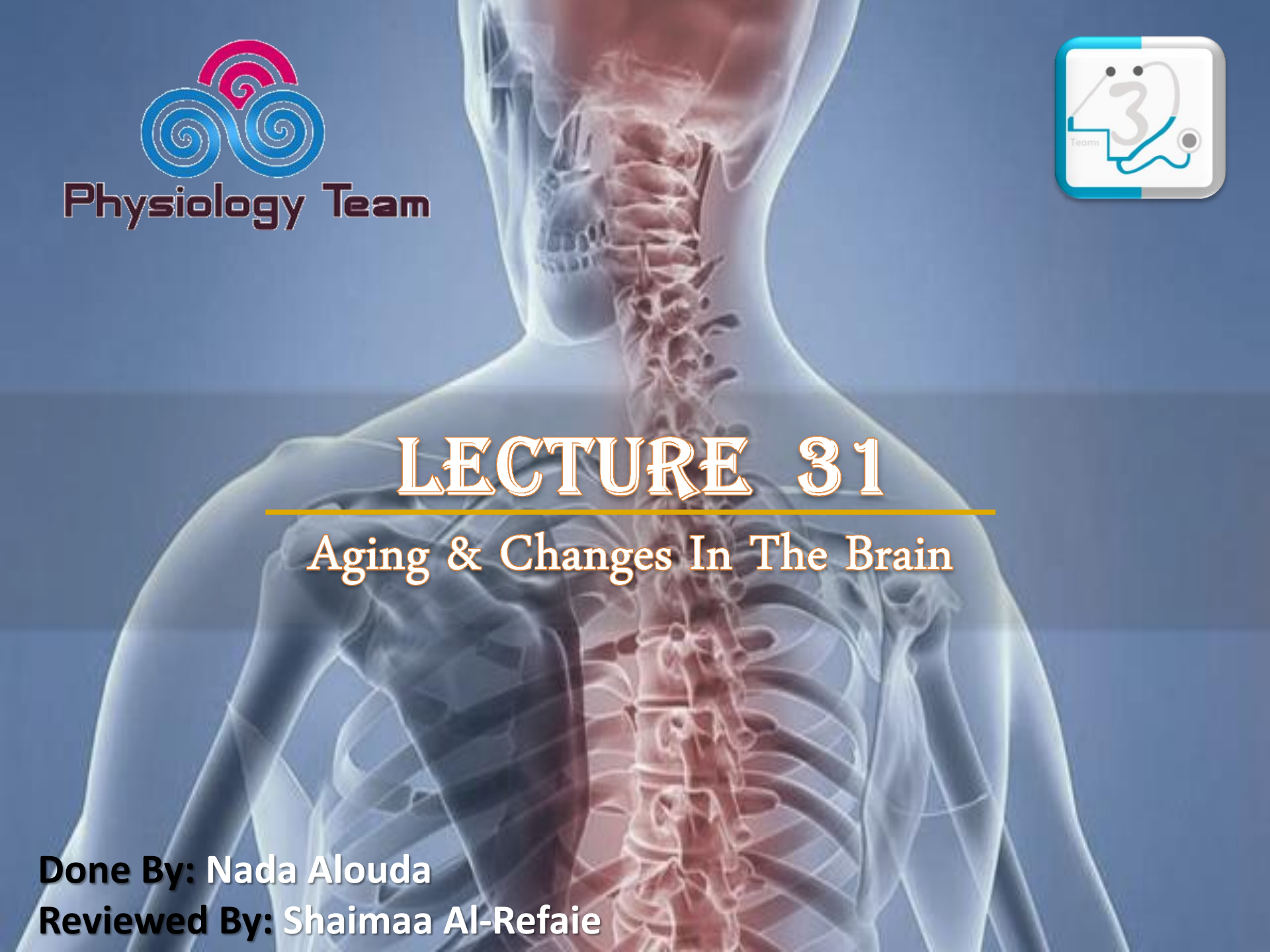

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LECTURE 31

Aging & Changes In The Brain

Done By: Nada Alouda
Reviewed By: Shaimaa Al-Refaie

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OBJECTIVES

At the end of this lecture, student should be able to describe:

1. ***Definition of Aging.***
2. ***Theories and terms Used.***
3. ***Body Changes in Aging.***
4. ***Brain Changes in Aging.***
5. ***Memory Changes in Aging.***
6. ***Carotid Hypersensitivity.***

