NUTRITION

For a 3rd-year medical college student

Nutrition

*All processes involved in how organisms obtain nutrients, metabolize them and use them to support all of life's processes.

*Adequate nutrition is essential for survival and type of food influences health. **Nutrients** *Substances that are not synthesized insufficient amount in the body and therefore must be supplied by the diet.

*Nutrients are classified into

1-Macronutrients include [protein, fat, carbohydrates],

2-Micronutrients include (vitamins and minerals).

Nutritional Physiology

*Glucose is essential for the Brain, Renal medulla, and Red cell metabolism. For this reason under normal circumstances, regulatory mechanisms maintain and control glucose levels in a tight range both at the time of eating and between meals.

*Insulin is the main glucose-regulatory hormone. Eating glucose is rapidly absorbed into the portal system, resulting in insulin secretion from the pancreas.

*Liver extracts a large amount of glucose and converts it to glycogen.

*Glucose is taken up first into muscle and then into adipocytes.

*Between meals glucose levels in the portal tract decrease and the result is the stimulation of Glycogenolysis, *Gluconeogenesis and *Lipolysis.

<u>Glycogenolysis occurs in the liver to maintain plasma glucose levels.</u> <u>Lipolysis is induced</u> and fatty acids are released and become the major energy substrate for the body.

<u>Gluconeogenesis</u> is induced in converting glycerol, amino acids, and fatty acids (via the citric acid cycle) to glucose.

Other hormones act on the regulatory mechanism. These include

Glucagon, Catecholamines, and Growth hormone. They have an anti-insulin effect, increasing glycogenolysis, gluconeogenesis, and release of fatty acids and glycerol from adipose tissue and amino acids from muscle.

Lipids enter the circulation as chylomicrons. When chylomicrons reach the peripheral capillaries lipoprotein lipase on the capillary endothelium binds them and the triglycerides at the core of the chylomicron are rapidly hydrolyzed to fatty acids, which are then taken up and utilized by peripheral tissues.

Between meals, chylomicrons disappear from the circulation and are replaced by verylow-density lipoproteins (VLDLs) which are secreted by the liver. They are also bound and metabolized by lipoprotein lipase in peripheral capillaries.

Energy Balance

Energy balance is achieved when energy intake = Energy expenditure. *Energy expenditure includes

1-The Basal Metabolic Rate (BMR) [energy required to maintain metabolic functions] 2-Extra Metabolic Energy is consumed during growth, pregnancy, lactation, fever, Thermal regulation, digestion of food, and muscular activity.

*Energy intake is determined by the 'macronutrient 'which provides fuel for oxidation in the mitochondria to generate ATP.

Regulation of Energy Balance

For weight to remain stable energy intake must match energy output.

The brain regulates energy homeostasis in response to signals from both adipose tissue and gastrointestinal tract.

Regulation occurs in the hypothalamus which receives afferent signals from the stomach, pancreas, small intestine, and adipose tissue.

The following hormones are involved in the regulation of food intake

*Ghrelin hormone It is produced and released by the gastric mucosa during fasting and falls immediately after eating, ghrelin H increase appetite.

*insulin secreted from Pancreas after meal inhibits food intake.

Hormones secreted by intestine after meal include

*PYY[peptide tyrosine tyrosine] *Glucagon-like peptide1

*Cholecystokinin[CCK],pancreatic like peptide and*Oxyntomodulin

All these hormones inhibit food intake.

*Leptin hormone which synthesized and secreted from adipose tissue also inhibits food intake. The absence of leptin hormone leads to hyperphagia and obesity.

<u>Hypothalamus affects the body by stimulation of secretion the following hormones</u> 1-Thyroxin 2- Growth hormone 3-Cortisol 4-Autonomic nervous system that regulates energy expenditure or storage.

Certain conditions affect hypothalamus like Craniopharyngioma or Gene mutation [Leptin or Melanocortin 4 receptors]lead to loss of receptor response in the hypothalamus lead to loss of satiety feeling Which leads to weight gain.



Regulation of energy balance and its link with reproduction. +indicates factors that are stimulated by eating and induce satiety. - indicates factors that are suppressed by eating and inhibit satiety.

Response to Under and Over Nutrition

When human consumes a small amount of diet or during starvation, the body tries to defend against weight loss through reducing energy loss by the following

1-Reduce basal metabolic rate

2-Decrease Reproductive Function

3-Depression and lethargy

All these happen to maintain body weight but this continued for a limit period after that the body use stored energy by

1-Glycogenolysis in the liver and muscle.

2-Lipolysis of the stored triglyceride in adipose tissue.

3-Proteolysis.

When humans consume Extra Energy. This leads to the following

1-Basal Metabolic Rate will be increased.

2-Excess energy will be stored in the body as triglyceride in adipose tissue or as glycogen in the liver and skeletal muscle.

Clinical Assessment and investigation of Nutritional Status includes

1-Nutritional history

Ask about weight •

Current weight • And Weight 2 weeks, 1 month and 6 months ago •

Assessment of degree of change

Ask about current food intake •

Quantity of food and if any change in Quality of food was taken.

Whether normal food is being eaten

Avoidance of specific food types (e.g. solids).

Any nutritional supplements.

Any change in appetite or interest in food.

Any taste disturbance

Ask about Symptoms that interfere with eating •

Oral ulcers or oral pain.

Difficulties swallowing.

Nausea/vomiting • Early satiety.

Alteration in bowel habits.

Abdominal (or other) pain.

Ask about activity levels/performance status •

Normal activity Slightly reduced activity.

Inactive < 50% of the time .

