Date

BONE REMODELING

1. BONE DEPOSITION

2. is the apposition or formation of new bone as a normal physiological process (specialized cells called osteoblasts)
3. The purpose remodeling regulate calcium homeostasis, repair micro- damaged bones and also to shape and sculpt the skeleton during growth.
4. Calcium balance
5. The process of bone resorption by the osteoclasts releases stored calcium into the systemic circulation and is an important process in regulating calcium balance.
6. **Osteoblasts**
7. Mononucleated cells that are responsible for bone formation
8. • synthesize most of proteins found in bone as well as various growth factors & cytokines.
9. • responsible for the deposition of new bone matrix ; Osteoid (is the unmineralized, organic portion of the bone matrix that forms prior to the maturation of bone tissue) and its subsequent mineralization.
10. • control mineralization by regulating the

11. BONE RESORPTION

is a process involving the breakdown of bone by specialized cells known as osteoclasts

Osteoclasts

Multinucleated cells

removes bone tissue by removing its mineralized matrix and breaking up the organic bone (organic dry weight is 90% collagen). This process is bone resorption

•mechanism

• A proton translocating ATPase expels protons across the ruffled border in to resorption area.

•This Lowers the Local PH to 4.0 or less, thus increasing the solubility of hydroxyapatite & allowing demineralization to occur.

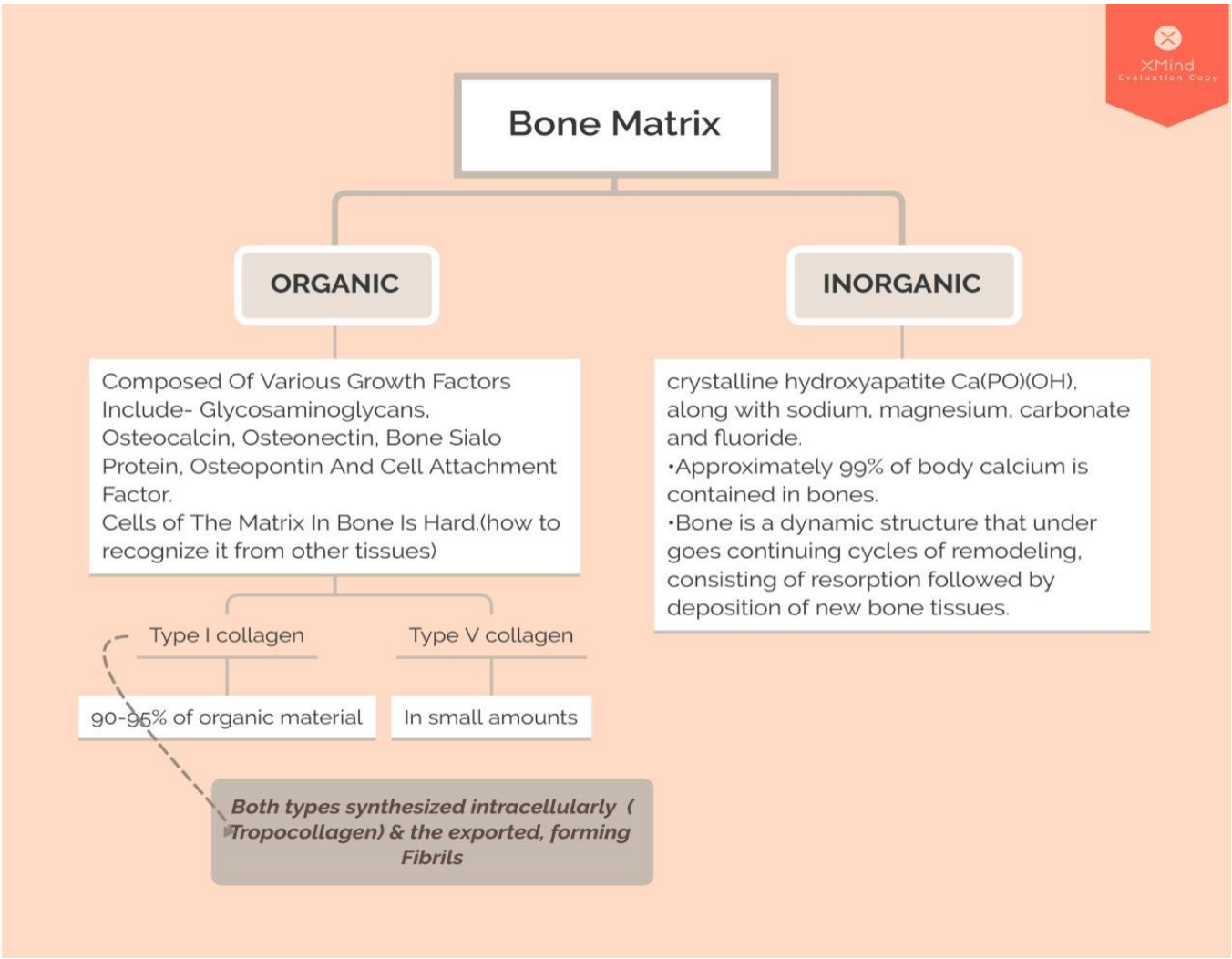
•Lysosomal acid proteases are released that digest the new accessible matrix proteins.

