Environmental Diseases

1.Diseases due to pollution.

2. Drugs and physical agents.

3. Over and undernutrition.

Environmental pollution

A pollutant is an agent in the environment that can cause disease in those who are exposed.

Acute toxicity may be produced directly by induction of

inflammation or necrosis, or indirectly by a hypersensitivity reaction

chronic toxicity by production of chronic inflammation and fibrosis or degenerative changes leading to organ malfunction

Air pollution

The lungs are the major organs affected by air pollution, ranging from minor irritation, to fibrosis and cancer

Lung injury by a pollutant depends on:

1. Solubility in water.

2. Particle size Particle with a size of 1-5 μm deposit at the bifurcations of air ways

3. Concentration and chemical reactivity.

4. Duration of exposure.

5. Host clearance mechanisms.

Tobacco Smoke:

Emphysema, chronic bronchitis and lung cancer are common lung diseases caused by cigarette smoking.

Agents in smoke have indirect irritant effect:

-producing inflammation and increased mucus production (bronchitis).

also cause recruitment of leukocytes and production of elastase lead to emphysema. -

- Tar present in smoke is a potent mutagen and cancer promoter, 85% of lung carcinomas are related to cigarette smoking -

-Atherosclerosis and myocardial infarction are strongly associated

Pneumoconiosis

non-neoplastic lung reactions to inhalation of mineral dusts, this term has been broadened to include diseases induced by organic and inorganic particulates.

The four most common diseases result from exposure to:

coal dust, silica, asbestos, and beryllium.

pathogenesis

Inhaled dust particles are engulfed by macrophages that release inflammatory mediators initiating fibroblast proliferation and collagen deposition.

Important mediators include:

1. oxygen free radicals and proteases.
2. Leukotreine B4, IL-8, MIP-1a, TNF-a, fibronectin, PDGF and IGF-1.

Some particles interact directly with fibroblasts, others migrate by lymphatics leading to a widespread reaction.

Coal Workers' Pneumoconiosis (CWP)

1.Pulmonary anthracosis: is also commonly seen in urban dwellers and tobacco smokers. Carbon is engulfed by alveolar macrophages which then accumulate in the connective tissue along the lymphatics seen as linear streaks and aggregates at autopsy. ١.

2. Simple CWP: Is characterized by coal macules and coal nodules Macule consisting of dust-laden macrophages. Nodules contain in addition collagen fibers. The upper lobes and upper zones of lower lobes are most commonly affected. Dilatation of adjacent alveoli result in centrilobular emphysema.

3. Complicated CWP (PMF): requires many years to develop, characterized by an intensely blackened scar, 2-10 cm in diameter, usually multiple consists of dense collagen and pigments with a necrotic center.

4. Caplan's syndrome: Is coexistence of rheumatoid arthritis with pneumoconiosis with large parenchymal nodules.

Silicosis

Caused by inhalation of crystalline silicone dioxide.

Is the most prevalent occupational disease in the world

usually present after decades as slowly progressing nodular fibrosing pneumoconiosis.

The initial lesion tends to be localized in the upper lung zones.

The lesion consists of concentric layers of hyalinized collagen with a capsule of more condensed collagen.

Some nodules cavitate as a result of tuberculosis or ischæmia.

Asbestosis

1. Parenchymal interstitial fibrosis (asbestosis).
2. Bronchogenic carcinoma.
3. Pleural effusion.
4. Localized fibrous plaques or diffuse pleural fibrosis.
5. Mesotheliomas.
6. Laryngeal neoplasms.
7. Extrapulmonary neplasms including the colon.

Two forms of asbestos are present; serpentine (curly and flexible) and amphiboles (straight, stiff and brittle). Amphiboles are more pathogenic

Asbestos can also act as a tumour initiator and promoter

It begins around the respiratory bronchioles and alveolar ducts, involving adjacent alveolar sacs and alveoli. Asbestosis begins in the lower lobes and subpleurally. The visceral pleura undergoes fibrous thickening. Pleural plaques are the most common manifestations, they develop on the parietal pleura.

Berylliosis

Heavy exposure may induce acute pneumonia.

Prolonged low dose exposure may cause pulmonary and systemic granulomas closely mimicking sarcoidosis.

Chronic berylliosis is caused by induction of T cell mediated immunity in genetically susceptible individuals.

