Environmental Pathology

* Environmental diseases: diseases that are not entirely genetic caused by exposure to chemical or physical agents in the ambient, workplace, and personal environments, including diseases of nutritional origin
* Can be a consequences of major disasters
* Physical Injuries:
	+ Mechanical injury :blunt, or sharp force injury, and gun shot injury.
	+ Thermal injury
	+ Radiation injury

**Mechanical Trauma**

* Mechanical forces may inflict a variety of forms of damage.
* The type of injury depends on the shape of the colliding object (Blunt vs. Sharp), the amount of energy discharged at impact, and the tissues or organs that bear the impact
* patterns of injury seen in mechanical force:
	+ **abrasion**:
		- is a wound produced by scraping or rubbing, resulting in removal of the superficial layer.
		- Skin abrasions may remove only the epidermal layer.
	+ **A contusion, or bruise:**
		- is a wound usually produced by a blunt object
		- characterized by damage to blood vessels and extravasation of blood into tissues.
	+ **A laceration**
		- a tear or disruptive stretching of tissue caused by the application of force by a blunt object.
		- In contrast to an incision, most lacerations have intact bridging blood vessels and jagged, irregular edges.
	+ **An incised wound:**
		- inflicted by a sharp instrument.
		- The bridging blood vessels are severed
	+ **A puncture wound :**
		- caused by a long, narrow instrument
		- termed penetrating when the instrument pierces the tissue and perforating when it traverses a tissue to also create an exit wound.
* One of the most common causes of mechanical injury is **vehicular accident** a common pattern of injury sustained by a driver who is not wearing a seat belt includes:
	+ trauma to the head (windshield impact),whith brain contusion.
	+ chest (steering column impact), common chest injuries include sternal and rib fractures, heart contusions, aortic lacerations, and (less commonly) lacerations of the spleen and liver.
	+ knees (dashboard impact)may lead to hip, femur and lower limp fracture
	+ in caring for an automobile injury victim, it is essential to remember that internal wounds often accompany superficial abrasions, contusions, and lacerations. in many cases, external evidence of serious internal damage is completely absent.
* **Causes of Death in Mechanical truma:**
	+ **Heamorrhage:**
		- Tear or ruptured spleen;liver,skin… large blood vessels
		- Hemorrhaging is broken down into four classes by the American College of Surgeons' [Advanced Trauma Life Support](http://en.wikipedia.org/wiki/Advanced_Trauma_Life_Support) (ATLS).
			* **Class I Hemorrhage** involves up to 15% of blood volume. There is typically no change in vital signs and fluid resuscitation is not usually necessary.
			* **Class II Hemorrhage** involves 15-30% of total blood volume. A patient is often tachycardic (rapid heart beat) with a narrowing of the difference between the systolic and diastolic blood pressures. The body attempts to compensate with [peripheral vasoconstriction](http://en.wikipedia.org/wiki/Peripheral_vasoconstriction). Skin may start to look pale and be cool to the touch. The patient may exhibit slight changes in behavior.
			* **Class III Hemorrhage** involves loss of 30-40% of circulating blood volume. The patient's [blood pressure](http://en.wikipedia.org/wiki/Blood_pressure) drops, the [heart rate](http://en.wikipedia.org/wiki/Heart_rate) increases,decrease in peripheral perfusion ([shock](http://en.wikipedia.org/wiki/Shock_%28circulatory%29)), such as [capillary refill](http://en.wikipedia.org/wiki/Capillary_refill) worsens, and the mental status worsens
			* **Class IV Hemorrhage** involves loss of >40% of circulating blood volume. The limit of the body's compensation is reached and aggressive resuscitation is required to prevent death.
	+ **Head injury**
		- Death in head injury is do to increased intracranial pressure and Herniation
		- Skull fractures
		- Intracranial hemorrhages:
			* + Epidural Hemorrhage: middle meningeal artery tear.
				+ Subdural Hematoma: connecting venous BV
				+ Subarachnoid Hemorrhage
		- Cerebral contusions & laceration
	+ **Fat embolism:**
		- fracture of long bones
		- injury to adipose tissue
		- Death 1–4 days following injury
	+ **Rapture viscera**
	+ **Secondary infection**
	+ **Renal shot down**

