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اسم المادة باللغة العربية: الامراض

اسم المادة باللغة الإنكليزية: Pathology

اسم المحاضرة الأولى باللغة العربية: علم الأمراض البيئية

اسم المحاضرة الأولى باللغة الإنكليزية: Environmental Pathology

محتوى المحاضرة الرابعة

- **ENVIRONMENTAL PATHOLOGY**
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- **FICMS Pathology/ Hematology**
- **What is Environmental Pathology?**
- “concerned with those diseases caused by specific agents imposed by mankind on mankind itself.”
- The term environmental disease refers to disorders caused by exposure to chemical or physical agents in the ambient, workplace, and personal environments, including diseases of nutritional origin.
- Environmental diseases are surprisingly common.
- Work-related injuries and illnesses kill more people per year globally than do road accidents and wars combined.
- Environmental diseases are significant because most are preventable.
- **Etiological agents**
- 1. Climate change
- 2. Nutritional factors
- 3. Air pollutants
- 4. Tobacco smoking
- 5. Alcohol
- 6. Chemicals/drugs

- 7. Physical factors/ionizing radiation.

- **HEALTH EFFECTS OF CLIMATE CHANGE**

- Global temperature measurements show that the earth has warmed significantly since the early 20th century, and especially since the mid-1960s.

- Climate change is expected to have a serious negative impact on human health by increasing the incidence of a number of diseases, including the following:

- Cardiovascular, cerebrovascular, and respiratory diseases (exacerbated by heat waves and air pollution).

- Gastroenteritis, cholera, and other food- and waterborne infectious diseases (caused by contamination as a consequence of floods and disruption of clean water supplies).

- Vector-borne infectious diseases, such as malaria and dengue fever (resulting from changes in vector number and geographic distribution related to increased temperatures).

- Malnutrition (caused by changes in local climate that disrupt crop production).

- **TOXICITY OF CHEMICAL AND PHYSICAL AGENTS**

- Toxicology is defined as the science of poisons. It studies the distribution, effects, and mechanisms of action of toxic chemical agents. More broadly, it also includes the study of the effects of physical agents such as radiation and heat.

- Exogenous chemicals, known as xenobiotics, may enter the body through inhalation, ingestion, and skin contact, and can either be eliminated or accumulate in fat, bone, brain, and other tissues.

- Xenobiotics can be converted into water soluble non-toxic products (detoxification) or activated to form toxic compounds through a two-phase reaction process that involves the cytochrome P-450 system.

- **Air pollution**

- “Loading the atmospheric air with noxious gases/fumes/particles etc.”

- Pollutant: “agent in the environment that causes disease in exposed individuals.”

- Air pollution is a significant cause of morbidity and mortality worldwide, particularly among at-risk individuals with preexisting pulmonary or cardiac disease.
- Air pollution is worst in industrialized areas
- Lungs are affected more than any other system.
- Air pollution contributes to causation/aggravation of many lung diseases.
- The most common outdoor air pollutants are ozone, sulfur dioxide, acid aerosols, and particles less than 10 μm in diameter.

- **Factors that determine injurious potential of air pollutants**
- 1. Water solubility
- 2. Size
- 3. Concentration
- 4. Duration
- 5. Reactivity
- 6. Clearance mechanisms

- 1. Water solubility. Water-soluble molecules (for e.g. SO_2) dissolve in the secretions of the upper airway passages.
- 2. Particle size.
- Particles that are 0.5 micron in diameter act like gases and move in & out of alveoli.
- Those that are 1-5 micron in diameter are the most dangerous because of their impaction at the distal airway passages. There they are engulfed by macrophages and neutrophils that release mediators (e.g. macrophage inflammatory protein MIP) leading to inflammatory reaction.

- Particles greater than 5-10 microns in diameter are unlikely to reach distal airways; they are filtered out in the nose or trapped and evacuated by the muco-ciliary escalators.

- 3. Concentration. This is directly related to the effects the agent produces. SO2 depending on its concentration may produce the following effects

- Less than 0.2 ppm eye irritation.

- 2-5 ppm increases airway resistance.

- More than 20 ppm decrease in muco-ciliary clearance and may cause pulmonary edema

- 4. Duration of exposure

- - The longer the duration of exposure the greater is its noxious effects.

- 5. Reactivity of pollutant

- - Coal dust is relatively inert

- - Silica, asbestos and beryllium are more reactive than coal

- 6. Host clearance mechanism.