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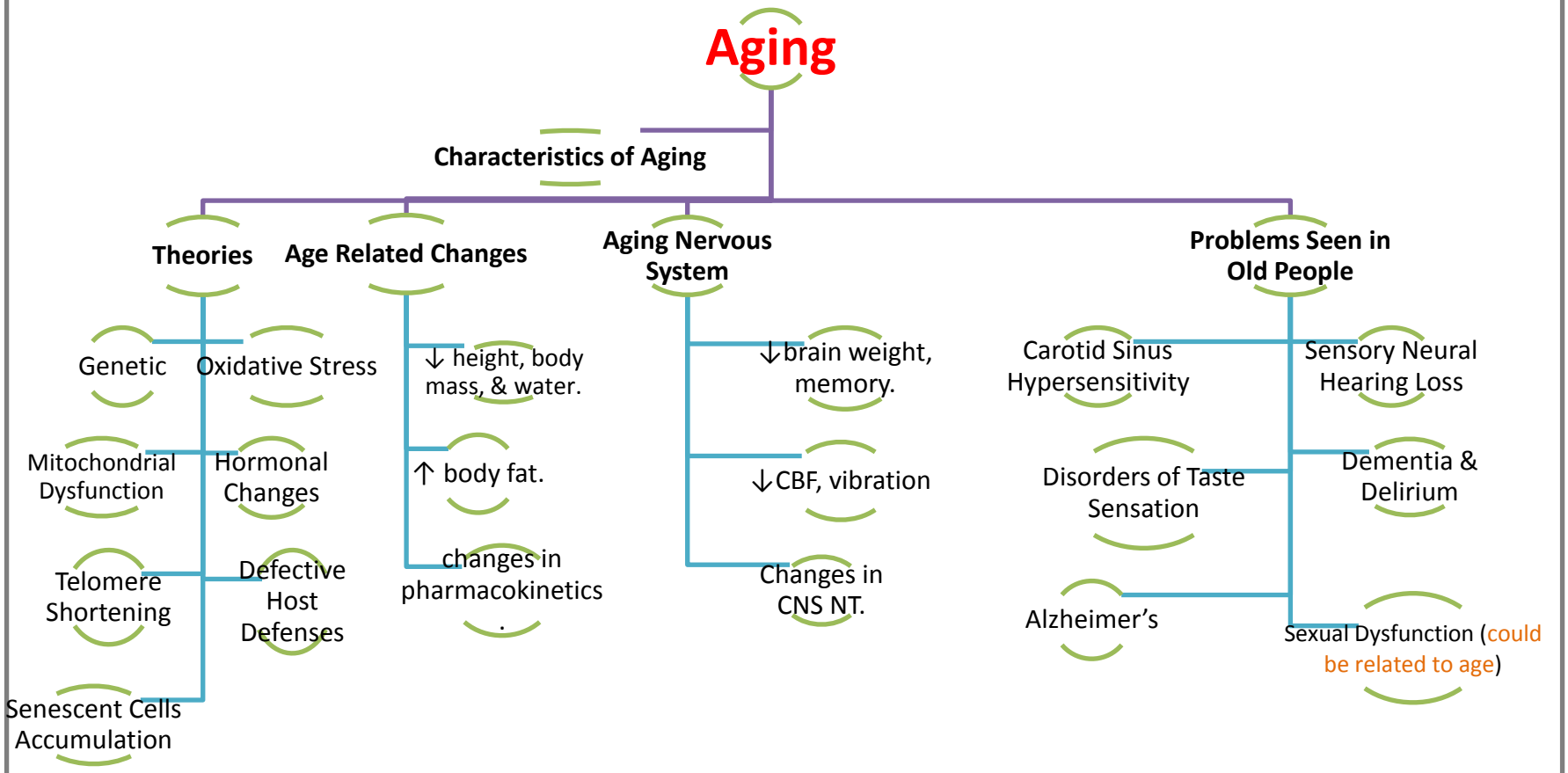
MIND MAP



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Aging

- Aging is the progressive, universal decline **first** in **functional reserve*** and **then** in **function** that occurs in organisms **over time**.
- IS decline in intrinsic physiological function, leading to an increase in age-specific **mortality rate** (i.e., a decrease in survival rate) and a **decrease in age-specific reproductive rate**
- *Reserve means something stored or kept available for future use or need. This mechanism prevents the person to undergo chronic changes early. However, the reserve decreases with time & will affect the normal function → aging.
- *All tissue cells do not work by using their maximal capacity in normal daily life BUT in case of injury, disease etc. the rest of our cells will work to respond to these changes.*
- Aging is **not** a disease; however, **the risk of developing disease is increased**, often dramatically, as a function of age.
- It's an *inevitable process* (عملية حتمية لا مهرب منها) but we can modify & slow it down to decrease the susceptibility of diseases, cognitive & physical functions…