Injury By Chemical Agents

Chemical injury depends on:

1. The dose.
2. Requirement for metabolic conversion.
3. Site of absorption, accumulation or excretion.
4. Individual variation (enzyme polymorphism).
5. The capacity of the chemical to induce an immune response

Lead Poisoning:

Lead is absorbed either through the GIT or through lungs.

Most of the absorbed lead (80-85%) is taken up by bones,

5-10% in the blood, the remainder in soft tissues.

It interferes with normal remodeling of calcified cartilage in the epiphysis, leading to increased bone density (lead lines).

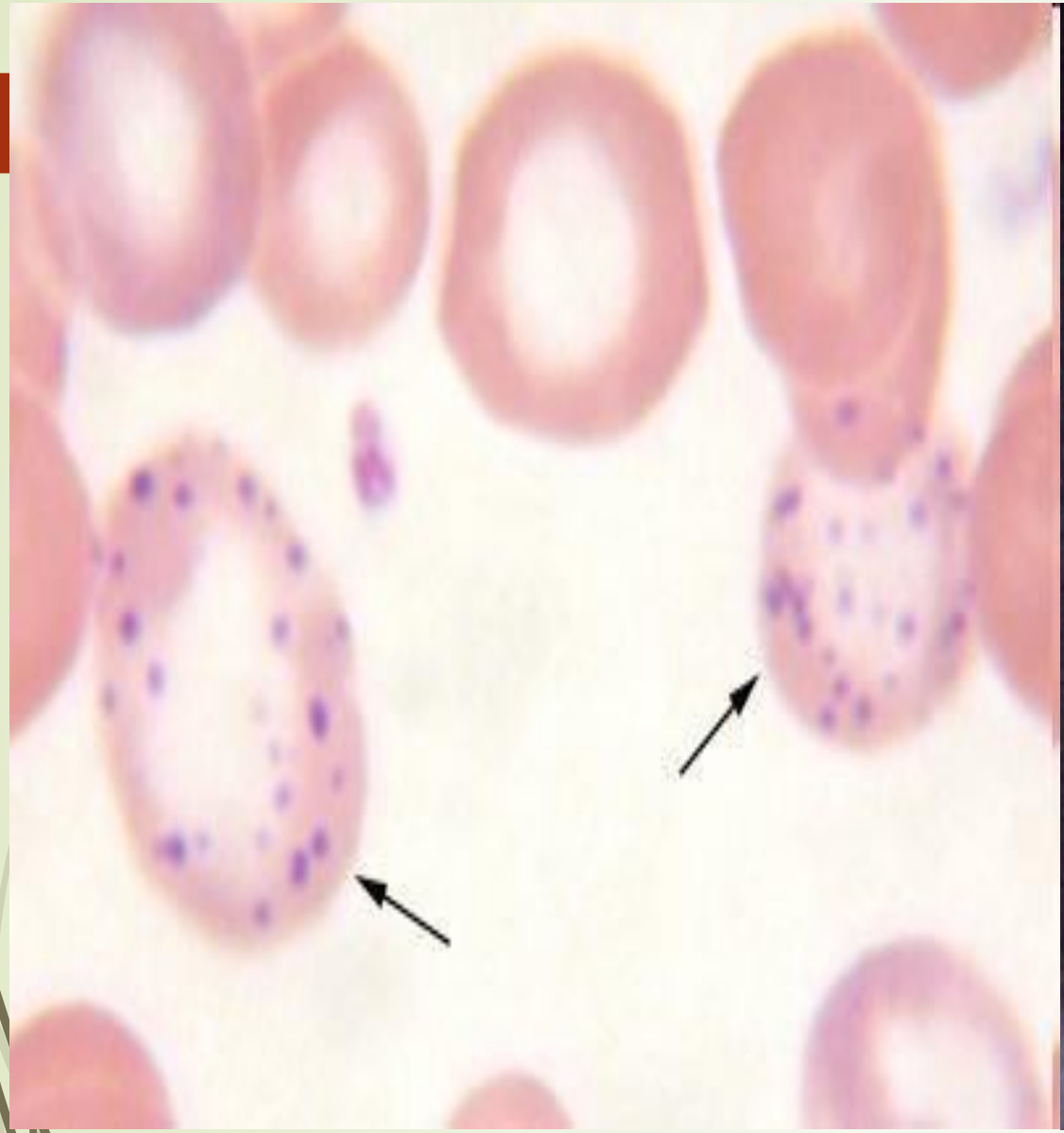
Lead lines may also occur in the gums.

