Nutritional Pathology

Topics

- Nutritional deficiencies
  - Protein - Energy Malnutrition
  - Anorexia Nervosa and Bulimia
  - Vitamin Deficiencies
  - Mineral Deficiencies
- Obesity
- Diet and Systemic Diseases

Nutritional deficiencies

An adequate diet should provide:
1. Energy, in the form of carbohydrates, fats, proteins
2. Essential (as well as nonessential) amino acids and fatty acids as building blocks
3. Vitamins and minerals function as coenzymes and hormones in vital metabolic pathways

Malnutrition

Primary malnutrition: missing from the diet
Secondary malnutrition: adequate nutrients supply, but malnutrition may result from
- Malabsorption
- Impaired nutrient use or storage
- Excess nutrient losses
- Increased need for nutrients (GI diseases, chronic wasting diseases, acute critical illness)

Common Causes

- Poverty (homeless, aged, children)
- Ignorance (infants, adolescents, pregnant women)
- Chronic alcoholism
- Acute and chronic illnesses (trauma, burn, cancer, etc.)
- Self-imposed dietary restriction
Protein - Energy malnutrition (PEM)

- PEM refers to a range of clinical syndrome characterized by an inadequate dietary intake of protein and calories to meet the body’s needs.

- Primary (children) and Secondary (illness) PEM
  - Two polar forms: - Marasmus, - Kwashiorkor

1. Marasmus
- Severe reduction in caloric intake
- Greater than 60% reduction in body weight
- Most common during the first year of life
- Use somatic protein component and subcutaneous fat as a source of energy
- Serum albumin levels are either normal or only slightly reduced
- Growth retardation, multivitamin deficiencies, anemia, immune deficiency

2. Kwashiorkor
- More severe form of malnutrition than marasmus
- Mainly occur in children 6 months to 3 years of age
- Occurs when protein deprivation is relatively greater than the reduction in total calories
- Loss of visceral protein component
- Hypoalbuminemia → generalized edema
- Fatty change of liver
- Skin lesion: hypo- and hyperpigmentation, desquamation
- Hair change: overall loss of color or alternating band (flag sign), straightening, loss of firm attachment to the scalp
- Multivitamin deficiencies, anemia, immune deficiency

Secondary PEM

<table>
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<tr>
<th>Syndrome</th>
<th>Clinical setting</th>
<th>Time course</th>
<th>Clinical features</th>
<th>Laboratory findings</th>
<th>Prognosis</th>
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<tr>
<td>1. marasmus-like PEM</td>
<td>Chronic illness</td>
<td>Months</td>
<td>History of weight loss muscle wasting, diastolic subcutaneous fat, &quot;Cachexia&quot;</td>
<td>Normal or mildly reduced serum proteins</td>
<td>Variable depending on underlying disease</td>
</tr>
<tr>
<td>2. kwashiorkor-like PEM</td>
<td>Acute, catabolic illness e.g. severe trauma burn sepsis</td>
<td>Weeks</td>
<td>Normal fat and muscle edema easily pluckable hair</td>
<td>Serum albumin &lt; 2.8 gm/dl</td>
<td>poor</td>
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Anorexia Nervosa

- Self-induced starvation, resulting in marked weight loss
- Manifested as severe PEM with endocrine abnormalities
  - Amenorrhea (GnRH, LH, FSH)
  - Decreased bone density (low estrogen level)
  - Decreased thyroid hormone release (cold intolerance, bradycardia, constipation)
- Increased susceptibility to cardiac arrhythmia and sudden death
Bulimia

- A condition in which the patient binges on food and then induces vomiting
- Amenorrhea occurs in less than 50% of Pt., Wt. and gonadotropin levels are near normal
- Major medical complications:
  - Electrolyte imbalances (Hypokalemia) and cardiac arrhythmia
  - Pulmonary aspiration of gastric content
  - Esophageal and cardiac rupture

Vitamin deficiencies

- Recommended dietary allowances (RDA)
  - Vit. A, D, E, K → fat soluble → storage
  - The remainders → water soluble
  - Vit. A, C, E + selenium → antioxidant
  - Vit.K + biotin → synthesis by intestinal flora
  - Vit.D → UV
  - Niacin → tryptophan (essential amino acid)
**Vitamin A Deficiency**

- night blindness
- Bitot's spot (small plaques of keratin debris, keratomalacia (corneal ulcer and destruction), xerophthalmia (dry eye), total blindness
- Squamous metaplasia → 2° pulmonary infection, KUB stone (keratin debris)
- vulnerability to infection (measle, pneumonia, diarrhea)

