



CNS PHYSIOLOGY

- Text.
- Important
- Formulas
- Numbers
- Doctor notes
- Extra notes and explanation

Lecture
No. 23

« إن معي ربي سيهدين »

Aging and changes in the brain

Objectives:

1. Definition of aging and its consequences
2. Theories and terms used
3. Body changes in aging
4. Describe Important clinical conditions
5. Brain changes in aging
6. Memory changes in aging
7. Carotid hypersensitivity
8. Elaborate Geriatric syndrome

What is aging ?

- ▶ Aging is the progressive, universal decline first in **functional reserve** and then in **function** that occurs in organisms over time.
- ▶ Aging is not a disease; however, the **risk** of developing disease is increased, often dramatically, as a function of age.
- ▶ A Developmental issue. Healthy older persons are a resource for their families, their communities and economy”- WHO brasilia declaration on aging, July 1996.
- ▶ Scientists used to try to stop ageing but this is impossible so they found out ways for successful ageing.

Successful aging

Active engagement with life



Low probability of disease or disability



- High cognitive and physical function capacity
- If we develop these function by deep mental thinking, we will increase the number of neurons and arborization.

Category	Interval	ONLY IN MALES' SLIDES
Elderly – Young old	65 – 74	
Aged – The middle old	75 – 84	
Very Old – Oldest old	85+	

Aging terms

- ▶ **Universal aging:** age changes that everyone shares (ex: Grey hair and wrinkles)
- ▶ **Probabilistic aging:** age changes that may happen to some (ex: Type two diabetes).

Probabilistic from “probability”

- ▶ **Chronological aging:** degrees of aging (ex: 50 decades different from 80).
- ▶ **Social aging:** society's expectations of a person's behavior as he/she grows older.
- ▶ **Biological aging:** a person's physical state as he/she ages.

Aging theories

Aging theories

Hypothesis	How it may work?
Genetic يبدأ الاجينج فيها من اليوم الاول في حياتنا بحيث تتغير اداء بعض الجينات واعدادها	Aging is a genetic program activated in post-reproductive life when an individual's evolutionary mission is accomplished.
Oxidative stress We relate a lot of diseases that we don't know their etiology to oxidative stress that's why they invented a lot anti oxidants.	Accumulation of oxidative damage to DNA, proteins, and lipids interferes with normal function and produces a decrease in stress responses.
Mitochondrial dysfunction	A common deletion in mitochondrial DNA with age compromises function and alters cell metabolic processes and adaptability to environmental change.
Hormonal changes زي الناس الي تنام وتصحى بدري يكون معدل عمل الهرمونات عندهم ممتاز	The decline and loss of circadian rhythm in secretion of some hormones produces a functional hormone deficiency state.

Cont.

Telomere ¹ 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 and the over-activity of natural immunity create vulnerability to Infection.
Accumulation of senescent cells	Renewing tissues become dysfunctional through loss of ability to renew.

