Vitamins Disorders

	Function	Deficiency	Excess
Fat Soluble Vitamins			
Vitamin A (retinol) Found in liver and leafy vegetables	1- Antioxidant 2- Constituent of **visual pigments (retinal)** 3- Essential for normal differentiation of epithelial cells into specialized tissue (pancreatic cells, mucus-secreting cells) 4- Prevents squamous metaplasia 5- Used to treat: **Measles & AML subtype M3.**	**3 Eyes :** 1- Night blindness (nyctalopia) 2- Corneal degeneration (keratomalacia) 3- **Bitot spots** on conjunctiva **Immunity:** Immunosuppression 	**Acute toxicity** 1- Nausea, vomiting, vertigo 2- Blurred vision. **Chronic toxicity**— 1- Alopecia, 2- Arthralgias 3- Pseudotumor cerebri. 4- Dry skin (e.g., scaliness) 5- Hepatic toxicity and enlargement 6- Teratogenic (cleft palate, cardiac abnormalities), ⊖ *pregnancy test and reliable contraception are required*
Vitamin C (ascorbic acid) Found in fruits and vegetables.	1- Antioxidant 2- Facilitates **iron absorption by reducing it to Fe^{2+} state**. - *Ancillary **treatment for methemoglobinemia** by reducing Fe^{3+} to Fe^{2+}.* 3- Necessary **for hydroxylation of proline and lysine** in **collagen synthesis**. 4- Necessary for dopamine β-hydroxylase, which converts dopamine to NE.	**SCurvy** : to a **C**ollagen synthesis defect **1-Swollen gums →** **2- Anemia** *3-Bruising 4- petechiae, 5-hemarthrosis* *6- Perifollicular & subperiosteal hemorrhages* 7- Poor wound healing, 8- "corkscrew" hair. **Immunity:** Weakened immune response. 	1-Nausea, vomiting, diarrhea, fatigue 2-Calcium oxalate nephrolithiasis 3-↑ risk of iron toxicity in predisposed individuals (e.g., those with transfusions, hereditary hemochromatosis).
Vitamin D D_2 = ergocalciferol—ingested from plants. D_3 = cholecalciferol—consumed in milk, formed in sun-exposed skin (stratum basale). **25-OH D_3** = storage form. **1,25-$(OH)_2$ D_3 (calcitriol)** = active form.	1- ↑ Intestinal absorption of calcium and phosphate. 2- ↑bone mineralization.	**In children :** Rickets (bone pain and deformity) **In adults:** Osteomalacia (bone pain & muscle weakness) + **hypocalcemic tetany**. **Vit. D. Deficiency is exacerbated by :** low sun exposure, pigmented skin, prematurity. 	→ **Seen in granulomatous disease** (↑activation of vitamin D by epithelioid macrophages). 1- Hypercalcemia / Hypercalciuria 2- Loss of appetite 3- Stupor
Vitamin E (tocopherol/tocotrienol)	1- Antioxidant : (protects RBCs and membranes from free radical damage). 2- Can enhance anticoagulant effects of warfarin.	1- **Hemolytic anemia** 2- **Acanthocytosis** 3- Muscle weakness 4- **Posterior column and spinocerebellar tract demyelination** : - Neurologic presentation may appear similar to vitamin B12 deficiency, but without: ***megaloblastic anemia, hypersegmented neutrophils, or ↑serum methylmalonic acid levels.***	
Vitamin K (phytomenadione, phylloquinone, phytonadione) Warfarin—vitamin K antagonist.	- **Cofactor** for **the γ-carboxylation of glutamic acid residues** on various proteins required for blood clotting. - Synthesized by **intestinal flora.** **K** is for **K**oagulation. Necessary for the maturation of **1- Clotting factors II, VII, IX, X** **2- Proteins C and S.**	**1- Neonatal hemorrhage with ↑PT and ↑ aPTT** *BUT normal bleeding time* *(neonates have sterile intestines → unable to synthesize vit. K).* → neonates are given **vitamin K injection** at birth to prevent hemorrhagic disease of the newborn. -- Also occur after prolonged use of **broad-spectrum antibiotics**	
Water Soluble Vitamins			
Vitamin B1 (thiamine) **Wernicke-Korsakoff syndrome & Beriberi** Seen in : 1- Malnutrition 2- **Alcoholism** (2ry to malnutrition and malabsorption) → **Most common** Diagnosis made by : ↑ in RBC **T**ransketolase activity following vitamin B1 administration.	**Thiamine PyroPhosphate (TPP), a cofactor** for several **dehydrogenase enzyme reactions**: Think **ATP** 1- **α**-ketoglutarate dehydrogenase (TCA cycle) 2- **T**ransketolase (HMP shunt) 3- **P**yruvate dehydrogenase (links glycolysis to TCA cycle) 4- Branched-chain ketoacid dehydrogenase **Deficiency:** Impaired glucose breakdown → ATP depletion worsened by glucose infusion; highly aerobic tissues (e.g., brain, heart) are affected first.	To determine thiamine deficency is to do **TRANSKETOLASE ASSAY** **Wernicke-Korsakoff syndrome:** Damage to 1- **M**edial dorsal nucleus of thalamus 2- **M**ammillary bodies. **Classic triad:** Wernicke: **1-** Cerebellar damage : **Ataxia** **2- Ophthalmoplegia** Korsakoff: **3-** psychiatric symptoms: **Confusion** + **1- Confabulation :** Inventing something to justify wrong as true (because of destruction of mamillary body) **2- Personality change** **3- Memory loss (permanent)**	**Dry beriberi** : **1-** Polyneuritis: **Symmetrical peripheral neuropathy with sensory & motor impairment** **2- Symmetrical muscle wasting.** **Wet beriberi** : **1- Neuropathy** **2- High-output cardiac failure** (dilated cardiomyopathy), **3-** Edema.