- - Impaired capacity to clear inhaled particles that occur in some lung diseases (such as emphysema, chronic bronchitis) leads to higher accumulation of potentially toxic substances in lung.

- **Carbon monoxide (CO)**

- It is a nonirritating, colorless, tasteless, odorless gas.

- CO is a systemic asphyxiant .It is an important cause of death from accidents and suicide. It kills by binding hemoglobin with high affinity and preventing oxygen transport resulting in CNS depression .

- Hemoglobin has a 200-fold greater affinity for CO than for O2. The carboxyhemoglobin, that is formed by binding of CO is incapable of carrying oxygen.

- Chronic poisoning by CO develops because carboxyhemoglobin, once formed, is remarkably stable. As a result, with low-level persistent exposure to CO, carboxyhemoglobin may accumulate to a life-threatening concentration in the blood. The slowly developing hypoxia can evoke widespread ischemic changes in the brain, particularly in the basal ganglia and lenticular nuclei. With cessation of exposure to CO, the patient usually recovers, but there may be permanent neurologic damage.

- Acute poisoning by CO generally is a consequence of accidental exposure or suicide attempt. In light-skinned people, it is marked by a characteristic generalized cherry-red color of the skin and mucous membranes, a color imparted by carboxyhemoglobin. If death occurs rapidly, morphologic changes may not be present; with longer survival, the brain may be slightly edematous and exhibit punctate hemorrhages and hypoxia induced neuronal changes. These changes are not specific; they simply imply systemic hypoxia .

- In victims who survive CO poisoning, complete recovery is possible; however, impairments of memory, vision, hearing, and speech sometimes remain.

- **Examples of environmental lung diseases**

- 1. COPD (COAD)

- - chronic bronchitis

- - emphysema

- 2. Laryngitis

- 3. Pneumoconiosis

- Pulmonary changes range

- - Minor irritations

- Fibrotic diseases
- Cancer

- **Tobacco smoke**
- Tobacco is the most common exogenous cause of human cancers, being responsible for 90% of lung cancers.
- Smoking is the most important cause of preventable human death.
- Substances present in cigarette smoke include
- 1. carcinogens
- 2. tumor promoters.
- Carcinogens include
- 1. Tar
- 2. Polycyclic aromatic hydrocarbons
- 3. Benzopyrene
- 4. Nitrosamine
- Promoters include
- 1. Nicotine
- 2. Phenol

- Cigarette smoking is by far the commonest cause of chronic obstructive pulmonary diseases COPD (chronic bronchitis and emphysema) as well as, the most serious of all, lung carcinoma. All these are common diseases nowadays.

- Agents in smoke have a direct irritant effect on the tracheo-bronchial mucosa, producing inflammation & increase mucus production.

- Cigarette smoke results in recruitment of leukocytes to the lung with local elastase production from these inflammatory cells and subsequent injury and damage to lung elastic tissue. The ultimate effect is the development of emphysema as a result of loss of the elastic recoil of lung tissue.

- Atherosclerosis and its major complication, myocardial infarction, are strongly linked to cigarette smoking. The causal mechanisms probably relate to several factors, including increased platelet aggregation, decreased myocardial oxygen supply accompanied by increased oxygen demand, and a decreased threshold for ventricular fibrillation. Almost one-third of all heart attacks are associated with cigarette smoking.

- Maternal smoking increases the risk of spontaneous abortions and preterm births and results in intrauterine growth retardation.

- **Pneumoconiosis**

- This term refers to a group of lung diseases that result from inhalation of specific organic & inorganic dust particulates.

- These diseases are basically occupational but people living near industries may also suffer.

- The most serious are those diseases having the potential of progression to irreversible lung fibrosis. These include:

- 1. Coal worker's pneumoconiosis (inhalation of coal dust)

- 2. Silicosis (inhalation of silica particles)

- 3. Asbestosis (inhalation of asbestos particles)

- Mineral (inorganic) dusts include
- 1. Coal dust
- 2. Silica
- 3. Asbestos
- 4. Beryllium

- **Pathogenesis**

The reaction of lung to dusts depends on the previously mentioned factors (size, duration of exposure, concentration ... etc).