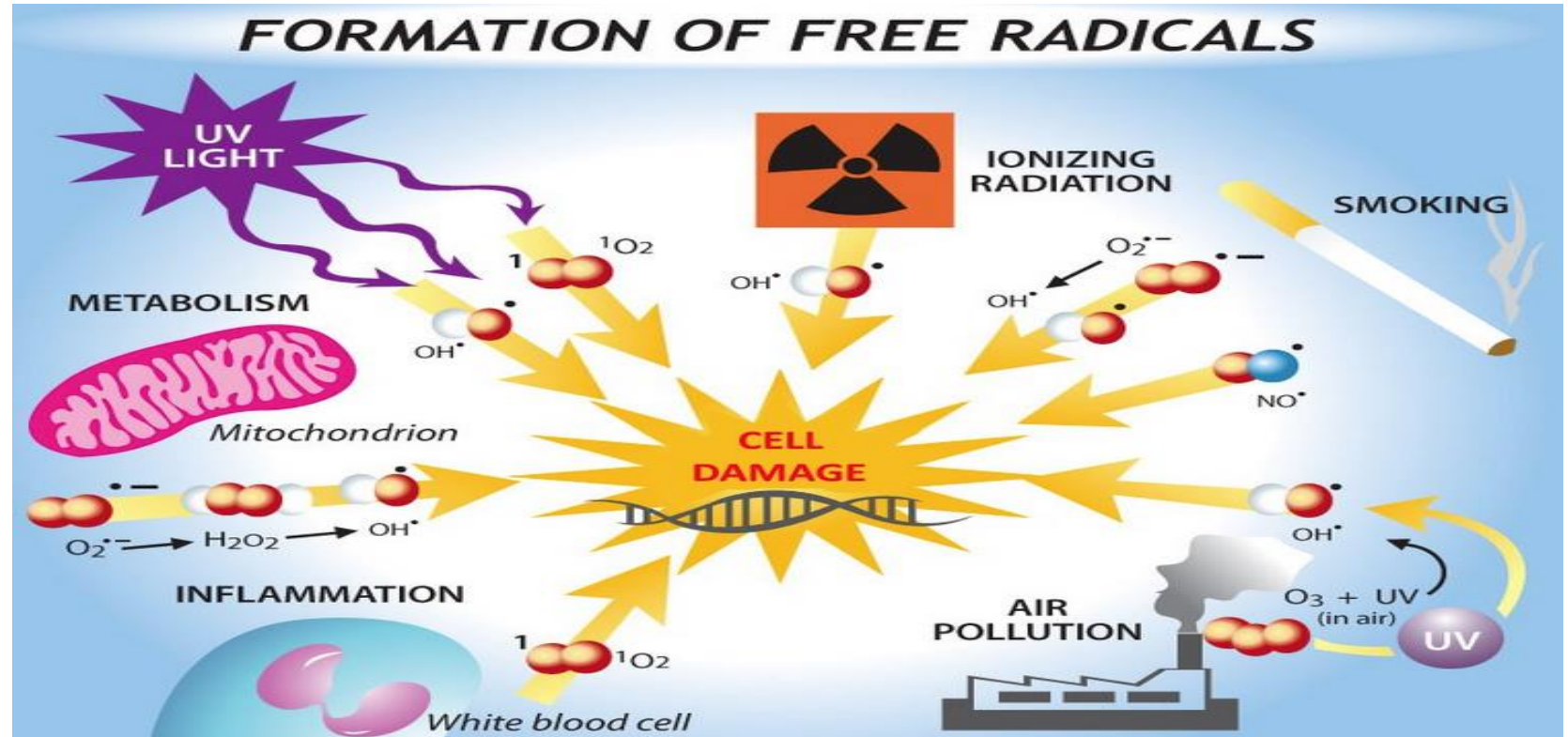
¹ The telomeres are special structures on the chromosome ends that are essential for providing protection from enzymatic end-degradation and maintaining chromosomal and genomic stability. This is the reason why adequate telomere structure (including the presence of telomere-binding proteins) remains pivotal for avoiding cellular dysfunction.

Doctors' notes

- ▶ Mitochondria uses its O_2 to oxidize food residues such as glucose and fatty acids to generate oxygen and at this level the oxygen free radical generate such as super oxide and hydrogen free radicals which will damage the protein and DNA and affect the cell function.
- ▶ Hormones have diurnal variation some are secreted at morning and others are secreted at night(during sleep).
- ▶ Exmample:
 1. Corticosteroids are secreted at morning.
 2. Melatonin is secreted at night.
- ▶ Aging disturb the secretion of biological hormones.