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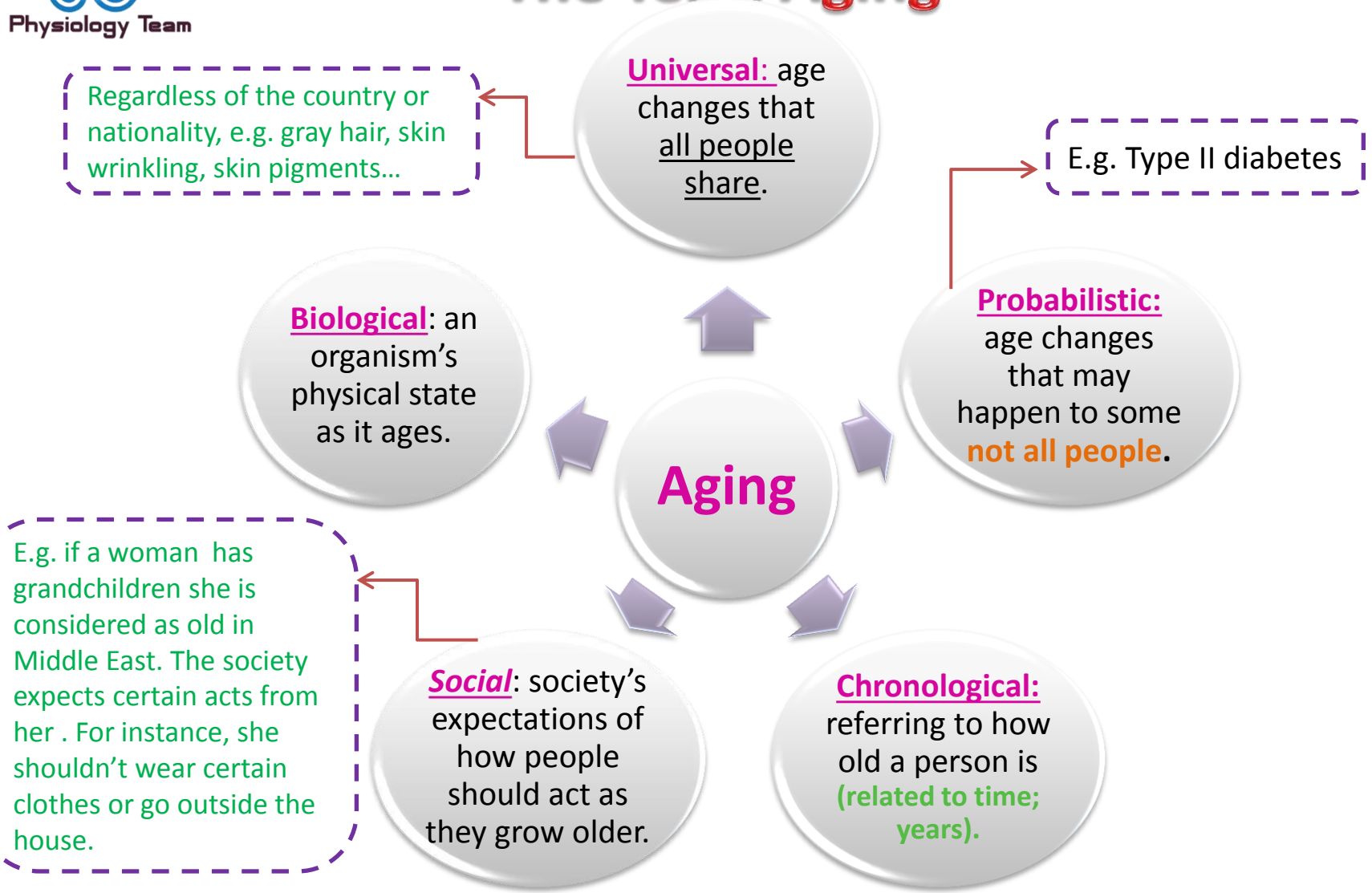
Aging is characterized by

1. Changes in appearance (gradual reduction in height and **weight loss** due to **loss of muscle & bone mass**).
2. A lower metabolic rate. ← **The person should decrease his calories intake as aging.**
3. Longer reaction times. Decrease in responses
4. Declines in certain memory functions. ← **Long-term memory remains intact.**
5. Declines in sexual activity and in women menopause.
6. A functional decline in audition, olfaction, and vision.
7. Declines in kidney, pulmonary, and immune functions, declines in exercise performance, and multiple endocrine changes.

The Term Aging



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Some Theories of Aging

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There is no specific cause of aging as it's an inevitable process but we can modify & slow it down.

Hypothesis	How it May Work.
Genetic	Aging is a genetic program activated in post-reproductive life when an individual's evolutionary mission is accomplished.
Oxidative stress	Accumulation of oxidative damage to DNA, proteins, and lipids interferes with normal function and produces a decrease in stress responses. ***People who live in nature or eat healthy food don't show patterns of age because they don't expose to ROS.***
Mitochondrial dysfunction	A common deletion in mitochondrial DNA with age compromises function and alters cell metabolic processes and adaptability to environmental change.
Hormonal changes	The decline and loss of circadian rhythm in secretion of some hormones produces a functional hormone deficiency state. ***E.g. sleeping & waking up early & thyroid gland control metabolism, insulin – energy).***
Telomere shortening	Aging is related to a decline in the ability of cells to replicate.
Defective host defenses	The failure of the immune system to respond to infectious agents create vulnerability to infection. host defenses that protect against infection include: natural barrier(skin, mucous membrane ..)
Accumulation of senescent cells	Renewing tissues become dysfunctional through loss of ability to renew *resulting in accumulation of senescent cells in the organs → senescent organs.*

OXYGEN - free radicals (FR) and reactive oxygen species (ROS)