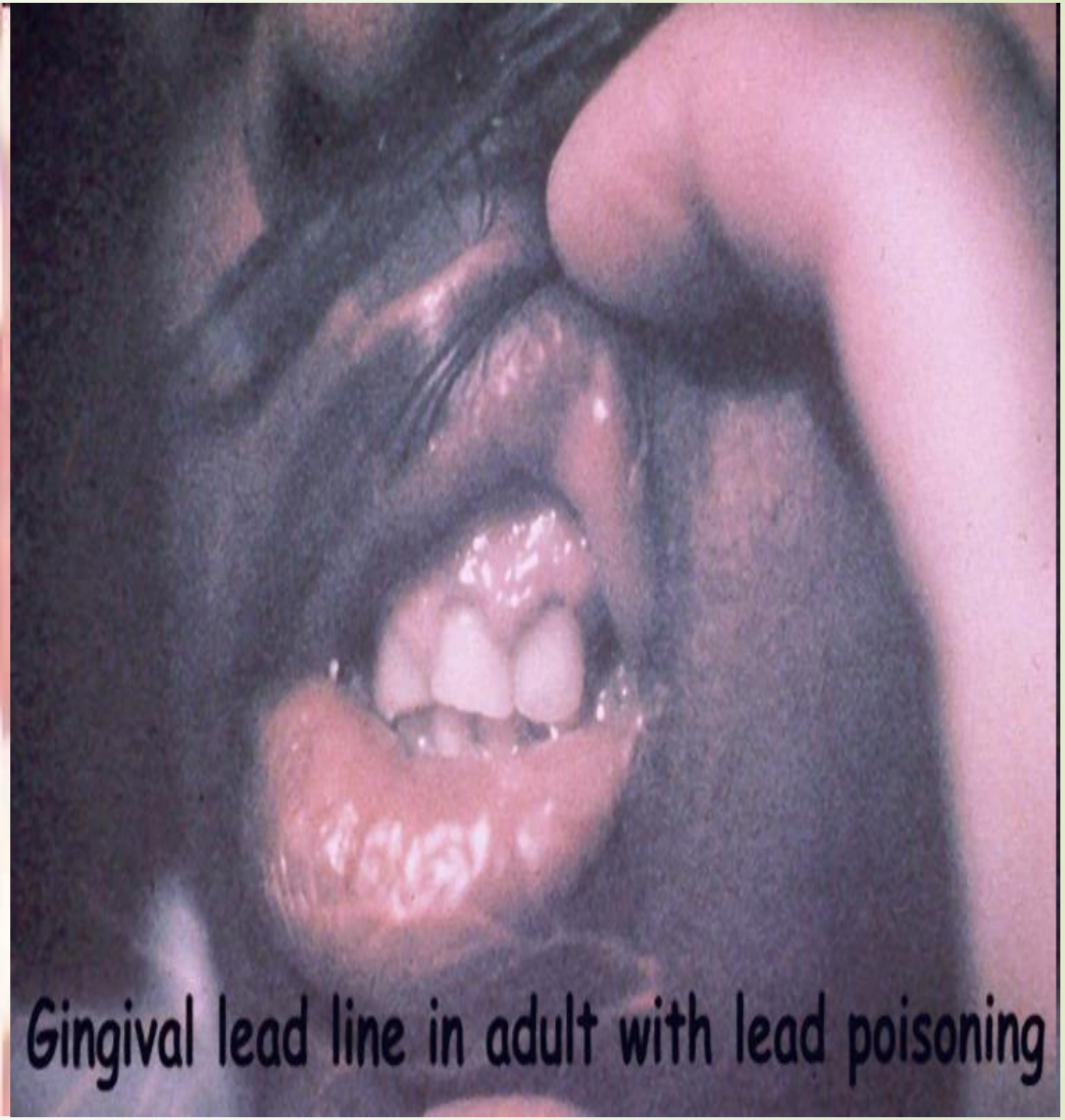
1. Blood changes: Hypochromic microcytic anæmias with punctuate basophilia, and hæmolytic anæmias.

