Summary

Vitamin B6 & B12

-What is the component of B-Complex?

-Thiamine B_1 -Riboflavin B_2 -Niacin B_3 -Pantothenic acid B_5

-Pyridoxine B_6 6-Biotin B_7 7-Cobalamin B_{12} -Folate B_9

-How vitamin B_6 forms be active?

Converted to pyridoxal phosphate (PLP)

-What is the mechanism of Condensation Reaction that vitamin B_6 required in?

Glycine and succinyl CoA condense in the presence of ALA synthase (Vitamin B_6 is the coenzyme) to form ALA.

-What is the mechanism of Decarboxylation Reaction that vitamin B_6 required in?

1-decarboxylation of Tyrosine to dopamine (then dopamine converted to epinephrine and norepinephrine).

2-decarboxylation of histidine to histamine.

3-decarboxylation of tryptophan to serotonin.

-What is the mechanism of Transamination Reaction that vitamin B_6 required in?

Conversion of alanine to pyruvate via ALT and PLP

-How Isoniazid treatment for tuberculosis can lead to vit B_6 deficiency?

by forming inactive derivative with PLP.

-How vitamin B_6 deficiency leads to demyelination of nerves and consequent peripheral neuritis?

PLP is involved in the synthesis of sphingolipids

-How vitamin B_{12} absorbed by/storaged in the body?

salivary glands secrete R protein which bind to vitamin B_{12} in stomach and will be removed in the intestine by pancreatic enzymes > the free B_{12} binds to the intrinsic factor which is released from the parietal cells of the stomach > intrinsic factor complex bind to their special receptors present on the intestinal epithelial cells and taken inside the enterocytes > thrown into the general circulation, bound to trans-cobalamin > goes to the liver to be stored. (whole explanation if the pic comes)

Short answer : it is absorbed by intrinsic factor (released from parietal cells) and stored in the liver (4-5mg)

-What is the mechanism of Reaction that vitamin B_{12} required in?

1-Conversion of homocysteine to methionine by methionine synthase (requires Methylcobalamin) (take methyl group N^5-methyltetrahydrofolate which gets converted to tetrahydrofolate)
2- Conversion of propionyl-CoA to succinyl-CoA by methylmalonyl-CoA mutase (requires deoxyadenosylcobalamin)

-What is the mechanism of folate trapping?

(Accumulation of N^5-methyltetrahydrofolate due to dysfunction of methionine synthase)
Homocysteine re-methylation reaction is the only pathway where N^5-methyl TH4 can be returned back to the pool. Thus, in B12 deficiency, folate is trapped as N^5-methyl TH4 → folate deficiency + deficiency of other derivatives (N^5-N^{10} methylene TH4 + N^{10} formyl TH4) required for purine/pyrimidine synthesis.

-How vitamin B_{12} deficiency cause neuropathy?

Deficiency of vitamin B12 leads to accumulation of methylmalonyl CoA which will be used instead malonyl CoA for fatty acid synthesis (unstable)

-What causes vitamin B12 Deficiency secondary to IF deficiency?

Intrinsic factor deficiency due to autoimmunity or by partial or total gastrectomy

Vitamin A & VISUAL CYCLE

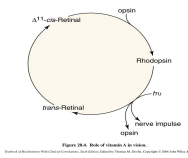
- **Enumerate the fat soluble vitamins.**
  - A - K - E - D

- **Enumerate vitamin A compounds and their sources.**
  - Vitamin A from animal sources (called Retinoids) found in three forms 1- Retinol 2- Retinal 3-Retinoic acid
  - vitamin A from plant sources 1- carotenoids (beta carotene) 2-cryptoxanthin

- **Enumerate vitamin A compounds from animal sources and their roles.**
  1- retinol (alcohol form)
  2- retinal (or retinaldehyde form) essential in vision
  3- retinoic acid (acid form) essential for skin and bone growth

- **List vitamin A functions.**
  1- vision
  2- skin health & antioxidant activity
  3- bone metabolism
  4- embryonic development and reproduction
  5- immune function
  6- gene transcription

- **Explain the role of vitamin A in vision.**
  In Retina Vitamin A in the form of Retinal binds to protein called opsin to make rhodopsin (in rods) and iodopsin (in cones) Once its stimulated by light Vitamin A isomerizes from bent "cis" form to straighten " trans" form and detaches from opsin The opsin change shape and send signal to the brain via optic nerve and the image is formed.
  Most retinal released is converted to " trans " retinol then to "cis" retinal to begin a new cycle .



- **Explain the role of vitamin A in other tissues.**
  retinol oxidized into retinoic acid(steroid hormone) which bind to nuclear receptors and cause gene activation lead to activation of mRNA and that lead to cellular differentiation

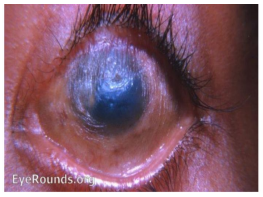
- **Define the adaptation time and mention what does increase it?**
  Its the time required to synthesis rhodopsin in the dark
  And its increased due to vitamin A deficiency

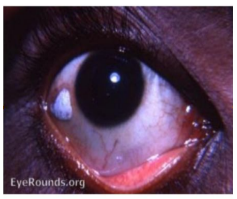
- **What is the storage form of Vitamin A?**
  Retinyl ester

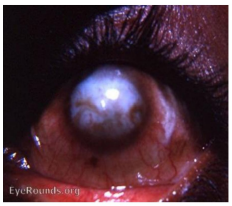
- **What are the diseases caused by vitamin A deficiency?**