Inactive most of the time

Clinical Examinations

Signs of weight loss:

Prominent ribs, Muscle wasting, ↓Skin turgor, and Scaphoid abdomen

Eyes -Sunken eyes, Pallor, Jaundice, Bitot spots, vitamin A deficiency

Mouth- Pallor, Angular stomatitis (↓B12, folate, iron), Glossitis (↓B12, folate, iron),

Gingivitis, bleeding gums ↓vitamin C, Poorly fitting dentures, Gingivitis

Skin -Dry, flaky skin, or dermatitis. Hair loss. Petechiae, corkscrew hairs (↓vitamin C), Dermatitis of pellagra (↓niacin)

Hands -Muscle wasting (dorsal interossei, thenar eminences), Finger clubbing Leukonychia (low albumin), Koilonychia (iron deficiency

Legs -Pitting edema,Ulcers

Simple Anthropometrics

1-Body mass index (BMI) is useful for categorizing under and over-nutrition. BMI= the weight in kilograms divided by the height in meters squared. For example, an adult weighing 70 kg with a height of 1.75 m has a BMI of $70/1.75^2 = 22.9 \text{ kg/m}^2$ BMI does not discriminate between fat mass and lean body mass and can be increased by muscle mass. For optimal health, the BMI should be 18.5-24.9 kg/m².

2-in older people with kyphosis or in those who cannot stand and height cannot be determined. height can be determined by-

<u>A-Demispan Measure</u> - This done by measuring the distance from the suprasternal notch to the middle finger then height = $0.73 \times (2 \times \text{demispan}) + 0.43$.

B-Measurement of the femoral length or 'knee height' is a good surrogate

males: Height in cm = 84.88 - (0.24 x age) + (1.83 x knee height)

females: Height in cm = 64.19 - (0.04 x age) + (2.02 x knee height)

<u>3-Triceps skin fold thickness</u> measured by skin fold caliper.

Lean patients 6–12 mm;

obese patients 40-50 mm

Triceps skinfold thickness (when combined with mid-/upper arm circumference MAMC estimates muscle mass.

muscle mass calculated as follows

MAMC = upper arm circumference[cm]–[0.314 ×triceps skinfold thickness[mm]. 4-Waist circumference[Land mark around umbilicus] normal –man <37 inch or 94 cm, female< 31.5 inch or < 80cm



Triceps skinfold thickness

knee height'

Nutrients include *Macronutrients 1-Carbohydrates-

An average adult consumes 55 to 65% of calories as carbohydrates and they form the major source of energy.

Source of Carbohydrates

1.Sugars—Mono [Glucose, fructose]and disaccharides(sucrose, maltose, lactose) *Fruits and milk (good for health)

*Cane sugar and beet-root sugar increase risk of dental caries and diabetes mellitus 2.Polysaccharides—Starch, glycogen

*Starch is available in cereals (wheat, rice, maize,), roots (Potatoes and legumes. starches and sugars are broken down to monosaccharides before absorption.

*Starches in cereal foods, root foods, and legumes provide the largest proportion of energy.

*When carbohydrate intake is less than 100 g per day this leads to increased lipolysis with ketone production.

Non-energy Yielding Carbohydrates

Dietary Fiber

It is the natural packing of plant foods and not digested by human enzymes. They are of two types:

A-Water Soluble Fibers

Oat bran, beans, pectin, and guar gum.

These fiber Slow gastric emptying which contributes to satiety And Reduces bile salt absorption and plasma cholesterol concentration.

B. Water Insoluble Fibers

Wheat bran—hemicellulose of wheat because of increased water holding capacity increases the bulk of the stool and prevents constipation, diverticulosis, and colonic cancer. Flatus formation is common with fiber diet.

*Dietary fibers are broken down by colonic bacteria to produce short-chain fatty acids which are essential fuel for the enterocytes and bowel health.

1gr of carbohydrate provide 4 kilocalories

<u>2-Fat</u>

It has the highest energy source and excessive consumption may cause obesity. Free fatty acids are absorbed in chylomicrons allowing access of complex molecules into the circulation.

Cholesterol is also absorbed directly from food in chylomicrons and is an important substrate for steroid synthesis.

There are three types of fats.

1. Saturated fats animal sources include butter, ghee, or lard.

They increase plasma LDL and total cholesterol. They predispose to CAD.

2. Monounsaturated fatty acids include -Oleic acid,

3. Polyunsaturated fatty acids include -Linoleic acid in plant seed oils and its derivatives—gamma-linolenic acid, arachidonic acids are the essential fatty acids. They are precursors of prostaglandins, eicosanoids and they form part of the lipid membrane in all cells.

The omega 3 in fish oil. By antagonizing thromboxane A-2, they inhibit thrombosis. Replacing saturated fat (i.e. from animal sources: butter, ghee, or lard) with PUFA in the diet can lower the concentration of circulating low-density lipoprotein (LDL) cholesterol and may help prevent coronary heart.

1 gr of fat provides 9 kcal of energy.

<u>3-Proteins</u>

Proteins form the basic building units of tissue. They play a major role in the formation of enzymes and hormones and also in the transport mechanisms.

There are 20 different amino acids of which 9 amino acids are essential-Tryptophan, threonine, histidine, leucine, isoleucine, lysine, methionine, phenylalanine, valine. <u>They cannot be synthesized in humans but are essential for the synthesis of different proteins in the body</u>.

Another group of five amino acids is termed 'conditionally essential' [Cysteine, Tyrosine, Arginine, Proline, Glycine], meaning that they can be synthesized from other amino acids, provided there is an adequate dietary supply. The remaining amino acids can be synthesized in the body by transamination

*Proteins of animal origin—eggs, milk, meat—have higher biological value than the proteins of vegetable.

*An average adult requires 10 to 15% of total calories as proteins. It is equivalent to 1 gm/kg body weight.

Protein requirements are highest during growth and adolescence Protein provides 16 KJ/ gr(4 KCL/gr

Daily adult energy requirements in health

Energy requirements depend on—age, sex, and body weight. Growing children, pregnant and lactating mother need more calories.,

Circumstances	Females	Males
At rest	(1600 kcal)	(2000 kcal)
Light work	(2000 kcal)	(2700 kcal)
Heavy work	(2250 kcal)	(3500 kcal

Balanced Diet

A balanced diet contains carbohydrates, protein, fat, mineral, vitamins, and trace elements in an adequate amount and proportion to maintain good health.