Oxygen free radicals (FR) and reactive oxygen species (ROS) resources

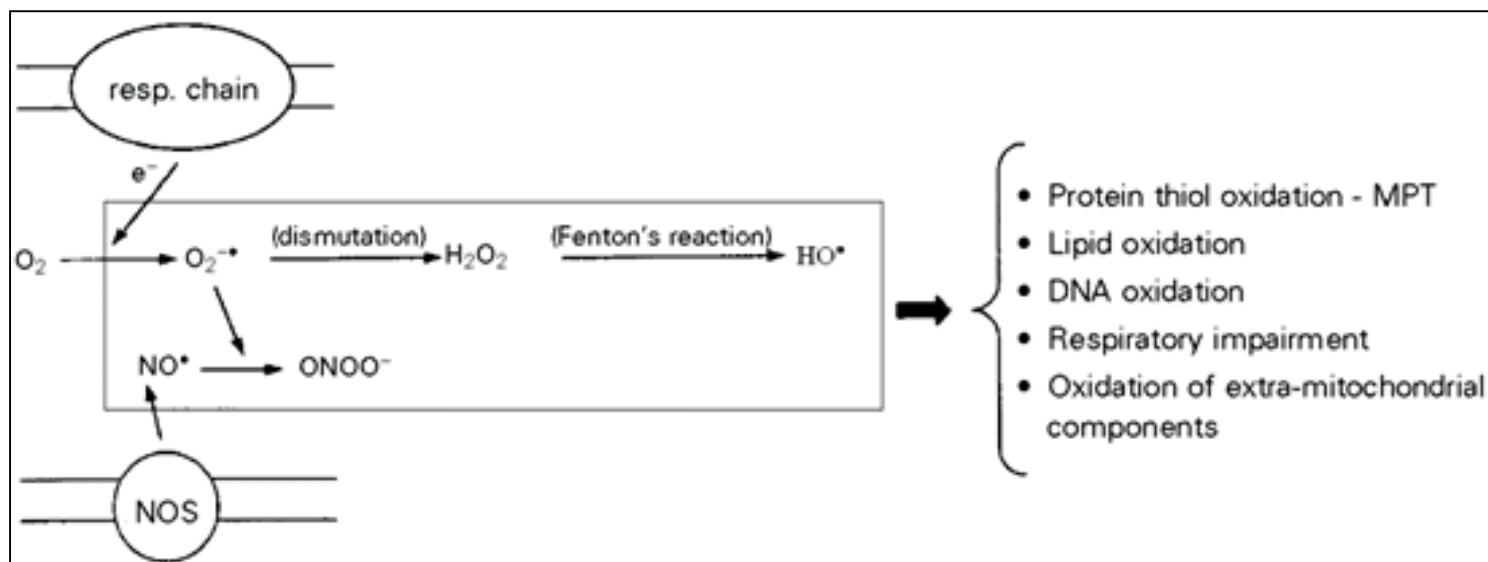
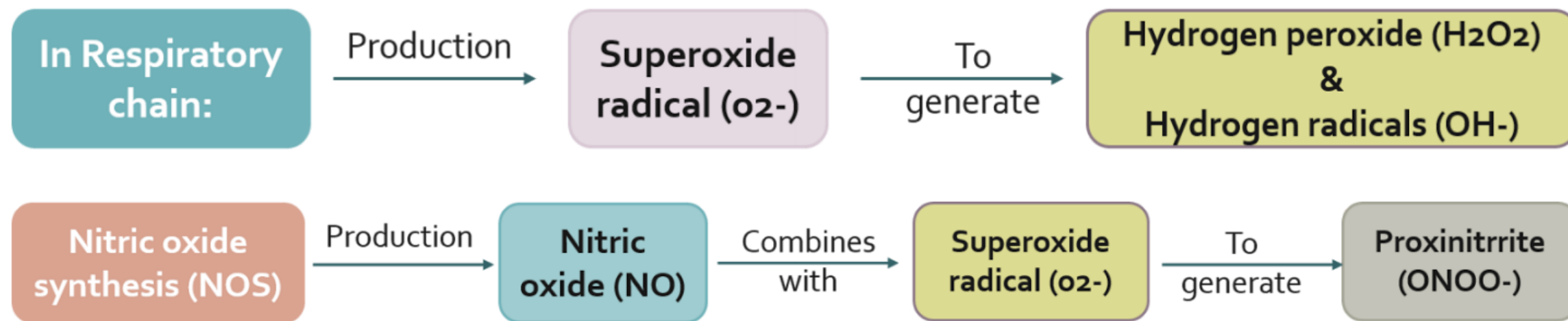
1. Cell metabolism.
2. Environment. (Radiation)
3. Lifestyle. (Smoking)
4. Pollution.
5. Diet.
6. Infection.



- ▶ Oxygen free radicals and reactive oxygen species (ROS) come from many sources.
- ▶ The most important for the cell is likely to be FR generated from oxidative phosphorylation in the mitochondrion respiratory chain.

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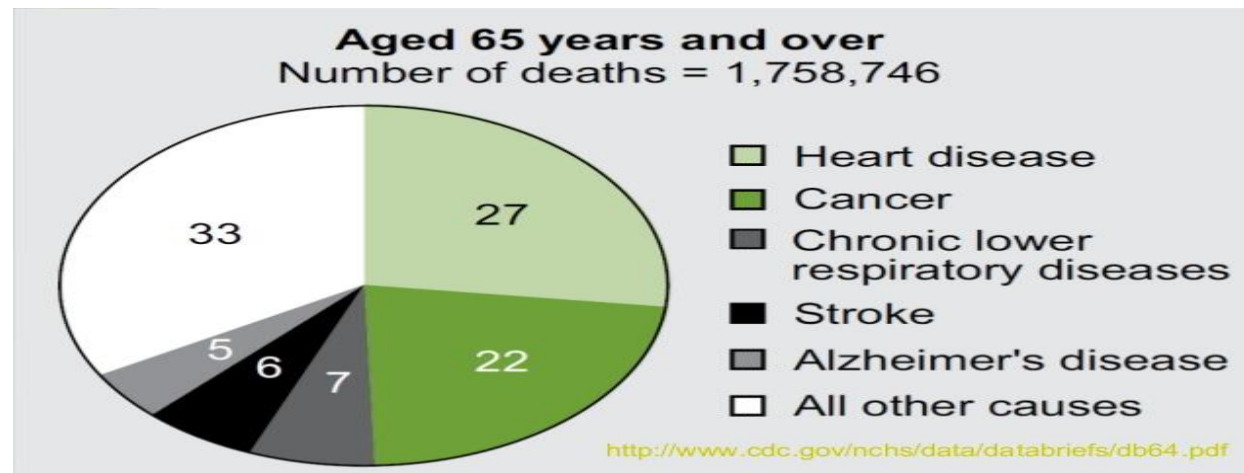
Mitochondria produce ROS