Cell metabolism

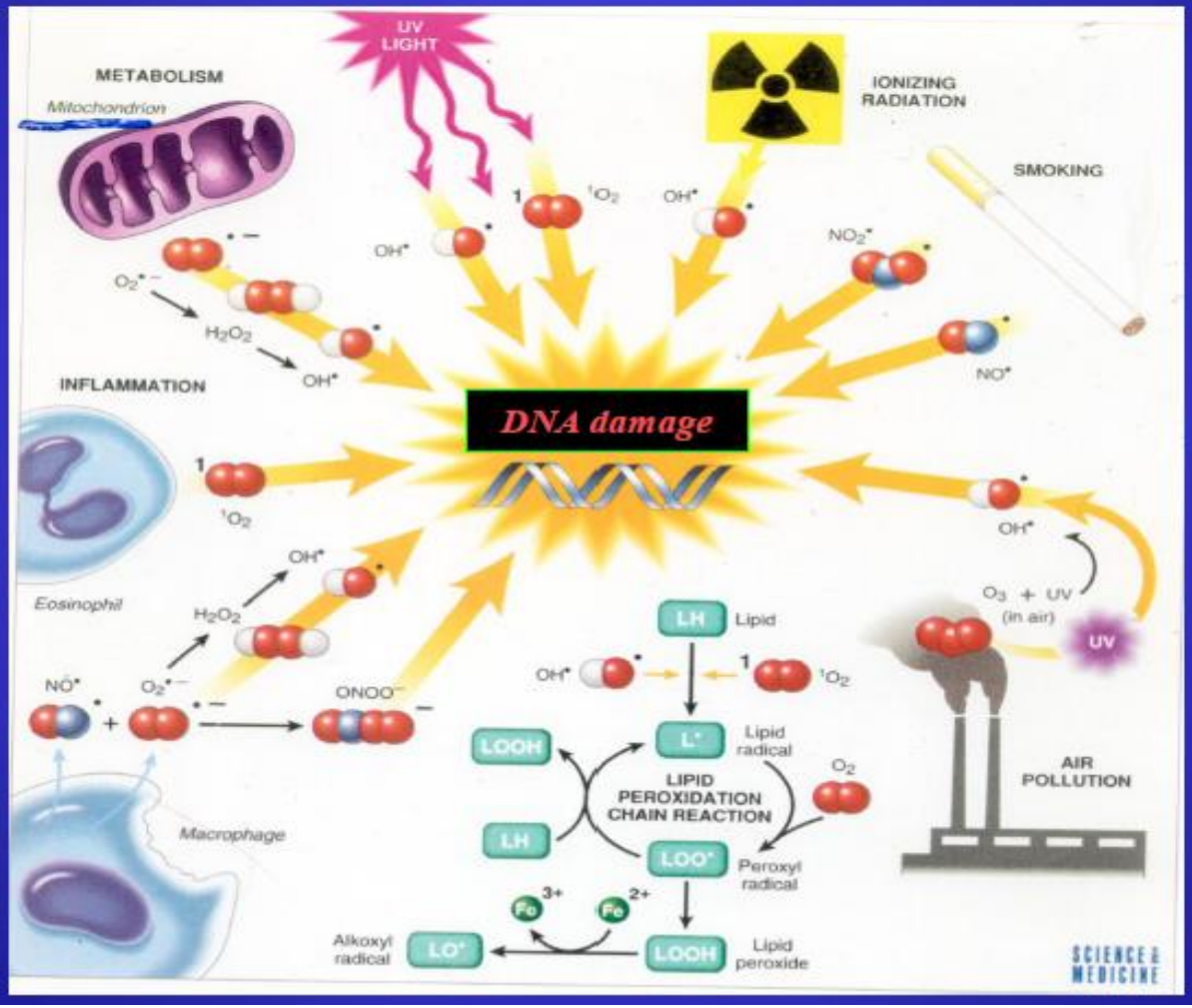
environment

Infection

lifestyle

diet

pollution



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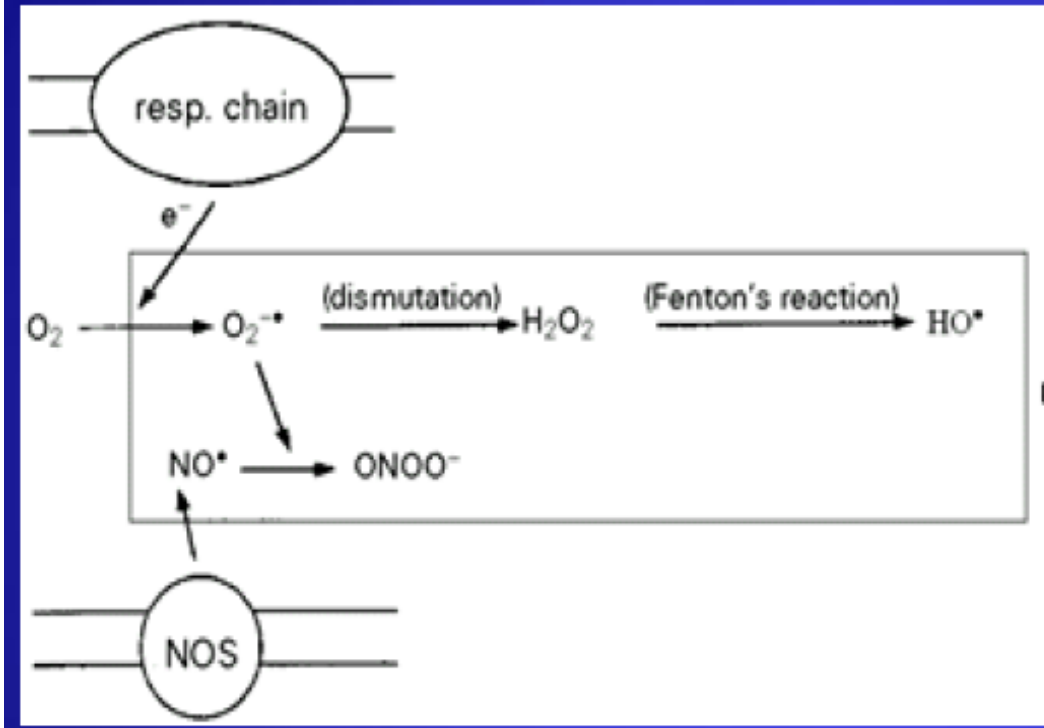
Mitochondria produce ROS:



Molecules damaged

- Protein thiol oxidation - MPT
- Lipid oxidation
- DNA oxidation
- Respiratory impairment
- Oxidation of extra-mitochondrial components

The respiratory chain (resp. chain) produces superoxide radicals ($O_2^{\cdot-}$), which generate hydrogen peroxide (H_2O_2) and hydroxyl radicals ($HO^{\cdot}$). Mitochondrial nitric oxide synthase (NOS) produces nitric oxide ($NO^{\cdot}$), which combines with $O_2^{\cdot-}$ to generate peroxinitrite ($ONOO^-$). All these ROS may cause mitochondrial and cellular damage if present in excess. MPT, Mitochondrial permeability transition.