2. Brain damage and demyelinating neuropathy.

3. GIT: Severe abdominal pain.

4. Chronic tubulointerstitial renal disease.




Gingival lead line in adult with lead poisoning

Alcohol:

After ingestion, ethanol is absorbed from the stomach and small intestine unaltered.

Less than 10% of ethanol is excreted unchanged in the urine, sweat and breath

. Most of alcohol is converted to acetaldehyde in the liver by: 1. Alcohol dehydrogenase at low levels. 2. Microsomal p-450 at high levels. Acetaldehyde is metabolized to acetate by acetaldehyde dehydrogenase. Chronic alcoholism develops tolerance through induction of microsomal p-450 system.

Acute Alcoholism:

1. CNS Effects: It has a depressant effect on the brain stem and reticular formation with stimulation of the cortical motor and intellectual behavior. Higher doses result in depression of cortical neurons and lower medullary centers.

2. Acute gastritis and ulceration.

3. Hepatic changes: Alcoholic hepatitis.

A blood level of 100 mg/dl induces ataxia, 200 mg/dl induces drowsiness, 300 mg/dl induces stupor and profound amnesia and death happens at 400-500 mg/dl.

Chronic Alcoholism:

Damage is mediated by acetaldehyde, free radicals and immune reactions.

1. Liver changes: Alcoholic hepatitis, steatosis and cirrhosis.

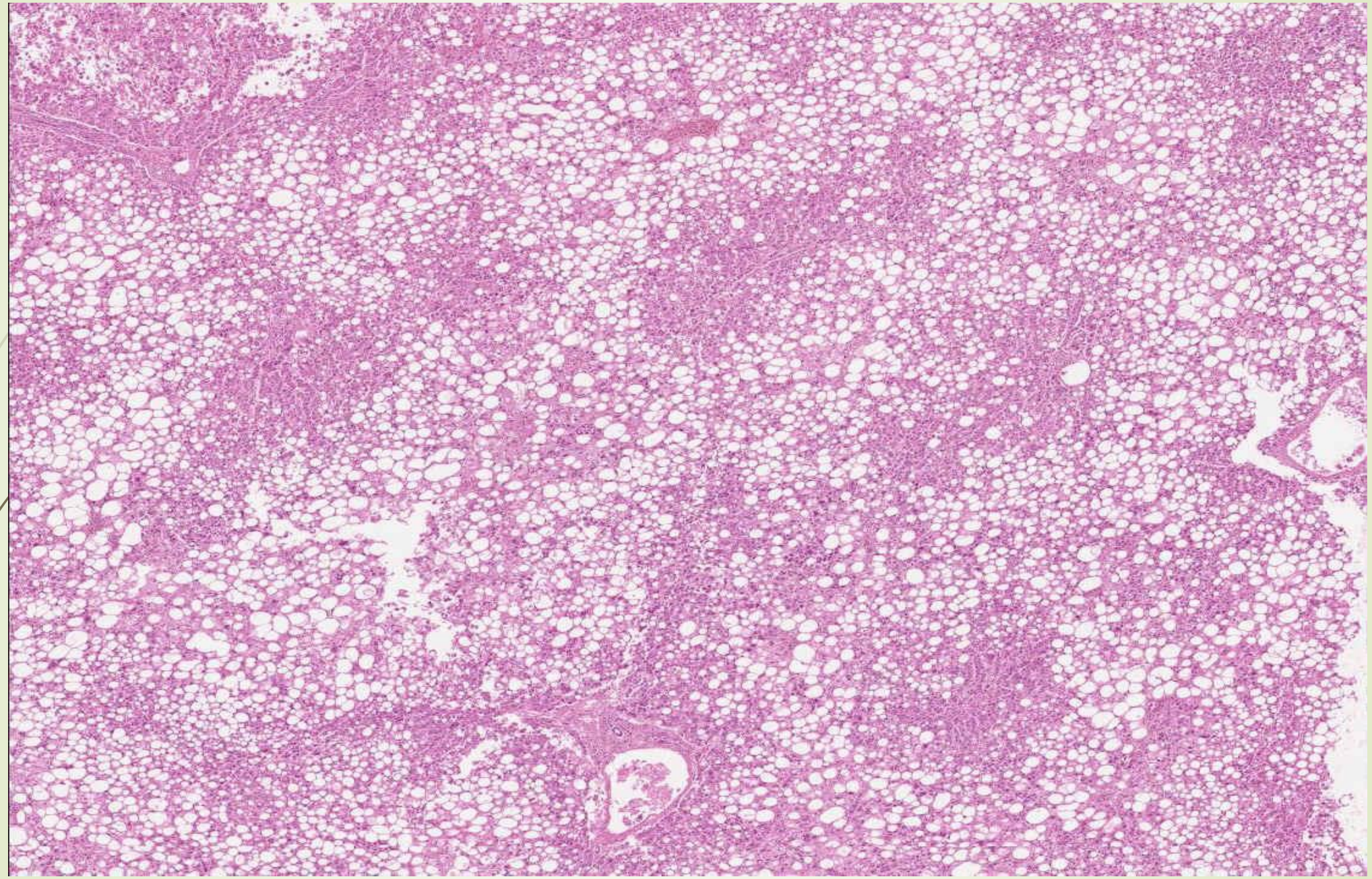
2. GIT: Gastritis, gastric ulcer, esophageal varices.