**Gunshot wounds**

* 1. Contact wounds
		1. grey-black discoloration from the soot
		2. abrasion ring
		3. Some times the gases released go into the subcutaneous tissue and cause the star-shaped laceration.
		4. muzzle imprint
	2. Intermediate-range wounds
		1. Powder tattooing (stippling) of the skin around the entrance site
		2. Irregular
	3. Long-range wounds
		1. No powder tattooing
		2. The entrance wound roughly equal projectile fired
	4. Exit wounds
		1. Typically larger and more irregular than entrance wounds

**Thermal injury:**

**Burns**

* 1. **First-degree**
		1. Painful partial-thickness burns (e.g., sunburn)
		2. Heal without scarring
	2. **Second-degree**
		1. Painful partial-thickness burns
		2. Damage to entire epidermis
		3. Blister formation
		4. Usually heal without scarring
	3. **Third-degree**
		1. Painless full-thickness burns
		2. Extensive necrosis of epidermis and adnexa
		3. Scarring is inevitable.
			+ Keloids (exaggerated scars) commonly occur.
			+ Potential for developing squamous cell carcinoma
		4. Healing of epithelial surface
			+ Proliferation of residual epithelium located at burn margins and lining adnexal structures

**Outcome of burns depends upon:**

* Depth
* Percentage of body involved (role of nine).
* Internal injury because of fume inhalation



Despite continuous improvement in therapy, any both at the burn site and systemically, which can result in hypovolemic shock

**Complications**

* Inhalation of smoke and toxic fume: produce inflammation and swelling, which may lead to partial or complete airway obstruction. Lipid-soluble gases, such as nitrous oxide and products of burning plastics, are more likely to reach deeper airways, producing pneumonitis which show after 48h
* Hypovolemic shock: develops within hours, burn exceeding 50% of the total body surface, whether superficial or deep, is grave and potentially fatal. With burns of more than 20% of the body surface, there is a rapid shift of body fluids into the interstitial compartments
* Infection
	+ Sepsis due to *Pseudomonas aeruginosa* is the most common cause of death.
	+ antibiotic-resistant strains of other common hospital-acquired bacteria, such as *S. aureus,* and fungi, particularly *Candida* specie,
	+ septic shock with renal failure and/or the acute respiratory distress syndrome (ARDS) are the most common serious sequelae
* Curling's ulcers in stomach (acute hemorrhagic gastritis)
* Post burn Contracture & deformaties

**Cold-Induced Injuries:**

* **Frostbite**
	+ Pathogenesis
		- Localized tissue injury caused by direct damage (e.g., ice crystallization intra &extracellular)
		- Indirect damage :Depending on the rate at which the temperature drops and the duration of the drop, induce vasoconstriction and thrombosis.
	+ Clinical findings
		- Loss of pain sensation
		- Waxy appearance
		- Gangrene

|  |
| --- |
| * **Hypothermia**
 |

|  |
| --- |
|  |

|  |
| --- |
| * Prolonged exposure to low ambient temperature leads to hypothermia, a condition seen frequently in homeless & alcohol persons.
* At about 90°F(32.2°C) loss of consciousness occurs, followed by

 bradycardia and atrial fibrillation . |

**Radiation Injury:**

* Radiation is energy distributed across the electromagnetic spectrum as waves (long wavelengths, low frequency) or particles (short wavelengths, high frequency).
* it can be divided into nonionizing and ionizing radiation.
* **Nonionizing radiation** :
	+ characterized by long wavelengths and low frequencies
	+ they produce vibration and rotation of atoms in biologic molecules.
	+ E.g. electric power, radio waves and microwaves, infrared, and **ultraviolet light**
* **Ionizing radiation**:
	+ short wavelengths and high frequency
	+ ionize biologic target molecules and eject electrons.
	+ it can be in the form of :
		- Electromagnetic (x-rays, γ rays)
		- particulate (α particles, β particles, protons, neutrons
		- Alpha particles :consist of 2neutrons and 2 protons.they have strong ionizing power but low penetration because of their large size.
		- Beta particles: are electrons emitted from the nucleus of an atom these have weaker ionizing power but higher penetration than alpha particles.