A healthy diet includes 55-75 % of the diet as carbohydrates. Protein 10-15 % of the diet (minimum 65 -100 gr /day) and less than 40 gr /day with high biological value.

Fat 15-30 % of diet/day maximum as polyunsaturated fatty acids and low with trans fatty acids and saturated fatty acids.

because it associated with obesity, coronary heart disease) total dietary cholesterol should be 300 mg /day.

Micronutrients

Micronutrient include [vitamins and minerals]

Micronutrients not enter the energy yield to the body but enter the metabolic activity of the body.

1-Vitamins

*Vitamins are organic compounds in food

*Required in small amounts and are not synthesized in the human body.

They are classified into

1-Fat-soluble vitamins (A, D, E, and K)

2-water soluble vitamins (B and C).

Diseases of vitamins may be caused by vitamin excess or deficiency.

<u>1-Fat Soluble Vitamins include</u>

Vitamin A (Retinol)

* It is necessary for clear vision in dim-light and maintains the integrity of epithelial tissues.

Sources: It is available in food of animal origin like liver, milk, milk products, egg, and fish oil also it is available in the dark green and colored yellow vegetables and carrots. Daily requirements of vitamin A [700 micrograms] for men and [600 micrograms] for women

Functions of Vitamin A

*It is responsible for the differentiation of epithelial cells. Responsible for normal growth, fetal development, fertility, hematopoiesis, and immune function * Antioxidant activity.

Vitamin A deficiency: When there is vitamin A deficiency mucus-secreting cells will be replaced by keratin producing cells.

*Vit A deficiency may cause blindness in newborns.

*Vitamin A deficiency lead at first to dark blindness (loss adaptation to dark vision) then keratinization of cornea causes Bitot eyes, keratomalacia then progresses to corneal ulceration, Retinal fibrosis, and irreversible blindness.

This disease can be prevented by :

*Giving Pregnant women diet rich with vitamin A or supply with a low dose of vitamin A.

* Giving 200 mg retinol oral dose to preschool children. In addition to preventing blindness also improve immunity, prevents recurrent gastroenteritis and respiratory infection.

Vitamin A Toxicity Repeated moderate or high doses of retinol can cause

Liver damage, hyperostosis, and teratogenicity. Acute overdose leads to Nausea, headache, increased intracranial pressure, and skin desquamation.

Retinol intake may also be restricted in those at risk of osteoporosis.

*Excessive intake of carotene can cause pigmentation of the skin hypercarotenosis this gradually disappears when intake is reduced.

Vitamin D

Vitamin D is essential for the metabolism of calcium and phosphorus and the formation of bone. When adequately exposed to sunlight Dietary supplements are not required. *There are two forms of vitamin D.*

1-Vitamin D3[Cholecalciferol].The natural form of vitamin D is formed in the skin by the action of ultraviolet (UV) light on 7-dehydrocholesterol, a metabolite of cholesterol. Vitamin D is converted in the liver to 25-hydroxyvitamin D (25(OH)D), which is further hydroxylated in the kidneys to 1,25-dihydroxyvitamin D (1,25(OH)2D), the active form of the vitamin. This 1,25(OH)2D enhances the absorption of calcium and phosphorus from the gut, their mobilization from bone, and re-absorption of phosphorus and calcium from the kidneys.

2-Vitamin D2 [Ergocalciferol]. The synthetic form is considered to be less potent than endogenous D3

Dietary Sources--Fish, eggs, liver, milk, cheese, butter.

Daily Requirements

Pre-school children – 10 micrograms (400 IU/day)

Children and adults – 5 microgram (200 IU/day)

Pregnancy and lactation – 10 microgram (400 IU/day)

Causes of Vitamin D Deficiency

1. Intestinal Malabsorption—pancreatic insufficiency, coeliac disease, biliary tract obstruction.2. Kidney disease.3. Lack of exposure to sunlight.

4. Defective metabolism—either due to renal disorders or drugs like phenytoin, rifampin. **Vitamin D deficiency**. causes rickets and osteomalacia.

Excessive doses of cholecalciferol, ergocalciferol, or hydroxylated metabolites cause

hypercalcemia.

*Vitamin E

There are eight related fat-soluble substances with vitamin E activity.

The most important dietary form is α -tocopherol.

Vitamin E has many direct metabolic actions:

*It prevents oxidation of polyunsaturated fatty acids in cell membranes by free radicals.

* Maintain cell membrane structure.*It affects DNA synthesis and cell signaling.

* It is involved in the anti-inflammatory and immune systems

Sources: Vitamin E is available in sunflower oil, vegetables, nut, and seeds oil. Daily requirement 4 mg for men and 3mg for women

Deficiency: Occur in premature and Malabsorption **Causing** hemolytic anemia, ataxia, and visual scotomas.

Vitamin E intakes of up to 3200 mg/day (1000-fold greater than recommended intakes) are considered safe.

*Vitamin K

2 Types

*Vitamin K1(phylloquinone) is supplied in the diet.

Sources - mainly in green leafy vegetables and soya oil.

*Vitamin K 2which is synthesized by intestinal bacteria.

Vitamin K required for the synthesis of clotting factors II, VII, IX, and X.,

Daily requirement: 80 microgram/day

Causes of vit K deficiency include

• Obstructive jaundice—defective absorption of vitamin K due to lack of bile.

• Anticoagulant therapy—Warfarin, act by antagonizing vitamin K.

• Prolonged antibiotic therapy—by eliminating bacteria from the gut

Management

When prothrombin time is prolonged, give vitamin K 10 mg IM for 3 to 5 days till prothrombin time is normal

Vitamin K has given routinely to newborn children to prevent the hemorrhagic condition,

Vit K in excess can cause liver damage and hemolysis.