**Vitamin A Toxicity**

- polar bear's liver
  - Acute → headache, vomiting, stupor, papilledema (increased ICP)
  - Chronic → weight loss, nausea, vomiting, dryness of lips, bone and joint pain, hyperostosis (excessive growth of bone), hepatomegaly with parenchymal damage and fibrosis

**Vitamin D**

1, 25 (OH)2 D is the active form of vitamin D (synthesis from kidney by α1-hydroxylase)

Function
- stimulate intestinal absorption of Ca and P.
- collaborates with PTH in the mobilization of Ca from bone.
- stimulate the PTH-dependent reabsorption of Ca in the distal renal tubules
Vitamin D
Deficiency: Rickets (children)
: Osteomalacia (adult)
: Hypocalcemia → tetany

Rickets
• overgrowth of epiphyseal cartilage.
• Persistence of distorted, irregular masses of cartilage projecting into marrow cavity.
• Deposition of osteoid matrix on inadequately mineralized cartilaginous remnants.
• Enlargement and lateral expansion of the osteochondral junction.
• Microfracture → overgrowth of capillaries and fibroblast (reparation)
• Deformation of skeleton due to loss of rigidity.

Morphology
- an excess of unmineralized matrix (osteoid)
- Intramembranous bone formation (direct ossification of embryonic connective tissue: membrane bone of skull)
- Endochondral bone formation (Intracartilaginous replacement of hyaline cartilage; bone of trunk and extremities cartilage)
**During nonambulatory stage of infancy:**
- **Head:** craniotabes, frontal bossing, squared appearance
- **Chest:** rachitic rosary at costochondral junction, pigeon breast deformity, Harrison's groove.

**During ambulatory stage of infancy:**
- Pelvis deformity, lumbar lordosis, bowing legs.

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**Rachitic rosary**

[Rachitic rosary image](http://www.patient.co.uk/doctor/Chest-Deformity.htm)

**Pectus excavatum (Funnel chest)**

[Pectus excavatum image](http://www.respir.com/images/SemeioPectusExt.jpg)

**Pectus carinatum (Pigeon chest)**

[Pectus carinatum image](http://www.nlm.nih.gov/medlineplus/ency/images/ency/fullsize/9583.jpg)

**Bowing legs**

[Bowing legs image](http://www.nlm.nih.gov/medlineplus/ency/images/ency/fullsize/9583.jpg)
**Osteomalacia**

- Vitamin D deficiency in adult
- Contour of the bone are not affected
- Bone is weak and vulnerable to fracture due to osteopenia

**Vitamin E (α-tocopheral)**

- Serves as a scavenger of free radicals, the antioxidant effect
- May reduce mutagenesis
- Cause of deficiency: Deficient diet is uncommon; occurs in association with malabsorption syndromes, infants of low birth weight, developmental defects in the GI tract, or lipoprotein disorders.

**Vitamin E Deficiency**

- Poor nerve conduction, axon degeneration on the posterior columns of the spinal cord, loss of nerve cells in the dorsal root ganglia, and degenerative changes in the spinocerebellar tracts
- The neurologic manifestations are ataxia, dysarthria, absent tendon reflexes, and loss of position sense and pain sensation.

**Vitamin K**

- Clotting factor 2, 7, 9, 10
- Anticoagulant protein C and S
- May favor calcification of bone proteins and inhibit bone resorption → prevent osteoporosis

**Cause of deficiency:**

- Fat malabsorption syndromes (biliary tract disease)
- Destruction of the endogenous vitamin
- Synthesizing flora (ingestion of broad-spectrum antibiotics)
- Neonatal period
- Diffuse liver disease
- Drug (e.g., warfarin)

**Deficiency state:**

- ภาวะเสี่ยงถลอกเลือด
- bleeding diathesis (intracranial hemorrhage of the newborn)
**Vitamin B1 (thiamine)**

Function: maintains neural membranes and normal nerve conduction, especially peripheral nerve.

