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, opthalmoplagia, nystagmus
            2. Korsakoff's psychosis: memory deficits
            3. Peripheral neuropathy
    - **Hepatobiliary:**
        - Fatty liver
        - alcoholic hepatitis
        - Liver cirrhosis
        - Hepatocellular carcinoma: preexisting cirrhosis, HCV,HBV

Hepatobiliary:	Stop drinking	Clinical finding	Gross finding	microscopy
Fatty liver	Reversible	Hepatomegally	Enlarged1.5-2.5kg, yellow	Macrovesicular steatosis
Acute alcohol hepatitis	Reversible	Fever, jaundice, mild hepatomegally, tenderness	Mild enlargement	Cetrolobular hepatnecrosis, ballooning degeneration PMN, Mallory hyaline body
Liver cirrhosis	Irreversible	Jaundice, PHT, loss of liver function	Shranking, micronodular cirrhosis	hepatocellular necrosis, fibrosis, and regeneration hepatocellular nodules

- **CVS:**
  - Cardiomyopathy
  - HT,IHD
- **GIT:**
  - Oropharyngeal and upper to midesophageal cancer: squamous cell carcinoma
  - Mallory-Weiss syndrome: tear of distal esophagus due to retching
  - Esophageal varices: caused by portal vein hypertension in alcoholic cirrhosis
  - Acute hemorrhagic gastritis
  - 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, diazepam's
- 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
  - Dilated pupils
  - Hallucinations
  - Nasal septal perforation.
- Acute overdose
  - Seizures
  - Cardiac Arrhythmias
  - Respiratory arrest
- Mechanism of Action:
  - on CNS :Blocks reuptake of Dopamine and serotonin leading to 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
  - Hemorrhage
  - 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:

- **Chloroform and carbon tetrachloride**
  - Cleaning fluids and solvents
  - Exert anesthetic (depressant) effects on the CNS, and on the heart and blood vessels
  - Hepatotoxins: acute hepatic necrosis (centrilobular fatty changes or necrosis), fatty liver, and liver failure
  - Renal tubular necrosis :Oliguria
  - Toxicity may persist for long periods
- **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(due to carboxyHb) 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.

Cyanide

- Very toxic kills in minutes
- classic murderer's tool
- smell of bitter almonds
- Cyanide blocks cellular respiration by binding to mitochondrial cytochrome oxidase,
- Generalized petechial hemorrhage

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 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.

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 is a disorder with a multifactorial complex etiology
  - environmental,
  - Genetic
  - Psychological
- Obesity:Body mass index (BMI) ≥ 30kg/m^2 (normal: 18.5-24.9kg/m^2) :BMI = weight (kg)/height (m^2)
- Other factors than body weight
  - 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
- 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)
- 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
  - Some Ca-Colon, breast

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
    a. Inadequate protein intake
    b. Adequate caloric intake consisting mainly of carbohydrates
    c. Protein in liver and other organs (i.e., visceral protein) is decreased.
    d. Muscle protein (i.e., somatic protein) is relatively unchanged.
  - Clinical findings
    e. Pitting edema and ascites
       - Caused by hypoalbuminemia and loss of plasma oncotic pressure
    f. Fatty liver
    Diarrhea
       - Caused by loss of the brush border enzymes and parasitic infections
    h. Anemia and defects in cell-mediated immunity (CMI)
  - **Marasmus**
  - Pathogenesis
    a. Dietary deficiency of both protein and calories
    b. Decrease in somatic protein
  - Clinical findings
    a. Extreme muscle wasting ("broomstick extremities")
       - Breakdown of muscle protein for energy
       - Loss of subcutaneous fat
    b. 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