**The dose of ionizing radiation is measured in several units:**

* **A roentgen** :the amount of ionization produced in air.
* **RAD** :**A**bsorption Of **R**adiant **E**nergy
	+ Biologically the more important parameter.
	+ A rad defines the energy, expressed as ergs, absorbed by a tissue.
	+ One rad equals 100 ergs(0.01joule) per gram of tissue.
* **Gray (Gy):**
	+ corresponds to 100 rads (1 joule/kg of tissue)
	+ centigray (cGy) is equivalent to 1 rad.
* **Pathophysiology**
	+ Injury correlates with type of radiation, cumulative dose, and amount of surface area exposed.
	+ Direct DNA,RNA & protiens injury, or indirect through formation of hydroxyl free radicals.
* **Morphology:**
	+ **Nuclear swelling** and condensation and clumping of chromatin; sometimes the nuclear membrane breaks.
	+ **Apoptosis** .
	+ Giant cells with pleomorphic nuclei or more than one nucleus may appear and persist for years after exposure.
	+ **cytoplasmic changes**, including cytoplasmic swelling, mitochondrial distortion, and degeneration of the ER.
	+ During the immediate post-irradiation period, vessels may show only dilation. Later, endothelial cell proliferation and collagenous hyalinization with thickening of the media, resulting in marked narrowing or even obliteration of the vascular lumina
* **Tissue susceptibility**
	+ Most radiosensitive tissues (highest mitotic activity)
		- Lymphoid tissue (most sensitive)
		- Bone marrow
		- Mucosa of gastrointestinal tract, germinal tissue
	+ Least radiosensitive tissues
		- Bone (least sensitive)
		- Brain, muscle, skin
* **Radiation effects in different tissues**
	+ **Hematopoietic**
		- Lymphopenia (first change)
		- Thrombocytopenia
		- Bone marrow hypoplasia
	+ **Vascular**
		- Thrombosis (early), fibrosis (late)
		- Ischemic damage
	+ **Epidermal**
		- Acute effects are erythema, edema, blistering
		- Chronic effect is radiodermatitis
			* Potential for squamous cell carcinoma
	+ **Gastrointestinal**
		- Acute effect is diarrhea.
		- Chronic effects are adhesions with potential for bowel obstruction.
* **Cancers caused by radiation**
	+ Acute leukemia (most common)
	+ Papillary carcinoma of the thyroid
	+ Osteogenic sarcoma

|  |  |  |
| --- | --- | --- |
| **Organ** | **Ac. Injury** | **Delayed complications** |
| **Bone marrow**  | **Atrophy**  | **Hypoplasia, leukaemia**  |
| **Skin** | **Erythema** | **Atrophy of epidermis & fibrosis of dermis, cancer**  |
| **Heart**  | **----**  | **pericardial fibrosis**  |
|  **Lung** | **Edema,endo.&ep.cell** **death**  |  **Interstit. & intra-alveol. fibrosis, Ca**  |
| **GIT**  | **Edema, mucosal ulcers**  | **Ulcers, fibrosis, strictures, adhesions,**  |
| **Liver**  | **Veno-occlusive disease**  |  **Cirrhosis, liver tumors**  |
| **Kidney**  | **Vasodilation**  | **Cortical atrophy, interstitial fibrosis**  |
| **Urin. Blad.**  | **Mucosal erosion**  | **Submucosal fibrosis, Ca**  |
| **Brain**  | **Edema ,necrosis**  | **Necrosis of white matter, gliosis,**  |
| **Testis**  | **Necrosis**  | **Tubular atrophy**  |
| **Ovary**  | **Atresia of follicle**  | **Stromal fibrosis**  |
| **Thyroid**  | **------**  | **Hypothyroidism, Ca**  |
| **Breast** | **-----** | **Fibrosis, Ca** |

* **Total-Body Irradiation:**
	+ atomic bomb, nuclear power plant accident
	+ even in very low doses - devastating effect
	+ effect on hematopoietic system, GIT and brain
	+ 1-5 Gy - hematopoietic form - nausea, vomiting, lymphopenia, thrombocytopenia, neutropenia, later anemia
	+ 5-50 Gy - gastrointestinal form - diarrhea, hemorrhage, toxemia (from large bowel) - death in 8-9 days
	+ >50 Gy - cerebral form - drowsiness, listlessness, convulsions, coma (death within hours, max. 3 days)
* **Acute radiation syndrome:**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | 0-1 Sv | 1-2 Sv/≤1Gy | 2-10 Sv/1-5 Gyacute radiation syndromes | 10-20 Sv/5-50 Gy - | >50 Sv/>50 Gy  |
|  |  |  |  |  |  |
| Main site of injury | None | Lymphocytes | Bone marrow | Small bowel | Brain |
|  |  |  |  |  |  |
| Main signs and symptoms | - | Moderate leukopenia | Leukopenia, hemorrhage, epilation, vomiting | Diarrhea, fever, electrolyte imbalance, vomiting | Ataxia, coma, convulsions, vomiting |
|  |  |  |  |  |  |
| Timing | - | 1 day to 1 week | 4-6 weeks | 5-14 days | 1-4 hours |
|  |  |  |  |  |  |
| Lethality | - | None | Variable (0% to 80%) | 100% |  |