<u>2-Water Soluble Vitamins</u>

*Thiamin (vitamin B1)

Thiamin is found in foods of both vegetable and animal origin. Thiamin pyrophosphate (TPP) is a co-factor for enzyme reactions involved in the metabolism of macronutrients (carbohydrate, fat , and alcohol),

In thiamin deficiency, cells cannot metabolize glucose aerobically to generate energy as ATP. Neuronal cells are most vulnerable because they depend almost exclusively on glucose for energy requirements. Impaired glucose oxidation causing accumulation of pyruvic and lactic acids, which produce vasodilatation and increased cardiac output.

Causes of thiamin Deficiency include:

*Chronic alcoholics. [increased requirements for thiamin to metabolize ethanol].

* a diet based on polished rice

*impaired absorption, storage, and phosphorylation of thiamin in the liver.

The body has very limited stores of thiamin so deficiency is manifest after only 1 month on a thiamin-free diet.

Clinical Features

Thiamin deficiency in adults causes either cardiac involvement (Wet beriberi) or nervous system involvement (Dry beriberi).

1-Cardiac Manifestations

They are due to:

1. High output state due to peripheral vasodilatation.

2.Edema due to retention of sodium and water.

3.Biventricular failure.

Examinations revealed

*Raised jugular venous pulse, *Tachycardia, *cyanosis, *cardiomegaly, *hepatomegaly, *edema.

2-Neurological Manifestations

1-Chronic peripheral neuropathy with wrist and/or foot drop.

2. Wernicke's encephalopathy-[confusion, vomiting, nystagmus, ophthalmoplegia, fever, ataxia, coma].

3. Korsakoff's syndrome

*impaired ability to learn

*Retrograde amnesia,

*Confabulation (amnestic—confabulatory syndrome).

Investigations

*Low blood thiamine level,

*Raised pyruvate and lactate levels.

*Low blood or erythrocyte transketolase activity, which increases by more than 15% after administration of thiamine, is diagnostic

Management

Wernicke's encephalopathy and wet beriberi should be treated without delay with intravenous vitamin B and C mixture.

Korsakoff's psychosis is irreversible and does not respond to thiamin treatment. ***Riboflavin (Vitamin B2)**

It is a co-enzyme and takes part in various oxidation-reduction reactions.

Dietary sources:

Milk, cheese, butter, liver, kidney, meat, whole cereals, legumes, and green leafy vegetables.

Daily requirement:1 to 2 mg/day.

Causes of deficiency:

Malnutrition, malabsorption, and dialysis.

Clinical manifestations:

It mainly affects the tongue and lips and manifests as Glossitis, angular stomatitis, and cheilosis. The genitals may be involved, as well as the skin areas rich in sebaceous glands, causing nasolabial or facial dyssebacea

Management

Rapid recovery usually occurs after administration of riboflavin 10 mg daily by mouth ***Niacin (Vitamin B3)**

Niacin encompasses nicotinic acid and nicotinamide. Nicotinamide is an essential part of the two pyridine nucleotides, nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP), which play a key role as hydrogen acceptors and donors for many enzymes.

Niacin can be synthesized in the body in limited amounts from the amino acid tryptophan, so niacin became deficient from excessive consumption of niacin in carcinoid syndrome where tryptophan used for the synthesis of 5HT.

Dietary sources:

Whole cereals, pulses, nuts, meat, fish, liver, kidney yeast, and coffee. *Causes of deficiency:*

1. Chronic small intestinal disorders

2. Alcoholics

3. Food habit—high intake of maize which contains niacytin, a form of niacin that the body is unable to utilize.

4-Hartnup's disease, a genetic disorder characterized by impaired absorption of several amino acids, including tryptophan

5-Carcinoid syndrome when tryptophan is consumed in the excessive production of 5hydroxytryptamine (5-HT, serotonin).

Deficiency causing Pellagra

Pellagra called the disease of the three **Ds**

Chronic wasting disease with signs of Dementia, Diarrhea and Dermatitis.

Dermatitis -Characteristically, there is erythema resembling severe sunburn, appearing symmetrically over the parts of the body exposed to sunlight, particularly the limbs and especially on the neck but not the face (Casal's necklace, The skin lesions may progress to vesiculation, cracking, exudation and secondary infection



Diarrhea. associated with anorexia, nausea, glossitis, and dysphagia.

Dementia. In severe deficiency, delirium occurs acutely and dementia develops in chronic cases.

Management

Nicotinamide 100 mg tid PO or 100 mg IM/IV for 2 weeks followed by niacin 10 mg od. The response is usually rapid. Within 24 hours the erythema diminishes, diarrhea ceases and improvement in the patient's mental state

Excessive intakes of niacin

may lead to reversible hepatotoxicity. Nicotinic acid is a lipid-lowering agent but at doses above 200 mg a day causing vasodilatory symptoms ('flushing' and/or hypotension).

***Pyridoxine (Vitamin B₆)** :

* It is available in meat, fish, banana, vegetables and it synthesizes in intestinal microflora

*It enters in amino acids metabolism.

*Vitamin B6 deficiency is rare. However certain drugs such as isoniazid and penicillamine act as chemical antagonists to pyridoxine.

*Pyridoxine administration is effective in isoniazid-induced peripheral neuropathy and some cases of sideroblastic anemia. Large doses of vitamin B6 have an antiemetic effect in radiotherapy-induced nausea.

*vitamin B6 supplements may have benefit in the treatment of nausea in pregnancy, carpal tunnel syndrome, and premenstrual syndrome.

*Biotin :

Causes of deficiency:

1. Prolonged consumption raw egg whites— because the avidin they contain binds biotin and prevents absorption from the gut.

2. Prolonged parenteral nutrition.

Clinical Features

scaly dermatitis, alopecia, and paraesthesias,

Management

Biotin 100 microgram/day.