Kowaltowski 2002

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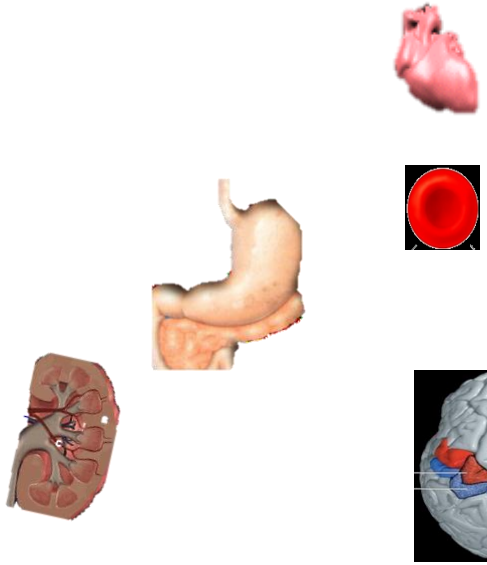
Successful Aging

- Active engagement with life.
- Low probability of disease or disability.
- High cognitive (mental) & physical function capacity.

Leading Causes of Death Age 65+ "Medical Diagnoses"

1.	**Heart Disease**	32%
2.	Cancer	22%
3.	Stroke	8%
4.	Chronic respiratory	6%
5.	Flu/Pneumonia	3%
6.	Diabetes	3%
7.	Alzheimer's	3%



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Age Related Changes

- ↓ height, lean body mass, & body water.
- ↑ body fat.
- Consequence changes in pharmacokinetics.

Healthy males are about 60% of water.
Total water content declines throughout life.
E.g. in old age becomes 45%.

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Aging and Nervous System

Changes	Consequences
• ↓ brain weight and volume. • ↓ Cerebral blood flow. • ↓ memory. • Alteration in CNS neurotransmitters. • ↓ vibratory sense. • Enlargement of ventricular system of brain (because cells surrounding the ventricles are lost)	• Drug toxicities *(especially ones that cross BBB).* • Delirium. • Altered mood *(they get happy or sad easily).* • Decreased IQ scores. • "Benign senile forgetfulness". • Increased postural instability *(balance).* • Altered gait. • Falls, accidents.

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Neurological System

1. Neuronal loss is normal in the aging brain but the *ability to learn remains generally unchanged.*
2. There is loss of dendritic arborization.
3. ***Recall memory is affected*** more than cognitive function in normal aging.
4. Cerebral atrophy shows up on CTs and MRI scans.
5. Lowered seizure threshold.
6. Reduced Sympathetic nervous system activity.
7. Reduced Neurotransmitter levels.
8. Changes in sleep patterns.
9. Abnormalities in EEG tracings.
10. Increased risk of stroke ***(due to atherosclerosis).***
11. ***Neurological disorders: Alzheimer's disease & Parkinson's disease .***

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Nervous System

1. Aging leads to increased cerebral amyloid.
2. Amyloid is a general term for protein fragments that the body produces normally. Beta amyloid is a protein fragment snipped from an amyloid precursor protein (APP).
3. Average amount of brain protein is reduced with a **marked loss in multiple enzymes** *(carbonic anhydrase and the dehydrogenases)* but with a relative *increase in abnormal proteins such as amyloid* in **tangles** and **plaques**.
4. **Loss of RNA** (messenger and transcription) but **not DNA**.
5. Loss of lipids, and lipid turnover rate, and a decrease in catabolism and synthesis (&↓ metabolic rates in general).

Carotid Sinus Hypersensitivity

- ✓ Carotid sinus syncope occurs when there is an exaggerated vagal response to carotid sinus stimulation.
- ✓ Provoked by wearing a tight collar, looking upwards or turning the head.
- ✓ **Carotid sinus syndrome occurs in the elderly** and mainly results in **bradycardia**.
- ✓ Most common etiologies of atrio-ventricular block.
- ✓ Do not massage both carotids simultaneously.

Carotid Sinus Stimuli:

1. **Wearing a tight collar.**
2. **Looking upwards.**
3. **Turning the head.**
4. **Massage.**

Control of blood pressure	The mechanism	The characteristics of the mechanism
A) Short-term control (rapid)	Baroreceptor reflex.	1. Quick operation (within few seconds). 2. Mediated through autonomic nerves. 3. Adjusts cardiac output (CO) & total peripheral resistance (TPR) to restore BP to normal. 4. Influences heart & blood vessels.
B) Long-term control	Renal compensation.	-------

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Baroreceptor Reflex Arc

Receptors	• Baroreceptors in carotid sinuses, Aorta
Afferents	• Vagus nerve
Center	• Vasomotor center in medulla oblongata
Efferents	• Sympathetic & parasympathetic nerves
Effectors	• Heart & blood vessels

According to the stimulus: IF:
↑ BP: parasympathetic activated.
↓*BP:* sympathetic activated.