 1 Sv ≈Gy= 100 rad. / 1 rad = 1 rem



 Chemical injury:

* Injury By Therapeutic Agents
* Tobacco Abuse
* Alcohol Abuse
* Drug Abuse: Cocaine And Heroin Abuse
* Exposure To Toxic Chemical Substance:
	+ Carbone monoxide
	+ carbon tetrachloride
	+ Cyanide ,lead poisoning, Mercuric chloride
* **Adverse effects of Therapeutic Drugs:**
	+ Adverse drug reactions - extremely common in practice of medicine
	+ believed to affect 7% to 8% of patients admitted to a hospital, about 10% of these prove fatal
	+ Most frequently in : antibiotics, antineoplastic agents, immunosuppressive drugs
	+ adverse reaction:
		- Predictable (dose-dependent) - purposeful over dosage: digitalis, streptomycin , sedatives
		- Unpredictable
			* idiosyncrasy - massive necrosis of the liver after paracetamol
			* Hypersensitivity :Anaphylactic shock

|  |  |
| --- | --- |
| **Adverse effects**  | **Drugs**  |
| agranulocytosis, pancytopenia aplastic anemia  | chloramphenicolAntineoplastic agents, immunosuppressives  |
| urticaria, expholiative dermatitis  | Antineoplastic agents, sulfonamides, hydantoins, some antibiotics, and many other agents  |
| acute tubular necrosis, Tubulointerstitial disease necrosis of papillae,  | sulphonamides, analgetics :Phenacetin, salicylates  |
| lung fibrosis, Asthma  | bleomycine, busulphan Salicylates  |
| liver steatosis, cholestasis, necrosis of hepatocytes  | tetracycline, estrogens, halothane, chlorpromazine.  |
| Respiratory depression | Sedatives |

* **Broad spectrum antibiotic side effect:**
	+ Diarrhea: pseudomembranous colitis
	+ Candidacies :mouth, vagina
	+ Skin eruption
	+ develop of bacterial resistance
	+ Other drug specific
* **cancer chemotherapeutic:**
	+ Nausea and vomiting
	+ Susceptibility to infection even minor infection can be fatal
	+ Tumor lysis syndrome
	+ Malignancy: lymphoma
* **Acetaminophen:**
	+ very safe :The window between the usual therapeutic dose (0.5 gm) and the toxic dose (15-25 gm) is large
	+ accidental over dosage occurs in children, and suicide attempts
	+ Conversion to free radicals in the liver
	+ Toxicity begins with nausea, vomiting, diarrhea, and sometimes shock, followed in a few days by jaundice
	+ very large doses May result in damage to the liver at centrilobular areas of the hepatic lobules
	+ May result in damage to the kidneys (e.g., renal papillary necrosis)
* **acetylsalicylic acid(Aspirin):**
	+ accidental overdosage occurs in children, and suicide attempts
	+ Stomach :ulcer, acute hemorrhagic gastritis
	+ Platelet dysfunction &bleeding
	+ Asthma
	+ Reyes Syndrome
	+ In Acute over dose:
		- Tinnitus, vertigo, change in mental status (confusion, seizures), tachypnea
		- Acid-base disorders
		- Hyperthermia
		- fulminant hepatitis.
* **Proprietary analgesic mixtures of aspirin and phenacetin or its active metabolite, acetaminophen, when taken over several years, can cause tubulointerstitial nephritis with renal papillary necrosis, referred to as *analgesic nephropathy***

