



الكلية: الطب

القسم او الفرع: الامراض والطب العدلي

المرحلة: الثالثة

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اسم المادة باللغة العربية: الامراض

اسم المادة باللغة الإنكليزية: **Pathology**

اسم المحاضرة الأولى باللغة العربية: علم أمراض التغذية

اسم المحاضرة الأولى باللغة الإنكليزية: **Nutritional Pathology**

- **INJURY BY CHEMICAL AGENTS (Therapeutic and Non-therapeutic)**
- **Factors influencing chemical injury:**
- 1. Dose; the higher the dose the greater the toxicity.
- 2. Metabolic conversion e.g. alkaline cleaning materials are directly toxic to cells and cause injury to oral mucosa, esophagus & stomach. While alcohol should first be converted in the liver to compounds that are more toxic than the original compound.
- 3. Sites of absorption, accumulation and excretion, e.g. the aminoglycosides accumulate in the endolymph & perilymph of ear and the renal cortex, so they are ototoxic and nephrotoxic.
- 4. Individual variations, which is due to variations in the enzymes that metabolize the drugs.
- 5. Capacity of inducing immune responses. Many chemicals are not directly toxic but induce injury by immune response e.g. penicillins

- **Injury by therapeutic agents**
- **Exogenous estrogens (Menopausal Hormone Therapy MHT)**
- used for postmenopausal women to slow adverse effects of osteoporosis.
- Adverse effects
- 1. Endometrial carcinoma
- - 3-6 times after 5 years

- - risk reduced by addition of progestogens.
- 2. Increased risk of breast carcinoma
- 3. Increased risk of stroke and venous thromboembolism.
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- **Oral contraceptives**

- Adverse effects
- Increased risk/incidence of :
 - 1. cervical carcinoma.
 - 2. thromboembolism
 - 3. hypertension.
 - 4. hepatic adenoma.
 - 5. gall bladder diseases.

- **Acetaminophen**

- Causes centrilobular hepatic necrosis.
- Toxic dose is 15 – 25 gram
- Toxicity begins with
 - -nausea/vomiting
 - - diarrhea
 - - sometimes shock

- Later
- - jaundice
- Eventually
- - liver failure.
- In the United States, acetaminophen toxicity causes about 50% of acute liver failure.
- Overdoses of acetaminophen can be treated in early stages by the administration of N-acetylcysteine.
- **Acetylsalicylic acid (aspirin)**
- Aspirin overdose may result from accidental ingestion in young children or suicide attempts in adults.
- At first respiratory alkalosis develops, which is followed by metabolic acidosis.
- The toxic dose for children is 2-4 grams, and for adult 10-30 grams.
- Chronic aspirin toxicity occurs in patient with chronic inflammatory conditions (such as rheumatoid arthritis). The drug is taken as an analgesic to ameliorate the pain.
- These patients take an average of 3 grams (or more) of aspirin daily or for long periods.
- Chronic toxicity is manifested by headache, dizziness, tinnitus, mental confusion, nausea , vomiting, diarrhea, acute erosive gastritis & GIT bleeding.
- The bleeding occurs because aspirin acetylates platelet cyclo-oxygenase & blocks its ability to make thromboxane A₂ (an activator of platelets aggregation).
- Petechial hemorrhages may appear in the skin and internal viscera, and bleeding from gastric ulcerations may be exaggerated.
- **Injury by Nontherapeutic Agents (Drug Abuse)**
- **Cocaine**

- Cocaine produces a sense of intense euphoria and mental alertness, making it one of the most addictive of all drugs.
- Manifestations of cocaine toxicity:
 - 1. Cardiovascular effects: tachycardia, hypertension, and peripheral vasoconstriction, myocardial ischemia, also can precipitate lethal arrhythmias.
 - 2. CNS effects: hyperpyrexia and seizures.
 - 3. Effects on the fetus: fetal hypoxia and spontaneous abortion.
 - 4. Dilated cardiomyopathy.

- **Heroin and Other Opioids**

- Heroin is an addictive opioid derived from the poppy plant and is closely related to morphine. Its effects are even more harmful than those of cocaine.
- Most important adverse effects:
 - 1. Sudden death
 - 2. Pulmonary disease: edema, septic embolism, lung abscess, opportunistic infections, and foreign body granulomas from talc.
 - 3. Infections of the skin and subcutaneous tissue, heart valves, liver, and lungs. Most cases are caused by *Staphylococcus aureus*. Viral hepatitis is the most common infection among addicts. High incidence of HIV infection.
 - 4. Skin lesions: abscesses, cellulitis, and ulcerations.
 - 5. Renal problems.

- **Lead poisoning**

- Lead is a readily absorbed metal that binds to sulfhydryl groups in proteins and interferes with calcium metabolism, leading to hematologic, skeletal, neurologic, GI, and renal toxicities.