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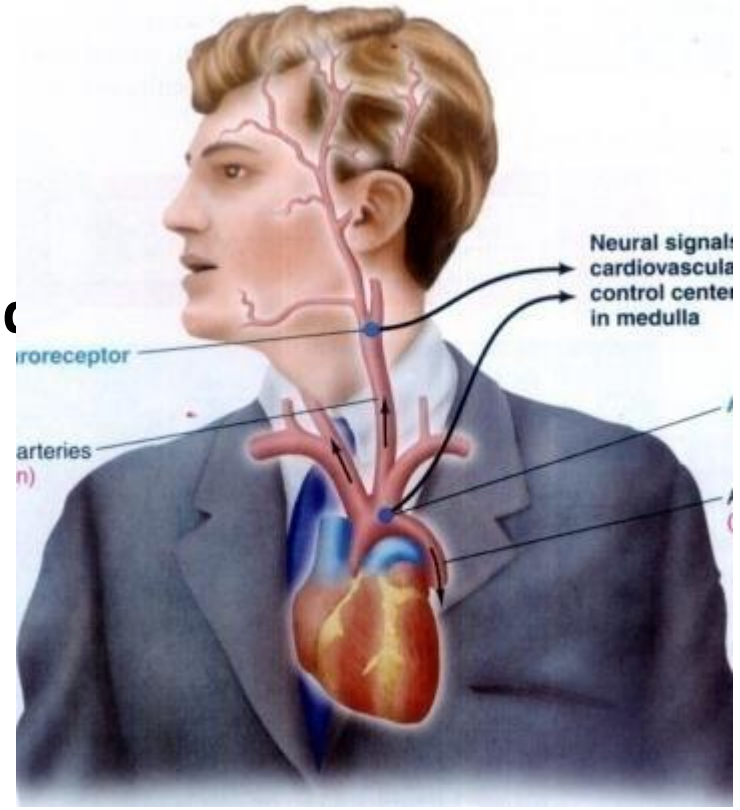
Pressure on the carotid sinus, produced by the tight collar or carotic massage can cause:

1- Vasodilatation.

2- Marked bradycardia.

Fainting or syncope.



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Age-related changes

Boy's slide

Touch:

Age-related changes in the ability to perceive tactile stimuli may be due to:

Loss of various receptors (for example, Meissner's and Pacinian corpuscles) in the skin.

Reductions in the number of sensory fibers innervating the skin.

Vision:

Lens: proteins in the lens change with age and the elasticity of the lens is reduced. Therefore, many elderly individuals have trouble focusing their eyes.

Cornea: the cornea may become less transparent and more flat. This may cause images to appear distorted or blurred. There may also be a loss of color sensitivity to green, blue and violet shades.

Pupil: changes in the autonomic nervous system alter the ability of older people to dilate the pupil. By age 70, the pupil may not dilate easily in low lighting conditions (Hampton, 1997).

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Boy's slide

Vision Cont..

Cataracts: cloudy areas of the lens. Cataracts decrease the amount of light that passes through the lens and can bend lig abnormally. The National Eye Institute estimates that more than 50% of Americans age 65 years and older have a cataract.

Retina: the peripheral retina is thinner and contains fewer rods in older individuals.

Olfaction:

Changes in the nasal mucosa, cribriform plate (which separates the nasal cavity from the brain **)and air passages may contribute to impaired odor recognition. The amygdala (**is an almond-shape set of neurons located deep in the brain's medial temporal lobe) **and other brain areas involved with smell may be damaged in older individuals.**

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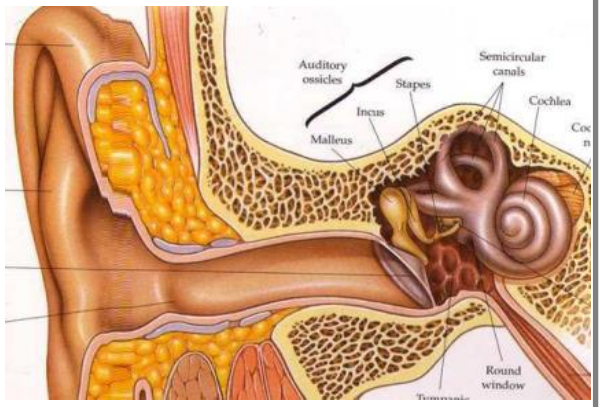
Sensory Neural Hearing Loss



Damage to the hair cells of the organ of Corti may be caused by:

1- **Intense noise.**
2- **Viral infections.**
3- **Ototoxic drugs.**
4- **Fractures of the temporal bone.**
5- **Meningitis.**
6- **Cochlear otosclerosis.**
7- **Ménière's disease.**
8- **Aging.**

Ototoxic Drugs:

1. Salicylates.
2. Quinine and its synthetic analogues.
3. Aminoglycoside antibiotics.
4. Loop diuretics such as furosemide and ethacrynic acid.
5. Cancer chemotherapeutic agents such as cisplatin.

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Disorders of the Sense of Taste

❑ **Disorders of the sense of taste are caused by:**

- Sensory loss.
- Neural loss.

❑ ***Sensory gustatory losses* are caused by:**

1- Inflammatory and degenerative diseases in the oral cavity.
2- A vast number of drugs, particularly those that interfere with cell turnover such as Antithyroid and antineoplastic agents.
3- Radiation therapy to the oral cavity and pharynx.
4- Viral infections.
5- Endocrine disorders.
6- Neoplasms.
7- Aging.

Geriatric Syndromes

- **Geriatrics**: A branch of medicine that deals with the problems and diseases of old age and aging people.