3. CNS: Korsakoff syndrome, cerebral atrophy, cerebellar degeneration and optic neuropathy.

4. Cardiovascular system: Dilated congestive cardiomyopathy, hypertension.

5. Pancreas: Acute and chronic pancreatitis.

6. Fetal alcohol syndrome: Growth retardation and mental function reduction.



Ultraviolet Radiation

Solar radiation spans the spectrum of wavelengths between 200 and 4000 nm

including ultraviolet, visible, and infrared radiation.

Ultraviolet radiation is divided into ultraviolet A (UVA), ultraviolet B (UVB), and ultraviolet C (UVC)

3% to 5% of the total solar radiation that penetrates the earth's surface is ultraviolet radiation.

Radiation	Wavelength (nm)	Acute Effects	Delayed Effects
UVA	320-400	Erythema 8-48hr	Tanning
		Depletion of Langerhans cells	Skin cancer?
		Pigment darkening	
		Dermal inflammation	
UVB	290-320	Erythema 3-24hr	Tanning
		Apoptosis of keratinocytes	Solar elastosis
		Depletion of Langerhans cells	Premature aging
			Actinic keratosis
			Skin cancer
UVC	200-290		skin cancer?

Therapeutic Drugs(Medications)

Oral Contraceptives

breast cancer no increased risk, or at most a very low increase among young long-term users

decrease endometrial and ovarian cancers

Increase risk of cervical cancer in woman infected with human papillomavirus.

Thromboembolic events :VT and Pulmonary Embolism increased(hepatic synthesis for coagulation factor increased) ,adds to other risk factors (e.g. Factor V Leiden)

Cardiovascular disease ,with current low estrogen pills, risk of MI and atherosclerosis not increased in non-smoking women < 45 y

Liver tumors ,benign hepatic adenomas ,older women with prolonged use may rupture and cause intra-abdominal bleeding

Hormone Replacement Therapy (HRT)

Cancer in women with a uterus combined estrogen and progestin Rx necessary to reduce endometrial cancer

WHO showed increased risk of breast cancer in women who used HRT combined therapy for 5 years.

Thromboembolic events elevated approximated two fold in HRT users, especially within the first 2 years

Cardiovascular disease WHO reported 29% increased risk of myocardial infarction, especially during the first year of combined HRT

use Exogenous esterogen is used for distressing menopausal symptoms

Acetaminophen

Does not affect cyclooxygenase so bleeding associated with aspirin does not occur

Has analgesic and antipyretic actions but no anti-inflammatory action

Large doses may produce hepatic necrosis caused by reactive oxygen species patients should not exceed recommended dose (4 grams/day)

toxic dose in adults is 15 to 25 gm dose should be reduced in children with fever or dehydration

Aspirin

Overdose respiratory alkalosis followed by metabolic acidosis that may be fatal. Chronic aspirin toxicity (salicylism)

headache, dizziness, ringing in the ears (tinnitus), mental confusion, drowsiness, nausea, vomiting, and diarrhea ,CNS changes, coma, convulsion.