**Tobacco Smoking:**

* Smoking is the most preventable cause of human death.
* It reduces overall survival, and the impact is dose dependent
* Cessation of smoking greatly reduces the risk of death from lung cancer
* Nicotine is an important constituent responsible for tobacco addiction
* Nicotine is an alkaloid that readily crosses (7sec)the blood-brain barrier and stimulates nicotine receptors in the brain.It immediately stimulates the release of many chemical messengers including acetylcholine, catecholamine: increase : heart rate and blood pressure, coronary artery blood flow, contractility and cardiac output), dopamine, and beta-endorphins. This results in enhanced pleasure, decreased anxiety, and a state of alert relaxation.
* Most of the deaths related to smoking :lung cancer, cardiovascular disease, and chronic respiratory disease
* Directly linked to the action of carcinogens in smoke are:
	1. Bronchial carcinoma.
	2. Oral cancer.
	3. Carcinoma of the larynx.
* The incidence increased significantly in smokers:
	1. Carcinoma of the esophagus.
	2. Carcinoma of the urinary bladder.
	3. Carcinoma of the uterine cervix.
	4. Carcinoma of the kidney.
* Carcinoma of the pancreas. Polycyclic hydrocarbons are the primary carcinogens.
* Systemic effect:
	1. RS:

Laryngeal cancer: squamous cell carcinoma
Chronic obstructive pulmonary disease: chronic bronchitis, emphysema
Lung cancer: squamous cell carcinoma, small cell carcinoma, some types of adenocarcinoma

* 1. CVS:

 Acute myocardial infarction (AMI)
Sudden cardiac death
Peripheral vascular disease(Burger disease)
Hypertension; cardiac arrest in women who take oral contraceptives

* 1. CNS:

Strokes: intracerebral bleed, subarachnoid hemorrhage

* 1. GI:

Oropharyngeal cancer: squamous cell carcinoma
Upper, midesophageal cancer: squamous cell carcinoma
Gastroesophageal reflux disease: decreases tone of lower esophageal sphincter
Delayed healing of peptic ulcers
Pancreatic cancer: adenocarcinoma

* 1. GUS:

Cervical cancer: squamous cell carcinoma
Decreased testosteronein males
Decreased estrogen in females
Kidney cancer: renal cell carcinoma
Urinary bladder cancer: transitional cell carcinoma

* 1. Maternal smoking:

increases the incidence of sudden infant death syndrome, even 10 cigarettes per day can cause fetal hypoxia; low birth weight, prematurity, and increased incidence of spontaneous abortion

* Passive (secondhand) smoke inhalation
	1. Greatest impact on children
		+ Increased risk of respiratory and middle ear infections
		+ Exacerbates asthma
	2. Increased risk for lung cancer and coronary artery disease
* Beneficial effects of smoking cessation
	1. Risk for cardiovascular disease
		+ Approaches nonsmoker after 15 years
	2. Risk for lung cancer
		+ Approaches nonsmoker after 15 years
	3. Risk for stroke
		+ Approaches nonsmoker after 5 to 15 years
	4. Other benefits
		+ Reduced risk for cancers of the mouth, larynx, esophagus, pancreas, and urinary bladder
		+ Improved pulmonary function regardless of severity of the disease
		+ Reduced risk for pneumonia, influenza, and bronchitis

|  |  |
| --- | --- |
| Tar | Carcinogenesis |
| Polycyclic aromatic hydrocarbons | Carcinogenesis |
| Nicotine | Ganglionic stimulation and depression, tumor promotion |
| Phenol ,acetaldehyde  | Tumor promotion; mucosal irritation |
| Benzopyrene  | Carcinogenesis |
| Carbon monoxide | Impaired oxygen transport and utilization |
| Formaldehyde hydrogen cyanide;  | Toxicity to cilia; mucosal irritation |
| Oxides of nitrogen | Toxicity to cilia; mucosal irritation |
| Nitrosamine | Carcinogenesis |