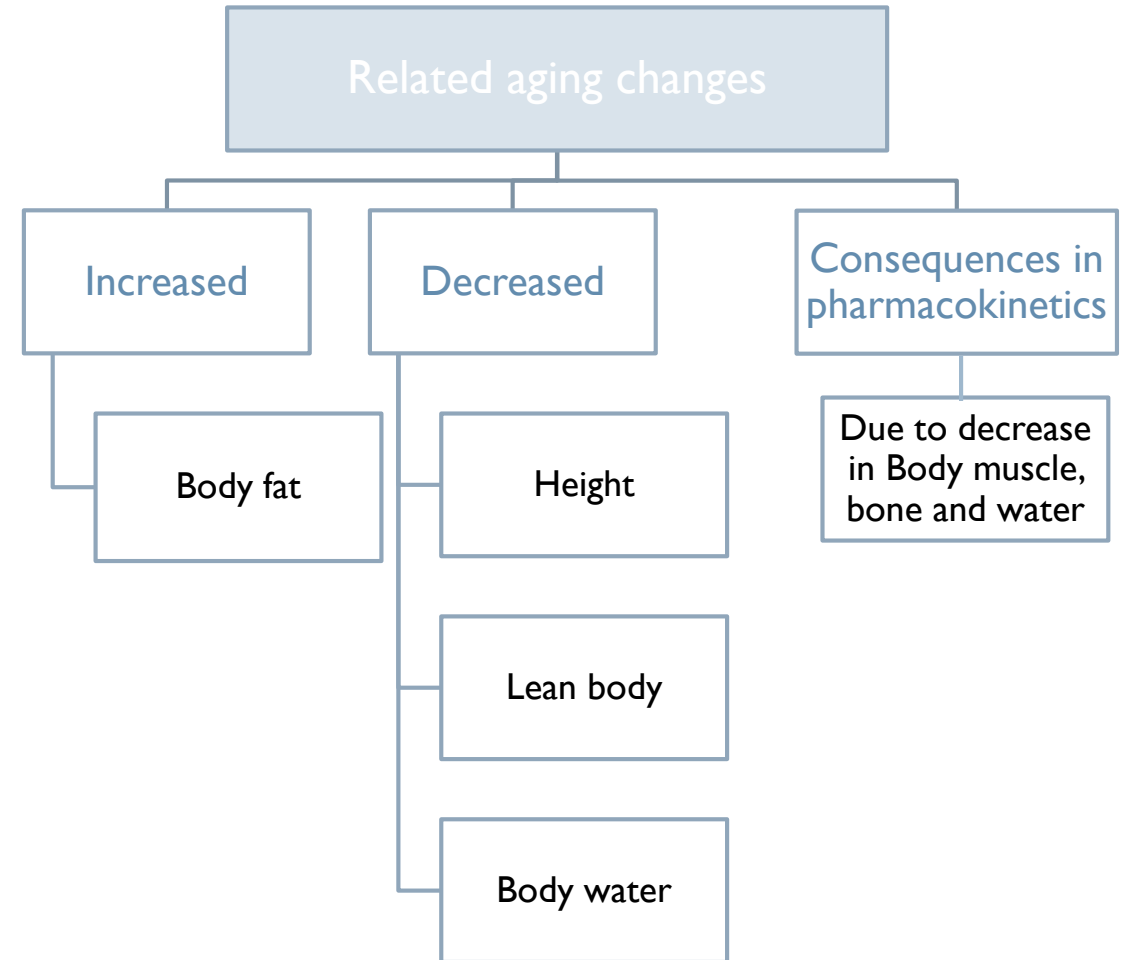
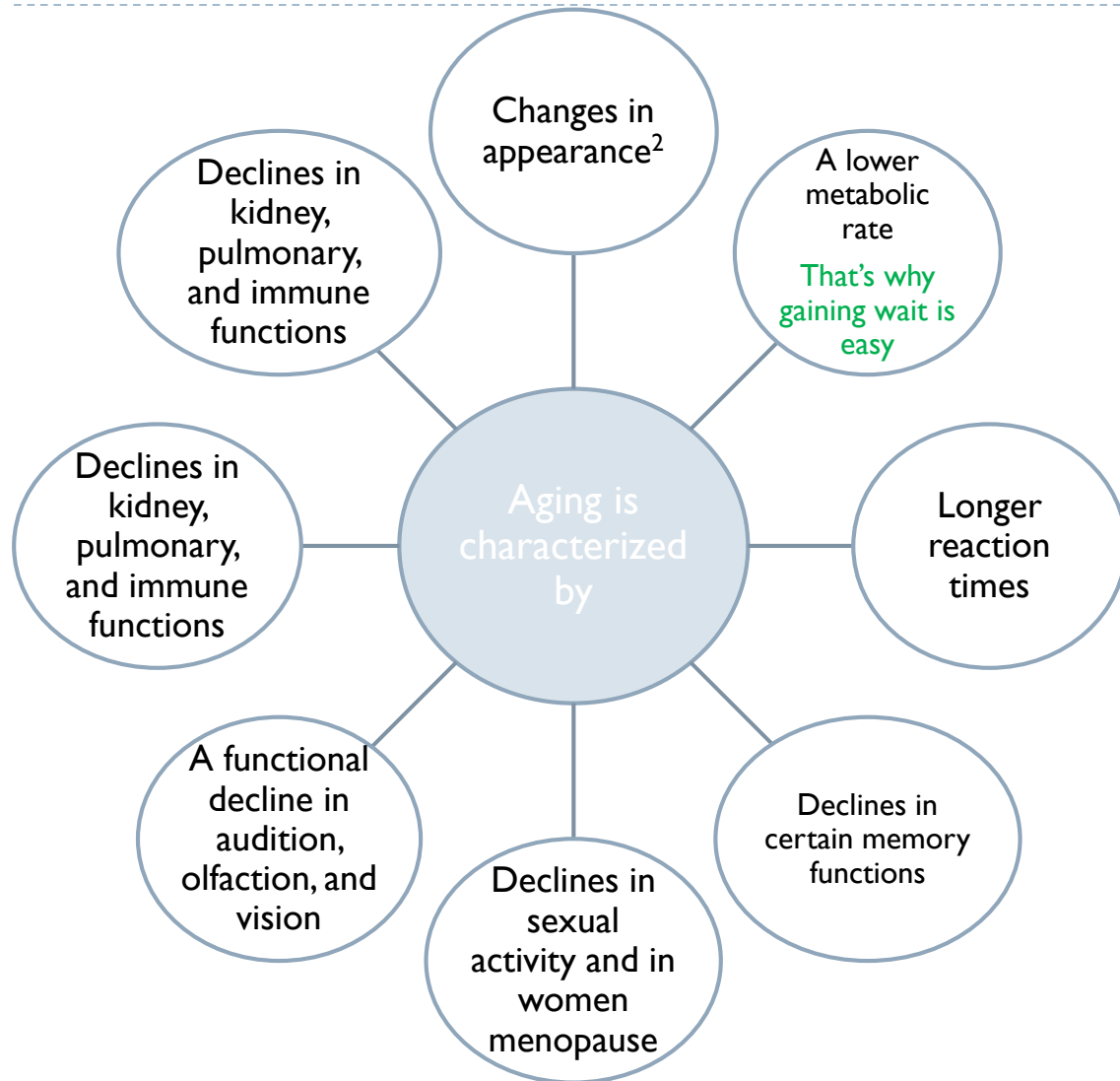
- The respiratory chain produces superoxide radicals which generate peroxynitrite in the end after series of reactions.
- All these ROS may cause mitochondrial and cellular damage if present in excess. Vitamin E, Vitamin C and citation in green tea are factors that help increase antioxidants which will degrade oxygen free radicals.