Inhibits cyclooxygenase(COX 1 & 2) Erosive gastritis is a major cause of GI bleeding

Reye syndrome occurs in children following an acute fibrile viral illness

Injury by Nontherapeutic Toxic Agents(Drug Abuse)

- Cocaine: can result in the following effects and complications:
- Mood elevation followed by irritability, anxiety, and depression.
- Increased myocardial irritability lead to arrhythmia.
- Hypertension can lead to cerebral hemorrhage
- Nasal congestion, ulceration, septal perforation
- Epileptic seizures, respiratory arrest, myocardial infarction, cerebral infarcts in the fetus of addicted mothers

Heroin

- Administered intravenously, results in:
- Physical dependence with sever withdrawal symptoms
- Infection: like HIV, Hepatitis B, Infective endocarditis.
- Adult respiratory distress syndrome.
- Death from respiratory or cardiac arrest or from pulmonary edema

Marijuana:

- Laryngitis, pharyngitis, bronchitis, cough and hoarseness. Increase in heart rate and blood pressure
- CNS changes include psychomotor impairments, such as inability to judge time, speed, and distance

HYPERTHERMIA Prolonged exposure to elevated temperatures can result in:

Heat cramps:Electrolyte loss via sweat

Heat exhaustion:Water depletion and lack of cardiovascular compensation for hypovolemia

Heat stroke:Extensive peripheral vasodilatation, i.e., “shocky”, very serious, T>106°, over 110° have been reported, high mortality

NUTRITIONAL DISEASE / Protein-Energy Malnutrition

Marasmus

Caused by widespread deficiency of almost all nutrients (protein and calories), often coexists with vitamin deficiencies.

clinically characterized by growth retardation -arrest, loss of muscle mass, serum albumin is normal, subcutaneous fat is used as a fuel -extremities are emaciated, the head appears too large.

Anaemia, multivitamin deficiency, and evidence of immunedeficiency (namely cellular immunity)

Kwashiorkor

Caused by protein deficiency but adequate calorie

more severe than marasmus-loss of visceral proteins -hypoalbuminemia-generalized edema, ascites skin lesions, hair changes are characteristic Fatty liver, defects of immunity, secondary infections, anemia

Clinically characterized by retarded growth and muscle wasting caused by inadequate protein intake, but with preservation of subcutaneous fat

Vitamin Deficiency and Excess

Vitamin A

retinol and related substances

important for vision (visual pigment) and differentiation of some types of epithelial cells (mucus-secreting)

changes:

impaired vision in reduced light , xerophtalmia

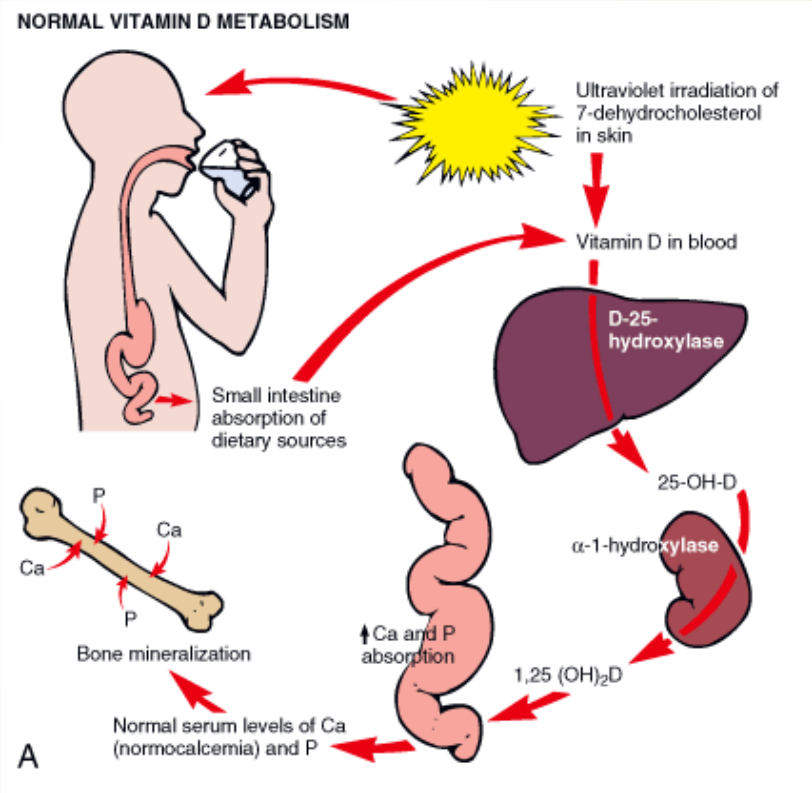
Respiratory tract -squamous metaplasia, pulmonary infections