**Alcohol abuse:**

* Fifty percent of adults in the western world drink alcohol
* about 5% to 10% have chronic alcoholism.
* It is estimated that *there are more than 10 million chronic alcoholics in the United States*
* *alcohol consumption is responsible for more than 100,000 deaths annually*.
* Almost 50% of these deaths result from accidents caused by drunken driving and alcohol-related homicides and suicides, and about 25% are a consequence of cirrhosis of the liver.
* Absorption occurs in the stomach (25%)
* Metabolism occurs in the stomach and liver
* Alcohol is oxidized to acetaldehyde in the stomach and liver by alcohol dehydrogenase ,& by Cytochrome P-450 & Catalase in liver
* Alcohol oxidation by alcohol dehydrogenase depletes NAD, leading to accumulation of fat in the liver and metabolic acidosis.
* Legal blood alcohol limit for driving (in western word) ranges from 80 to 100mg/dL
* Blood alcohol levels and their effects:
	+ 100 mg/dl ataxia, decreased motor response time
	+ 200 mg/dl drowsiness
	+ 300 mg/dl Stupor
	+ 400 mg/dl Profound anesthesia (may be fatal)
* **Systemic Manifestation:**
	+ **CNS:**
		- Depressant
		- thiamine deficiency :
1. Wernicke's syndrome: confusion, ataxia, nystagmus
2. Korsakoff's psychosis: memory deficits
3. Peripheral neuropathy
	* **Hepatobiliary:**
		+ Fatty liver
		+ alcoholic hepatitis
		+ Liver cirrohsis
		+ Hepatocellular carcinoma: preexisting cirrhosis
	* **CVS:**
		+ Cardiomyopathy
		+ HT
	* **GIT:**
		+ Oropharyngeal and upper to midesophageal cancer: squamous cell carcinoma
		+ Acute hemorrhagic gastritis
		+ Mallory-Weiss syndrome: tear of distal esophagus due to retching
		+ Boerhaave's syndrome: rupture of distal esophagus due to retching
		+ Esophageal varices: caused by portal vein hypertension in alcoholic cirrhosis
		Acute and chronic pancreatitis
	* **GUS:**
		+ Testicular atrophy: decreased testosterone
		+ decreased spermatogenesis
		+ Increased risk for spontaneous abortion
	* **Fetus:**
		+ Fetal alcohol syndrome : mental retardation, microcephaly, atrial septal defect
	* **Hematopoietic:**
		+ Folate deficiency: decreased reabsorption in jejunum; macrocytic anemia
		+ Acquired sideroblastic anemia: microcytic anemia due to defect in heme synthesis
		+ Anemia chronic disease: most common anemia in alcoholics

|  |
| --- |
|  |

* + **Rhabdomyolysis:**
		- direct alcohol effect on muscle

**Drug abuse**:

Has been defined as “the use of any substance in a manner that deviates from

 the accepted medical, social or legal pattern within a given society:

* CNS depressants –alcohol, diazepines
* CNS stimulants – cocaine, amphetamine
* Narcotics – morphine
* Hallucinogens – marijuana

**Complications of intravenous drug use:**

* Infection:
	+ Hepatitis B
	+ Human immunodeficiency virus (HIV)
	+ Infective endocarditis
		- Caused by *Staphylococcus aureus*
	+ Tetanus
* Contaminants like powder talc etc.
	+ Pulmonary granuloma &fibrosis
	+ Cardiac arrest

**Cocaine Abuse:**

* Alkaloid extracted from the leaves of Erythroxylon coca.
* The pharmacologic actions of cocaine and crack are identical, but crack is far more potent
* Methods of abuse
	+ Chewing leaves
	+ Sniffing
	+ Smoking crack
	+ I/V use.
* Produces rapid *high* of short duration
	+ Euphoria
	+ Increased energy
	+ Stimulation
* Chronic Abuse
	+ Insomnia
	+ Increased anxiety
	+ Paranoia
	+ Hallucinations
	+ Nasal septal perforation.
* Acute overdose
	+ Seizures
	+ Cardiac Arrhythmias
	+ Respiratory arrest
* Mechanism of Action:
	+ on CNS :Blocks reuptake of Dopamine and serotonin leading dopaminergic effect in limbic area produces euphoria and hyperpyrexia
	+ Periphery: Blocks reuptake of adrenaline and noradrenalin catecholamine activity Stimulation of alpha and beta adrenergic receptors: Increased heart rate, Increased B.P, Coronary spasm, Increased myocardial oxygen demand, Decreased blood supply Causes Cardiac arrhythmias Ischemia ,Infarction
	+ Fetal risks
		- Decreased fetal blood flow to the placenta
		- Fetal hypoxia
		- Spontaneous abortions
		- Abruption of placenta
		- Haemorrhages
		- Neurological impairments

**Heroin:**

* Opioid derivatives
* Closely related to morphine.
* Derived from the poppy plant.
* Is usually self-administered intravenously or subcutaneously.
* Chronic Abuse Induces:
	+ Miotic pupils,
	+ noncardiogenic pulmonary edema (frothing from mouth),
	+ focal segmental glomerulosclerosis (nephrotic syndrome)
	+ Granulomatous reactions in skin and lungs from material used to "cut" (dilute) drug
* Overdose **:**
	+ Hypothermia
	+ Convulsions
	+ Cardiorespiratory arrest
	+ Coma &Death