Deficiency: most common in chronic alcoholism, result in syndromes of:
- dry beriberi (polyneuropathy)
- wet beriberi (heart failure, peripheral edema)
- Wernicke-Korsakoff Syndrome

**Wernicke-Korsakoff Syndrome**

- Lesions in the CNS: hemorrhage and degeneration of mammillary bodies, periventricular region of thalamus, floor of forth ventricle, anterior region of cerebellum
- Wernicke encephalopathy is marked by ophthalmoplegia, nystagmus, ataxia of gait and confusion
- Korsakoff psychosis consists of impairment of remote recall, confabulation, and inability to acquire new information

**Vitamin B2 (Riboflavin)**

- cheilosis (cheilitis, angular stomatitis): first + most characteristic sign (crack + fissure at the angles)
- Glossitis: tongue atrophy, red-blue discoloration
- Eye change: interstitial keratitis, corneal vascularization, corneal ulcer
- Scaling dermatitis: nasolabial folds and cheek (butterfly distribution), scrotal, vulva

**Vitamin B3 (Niacin)**

- an essential component of NAD⁺ and NADP⁺
- Pellagra (3 D's):
  - Dermatitis sharply demarcated scaling and desquamation of exposure area, bilaterally symmetric
  - Diarrhea caused by atrophy of the gastrointestinal epithelium
  - Dementia results from neuron degeneration in the brain, and in the spinal cord
**Vitamin B6 (Pyridoxine)**

Deficiency state
- Most common in chronic alcoholism and pregnancy
- Clinical findings resemble vit. B2 + niacin deficiencies (seborrheic dermatitis, cheilosis, glossitis, peripheral neuropathy, convulsion)

**Vitamin B12 (Cobalamin)**
- Coenzyme in the DNA synthetic pathway (as well as folic acid)
- Vit.B12 + R - binder (saliva) → protease (pancreas)
  ↓
  vit.B12 + intrinsic factor (gastric parietal cell)
  ↓
  absorb at ileum

**Vitamin B12 Deficiency**

1) Megaloblastic anemia
- RBC: anisocytosis, hyperchromia, macrocytic and oval shape
- Neutrophil: macropolycyte, hypersegmentation
- Bone marrow: erythroid to myeloid ratio = 1:1 (normal 1:3)
  : megaloblastic change in all stages of RBC development
- Leukopenia and thrombocytopenia

**Chronic atrophic gastritis**
- Autoantibody to parietal cell, IF or IF receptor
- Vitamin B12 cannot be absorbed
- Achlorhydria + intestinal metaplasia → gastric cancer

**"ผู้มีสิทธิ์"**
2.) Atrophic glossitis
3.) Myelin degeneration of the spinal cord

Anemia and neurologic changes can be cured after administration of Vitamin B12, but the changes in gastric mucosa are unaffected.

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**Folate**

- Coenzyme in the DNA synthetic pathway
- Absorb at proximal jejunum
- Deficiency: clinically some as vitamin B12 deficiency except neurologic change
  - Neural tube defects in the developing fetus (first few weeks post-conception)

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**Vitamin C (Ascorbic acid)**

- Function: hydroxylation of procollagen, antioxidant
- Deficiency: impaired synthesis of collagen (bone and vessel)

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**Morphology**

- Scurvy in growing child
- Hemorrhagic diathesis
- Inadequate synthesis of osteoid
- Cartilagenous overgrowth → widening of epiphysis
- Bowing of legs + abnormal depression of the sternum
- Impaired wound healing and local infection
- Skin lesions: perifollicular hemorrhage, hyperkeratotic, papular rash
Mineral deficiencies

Causes: inadequate supplementation
- interference with absorption by dietary constituents
- inborn errors of metabolism

Zinc
- Acrodermatitis enteropathica (often around eye, nose, mouth, anus and distal parts)
- Anorexia with diarrhea
- Growth retardation in children
- Impaired wound healing
- Hypogonadism
- Altered immune function
- Impaired night vision
- Depressed mental function
- Increased incidence of congenital malformations in infants of zinc-deficient mother

Iron
- Absorption at duodenum
  - Functional iron (80%): hemoglobin, myoglobin, iron-containing enzymes
  - Storage pool (20%): hemosiderin, ferritin-bound iron (liver, spleen, bone marrow, skeletal muscle)

Iron Deficiency
- dietary lack, increased requirement, chronic blood loss
  - koilonychia (spoon nail), alopecia
  - atrophic changes in the tongue and gastric mucosa, intestinal malabsorption
  - hypochromic microcytic anemia, poikilocytosis
  # Plummer-Vinson syndrome:
    1.) microcytic hypochromic anemia
    2.) Atrophic glossitis
    3.) Esophageal webs (dysphagia)
Hypochromic microcytic anemia with poikilocytosis

Koilonychia

Fe Excess: Hemochromatosis
- Defined as the excessive accumulation of body iron, deposited in the parenchymal cells of various organs, particularly liver and pancreas.