• Pulmonary alveolar macrophages play a central role in the pathogenesis of lung injury by promoting inflammation (proinflammatory factors LTB4, IL6, IL8, TNF, MIP) and producing reactive oxygen species and fibrogenic cytokines (TNF, PDGF, Fibronectin) .

- Most of the inhaled dust is removed by entrapment in the mucous blanket followed by rapid removal from lung by ciliary movement.
- Some of the particles become impacted at alveolar-duct bifurcation where macrophages accumulate and phagocytose the impacted materials.

- The more reactive the particulates are, the more likely their ability to :
- 1. Trigger of the macrophages to release a number of products that are toxic to the lung
- 2. Mediate an inflammatory response
- 3. Initiate fibroblastic proliferation and collagen deposition.
- The mediators include:
- 1. Reactive oxygen species
- 2. Proteases
- 3. Leukotriene B 4 (LTB 4)

- 4. IL8 & IL6 and (IL: interleukin)
- 5. TNF (Tumor necrosis factor)

- **Coal worker's pneumoconiosis (CWP)**

- This results from inhalation of coal dust particles.
- The spectrum of lung findings in coal workers is wide, ranging from:
- 1. Asymptomatic anthracosis , in which the carbon pigment accumulates without significant cellular reaction.
- 2. Simple coal workers' pneumoconiosis (CWP), in which there is accumulation of coal dust laden macrophages around respiratory bronchioles with focal fibrosis and secondary dilatation of the related alveoli (emphysema). There is little or no pulmonary dysfunction.
- 3. Complicated CWP or progressive massive fibrosis (PMF). A small proportion of those with simple CWP after 10 –20 years of exposure, develop this form of the disease, which is a more severe and serious form of CWP. The fibrosis is extensive & lung function is severely affected. The masses of black fibrous tissue may become infected by TB. The latter is a recognized complication of this condition.

- Progressive massive fibrosis (PMF) in a coal worker. A large amount of black pigment is associated with fibrosis.

- **Silicosis**

- the most prevalent chronic occupational lung disease.
- caused by inhalation of crystalline silicon dioxide particles.
- Several decades of exposure required.
- slowly progressing nodular/fibrosing pneumoconiosis.
- Encountered in :

- 1. Mining of metals e.g. gold, copper and coal.
- 2. Sandblasting
- 3. Metal grinding
- 4. Manufacture of ceramics

- **Gross features**
- Silicotic nodules in their early stages are tiny, barely palpable,discrete, pale-to-black (if coal dust is present) nodules in the upper zones of the lungs .
- With progression: individual nodules may coalesce into hard, collagenous scars,with eventual progression to PMF.
- Nodules blackened by accumulation of coal dust.
- Fibrotic nodules encroach on adjacent bronchioles and branches of pulmonary artery hyperinflation of related alveoli + pulmonary hypertension.
- May be complicated by TB.
- Cavitation when present should raise possibility of intercurrent TB.
- Hilar lymph nodes and pleura may be involved by fibrotic lesions.

- Advanced silicosis, seen in a transected lung. Scarring has contracted the upper lobe into a small dark mass (arrow). Note the dense pleural thickening
- **Microscopic features silicosis**
- Microscopically, the silicotic nodule demonstrates concentrically arranged hyalinized collagen fibers surrounding an amorphous center.
- The“whorled” appearance of the collagen fibers is quite distinctive for silicosis . (collagen laid down in concentric layers)

- Examination of the nodules by polarized microscopy reveals birefringent silica particles.
- Coalescent silicotic nodules

- By polarized light microscopy the silica crystals are seen.These are bright white (colorless) crystals of varying sizes.

- **Clinical features**
- detection by routine chest X-ray (in asymptomatic workers)
- - fine nodularity in upper zones
- shortness of breath late in course of disease
- disease may become progressive even if exposure discontinued
- disease impairment of lung function
- increased susceptibility to T.B.
- no evidence of increased risk of lung cancer.