*Folate (folic acid)

sources -Liver and leafy vegetables

Folates exist in many forms. The main circulating form is 5methyltetrahydrofolate. The natural forms are prone to oxidation. Folic acid is a stable synthetic form. Folate It is directly involved in DNA and RNA synthesis, and requirements increase during embryonic development

Folate deficiency may cause three major birth defects

(Spina bifida, anencephaly, and encephalocele) resulting from imperfect closure of the neural tube, which takes place 3–4 weeks after conception. so it is advised for pregnant women to use Folate from the first trimester.

Folate deficiency has also been associated with heart disease, dementia, and cancer.

*Vitamin B₁₂ :

It is present only in animal products, Vegans are at risk of deficiency

The Daily requirement is 1 microgram,

*Vit B 12 is required for the integrity of myelin

*The store of vit B B_{12} in the liver can last for five years.

In older people and chronic alcoholics, vitamin B12 deficiency arises from insufficient intake and/or from Malabsorption.

Vitamin B 12 deficiency causes megaloblastic anemia and peripheral neuropathy, subacute combined degeneration of the spinal cord, optic atrophy, and dementia

Vitamin B12 therapy improves symptoms in most cases.

*Vitamin C (ascorbic acid) :

It promotes collagen formation. It aids in the production of supporting tissues of mesenchyme

Dietary sources -citrus fruits, fresh fruit, fresh and frozen vegetables.

*Vitamin C very easily destroyed by heat, increased pH and light, and is very soluble in water

*Daily requirement 40 mg daily.

*it improves immunity against the common cold and improves the strength of collagen.

*It enhances the iron absorption from the intestine.

*As an antioxidant it reduces the risk for cancer formation.

Vitamin C deficiency leads to scurvy, the defective formation of collagen with impaired healing of wounds, capillary hemorrhage, and reduced platelet adhesiveness

Precipitants for scurvy

1-Increased requirement -Trauma, surgery, burns, infections, Smoking, Drugs (glucocorticoids, aspirin, indomethacin, tetracycline)

2-Dietary deficiency - Lack of dietary fruit and vegetables for > 2 months, Infants fed exclusively on boiled milk

Clinical features

- Swollen gums that bleed easily
- Perifollicular and petechial hemorrhages
- Ecchymoses
- Gastrointestinal bleeding

- Haemarthrosis
- Anaemia
- Poor wound healing

Treatment by Vitamin C 250 mg 8 hourly by mouth.

Vitamin C excess lead to oxalate renal stone and diarrhea

Inorganic Nutrients

*Calcium

Sources - milk and milk products and only 5% from vegetables.

*Calcium is absorbed from the gastrointestinal tract depending on vitamin D. *calcium is used in the formation of bone and teeth, Calcium also is essential for the transmission of nerve impulses and muscle contraction. It serves as an intracellular messenger of different hormones. It takes part in blood coagulation.

*Higher intakes usually recommended in places with higher fracture prevalence, pregnancy and lactation.

Calcium deficiency is usually due to vitamin D deficiency. Too much calcium can lead to constipation, and toxicity has been observed in 'milk-alkali syndrome'

*Phosphate

Phosphates are present in all- natural foods and dietary deficiency have not been described. Phosphate deficiency in adults occurs in

*Patients taking large amounts of aluminum hydroxide by binding phosphate in the gut lumen.

*in patients with renal tubular phosphate loss

*in alcoholics sometimes when they are fed with high carbohydrate foods •

*in patients receiving parenteral nutrition if inadequate phosphate is provided.

Excessive phosphorus intakes (e.g. 1–1.5 g/day) may cause hypocalcemia and secondary hyperparathyroidism

Deficiency causes hypophosphatemia and muscle weakness secondary to ATP deficiency

*Iron

Dietary Sources

Green leafy vegetables, fruits, onions, cereals, pulses, grapes, dates, animal foods like meat, liver, fish, kidney, egg yolk.

Food rich in vitamin C enhances the absorption of iron.

Dietary calcium reduces iron uptake from the same meal

*Non-haem iron in cereals and vegetables is poorly absorbed compared to the wellabsorbed haem iron from animal products

Daily Requirement

• For Males—1 mg

- For Females—2 mg
- Pregnant/lactating women—3 mg

Only 10% of consumed iron is absorbed in the duodenum and upper jejunum and so, the daily intake has to be 10 for males and 20 mg for females .

*There is no physiological mechanism for the excretion of iron so homeostasis depends on the regulation of iron absorption. This is regulated at the level of duodenal enterocytes by hepcidin (a peptide secreted by hepatocytes in the duodenum). The expression of hepcidin is suppressed when body iron is low, leading to enhanced efflux of iron into the circulation

The total body iron content is 4 gm. Sixty percent of that is present in hemoglobin. It is used in erythropoiesis. [synthesis of hemoglobin].

Normal serum level: 80 to 120 µgm/dl.

Iron Deficiency- leads to Iron deficiency causes microcytic hypochromic anemia with brittle nails, spoon-shaped nails (koilonychia), atrophy of the papillae of the tongue, angular stomatitis, brittle hair, a syndrome of dysphagia and glossitis [Plummer–Vinson or Paterson–Brown–Kelly syndrome].

*Iodine

It is required for the synthesis of thyroid hormones.

Sources - sea fish, seaweed and most plant foods grown near the sea.

The amount of iodine in soil and water influences the iodine content of most foods. Iodine is lacking in the highest mountainous areas of the world and in the soil of frequently flooded plains,

iodine deficiency causing endemic goiter, 1% or more of babies are born with cretinism (characterized by mental and physical retardation), deafness, slowed reflexes and poor learning . **Prevention** by Salt iodization

*Zinc

Dietary Sources- most foods of vegetable and animal origin.

It is an essential component of many enzymes, including carbonic anhydrase, alcohol dehydrogenase, and alkaline phosphatase.