**Exposure to Toxic Chemical Substance:**

* **Cyanide**
* Cyanide blocks cellular respiration by binding to mitochondrial cytochrome oxidase
* The effects of cyanide ingestion are very similar to the effects of suffocation/hypoxia
* Smell bitter almonds
* Immediate death:cardiac arrest ,coma
* Lower dose: General weakness, confusion, bizarre behavior, excessive sleepiness, shortness of breath, headeache ,dizzeness, and seizures
* **Chloroform and carbon tetracholoride**
	+ Cleaning fluids & industrial organic solvents
	+ **Acute central nervous system depression**
	+ Hepatotoxic:Centrilobular fatty changes or necrosis of the liver
	+ Nephrotoxcity: Renal tubular necrosis ,Oliguria
	+ Toxicity may persist for long periods:stored in adiopse tissue
	+ Carcinogenic in rodents
* **Carbon monoxide (CO) poisoning:**
	+ nonirritating, colorless, tasteless, odorless gas. come from Automobile exhaust, house fires
	+ Cause systemic asphyxia by forming stable carboxyHb which is incapable of binding oxygen.
	+ Affinity of CO for Hb is 200 times the affinity of oxygen
	+ The cherry red color of skin is hallmark in acute poisoning
	+ It is produced by the imperfect oxidation of carbonaceous materials
	+ Chronic exposure to CO seen in individuals working in confined environments with high exposure to fumes, such as tunnel and underground garage workers which may cause headaches.
	+ Systemic hypoxia appears when the hemoglobin is 20% to 30% saturated with CO, and unconsciousness and death are probable with 60% to 70% saturation.
* **LEAD:**
	+ Lead exposure occurs through contaminated air and food.
	+ Most of the absorbed lead (80% to 85%) is taken up by bone and developing teeth
	+ Major sources of lead in the environment were lead-containing house paints and gasoline.
	+ Lead contamination in houses and soil remains an important health hazard, particularly for children.
	+ Other sources of lead in the environment, mines, foundries, batteries, and spray paints,
	+ The maximal allowable level 10 μg/dL.
	+ Children absorb more than 50% of lead from food, while adults may absorb approximately 15%.
	+ A more permeable blood-brain barrier in children creates a high susceptibility to brain damage.
	+ The major anatomic targets of lead toxicity are
		- **The blood :**
			* **basophilic stippling** of the erythrocytes,
			* microcytic, hypochromic, hemolytic anemia
		- **nervous system:**
			* Children: low IQ ,mental retardation
			* Adult: head each ,memory loss
		- **GI tract**: Lead "colic"
		- **Kidneys**: develop proximal tubular damage with intranuclear lead inclusions

**Mercury:**

* + - The main sources of exposure to mercury are contaminated fish and dental amalgams
		- Mercury used in gold mining has contaminated rivers and streams.
		- The consumption of contaminated fish from the release of methyl mercury in Minamata Bay and the Agano River in Japan *:"Minamata disease,"* :cerebral palsy, deafness, blindness, and major CNS defects in children exposed in the uterus.
		- The consumption of bread containing grain treated with a methyl mercury-based fungicide in Iraq caused widespread mortality and morbidity.
		- There has been much publicity about a possible relationship between thimerosal (a compound that contains ethyl mercury, until recently used as a preservative in some vaccines) and the development of autism, but there is little evidence for a relationship between thimerosal and autism.

**NUTRITIONAL DISEASES:**

* Malnutrition
	+ Overnutrition: Obesity
	+ Protein-Energy Malnutrition (PEM):Marasmus, Kwashiorkor
* Eating disorder: Anorexia Nervosa and Bulimia