- Lead exposure occurs through contaminated air, food, and water. For most of the 20th century the major sources of lead in the environment were house paints and gasoline. Two forms
- A. Acute lead poisoning
 - - unusual circumstances (e.g. battery burning).
- B. Slow accumulation of lead compounds (weeks/ months until reach toxic levels)
- Manifestations in adults differ from those in children
- In Adults
 - 1. Colicky abdominal pain
 - 2. Fatigue
 - 3. Headache
- In Children
 - - encephalopathic crises.
- Sites of deposition
 - 1. Bone and teeth: most of the absorbed lead (80%) is taken up by bone and developing teeth
 - 2. 5% to 10% of the absorbed lead remains in the blood .
 - 3. The remainder is distributed throughout the soft tissues.
- Blood changes are one of the earliest signs of lead accumulation and are characteristic, consisting of a microcytic, hypochromic anemia associated with a distinctive punctate basophilic stippling of red cells. Elevated blood levels of zinc protoporphyrin is an important indicator of lead poisoning.

- In children, excess lead interferes with the normal remodeling of calcified cartilage and primary bone trabeculae in the epiphyses leading to increased bone density, which is detected as radiodense "lead lines" on radiographs .
- Lead lines may also occur in the gums, where excess lead stimulates hyperpigmentation of the gum tissue adjacent to the teeth.
- Excretion of lead occurs via the kidneys, thereby exposing these organs to potential damage (interstitial fibrosis and possibly renal failure).
- Excess lead is toxic to nervous tissues in adults and children; peripheral neuropathies predominate in adults, whereas central effects are more common in children. In young children, chronic lead exposure causes sensory, motor, intellectual (including reduced IQ), psychological impairment, retarded psychomotor development and in more severe cases blindness, seizures and coma.

- Impaired remodeling of calcified cartilage in the epiphyses (arrows) of the wrist has caused a marked increase in their radiodensity, so that they are radiopaque as the cortical bone.

- **Injury by ionizing radiation (IR)**

- Two forms of IR
 - 1. Electromagnetic waves (X-ray/gamma rays)
 - 2. High energy neutrons & charged particles (alpha/beta)
- Radiation is used in the treatment of cancer, in diagnostic imaging, and as therapeutic or diagnostic radio isotopes. However, it is also mutagenic, carcinogenic, and teratogenic.
- Effects of IR on tissues & cells
- The most important cellular target of ionizing radiation is the DNA

- DNA damage is compatible with survival if cells remain in inter-mitotic phase.
- Simple defects may be repairable by various enzyme repair systems.
- During mitosis, cells with irreparable DNA damage die.
- Damage to DNA that is not precisely repaired leads to mutations, which can manifest years or decades later as cancer.

- Tissues containing rapidly dividing cells show evidence of radiation injury, while tissues containing few dividing cells show little injury.
- The most sensitive organs and tissues are the gonads, the hematopoietic and lymphoid systems, and the lining of the GI tract.

- **Morphology of IR damage**

- At molecular level;
 - Cells surviving radiant energy damage show a wide range of structural changes in chromosomes:
 - - deletions
 - - breaks
 - - translocation
 - - fragmentation
 - - mitotic disorders (aneuploidy or polyploidy)

- At cellular level;
 - a. Nuclear damage

- b. Nuclear swelling
- c. Condensation & clumping of chromatin
- d. Apoptosis may occur
- e. Formation of giant cells with pleomorphic nuclei
- f. Cytoplasmic damage
- g. Cytoplasmic swelling
- h. Mitochondrial distortion
- i. Degeneration of endoplasmic reticulum
- These changes are similar to those seen in cancer cells.

- **Vascular changes**

- At the light microscopic level, vascular changes and interstitial fibrosis are prominent in irradiated tissues. During the immediate postirradiation period there is vasodilatation and later there are degenerative changes including endothelial swelling and vacuolation ,or even necrosis of the walls of small vessels such as capillaries and venules.
- Affected vessels may rupture or get thrombosed.
- Later on, the endothelial cells proliferate & collagenous hyalinization with thickening of the media occur (fibrosis) that result in marked narrowing or obliteration of the vascular lumina.

- **Nutritional diseases**

- A healthy diet provides
- (1) sufficient energy, in the form of carbohydrates, fats, and proteins, for the body's daily metabolic needs

- Adipose tissue stores (9-15 kg) provide energy for about 40-70 days.
- Total body protein (9-11 kg)
- muscle proteins (3-4 kg)
- Muscle stores allow survival for about 75 days
- **Nutrients deficiency**
- Classified into
 - Type 1
 - - specific S&S reflecting reduced tissue concentration of such elements or nutrients as iron, iodine, and vit. B
 - Type 2
 - - reduction in growth rate as in severe acute malnutrition (previously called protein-energy malnutrition PEM)
 - - effects are more severe
 - - evident in infancy and early childhood.
- **SAM**
- The WHO defines severe acute malnutrition (SAM) as a state characterized by a greatly reduced weight for height ratio that is below 3 standard deviation of WHO standards. Worldwide about 16 million children under the age of 5 years are affected by it. It is common in poor countries, where as many as 25% of children may be affected and where it is a major contributor to the high death rates among the very young.
- It is characterized by
 - 1. Loss of adipose tissue and loss of tissue proteins

- skin: thin/inelastic
- hair : dry/fall easily.
- 2. ↓basal metabolic rate/↓heart rate/ ↓ blood pressure
- 3. Amenorrhea.