- **Asbestosis and related diseases**
- Asbestos: family of crystalline hydrated silica.
- Exposure to asbestos leads to
- 1. Parenchymal interstitial fibrosis (asbestosis)
- 2. Bronchogenic carcinoma
- 3. Pleural effusion
- 4. Localized fibrous plaques of the pleura (rarely diffuse)

- 5. Mesotheliomas of pleura/ peritoneum
- 6. Laryngeal carcinoma

- Asbestos has the following effects
- 1. Induces cellular & fibrotic lung reactions.
- 2. Acts as a tumor initiator & promoter.
- **** There is an increased incidence of asbestos-related cancers in family members of asbestos workers.
- **** The adsorption of carcinogens in tobacco smoke onto asbestos fibers may be the basis for the remarkable synergy between tobacco smoking and the development of lung carcinoma in asbestos workers.
- **MORPHOLOGY**
- Asbestosis is marked by diffuse pulmonary interstitial fibrosis, characterized by the presence of **asbestos bodies**, which are seen as golden brown, fusiform or beaded rods with a translucent center. They consist of asbestos fibers coated with an iron-containing proteinaceous material .
- Asbestos bodies apparently are formed when macrophages attempt to phagocytose asbestos fibers; the iron “crust” is derived from phagocyte ferritin.
- In contrast with CWP and silicosis, asbestosis begins in the lower lobes and subpleurally, spreading to the middle and upper lobes of the lungs as the fibrosis progresses. Contraction of the fibrous tissue distorts the normal architecture, creating enlarged air spaces enclosed within thick fibrous walls; eventually, the affected regions become honeycombed.
- Simultaneously, fibrosis develops in the visceral pleura, causing adhesions between the lungs and the chest wall. The scarring may trap and narrow pulmonary arteries and arterioles, causing pulmonary hypertension and cor pulmonale
- Markedly thickened visceral pleura covers the lateral and diaphragmatic surface of the lung . There is also severe interstitial fibrosis diffusely affecting the lower lobe of the lung .

- Lt photo. lung (HE x 360) Asbestos fibers in the lung often acquire a proteinaceous golden-yellow "coat" which is rich in hemosiderin. Several clusters of asbestos bodies of various lengths are present in the bronchiole and alveolus. The coat of most of the bodies is highly segmented and most have bulbous swellings, usually at the ends of the fiber.

- Rt photo. The asbestos fiber becomes coated with iron and calcium. Thus it could be demonstrated by using iron stain, as in this example (dark blue elongated structures).

- Pleural plaques are the most common manifestation of asbestos exposure and are well-circumscribed plaques of dense collagen , often containing calcium.

- They develop most frequently on the anterior and posterolateral aspects of the parietal pleura and over the domes of the diaphragm. Uncommonly, asbestos exposure induces pleural effusion or diffuse pleural fibrosis.

- Incidence of bronchogenic carcinoma is 5 times higher in asbestos workers than in general population.

- Incidence of mesotheliomas is 1000 times higher compared to general population.

- Concomitant cigarette smoking greatly increases the risk for lung carcinoma but not for mesothelioma. Lung or pleural cancer associated with asbestos exposure carries a particularly poor prognosis.

- **Alcohol**

Acute alcoholism exerts its effects mainly on the CNS but also may induce reversible hepatic and gastric injuries.

- At first there is depression (of sub-cortical structures), later on there is stimulation and disordered cortical, motor and intellectual behavior. With progressive high levels there is depression of medullary centers and cortical neurons.

- Acute lcohol buse auses rowsiness t lood evels f approximately 200 g/dL. tupor nd oma evelop t igher levels.

- Alcohol s xidized o cetaldehyde n he iver rimarily y alcohol ehydrogenase which results in depletion of NAD and accumulation of at n he iver nd o etabolic acidosis.

- Affection of stomach will cause acute gastritis & ulcerations.

- Chronic alcoholism
- Alcohol s xidized o cetaldehyde n he iver .Chronic ethanol consumption increase blood level of acetaldehyde.
- Acetaldehyde is a mediator of wide spread tissue & organ damage.
- Chronic alcoholism may lead to:
- 1. Liver
- - Fatty liver
- - Alcoholic hepatitis
- - Alcoholic cirrhosis which eads o ortal ypertension nd increases he isk or evelopment f epatocellular carcinoma.

- 2. GIT
- - Gastritis
- - Gastric ulcers
- - Esophageal varices.
- - Acute and chronic pancreatitis.

- 3. CNS: deficiency of thiamine (vitamin B1)
- - Peripheral neuropathies
- - Wernicke–Korsakoff psychosis (ophthalmoplegia, ataxia and confusion)

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- 4. CVS
- - Dilated congestive cardiomyopathy.
- 5- Cancers
- major isk actor or ancers f he oral avity, arynx, nd sophagus. he isk s reatly ncreased by oncurrent moking r he se f mokeless obacco.