Acute zinc deficiency occurs in prolonged zinc-free parenteral nutrition and causes diarrhea, mental apathy, a moist, eczematoid dermatitis, especially around the mouth, and loss of hair.

Chronic zinc deficiency occurs in dietary deficiency, Malabsorption syndromes, alcoholism, and its associated hepatic cirrhosis. It causes the clinical features of *acrodermatitis enteropathica* (growth retardation, hair loss and chronic diarrhea). dwarfism and Hypogonadisim and thymic atrophy.

zinc supplements may accelerate the healing of skin lesions, promote general well-being, improve appetite and reduce the morbidity associated with the under-nourished state, and lower the mortality associated with diarrhea and pneumonia in children.

*Selenium -The family of seleno-enzymes includes

*Glutathione peroxidase-which helps prevent free radical damage to cells.

*Monodeiodinase- which converts thyroxin to triiodothyronine.

Selenium deficiency can cause hypothyroidism, cardiomyopathy in children (Keshan's disease) and myopathy in adults.

Excess selenium can cause heart disease

*Fluoride.

*Prevent dental caries because it increases the resistance of the enamel to acid attack. If the local water supply contains more than 1 part per million (ppm) of fluoride, the incidence of dental caries is low.

*Soft waters usually contain no fluoride, while very hard waters may contain over 10 ppm.

*The benefit of fluoride is greatest when it is taken before the permanent teeth erupt, while their enamel is being laid down.

Chronic fluoride poisoning is occasionally seen where the water supply contains > 10 ppm fluoride

Clinical features include

yellow staining and pitting of permanent teeth, osteosclerosis, soft tissue calcification, deformities (e.g. kyphosis) and joint ankylosis.

<u>Very high doses of fluoride</u> may cause abdominal pain, nausea, vomiting, seizures and muscle spasm.

Prevention of Caries

When fluorine level is low, the addition of traces of fluoride—1 ppm to the public waters supplies

Presenting the problem of altered energy balance

1-Obesity

Obesity means excess storage of fat and BMI > 30 kg/m^2 .

Obesity is of two types

1-Central type (android, apple shape, abdominal or visceral) where fat accumulate around the abdomen and trunk and it is associated with a high risk of cardiovascular complications and it usually obesity in male

2-Gynoid type (generalize, pear shape) where fat accumulates around limbs and other bodies usually common in females.

To differentiates gynoid from android obesity by measuring

Waist circumference [Land mark around umbilicus] and Hip circumference [Landmark around greater trochanters]. If waist circumference is more it is central obesity and if the Hip circumference is more it is gynoid obesity.

Waist and Hip circumference also used to detect obesity according to charts of normal and abnormal values. Waist circumference if more than 102 cm in male and more than 88 cm in a female is associated with cardiovascular complications.

Lean body mass = Total body mass – Fat mass.

Normal BMI =18.5 -24.9 kg/ m2. BMI Below 18.5 kg/ m2 is under weight .

Overweight $BMI = 25 - 29.9 \text{ kg/m}^2$ associated with a low risk of comorbidity.

Obesity more than 30 kg/ m2 . Classification

Class 1: 30-34.9 kg/m2 associated with moderate risk of comorbidity.

Class 2: 35-39.9 kg/ m2 associated with sever risk of comorbidity

Class 3: more than 40 kg/ m2 associated with very severe risk of comorbidity.

Causes of obesity include

A-abnormal energy balance by the discrepancy between energy intake and expenditure where energy intake is increased by

*increase diet Portion sizes, * increase fat size *increase snacks

Loss of energy expenditure by

*Physical inactivity -decrease exercise by using cars instead of walking for daily activities *Long time sitting for TV and computers.

B- Genetic factor:include*mutation in Melanocortin 4 receptor (MC4R) *Defect in enzyme processing propiomelanocortin (POMC) the precursor for ACTH hormone in the

hypothalamus * Mutation in Leptin hormone gene has associated with massive obesity, Leptin has a dual effect of reducing food intake and increasing energy expenditure * Pradder –Willi syndrome * Lawrence –moon biedl syndrome.

C-Reversible causes of obesity: include endocrine causes like *insulinoma

*hypothyroidism, *Cushing 's syndrome * hypothalamic tumor, or injury*.

*drugs like tricyclic antidepressants, sulphonylureas, estrogen-containing oral

contraceptive pill, corticosteroids, sodium valproates and B- Blockers

Complications of obesity include

Cardiovascular include .hypertension, dyslipidemia, coagulopathy, chronic inflammation, endothelial dysfunction.

Pulmonary –exercise intolerance, obstructive sleep apnea, asthma

Gastrointestinal-gallstone, Gastroesophageal reflux disease, non-alcoholic fatty liver, colon cancer.

Renal- glomerulosclerosis, renal cancer.

Endocrine-insulin résistance, glucose intolerance, type 2 diabetes, precocious puberty, menstrual irregularity, polycystic ovary syndrome, hormone-related cancer[breast, endometrium, prostate].

Musculoskeletal-osteoarthritis, back pain, flat feet.

Neurological-idiopathic intracranial hypertension.

Psychological-eating disorders, poor self-esteem, social isolation, depression.

MANAGEMENT

Steps in obesity management include

History

*Sudden or gradual increase in weight

*Family history of obesity

Physical examination

*Determine vital signs and BMI and waist circumference

*Acanthosis nigricans[Acanthosis nigricans is a skin condition characterized by areas of dark, velvety discoloration in body folds and creases].



Acanthosis nigricans

Investigations •

*Height and weight - BMI (≥ 25 overweight, ≥ 30 obese).

*Waist circumference (>102cms for men and >88cms for women lead to significantly greater health risks).

*Blood pressure, *Urinalysis * Blood tests: fasting glucose, Glucose tolerance test, HbA1c, U&E's, TFT's, LFT's, and lipids, (Include an assessment of sex hormones and cortisol if hirsute or moon-faced with central obesity) •

*ECG or exercise stress test.