1. Genetic hemochromatosis (hereditary hemochromatosis) is a homozygous recessive heritable disorder, rarely

2. Secondary hemochromatosis denotes disorders with identifiable sources of excess iron, more common, ex. Thalassemia

Clinical features
- Hepatomegaly, abdominal pain, micronodular cirrhosis, hepatocellular carcinoma, diabetes mellitus, skin pigmentation, cardiac dysfunction, hypogonadism and arthritis

Copper
- Absorb in stomach and duodenum
- Uptake by hepatocyte and 90-95% bind with ceruloplasmin (resecrete into plasma)
- Wilson disease (hepatolenticular degeneration): autosomal recessive disorder
  - Decrease serum ceruloplasmin, accumulation of Cu in liver, brain, eye, increase urinary excretion of copper
  - Liver: fatty change, acute/chronic hepatitis, cirrhosis, massive liver necrosis
  - Brain: injury to basal ganglia
  - Eye: deposition of copper in Descemet's membrane in the limbus of cornea (Kayser-Fleischer rings)
**Obesity**

Mesurement: Body mass index (BMI) = Wt (kg)/Ht(m)^2
- Body-fat percentage (skin fold measurement) and lean body weight

BMI:
- normal = 18.5 - 24.9 kg/m^2
- overweight = 25.0 - 29.9 kg/m^2
- obesity > 30.0 kg/m^2

**Neurohumoral mechanism**

- Afferent (humoral) signals: leptin(adipose tissue), insulin, ghrelin(stomach)
- Hypothalamus (central melanocortin system)
- Efferent: feeding behavior + energy expenditure (TRH and autonomic pathway)

**Food-derived energy > energy expenditure**

Storage as triglycerides in adipose tissue (insulin effect)
- Daily energy expenditure = Basal energy expenditure (BEE) + Activities.

BEE man = 66 + (13.7 x Wt.) + (5 x Ht.) - (6.8 x age)
BEE woman = 655 + (9.5 x Wt.) + (1.8 x Ht.) - (4.7 x age)

Wt (Kg), Ht (cm.), Age (yrs)

**Exercise more than 3 times per week**

1. **Aerobic exercise** - moderate intensity + long duration (20 - 45 min)
   - use oxegen to burn fat
   - Cardiovascular protection

2. **Anaerobic exercise** - high intensity + short duration
   - glycogenolysis + muscular hypertrophy

CHD 1 gm. = 4 kcal.
Protein 1 gm. = 4 kcal.
Fat 1 gm. = 9 kcal.

Daily energy suitable:
CHD : Protein : Fat = 3:2:1

The adult RDA for protein is 0.6 g./kg. Body weight.
Factors contributing to obesity:

1. Genetic predisposition
2. Decreased lipid utilization: aging, defective thermogenesis, inactivity, underexercising
3. Sociocultural environment: stress, emotional disturbances
4. Diseases: hypothalamic disorder:
   - hypothyroidism
   - Cushing’s syndrome
   - Polycystic ovary syndrome

Complication of obesity

<table>
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<tr>
<th>Gastrointestinal tract</th>
<th>Gallstones, pancreatitis, abdominal hernia, nonalcoholic fatty liver diseases, steatosis, steatohepatitis, and cirrhosis, and possibly gastroesophageal reflux</th>
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<tbody>
<tr>
<td>Endocrine/Metabolic</td>
<td>Metabolic syndrome, insulin resistance, impaired glucose tolerance, type 2 diabetes mellitus, dyslipidemia, polycystic ovary syndrome</td>
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Cardiovascular

- Hypertension
- Coronary artery disease
- Congestive heart failure
- Arrhythmias
- Pulmonary hypertension
- Ischemic stroke
- Venous stasis
- Deep vein thrombosis
- Pulmonary embolus

Respiratory

- Abnormal pulmonary function
- Obstructive sleep apnea
- Obesity hypoventilation syndrome
- Pickwickian syndrome

Musculoskeletal

- Osteoarthritis
- Gout
- Low back pain

Gynecologic

- Abnormal menses
- Infertility

Genitourinary

- Urinary stress incontinence

Endocrine/Metabolic

- Metabolic syndrome
- Insulin resistance
- Impaired glucose tolerance
- Type 2 diabetes mellitus
- Dyslipidemia
- Polycystic ovary syndrome

Diet and systemic diseases

- Fiber → ↓ cholesterol level
  → ↓ diverticulosis, CA colon
- Fish oil → omega-3 FA → ↓ cholesterol and coronary heart disease
- Restricted Na intake → ↓ HT
- Restricted protein diet in liver disease and chronic renal failure
- ↑ Meat intake & ↓ vit. B6, B12 and folate → Hyperhomocysteinemia → atherosclerosis

Dietary factors:

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