***♥As a refreshment :***

* 3-5% of O2 we breathe goes for the formation of reactive oxygen species.
* ROS could be generated by environmental factors, radiations, chemicals, infection, inflammatory diseases & others.
* Cellular reactions that produce ROS are : oxidases – cytochrome p450 (superoxide ion O2- could be produced & leak to the environment by this cytochrome, this accidental release of O2- could occur, but sometimes its increased in the case of infection, inflammatory disease, etc..).
* ROS are normally produced up to some extent but it can be increased in certain conditions as we mentioned earlier.
* Body should develop a defense system against ROS that are damaging all molecules & causing several diseases, disorders & cancers.

***♥Defense system***: composed of primary & secondary defense systems.

1. ***Primary defense system:***

-its composed of enzymes that neutralize O2, & these enzymes are: (superoxide dismutase – catalase – GSH peroxidase) , these enzymes calles: AntiOxidant Enzymes –AOE-.

-as a counter action by the body for some diseases or O2 stress, the AOE increases .

 

-these reactions occur in complex 4, & none of them leak.

-superoxide ion can be neutralized by superoxide dismutase ,cause this O2- can attack variety of compounds & produce ROS.

-by the superoxide dismutase enzyme , O2- converts to O2 atom & H2O2.

- H2O2 is weak oxidizing reagent , but it could be a source of hydroxyl radical by fenton reaction.



***♥Hydrogen peroxide can be neutralized by:***

***1-****catalase*: this enzyme is not widely spread, its mostly located in peroxisomes . it converts hydrogen peroxide to water & oxygen atom (that’s why when we put hydrogen peroxide on a wound , we see bubbles getting out).

*2- GSH peroxidase*: this enzyme :

 a)requires Selenium (Se) metal as a cofactor.

 b) neutralizes hydrogen peroxide by using 2 Glutathione (GSH is known as the most important antioxidant compound in the body, specially in blood, its an antioxidant scavenger compound) to reduce hydrogen peroxide ,& then it becomes oxidized.

c) Glutathione could be regenerated by GSH reductase (this is a FAD or falvin enzyme that reduce oxidized glutathione using e- of NADPH).

***♥Glutathione***:

* It’s a tripeptide composed of Glutamate, Cystine ,Glycine .
* Glutamate makes a peptide bond with cystine by Gama carboxylate not alpha , & the SH group in cystine is the projective group that undergoes oxidation & protect neighbouring molecules. When Glutathione undergoes oxidation , the disulfide will attach one glutathione to the other.

We talked about the three AOE that are considered the primary defense mechanisms, in addition we will now talk about the secondary one.

***♥Secondary defense mechanisms:***

1-dietary : antioxidant vitamins ( vitamin E & C) & B carotene.

2-endogenous antioxidant.

3- repair mechanism of DNA.

4- compatmentation .

***♥Compartmentation :***

-using different compartments in the cell, or compartmentation of molecules within defined organelle , this protects oxidant to diffuse everywhere.

- we notice that in specific places in the cell ,there is a production of ROS, such as in mitochondria, peroxisomes, ER, cytochrome p450, etc… , & at the same place ,there is a production of antioxidant enzymes , so, ROS are produced & neutralized at the same place or compartment.

 -these enzymes are rich in tissues of (liver, adrenal gland ,kidney) that have high concentration of mitochondria , peroxisomes, etc…

-ferritin → has high affinity for iron , so, it traps iron in the cell & not letting it to float around, cause iron is a catalyst in fenton reaction , that’s why we could consider ferritin as an antioxidant reactants. When ferritin binds too much iron , it will become Hemosiderin , & this means that there is an overload.

***♥Vitamin C & E:***

-vitamin E is the most powerful antioxidant & its good for heart problems.

-alpha tocopherol is the most type famous & wide spread of vitamin E.

-alpha tocopherol has an antioxidant action by termination free radical lipid peroxidation , it does so, by donating single e- to this lipid radical , so the vitamin will be oxidized.

-the oxidized vitamin can be reduced by vitamin C , so, vitamin C preserve the level of vitamin E.

- vitamin C & beta carotene are also antioxidant , but they act by accepting e- from lipid radical, unlike vitamin e- which donates e-.

-vitamin C also can regenerate reduced vitamin E from the oxidized one.

***♥Other dietary antioxidant:***

***♥Flavenoids:***

-they are polyphenolic compounds connected together.

***♥-functions:***

1-they can inhibit superoxide ion production.

2-chelate Fe & Cu.

3-free radical scavenger .

4- preserve vitamin E.

-it could exist in: green tea, chocolate, red wine, fruits.

-other flavenoids in other names (not that important): catechins – kaempherol – guercetin) they exist more in colored vegetables & red fruits.

-endogenous compounds that have an antioxidant activity:

1- uric acid (the end product of purine metabolism).

2-bilirubin (the end product of heme metabolism).

3-GSH

4-lipoic acid

5-ubiquinone

6-melatonin

***♥Chapter 14 >> Glycoseaminoglycan – glycoprotein***

-in synthesis of glycoseaminoglycan , glycoprotein or glycolipid, we always have a donor sugar. ( the sugar should be activated by forming UDP sugar, which can then be donated to protein, lipid, or, polysaccharide to form glycoprotein , glycolipid, or glycosaminoglycan).

-there is a specific enzymes for the donor sugar & acceptor , some have several glucose transferase enzymes.

-for example→ formation of UDP glucose from glucose 1 phosphate & UDP, & then using this UDP Glucose in producing proteoglycan , glycoprotein , UDP glucoronate & UDP galactose that has a role in making lactose.

-when the donated sugar binds a protein, it will make a glycosedic bond with serine (o-glycosedic bond) or asparagines ( N-glycosedic bond).

***♥Formation of Glucornic acid:***

-its formed by UDP Glucose dehydrogenase from UDP glucose , resulting UDP glucornate ( it’s a precursor of glycosaminoglycan, & an important compound cause its used to solubelize insoluble compounds & therefore it can be transported to tissues.

-the best example for the usage of glucornic acid is bilirubin. Bilirubin is not soluble, & in order to be secreted in the bile & reach the feces, this bilirubin in the liver undergoes conjugation with 2 glucornic acid , & this compound then will be called: bilirubin diglucuronide ( the soluble bilirubin).

-when gluconic acid is metabolized , it will be converted to xylulose –pentose- (knowing the details of this pathway is not important).

-other animals & plants contain enzymes that converts glucornic acid to vitamin C (ascorbic acid) , that’s why we have to take vitamin C , unlike plants which produces it.