Leading causes of death age 65+ “medical diagnoses”

Heart disease	32%
Cancer	22%
Stroke	8%
Chronic respiratory	6%
Flu/pneumonia	3%
Diabetes	3%
Alzheimer's disease	3%



Aging characterization and changes



▶ 11 ² gradual reduction in height and weight loss due to loss of muscle & bone mass.

Aging in nervous system

- Pink color refer to (ONLY IN FEMALES' SLIDES)
- Brown color refer to (ONLY IN Males' SLIDES)

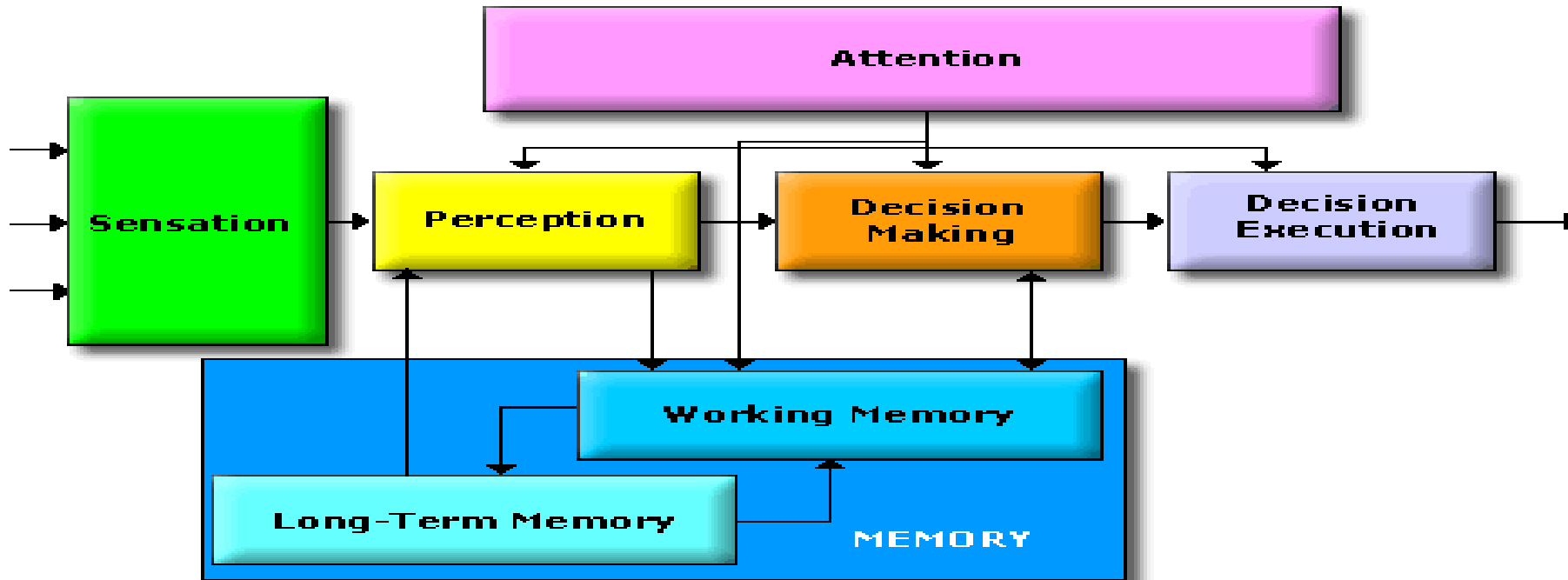
Aging in nervous system	
Changes	consequences
Decreased brain weight	Drug toxicities
	Delirium
Decreased Cerebral blood flow	Altered mood لذلك يكون عرضه اكثر لضعف في الذاكرة بسبب قلة السييريال بلود فلو Decreased IQ scores
Decreased Memory Just the short term memory بس الاشياء القديمة يقدر يتذكرها	Decreased IQ scores
Alteration in CNS neurotransmitters	“Benign senile forgetfulness”
Decreased vibratory sense	Increased postural instability
	Altered gait
	Falls, accidents

Aging in nervous system (structure-function related)

Structure	Regional function
<p>Basal ganglia</p> <p>The iron that is accumulated in basal ganglia comes from the destruction from the RBCs that happens every day (this iron suppose to go to the iron storage in).</p>	<p>Becomes bright in appearance due to iron accumulation.</p>
<p>Subarachnoid space</p>	<p>Increase in size due to brain shrinkage.</p>
<p>Hippocampus</p>	<p>Reduction in size due to cell loss in the structure.</p>
<p>Ventricles</p>	<p>Increase in size due brain shrinkage.</p>
<p>Matter</p>	<p>Reduction in size due to neuronal atrophy in the deep brain.</p>

Cognitive changes in aging (mental processing)

- ▶ Attention and Sensation are both included in three things : **perception** , **decision making** and **decision execution**. And all these can be **affected** or reduced with **aging**.
- ▶ There are two types of memories known as:
 1. Long-term memory.
 2. Short-term memory: working memory.



مثال لطيف:
مثل لما صديقتي تلمسني
واحس ان اللمسة للمسة حنينة
والتفت واتذكر انها صديقتي من
١٠ سنوات وينتج عني ردة فعل
اني احضنها مثلاً، ونقيس عليها
اشياء كثير مثل لما نمسك
حاجة ساخنة فإذا صار فيه
خطأ في العملية راح ينتج تأخير
في ردة الفعل او خطأ في الفعل
نفسه.

Nervous system changes

What happens to the nervous system when we get older?