**Overnutrition: Obesity:**

* Obesity is a global epidemic resulting from sedentary lifestyles, improved socioeconomic conditions, and availability of processed, high calorie foods and soft drinks in industrialized societies.
* Obesity is a disorder of energy balance. When food-derived energy chronically exceeds energy expenditure.
* Obesity:Body mass index (BMI) ≥ 30kg/m2 (normal: 18.5-24.9kg/m2) :BMI = weight (kg)/height (m2)
* Other factors than body weight associated with a much higher risk for several diseases
	+ Excess fat in the waist and flanks is more important than an excess in the thighs and buttocks.
	+ Excess visceral fat in the abdominal cavity has greater significance than excess subcutaneous fat.
* **Pathogenesis**
	+ Genetic factors
		- Examples-defects in the leptin gene, syndrome X (obesity, hypertension, diabetes)
	+ Acquired causes
		- Endocrine disorders-hypothyroidism, Cushing syndrome
		- Hypothalamic lesions, menopause
* Gherlin:Produced by stomach, before meals and fall after, gastric by pass surgery
* Leptin : It is now established that adipocytes communicate with the hypothalamic centers that control appetite and energy expenditure by secreting leptin (a member of the cytokine family).
	+ Hormone is secreted by adipose tissue that maintains energy balance.
	+ Leptin increases when adipose stores are adequate.
		- Decreases food intake
		- Increases energy expenditure (stimulates β-oxidation of fatty acids)
	+ Leptin decreases when adipose stores are inadequate.
		- Increases food intake
		- Decreases energy expenditure (inhibits β-oxidation of fatty acids)
	+ Obesity may be due to several factors:
		- Resistance to leptin effects
		- Decreases energy expenditure (inhibits β-oxidation of fatty acids)
* Behavioral and dietary changes are the initial therapeutic strategies; weight-loss drugs should be used with caution
* Associated disorders
	+ Atherosclerosis
	+ Hypertension
	+ Diabetes-ii
	+ Gallbladder disease
	+ Osteoarthritis.
	+ Hypoventilation syndrome (pickwickian syndrome)
	+ Stroke
	+ Some ca: colon, breast, endometrial

**Undernutrition**:

* Starvation: Calorie intake inadequate to sustain normal metabolic process
* Causes in affluent society
	+ Ignorance & poverty
	+ Chronic alcoholism
	+ Acute & Chronic illness
	+ Self imposed
		- Anorexia nervosa
		- Bulimia nervosa
* In poor societies
	+ Poverty & deprivation
	+ Severe protein-Energy malnutrition (PEM)
	+ Children& pregnant ladies affected more
* Other causes
	+ Malabsorption
	+ Genetic disease
	+ Specific drug therapies
	+ Total parentral nutrition
* PEM refers to a *range of clinical syndromes* characterized by an inadequate dietary intake of protein and calories to meet the body's needs
* In third world countries PEM major factor in the high death rates among children younger than age 5 years.
* Include two disease :marasmus (calorie deficiency), and kwashiorkor (protein deficiency)
* **Kwashiorkor:**
* Pathogenesis
	1. Inadequate protein intake
	2. Adequate caloric intake consisting mainly of carbohydrates
	3. Protein in liver and other organs (i.e., visceral protein) is decreased.
	4. Muscle protein (i.e., somatic protein) is relatively unchanged.
* Clinical findings
	1. Pitting edema and ascites
		+ Caused by hypoalbuminemia and loss of plasma oncotic pressure
	2. Fatty liver
	3. Diarrhea
		+ Caused by loss of the brush border enzymes and parasitic infections
	4. Anemia and defects in cell-mediated immunity (CMI)

|  |
| --- |
|  |

|  |
| --- |
| * **Marasmus**
* Pathogenesis
	1. Dietary deficiency of both protein and calories
	2. Decrease in somatic protein
* Clinical findings
	1. Extreme muscle wasting ("broomstick extremities")
		+ Breakdown of muscle protein for energy
		+ Loss of subcutaneous fat
	2. Growth retardation, anemia, defects in CMI
 |

* **Eating disorder: Anorexia Nervosa and Bulimia**
	+ - *Anorexia nervosa* is 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 generally has a better prognosis.
		- It is estimated to occur in 1% to 2% of women and 0.1% of men, with an average onset at 20 years of age.
		- These eating disorders occur primarily in previously healthy young women who have developed an obsession with attaining thinness.
		- Clinical findings in *Anorexia nervosa*
			* Secondary amenorrhea: Decreased gonadotropin-releasing hormone Caused by loss of body fat and weight produces hypoestroginism.
			* Osteoporosis :Caused by hypoestroginism
			* decreased thyroid hormone release, include cold intolerance, bradycardia, constipation,
			* dehydration and electrolyte abnormalities are frequently present.
			* Increased lanugo (fine, downy hair)
			* Increased hormones associated with stress (e.g., cortisol, growth hormone)
		- Clinical findings in Bulimia due to continual induced vomiting and chronic use of laxatives and diuretics.
			* electrolyte imbalances (hypokalemia), which predispose the patient to cardiac arrhythmias;
			* pulmonary aspiration of gastric contents;
			* Esophageal and stomach rupture.
			* Acid injury to tooth enamel