1. *Dementia and Delirium.*
2. *Falls.*
3. *Urinary Incontinence.*
4. *Pressure Ulcers.*
5. *Functional Decline.*

Dementia & Delirium

- **Dementia** is a syndrome of **progressive decline** in which multiple intellectual abilities deteriorate, causing both cognitive and functional impairment.

- **Delirium** is an **acute state of confusion**.

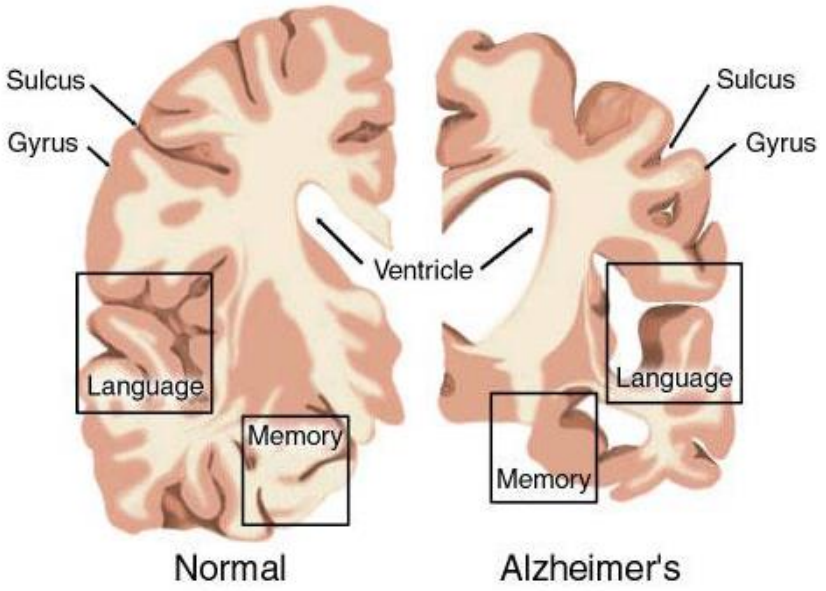
Delirium may be the only manifestation of a life-threatening illness in the older adult.
(We need to take it seriously because maybe there is transient ischemic attacks which is a warning of stroke.)

Alzheimer's Disease

Alzheimer's disease is defined as premature aging of the brain, usually beginning in mid-adult life and progressing rapidly to extreme loss of mental powers similar to that seen in very, very old age.

Features:

(1) An amnesic type of memory impairment.
(2) Deterioration of language.
(3) Visuospatial deficits;
(impaired of direction & position).



Features that are uncommon until the late phases of the disease:

- Motor and sensory abnormalities.
- Gait disturbances.
- Seizures.

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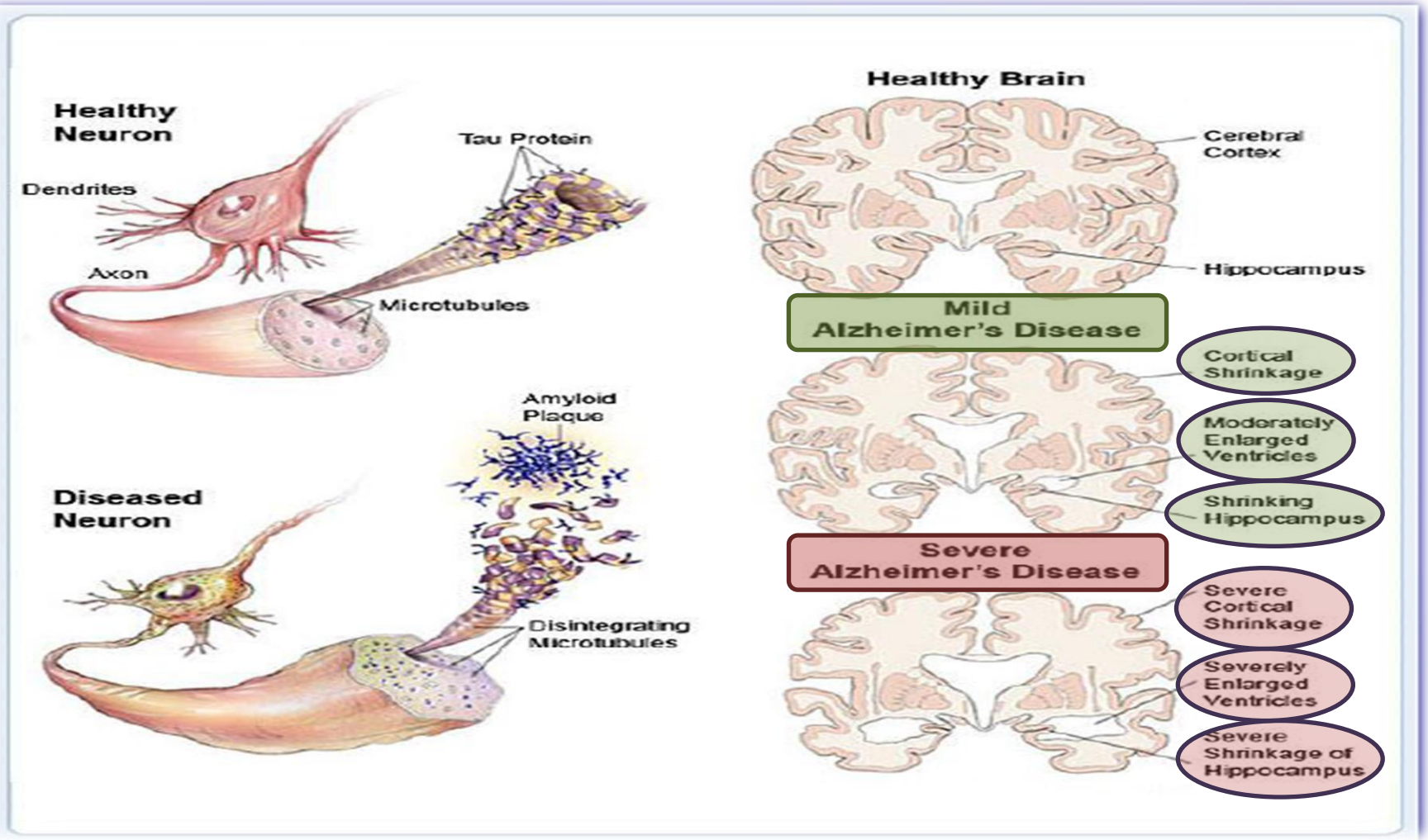
Alzheimer's Disease