- ▶ Aging leads to increased cerebral amyloid.
- ▶ 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.
- ▶ Loss of RNA (messenger and transcription) but not DNA.
- ▶ Loss of lipids, and lipid turnover rate, and a decrease in catabolism and synthesis.
- ▶ Neuronal loss is normal in the aging brain but the ability to learn remains generally unchanged.
- ▶ There is loss of dendritic arborization³.
- ▶ Recall memory is affected more than cognitive function in normal aging.
- ▶ Cerebral atrophy shows up on CTs and MRI scans.
- ▶ Reduced Sympathetic nervous system activity.
- ▶ Reduced Neurotransmitter levels. Ex: Dopamine, Serotonin, Glutamate (Intellectual functioning defined as “Stored” memory increases with age Problem solving skills increase with age).
- ▶ Changes in sleep patterns.
- ▶ Abnormalities in EEG tracings.
- ▶ Increased risk of stroke.
- ▶ Lowered seizure threshold.

لذلك نقدر نتعلم ايا كان عمرنا لكن المشكلة هي مشكلة الذاكرة
وليست القدرة
على التعلم

So we have to differentiate between cognitive
function and memory impairment

▶ 15³ the communication between different neurons will decrease.

Geriatric⁴ syndromes

- ▶ Dementia and delirium
- ▶ Falls
- ▶ Urinary incontinence
- ▶ Pressure ulcers
- ▶ Functional decline

Dementia and Delirium

Dementia and Delirium	
Dementia	Delirium
<ul style="list-style-type: none">• Syndrome of progressive decline in which multiple intellectual abilities deteriorate , causing both cognitive and functional impairment. <p>خرف يعني الفنكنشين حقت المخ متعطلة وتتبعها تعطل في الاعضاء</p>	<ul style="list-style-type: none">• An acute state of confusion.• It may be the only manifestation of a life-threatening illness in the older adult. e.g. infection, Drugs.• May be because of a cerebral circulation dysfunction (e.g. cerebral stroke). <p>يعني فجأة يفصل ويسألك انت مين او انا وين ؟</p>

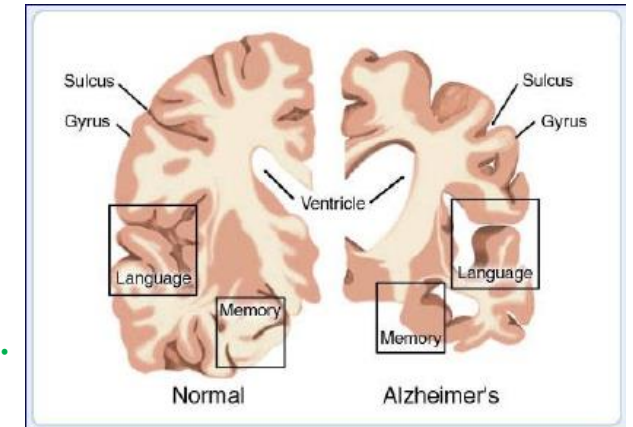
Alzheimer's disease

- ▶ 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 (loss of vocabulary and expressions).
3. Visuospatial deficits (Difficulties in identifying directions and shapes circle, square).

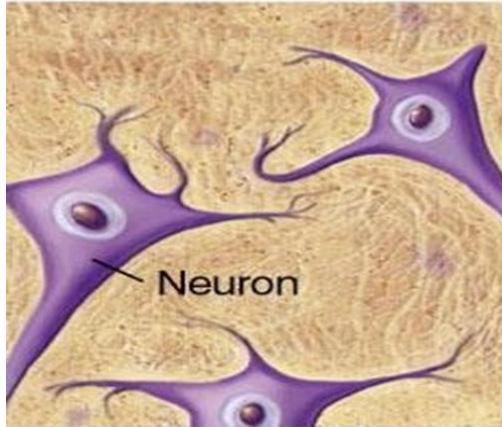
يعني مشكلة في الاتجاهات والاشكال وعلاقة الاشياء ببعضها لذلك كثير منهم يطلع من البيت وما يعرف يرجع