decreased resistance to infections

Urinary tract -pelvic keratinization - stones

Skin -hyperkeratosis

Vitamin D Metabolism



Functions of Vitamin D

Stimulates intestinal absorption of calcium and phosphorus

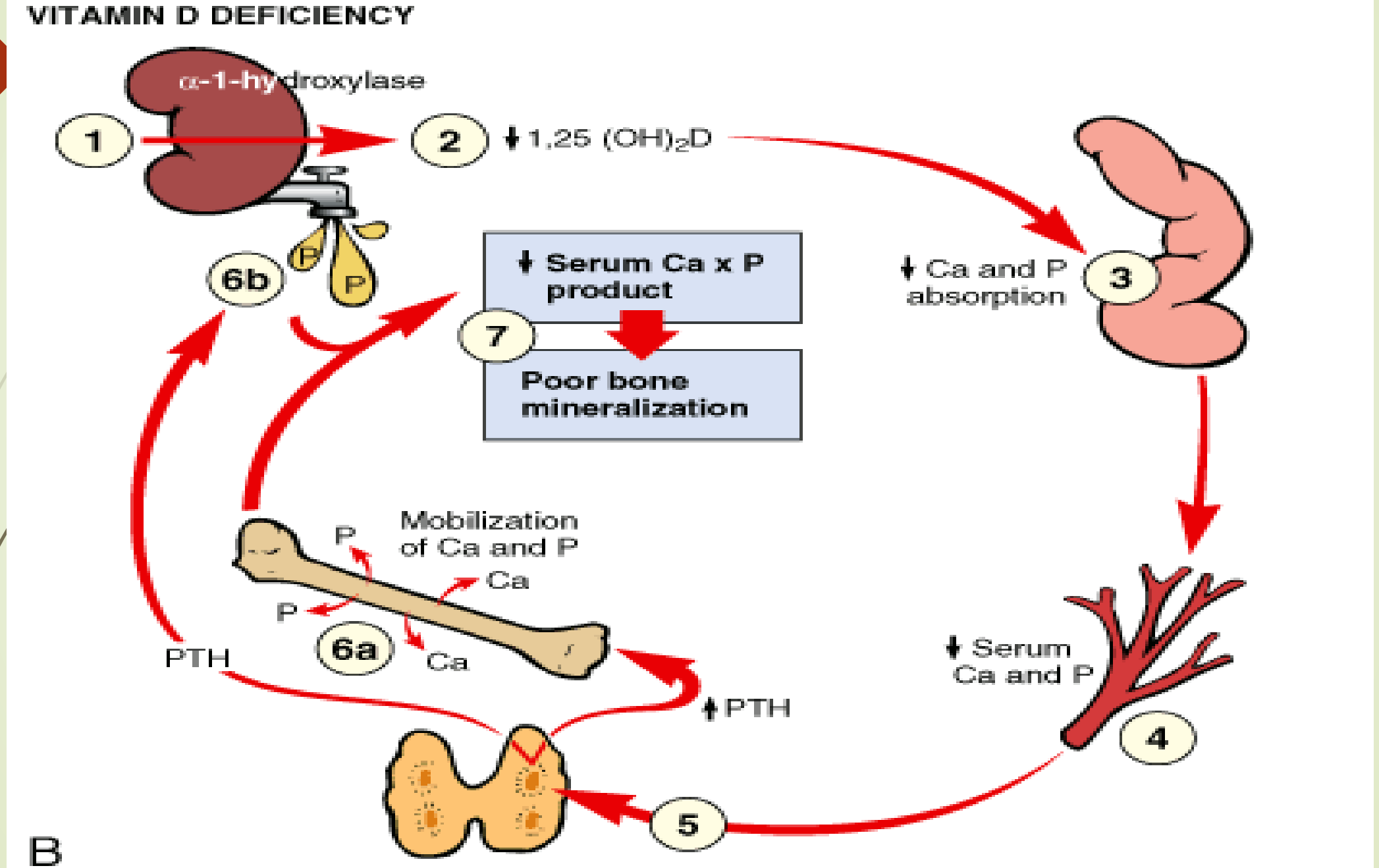
Collaborates with PTH in the mobilization of calcium from bone

Stimulates the PTH-dependent reabsorption of calcium in the distal renal tubules

1,25(OH)2 D, the biologically active form of vitamin D, is best regarded as a steroid hormone which acts by binding to a high-affinity receptor