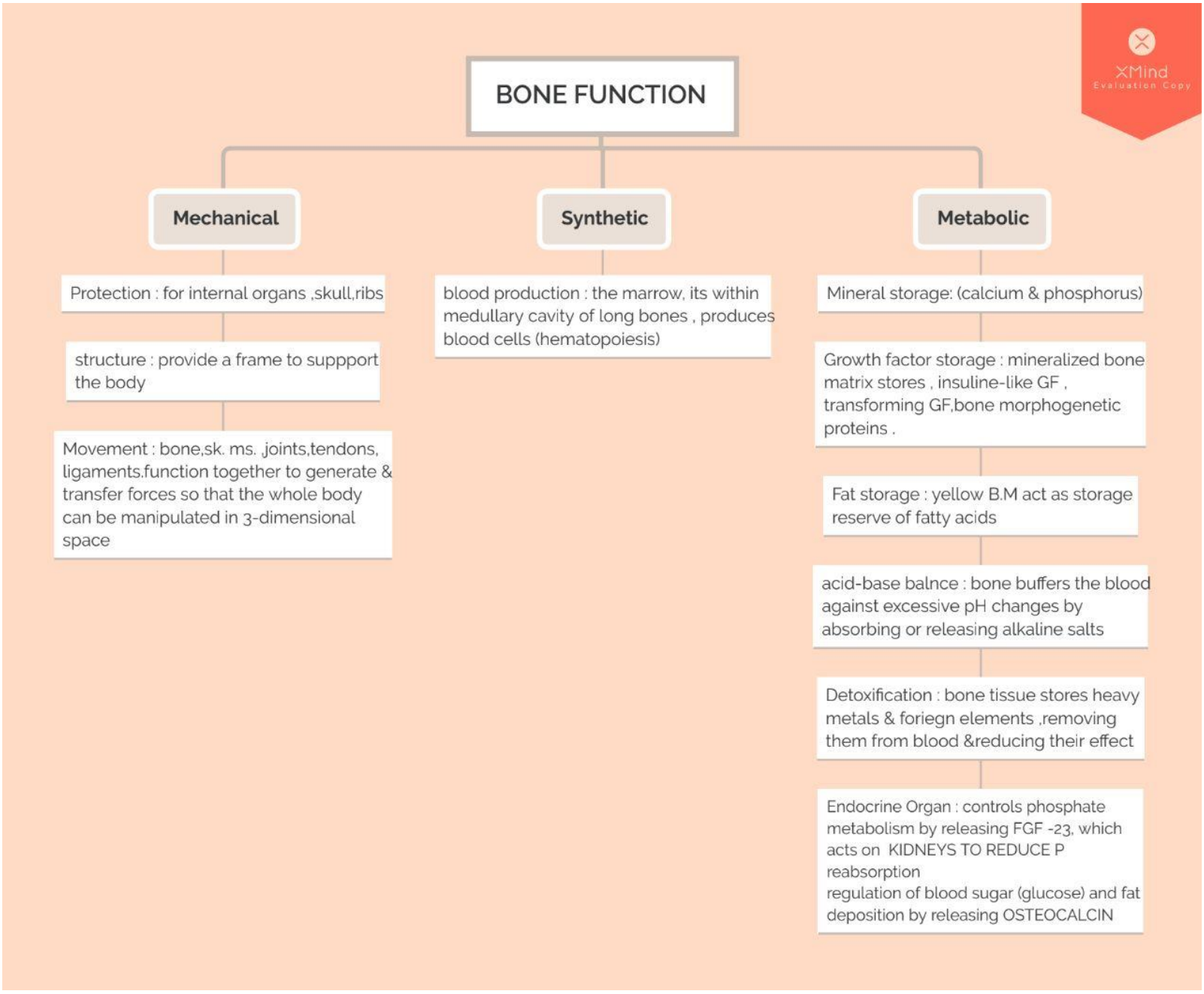
Regulation

Osteoclasts are regulated by several hormones :

1- Parathyroid hormone (PTH) from the parathyroid gland
2-calcitonin from the thyroid gland.