Nyctalopia (night blindness)	Xerophthalmia	Bitot's spots	Keratomalacia	Complete blindness
Patient cannot see in low light or near darkness conditions	Dryness of the conjunctiva and cornea	Localized increased thickness of the conjunctiva	Prolonged xerophthalmia leads to drying and clouding of cornea	In severe deficiency

One of the earlier signs of vitamin A deficiency







Sorry not sorry i had to :)

Alzheimer disease

- **Mention 3 major microscopic findings of Alzheimer's disease.**

1. Neuritic Plaques
2.Neurofibrillary Tangles
3. Amyloid Angiopathy

- **Compare between:**

Neuritic Plaques	Neurofibrillary Tangles	Amyloid Angiopathy
• Extracellular • Spherical with 20-200 µm in diameter • **Contain**: partial helical filament, synaptic vesicles, abnormal mitochondria • **Dominant component**: Aβ40 & Aβ42 • **Less abundant proteins:** complement protein, cytokines, α1-Antichymotrypsin, Apolipoproteins	• Cytoplasmic (intracellular) • Hyperphosphorylated tau protein (due to presence ofAβ) • Displace or encircle nucleus	• Amyloid proteins build up on the walls of the arteries in the brain. • increases the risk of hemorrhagic, stroke and Dementia.

- **What has strong correlation with the degree and severity of Dementia in Alzheimer's?**

- In comparison to plaques, tangles have a stronger correlation to the degree of dementia. HOWEVER, it is not the strongest correlation because loss of synapses have the best correlation to the degree/severity of dementia.

- **Enumerate 3 Biochemical markers correlated to degree of dementia.**

1. Loss of choline acetyltransferase
2. Synaptophysin immunoreactivity
3. Amyloid burden

- **Briefly, explain the 2 Pathways of APP processing.**

1. **Normal pathway**: APP is cleaved by α-secretase, followed cleavage by γ-secretase (gives soluble fragments).
2. **Abnormal Pathway**: APP Cleavage by β-secretase followed by γ-secretase results in production of Aβ (insoluble fragments).

- **How does the accumulation of Aβ protein affect neurons & neuronal function?**

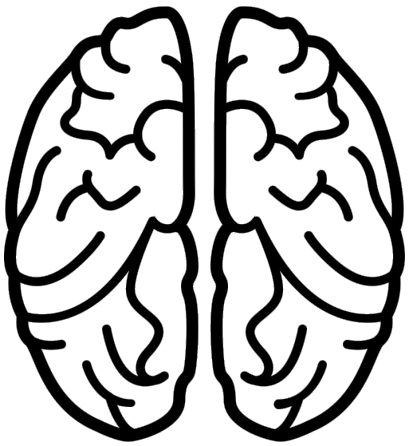
Small aggregates of Aβ alters neurotransmission and it can be toxic to neurons and synaptic endings. Larger deposits (plaques) also cause neuronal death. Elicit a local inflammatory response.

- **Mention the genetic mutations and their chromosomes that related to Alzheimer's disease.**

Gene	Amyloid Precursor Protein (APP)	Presenilin-1 (PS1)	Presenilin-2 (PS2)	Apolipoprotein E (ApoE)
Chromosome	21	14	1	19

- **List the therapeutic approach of Alzheimer's disease**

NSAIDs, AchE inhibitors, Flavonoids, Stem cell therapy.



Drawing break!!

Pathogenesis of cerebral infarction

- what are the biochemical responses to an Ischemic brain injury?
  Oxidative stress, metabolic stress, and neurochemical response.

- Mention three antioxidant enzymes and where do they perform their function? And which ROS they work on?
  - Superoxide dismutase in the mitochondria and cytosol (works on superoxide and convert it into oxygen or hydrogen peroxide)
  - Glutathione peroxidase in the mitochondria and cytosol (works on hydrogen peroxide and convert it into water)
  - Catalase in the peroxisomes (works on hydrogen peroxide and convert it into oxygen or water)

- What is The Role of Reactive Oxygen Species (ROS) & Reactive Nitrative Species (RNS) in Normal Brain Physiology?
  - They modulate synaptic transmission & non-synaptic communication between neurons & glia.
  - During periods of increased neuronal activity, ROS & RNS diffuse to the myelin sheath of oligodendrocytes activating Protein kinase C (PKC) → posttranslational modification of myelin basic protein (MBP) by phosphorylation.
  - regulate neuronal signaling.

- Why is the brain susceptible to ROS-induced damage?
  - High concentrations of peroxidisable lipids, Low levels of protective antioxidants
  - High oxygen consumption, High levels of iron
  - The occurrence of reactions involving dopamine & Glutamate oxidase in the brain

- Explain how can NOrelease be beneficial or detrimental?
  - NO produced by endothelial NOS (eNOS) improves vascular dilation & perfusion and prevention of platelet aggregation → beneficial
  - NO produced by neuronal NOS (nNOS) or by the inducible form of NOS (iNOS) → detrimental (harmful)

- Inhibition of ATP-dependent ion pump in an ischemic brain injury does what change to the ions transport?
  Na^+ influx , K^+ efflux , Ca^{2+} influx

- List the neurotransmitters increased during neurochemical response.
  Glycine , GABA , Glutamate , Dopamine

- List the molecular and vascular effects of ROS in ischemic stroke

Molecular	Vascular
• **DNA** damage • **Lipid** peroxidation of **unsaturated fatty acids** • **Protein** denaturation • Inactivation of **enzymes** • Cell **signaling** effects (e.g. release of Ca^{2+} from intracellular stores) • **Cytoskeletal** damage • **Chemotaxis**	• Altered vascular tone and cerebral blood flow • Increased platelet aggregability • Increased endothelial cell permeability

☆ وَحِين تُسأل يومئذٍ عن شَبابك فِيما أفْنيتهُ
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