Causes of hypovitaminosis

- decreased endogenous synthesis (inadequate exposure to sunlight)
- decreased absorption (dietary lack, malabsorption syndrome)
- enhanced degradation(drugs)
- impaired synthesis of metabolites (liver diseases, renal disorders)
- target resistance (congenital lack of receptors)
- phosphate depletion (renal tubular disorders, long-term use of antacids)


VITAMIN D DEFICIENCY
α-1-hydroxylase
1
2
↓1,25 (OH)2D
3
↓ Ca and P absorption
6b
P
P
↓ Serum Ca x P product
7
Poor bone mineralization
Mobilization of Ca and P
P
Ca
P
6a
Ca
PTH
↑PTH
↓ Serum Ca and P
4
5
B

Deficiency state

- children -before closing of epiphyses -rickets (rachitic rosary, pigeon chest deformity, lumbar lordosis, bowing of the legs)
- adults -after closing of epiphyses -osteomalacia (impaired remodelation of bone mass, no mineralization of osteoid -microfractures (vertebral bodies, femoral necks)
- Hypervitaminosis D -hypercalcaemia -metastatic calcification, urolithiasis

Vitamin K

- required cofactor for synthesis of clotting factors VII, IX, X

Causes of hypovitaminosis:

- fat malabsorption syndromes
- destruction of endogenous vit. K synthesizing flora (broad spectrum ATB)
- neonatal period (low reserve, no bacterial flora)
- diffuse liver disease
- iatrogenic decrease (warfarin

Vitamin B1 (thiamine)

widely available in the diet -nonpolished rice, grains

avitaminosis -in severe malnutrition-in chronic alcoholics

affected peripheral nerves, heart, brain

dry beri-beri (polyneuropathy) -degeneration of myelin sheaths and axons (motoric, sensoric and vegetative)

wet beri-beri (cardiovascular syndrome) -dilatation, right heart failure, peripheral edema

Wernicke-Korsakoff syndrome -ophthalmoplegia, nystagmus, ataxia of gait and stance, confusion, apathy, amnesia, psychosis

Vitamin B2 (riboflavin)

- avitaminosis associated with changes at the angles of the mouth (cheilosis or cheilitis), glossitis, ocular (keratitis) and skin changes (nasolabial dermatitis), bone marrow (erythroid hypoplasia -anemia)

Niacin (nicotinic acid)

Deficiency state:

- pellagra (rough skin) -3 Ds: diarrhea , dementia , dermatitis

Vitamin B12 (cyanocobalamine)

deficiency in strict vegetarians or in chronic atrophic gastritis -pernicious anemia (lack of synthesis of intrinsic factor in gastric mucosa due to autoimmune inflammation with severe destruction of corporal glands)

in deficiency -megaloblastic anemia (decreased number of RBC, increased size; hypersegmentation of neutrophilic leucocytes) and demyelinization of spinal cord and peripheral nerves = neuroanemic syndrome

Vitamin C (ascorbic acid)

fruits and vegetables -not synthesized endogenously

involved in metabolism of collagen and basic intercellular matrix -involvement of vessel walls -increased fragility -bleeding

deficiency in adults -scurvy

deficiency in children -Möller-Barlow disease -subperiosteal hematomas

Hypervitaminosis C

mega doses of vit. C (several grams/day) -no effect in prevention or in treatment

excretion into urine -urolithiasis

hyperacidity in stomach -mucosal erosions

Trace elements

14 anorganic elements -Fe, Cu, Co, I, Zn, Se, Mn, Mo, Cr, F, Si, Ni, Sn (tin), Va

activity in enzymes

primary deficiency -only I (thyroid gland -goiter)

secondary deficiency:

Zn -skin lesions, neurological and psychiatric syndromes, growth retardation, hypogonadism in males

Cu -anemia, impaired synthesis of connective tissue matrix

Se - dilated cardiomyopathy

Obesity

20% of world population

disorder of energetic balance -food derived energy chronically exceeds energy expenditure, excess calories are stored as fat

some genetic predispositions (multifactorial disease)

Results

hypertension -3x more frequent

DM type II. -3x more frequent

hypercholesterolemia -MI

more frequent malignant tumors -colon ca, breast ca, gallbladder ca, endometrial ca

cholelithiasis (gallstones)