- *These processes control the reshaping or replacement of bone following injuries like fractures also micro-damage, which occurs during normal activity.*
- *Remodeling functional responds also to demands of the mechanical loading.*




BONE FUNCTION
Mechanical
Protection : for internal organs ,skull,ribs
structure : provide a frame to suppport the body
Movement : bone,sk. ms. joints,tendons, ligaments.function together to generate & transfer forces so that the whole body can be manipulated in 3-dimensional space
Synthetic
blood production : the marrow, its within medullary cavity of long bones , produces blood cells (hematopoiesis)
Metabolic
Mineral storage: (calcium & phosphorus)
Growth factor storage : mineralized bone matrix stores , insuline-like GF , transforming GF,bone morphogenetic proteins .
Fat storage : yellow B.M act as storage reserve of fatty acids
acid-base balnce : bone buffers the blood against excessive pH changes by absorbing or releasing alkaline salts
Detoxification : bone tissue stores heavy metals & foriegn elements ,removing them from blood &reducing their effect
Endocrine Organ : controls phosphate metabolism by releasing FGF -23, which acts on KIDNEYS TO REDUCE P reabsorption
regulation of blood sugar (glucose) and fat deposition by releasing OSTEOCALCIN
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HORMONES IN BONE HEALTH		
Human Calcitonin	A 32-amino acid linear polypeptide hormone that is produced in humans primarily by the parafollicular cells (known as C-cells) of the thyroid. It acts to reduce blood calcium (Ca^{2+}), opposing the effects of (PTH)	1- lowers circulating calcium and phosphate levels. 2- It exerts its calcium lowering effect by inhibiting bone resorption. This action is direct, 3- inhibits the activity of osteoclasts. 4- increases Ca^{2+} excretion in Urine
G. H	(GH) is a growth promoting hormone produced by the pituitary gland. It is"anabolic" which means it stimulates bone formation.	* stimulates the production of insulin-like growth factor 1 (IGF-1) by the skeleton. * is important in stimulating longitudinal growth. * Can increase bone mass when given to adults.
Gonadal Steroids	Gonadal steroids are very important in maintaining bone balance. They are also important in normal growth and development and in development of peak bone mass. The mechanism of action is unclear but receptors for estrogen and Androgen are found in bone	1- Estrogens: are the principal circulating sex steroids in females. help to regulate the rates of bone formation and bone resorption. estrogen decrease after menopause, could contribute in development of osteoporosis. 2- Androgens (such as testosterone): Are necessary for bone strength in males
Thyroid Hormone	Produced by the thyroid gland. Bone cells have receptors for thyroid.	1- necessary for growth and maturation of the skeleton. 2- causes increased osteoclastic bone resorption and osteoporosis when levels are too high.
Glucocorticoids	(also called cortisol) is produced by the adrenal gland. Bone cells have receptors for glucocorticoid. This hormone is absolutely essential for life, but excess levels cause multiple deleterious effects on the skeleton.	1* decreases calcium absorption from the intestines. 2* inhibits bone formation. 3* increases bone resorption. 4* increases renal calcium excretion. 5* decreases sex steroid production.

LEC.2

Metabolic muscle diseases			
Name	**Is**	**Cause**	**Signs and Symptoms**
1. Acid Maltase Deficiency (AMD); also called glycogen storage disease type II	1. autosomal Recessive 2. break down of glycogen defect .	1. mutation in a gene (acid alpha-glucosidase: (acid 2. on long arm of chromosome 17 at 17q25.2-q25.3maltase	-accumulation of glycogen 1.muscle weakness (myopathy) 2. affecting major body tissues in the heart, skeletal muscles, liver and nervous system.
2.Carnitine deficiency	1. autosomal 2. defect in the transporter responsible for moving carnitine (is involved in the oxidation of fatty acids)	The gene responsible for the OCTN2 carnitine transporter is SLC22A5, located at 5 q31.1-32.	1. hypoglycemia 2. Cardiomyopathy 3. Muscle weakness
3. CPT Carnitine palmitoyl transferase deficiency	1. autosomal recessive 2. precursor CPT2(protein transport FA to the defect mitochendria)	enzymatic defect that prevents long-chain fatty acids from being transported into the mitochondria for utilization as an energy source	

Name	Is	Cause	Signs and Symptoms
4. Debrancher enzyme deficiency	carbohydrates	defect in the debrancher enzyme gene, which interferes with the **breakdown of glycogen** in the muscles and liver.	1. swelling of the liver 2. slowing of growth 3. low blood sugar level.
5.Lactate dehydrogenase deficiency	carbohydrates	genetic defect in the lactate dehydrogenase enzyme, which **normally recycles byproducts of carbohydrate metabolism**	
6.Myo-adenylate deaminase deficiency	**In adenosine triphosphate (ATP**	a genetic defect in the myoadenylate deaminase enzyme, which **affects the cell's ability to process ATP**	
7.Phosphofructokinase deficiency (Tarui disease)	carbohydrates	genetic defect in the phosphofructokinase enzyme, which affects the **breakdown of glucose**	
8.Phosphoglycerate kinase deficiency	carbohydrates	phosphoglycerate kinase enzyme, which normally **breaks down glucose** for energy production	

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