1-Life Style Modification. All successful treatments involve some form of lifestyle change affecting energy intake (diet) and energy expenditure (physical activity): This used for all types of obesity but it is usually indicated for overweight and class one obesity.

at least 60-minutes per day of physical activity, on 6 days a week, is the current consensus for achieving and maintaining weight loss.

2-Weight Loss diet: It is used for losing weight gradually by 0.5 kg /week means losing 600 kcal daily. There are many regimens are available (60 % carbohydrates,25 % fat, and 15 % proteins) another example (70% carbohydrates, 13 % fat and 13 % protein) .this regimen may be used for one year it need high understand and cooperation of the patients.

For more rapid weight loss diet for example preparation for surgery 1.5 -2.5 kg /week weight loss mean 500 kcal is consumed per day including 50 gr of protein as a minimum to prevent muscle loss and is used for a short period its *side effect* are orthostatic hypotension, headache, diarrhea, and nausea.

Starvation leads to muscle loss, increase free fatty acids, ketosis, and electrolytes derangement all these lead to cardiac arrhythmias and death.

3-Drugs should be coupled with dietary and behavioral changes. : used for BMI >27 with comorbidity and BMI >30 include

A-Fat absorption blocker

a-Orlistat act by inhibition of lipase enzyme in the gut so prevent hydrolysis of dietary triglycerides into fatty acids and absorption of fat leading to fat Malabsorption so causing (Steatorrhea) and lipid-soluble vitamins Malabsorption. Orlistat is given in a dose of 60-120 mg with or before the meal. It reduces weight by 3 kg/month and also improved lipid profile, glycemic index, and improve blood pressure .contraindicated in patients with Malabsorption or cholestasis.

b-Sibutramine: it is B1 agonist and 5HT (hydroxytryptamine and serotonergic

receptor agonist) in the brain reduced food intake. It reduces 5kg in weight and improves the lipid profile. *side effects* are dry mouth, constipation and insomnia noradrenergic side effects are tachycardia and hypertension so it is contraindicated in hypertension and cardiovascular diseases.

c-Lorcaserin- 5-HT2 C2 agonist]neurotransmitter serotonin is involved in regulating food intake and food preference *side effects*. Headache, nausea and dizziness

d-Litraglutide –GLP agonist-it is incretins, inhibit glucagon secretion, delays gastric emptying, stimulate hepatic gluconeogenesis,

e-combination of bupropion and naltrexone

Bupropion is a norepinephrine and dopamine reuptake inhibitor approved for the treatment of depression it reduces food intake by acting on adrenergic and dopaminergic receptors in the hypothalamus. Stimulate the production of a prohormone pro-

opiomelanocortin [POMC] which reduces food intake.

Naltrexone is an opioid antagonist and increases the release of &-MSH which inhibits food intake. *Side effects* nausea, constipation, and headache.

4-Surgery: Bariatric surgery Restrictive surgery, malabsorptive surgery, or combination of both is done to reduce stomach size and so reduce ghrelin and other small bowel peptides lead to satiety and create Malabsorption. and it is indicated in obesity associated with a high risk of complication and class 3 obesity.

5-Endoscopical treatment of obesity - intragastric balloon and endoscopically implantable sleeves. To create a duodenal- jejunal bypass effects.

2-Under nutrition

Mean body mass index less than 18.5 Kg/m².

Classifications-

*Mild under nutrition BMI 17 -18.4 kg \rm /m^2

*Moderate under nutrition 16-17Kg/m²

*Sever under nutrition $< 16 \text{ Kg/m}^2$.

Causes of under nutrition include

1-Decrease energy intake due to : Famine ,persistent regurgitation , vomiting ,anorexia ,Malabsorption[small intestinal disease], maldigestion [pancreatic exocrine Insufficiency].

2-Increased energy expenditure: a-Increased basal metabolic rate (cancer, thyrotoxicosis, trauma, and fever).b- Excessive physical activity(marathon running).

C-Energy loss (glycosuria in diabetes mellitus).d-Impaired energy storage [Addison disease, pheochromocytoma].

Example of undernutrition in children are Marasmus [malnutrition with muscle wasting] and Kwashiorkor (malnutrition with edema)

Clinical features of undernutrition include :

*Weight loss, nocturia, Thirst, craving for food, weakness and feeling cold, amenorrhea, impotence,

*Lax pale dry thin skin with loss of skin turgor and patchy pigmentation, Hair thinning, with hair loss.

*Muscle wasting [temporal and per scapular muscle and reduced mid-arm

circumference], Loss of subcutaneous fat,

*Bradycardia, hypotension, hypothermia and small heart, Edema which may present without Hypoalbuminemia due to functioning liver (called famine edema),

*Distended abdomen with diarrhea.

*Diminished tendon jerks., Apathy, depression.

*Susceptibility to infection [Gastroenteritis and Gram-negative septicemia, bronchopneumonia, measles, herpes simplex, Tuberculosis, Streptococcal, staphylococcal skin infections, and Helminthic infestations].

*Undernutrition leads to thiamine, folate, and vitamin C deficiency. Diarrhea leads to hyponatremia, hypokalemia, and hypomagnesemia.

*At the late stage, the patient is flexed posture, inactive, and died suddenly at the bed and quietly

* The main cause of mortality is infection and septicemia. At autopsy, all organs are atrophied except the brain

Investigations reveal :

*increased free fatty acids, ketosis, and metabolic acidosis

*Hypoglycemia but albumin concentration is maintained because the liver still functions normally

*Insulin secretion is diminished,

*glucagon and cortisol tend to increase and reverse T₃ replaces normal triiodothyronine.

*The resting metabolic rate falls, because of reduced lean body mass and hypothalamic compensation.

*The urine has a fixed specific gravity and creatinine excretion becomes low.

*mild anemia, leucopenia, and thrombocytopenia. The erythrocyte sedimentation rate is normal unless there is infection.