- Causes of SAM

- 1. Inadequate food intake.
- 2. Chronic diseases.
- 3. Anorexia nervosa.
- 4. Alcoholism.

- SAM in children includes

- 1. marasmus
- 2. kwashiorkor
- 3. intermediate forms

- **Marasmus**

- “disease of infancy develops when the diet is severely lacking in calories. The main features

- 1. Growth retardation.
- 2. Wasting/loss of subcutaneous fat.
- 3. The extremities are emaciated; by comparison, the head appears too large for the body
- 4. Edema usually absent (serum albumin levels are either normal or only slightly reduced).
- 5. Wizened face/premature aged appearance.

- 6. Patient alert/hungry.
- 7. Anemia and manifestations of multivitamin deficiencies
- 8. Evidence of immune deficiency, particularly of T-cell–mediated immunity (infections)

- **Kwashiorkor**
- Kwashiorkor occurs when protein deprivation is relatively greater than the reduction in total calories.
- Older children (18-24 months)
- Main features
 - 1. Growth retardation.
 - 2. Relative sparing of subcutaneous fat and muscle mass.
 - 3. Generalized edema (hypoalbuminemia)
 - 4. Characteristic skin lesions with alternating zones of hyperpigmentation, desquamation, and hypopigmentation, giving a “flaky paint” appearance.
 - 5. Straight friable depigmented hair/atrophy of the hair follicles.
 - 6. Enlarged fatty liver.
 - 7. Vitamin deficiency.
 - 8. Anemia.
 - 9. Defects in immunity and secondary infections.
 - 10. Apathy/irritability, loss of appetite.

- **Anorexia Nervosa and Bulimia**

- Anorexia nervosa is a state of self-induced starvation resulting in marked weight loss; bulimia is a condition in which the patient binges on food and then induces vomiting. Bulimia is more common than anorexia nervosa and carries a better prognosis. It is estimated to occur in 1% to 2% of women and 0.1% of men, with an average age at onset of 20 years.
- The clinical findings in anorexia nervosa generally are similar to those in SAM. In addition, effects on the endocrine system are prominent.
- Amenorrhea, hypothyroidism, decreased bone density, dehydration, electrolyte abnormalities, anemia, lymphopenia, and hypoalbuminemia.
- A major complication of anorexia nervosa is an increased susceptibility to cardiac arrhythmia and sudden death, both resulting from hypokalemia.
- **Vitamin Deficiencies**
- Thirteen vitamins are necessary for health; four —A, D, E, and K— are fat-soluble and the remainder are water-soluble.
- Certain vitamins can be synthesized endogenously— vitamin D from precursor steroids, vitamin K and biotin by the intestinal microflora, and niacin from tryptophan, an essential amino acid. However, a dietary supply of all vitamins is essential for health.
- Deficiency of a single vitamin is uncommon, and single- or multiple-vitamin deficiencies may accompany concurrent SAM.
- **Obesity**
- Excess adiposity (obesity) and excess body weight are associated with increased incidence of several of the most important diseases of humans, including type 2 diabetes, dyslipidemias, cardiovascular disease, hypertension, and cancer. It is a major public health problem in developed countries and an emerging health problem in developing nations.
- Obesity is defined as a state of increased body weight, caused by adipose tissue accumulation, that is of sufficient magnitude to produce adverse health effects.
- BMIs in the range 18.5 to 25 kg/m² are considered normal, whereas BMIs between 25 and 30 kg/m² identify the overweight, and BMIs greater than 30 kg/m², the obese. (BMI is calculated as (weight in kilograms)/(height in meters)², or kg/m²)

- Obesity is a disorder of energy balance.
- The regulation of energy balance is very complex. It has three main components:
- (1) afferent signals, provided mostly by insulin, leptin, ghrelin, and peptide YY
- (2) the central hypothalamic system, which integrates afferent signals and triggers the efferent signals
- (3) efferent signals, which control energy balance.
- In addition to diabetes and cardiovascular disease, obesity also is associated with increased risk for certain cancers, non alcoholic fatty liver disease, and gallstones.
- Obese persons generally have hypertriglyceridemia and low HDL cholesterol levels, factors that increase the risk of coronary artery disease.
- There is an increased incidence of certain cancers in the overweight, including cancers of the esophagus, thyroid, colon, and kidney in men and cancers of the esophagus, endometrium, gallbladder, and kidney in women.
- Possible mechanisms include:
- 1. Elevated insulin levels. Hyperinsulinemia causes a rise in levels of free insulin like growth factor-1 (IGF-1). IGF-1 is a mitogen, and its receptor, IGFR-1, is highly expressed in many human cancers.
- 2. Obesity has effects on steroid hormones that regulate cell growth and differentiation in the breast, uterus, and other tissues.
- 3. Adiponectin secretion from adipose tissue is reduced in obese individuals. Adiponectin suppresses cell proliferation and promotes apoptosis. It also counteracts the actions of p53 and p21. In obese individuals these anti-neoplastic actions of adiponectin may be compromised.
- 4. The proinflammatory state that is associated with obesity may itself be carcinogenic.