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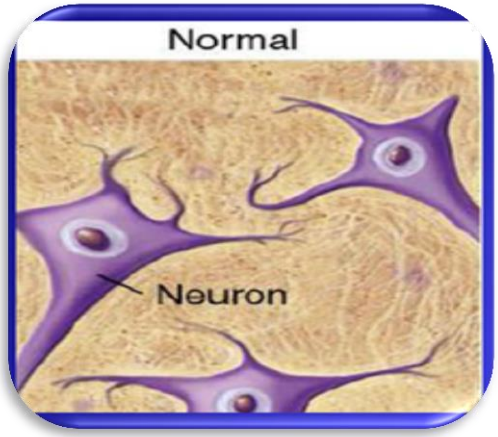
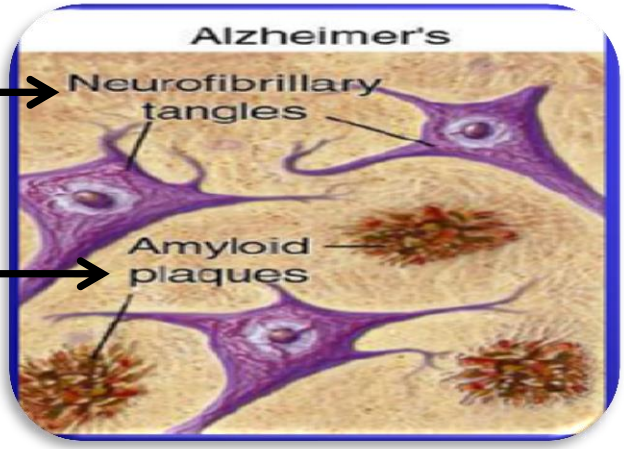
Alzheimer's Disease

Amyloid Plaques	Neurofibrillary Tangles
• It is **hallmark** of Alzheimer's disease. • There is **accumulation** of amyloid plaques **between nerve cells (neurons) in the brain**. • In a healthy brain, these protein fragments are broken down and eliminated. • In Alzheimer's disease, the fragments accumulate to form hard, insoluble plaques.	• These are insoluble twisted fibers **found inside the brain's cells**. • Consist primarily of a protein called tau, which forms part of a structure called a microtubule. The microtubule helps transport nutrients and other important substances from one part of the nerve cell to another. • In Alzheimer's disease, however, the **tau protein is abnormal** and the microtubule structures collapse.



They're found inside the brain's cells.

They're found between neurons in the brain.



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Sexual Dysfunction

- Erectile dysfunction (ED) is **not considered a normal part of the aging process.** Nonetheless, it is associated with certain physiologic and psychological changes related to age.

- In the Massachusetts Male Aging Study (MMAS), a community-based survey of men **as following:**

1. Men between the ages of 40 and 70, 52% of responders reported some degree of ED.
2. Complete ED occurred in 10% of respondents.
3. Moderate ED occurred in 25%.
4. Minimal ED in 17%

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SUMMARY

- The risk of developing disease is **increased** as aging.
- Aging is characterized by general **decline** of body systems' functions.
- The first 3 diseases that cause death in 65 yrs & above are (**1**) **heart**, (2) cancer, & (3) stroke diseases respectively.
- Cerebral atrophy shows up on CTs and MRI scans.
- Carotid sinus syncope occurs when there is an exaggerated (strong) vagal response (parasympathetic) to carotid sinus stimulation.
- Sensory neural hearing loss is due to damage to the hair cells of the organ of Corti.
- There is **accumulation** of amyloid plaques between (neurons) in the brain of Alzheimer's patient. However, in a healthy brain, these protein fragments are **broken down and eliminated**.

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QUESTIONS

Q1:A
Q2:A
Q3:A
Q4:B

Q1: In aging person there is weight loss due to:

A) loss of muscle & bone mass
B) Loss of fat.
C) Loss of water.

Q2: Which one of the following is seen in the late phases of Alzheimer's disease?

A) Motor and sensory abnormalities**.**
B) Language deterioration.
C) Memory Impairment.

Q3: Which one of the following is the most common etiology of atrio-ventricular block in old people?

A) Carotid sinus hypersensitivity.
B) Inflammation of the A-V node.
C) Drugs.

Q4: Which one of the following is may be the only manifestation of a life-threatening illness in the older adult?

A) Dementia.
B) Delirium.
C) Amnestic disorders.

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THE END

If there are any Problems or Suggestions,
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THANK YOU