*Tests of delayed skin hypersensitivity, e.g. to tuberculin are falsely negative the *Electrocardiogram shows Bradycardia and low voltage.

Management

Mild undernutrition has no risk, moderate undernutrition treated by extra energy diet, and sever undernutrition must be treated at the hospital. sever undernutrition causes atrophy of intestinal epithelium, small pancreas, and diluted bile so the diet should be in small frequent amounts till the growth of these organs. This is by F - 75 (it prepared from milk powder 25 g, sugar 70 g, cereal flour 35 g vegetable oil 27 g with minerals and vitamins in 1Liter of water). And F -100 diet (it prepared from milk powder 80g, sugar 50 g, vegetable oil 60 g with minerals and vitamins in 1Liter of water). The energy is given at the start in a small amount then increased,1600 -2000 Kcal is enough to stop the progression of undernutrition then energy builds up till normal body mass index return to normal .care needed for skin by adequate hydration and body temperature monitor.

Nutritional support of hospital patients.

A normal diet for inpatient must be encouraged and overcome conditions that prevent eating. Dietary supplements: It is formed of high energy and protein or manufactured from egg and milk and It is added to a normal diet to reach the energy requirements of the patient. When the patient cannot swallow diet normally due to diseases like *Throat surgery *Acute stroke * Motor neuron disease and *Multiple sclerosis.

Feeding can be done by

A-Enteral tube feeding.

1-Nasogastric tube feeding.

*Fine tube passed from the nose to the stomach and food and liquids is bushed either continuously or by bolus technique to the stomach. * The Presence of feeding tube in the stomach should be checked before pushing liquid to throw it by bushing air syringe through the tube to the stomach and heard by stethoscope over the Epigastric region or by X-ray to visualize the end of the tube in the stomach. Nasogastric tube feeding appropriate for patients needing up to 4 weeks of feeding If there is a gastric emptying delay, naso-jejunal tubes may be used.

2-Gastrostomy feeding

Percutaneous endoscopic gastrostomy (PEG) tube passed percutaneously to the stomach either endoscopically or surgically then fixed externally. PEG Used for patients needs feeding >4 weeks.

3- Jejunostomy indicated when there is gastric emptying delay or risk of aspiration with

gastric feeding.

Complications include puncture of other organs or peritonitis.

In enteral tube feeding the risk of bacteremia is low because of the integrity of gastrointestinal mucosa.

B-Parenteral nutrition [PN]: PN indicated when partial or complete intestinal failure has occurred and oral nutrition or enteral tube feeding (ETF) is not possible or has failed. In **PN** The main source of energy is carbohydrates(by glucose water 5%,10%,20%), and another solution formed of amino acids, lipids, trace elements, and vitamins all are infused intravenously. Parenteral feeding is expensive and has many complications In those receiving long-term PN there is a risk of cholestasis May relate to increased lithogenicity of bile with interruption of enterohepatic bile acid circulation, reduced gallbladder motility, and biliary sludge because of no oral intake, bacterial overgrowth and nutrient deficiencies, including choline, taurine, and carnitine. Long-term PN also places the patient at risk of metabolic bone disease and micronutrient deficiencies.

Routes for parenteral nutrition

1-Peripheral venous cannula. A 20 cm cannula is placed in a mid-arm vein

used for low-osmolality solutions due to the risk of thrombophlebitis and is unsuitable for patients with high nutritional requirements. hyperosmolar solutions cannot be used. peripheral veins cannot tolerate high infusion rates or high osmolarity solutions, such as lipid-free solutions.

2-Peripherally inserted central catheter (PICC). A 60 cm cannula is inserted into a vein in the antecubital fossa. The distal end lies in a central vein allowing hyperosmolar solutions to be used.

3-Central line. The subclavian or the internal jugular vein can be used. Hyperosmolar solutions can be used without difficulty.

Complications of **parenteral nutrition** can be divided into

A-line-related complications include- local hematoma, arterial puncture, and pneumothorax. Central vein thrombosis is relatively common, Catheter-related sepsis remains the most serious complication of PN.

infection that may lead to septicemia managed by removal of the central line, blood culture, and suitable antibiotics or reinsertion of the tube in the other site.

B-Metabolic complications include

Refeeding Syndrome -Definition-

The Refeeding syndrome can be defined as a syndrome consisting of metabolic disturbances that occur as a result of the reinstitution of nutrition whether enterally or parenterally to patients who are starved or severely malnourished

Pathogenesis

During undernutrition, the body regulates membrane pumping to conserve energy this causes leakage of intracellular potassium, magnesium, calcium, and phosphate. When nutritional support is given to an undernourished patient there is a rapid conversion from a catabolic to an anabolic state .in starvation the secretion of insulin is decreased in response to a reduced intake of carbohydrates .this result in further intracellular loss of electrolytes.

Refeeding leads to the reverse of the above processes and leads to the movement of electrolytes into cells. the refeeding syndrome is a potentially fatal process that results from fluid shifts and electrolyte abnormalities, which occurs when someone who has been chronically malnourished is refed, either orally or parenterally. In starvation, total body phosphorus is depleted although the serum phosphorus level usually remains normal because of adjustments in renal excretion. When carbohydrates are added through feeding, insulin is secreted, which stimulates anabolic protein synthesis and enhances the intracellular uptake of glucose, phosphate, and water. This can lead to significant extracellular hypophosphatemia. Because phosphate is needed for metabolic processes, potentially fatal cardiac, respiratory, and neurologic complications can ensue

Clinical manifestations and management

Decrease level of phosphate, potassium, magnesium may cause cardiac arrhythmias, convulsion, respiratory failure, muscle weakness, and pain These electrolytes disturbances should be managed by daily monitoring of blood urea, serum creatinine, electrolytes, glucose. Wernicke's encephalopathy can be prevented by administering thiamin before starting nutritional support to prevent all of these complications Refeeding should be started using only 5 Kcal /kg /day and increase slowly with continuous monitoring