Vitamin B2 (riboflavin) **F**AD and **F**MN are derived from ribo**F**lavin (B**2** ≈ **2** ATP).	Component of **flavins FAD and FMN**, used as **cofactors** in **redox reactions**, e.g., succinate dehydrogenase reaction in TCA cycle.	**Deficiency → 2 C's** of B**2**. **Cheilosis** (inflammation of lips, scaling and fissures at the corners of the mouth), **glossitis / Pharyngitis /edema & erythema of mouth / megenda tongue** **Corneal vascularization. / photophobia/ conjunctivitis ….. Seborrhic dermatitis**  	
Vitamin B3 (niacin) **N**AD derived from **N**iacin (B**3** ≈ **3** ATP). Causes of severe deficiency : 1- **Hartnup disease** (↓tryptophan absorption) 2- **Malignant carcinoid syndrome** (↑tryptophan metabolism) 3- **Isoniazid** (↓ vitamin B6). 4- **Malabsorption** (Ulverative colitis)	- Constituent of **NAD+, NADP+ (used in redox reactions)** - Derived from **tryptophan**. - Synthesis requires **vitamins B2 and B6**. - Used to treat dyslipidemia : 1- lowers VLDL 2- raises levels of HDL.	1- **Glossitis** (beefy tongue) 2- Severe deficiency leads to **Pellagra** : **3 D's** of B**3** • **D**iarrhea, • **D**ementia (also hallucinations), • **D**ermatitis : a- C3/C4 dermatome circumferential "broad collar" rash [Casal necklace] b- Hyperpigmentation & thickened skin of sun-exposed limbs c- Rash is burning. 	1- Facial flushing (induced by prostaglandin, not histamine; can avoid by taking aspirin with niacin) 2- Hyperglycemia 3- hyperuricemia.
Vitamin B5 (pantothenic acid) B**5** is "**pento**"thenic acid.	- **Essential component of :** 1- **coenzyme A** (CoA, a cofactor for acyl transfers) 2- **Fatty acid synthase.**	1- Alopecia 2- Adrenal insufficiency. 3- Dermatitis 4- Enteritis,	
Vitamin B6 (pyridoxine)	- Converted to **pyridoxal phosphate (PLP)**, **a cofactor** used in : **1- Transamination (e.g., ALT and AST),** **2- Decarboxylation reactions,** **3- Glycogen phosphorylase.** **4- Synthesis of :** - Cystathionine, Heme, Niacin, Histamine, - Neurotransmitters including serotonin, epinephrine, norepinephrine (NE), dopamine, and GABA.	**1- Hyperirritability** **2- Convulsions** **3- Peripheral neuropathy** : - Deficiency inducible by **isoniazid & OCP** **4- Sideroblastic anemias** - due to impaired hemoglobin synthesis & iron excess.	
Vitamin B7 (biotin)	- Cofactor for **carboxylation enzymes** (which add alpha 1-carbon group): * **Pyruvate carboxylase: pyruvate (3C)** → oxaloacetate (4C) * **Acetyl-CoA carboxylase: acetyl-CoA (2C)** → malonyl-CoA (3C) * **Propionyl-CoA carboxylase: propionyl-CoA (3C)** → methylmalonyl-CoA (4C)	- Relatively rare. - **Caused by**: **1- Antibiotic use** **2- Excessive ingestion of raw egg whites.** **1- Alopecia 2- Dermatitis 3- Enteritis** 4- Fasting hypoglycemia 5- Bowel inflammation 6- Muscle pain	
Vitamin B9 (folate) *Most common vitamin deficiency in U.S* Deficiency can be caused by several drugs : **1- Phenytoin** **2- Sulfonamides** **3- Methotrexate** Can be seen in : **1- Alcoholism** **2- Pregnancy → Neural tube defects**	- Converted to **tetrahydrofolic acid (THF),** a **coenzyme** for : **1-carbon transfer/methylation reactions.** - Important for **synthesis of nitrogenous bases in DNA & RNA** - Found in **leafy green vegetables.** - Absorbed in **jejunum**. - **Small** reserve pool stored primarily in the **liver**.	**1- Macrocytic, megaloblastic anemia** **2- Hypersegmented polymorphonuclear cells (PMNs)** **3- Glossitis** → **NO** neurologic symptoms (as opposed to vitamin B12 deficiency). **Labs:** 1- **↑ Homocysteine** 2- **Normal methylmalonic acid**	
Vitamin B12 (cobalamin) **- Deficiency is usually caused by :** 1- Insufficient intake (e.g., veganism) 2- Malabsorption : - Sprue - enteritis - *Diphyllobothrium latum* 3- Lack of intrinsic factor : - pernicious anemia: *"Anti-intrinsic factor antibodies" diagnostic for pernicious anemia.* - gastric bypass surgery 4- absence of terminal ileum: - Crohn disease	**Cofactor** for : **1- Homocysteine methyltransferase** (transfers CH3 groups as methylcobalamin) **2- Methylmalonyl-CoA mutase** - Found in **animal products** - Synthesized only by **microorganisms** - Absorbed in **terminal ileum** - **Very large** reserve pool (several years) stored primarily in **liver**. Prolonged deficiency → **irreversible nerve damage**	**1- Macrocytic, megaloblastic anemia** **2- Hypersegmented PMNCs** **3- Neurological Manifestation :** **A) Paresthesias** **B) Subacute combined degeneration** Degeneration of **:** - Dorsal columns - Lateral corticospinal tracts - Spinocerebellar tracts → due to **abnormal myelin.** **Labs:** 1- **↑ Homocysteine** 2- **↑ methylmalonic acid**