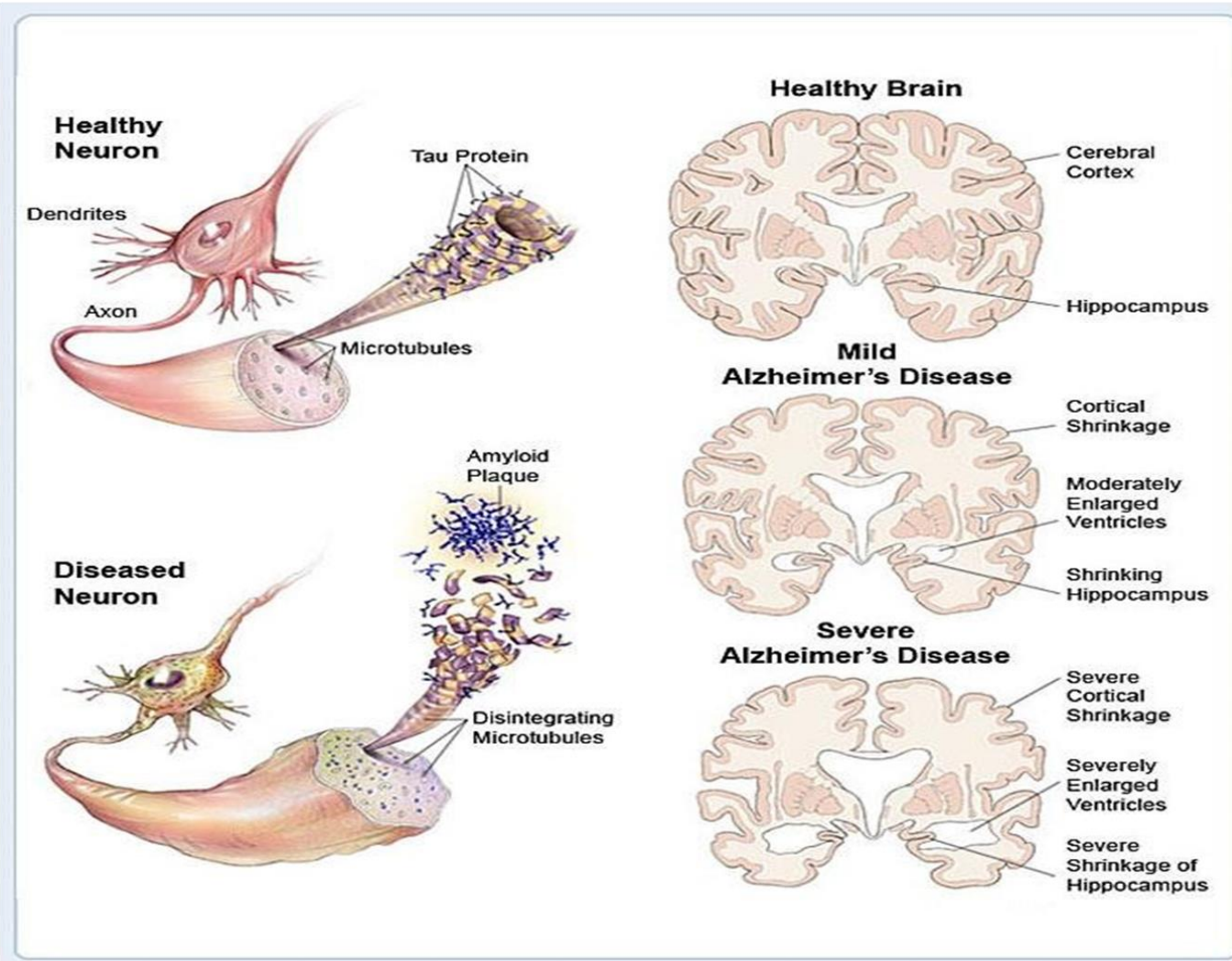
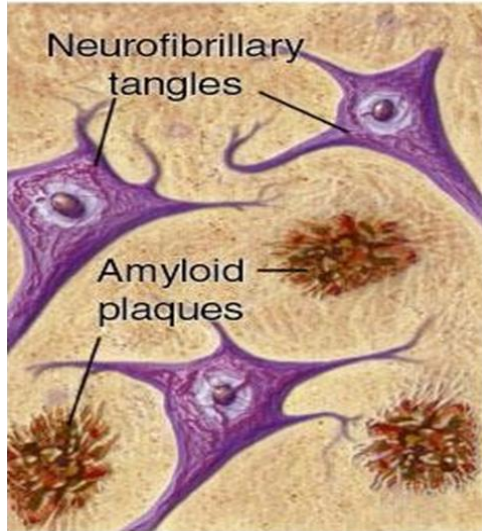
- ▶ **Motor and sensory abnormalities, gait disturbances, and seizures are uncommon until the late phases of the disease.**

Cont.

Normal



Alzheimer's



لاحظوا كيف حجم
الدماغ يقل مثل
White matter and
cortex

Amyloid plaques

- ▶ It is hallmark of Alzheimer's disease .
- ▶ There is accumulation of amyloid plaques between nerve cells (neurons) in the brain.
- ▶ 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).
- ▶ In a healthy brain, these protein fragments are broken down and eliminated. In Alzheimer's disease, the fragments accumulate to form hard, insoluble plaques.
- ▶ It is normal to find amyloid plaques in the brain of a person who is 80 but when you see it in a person who is 40-50 this would be due to Alzheimer's disease.

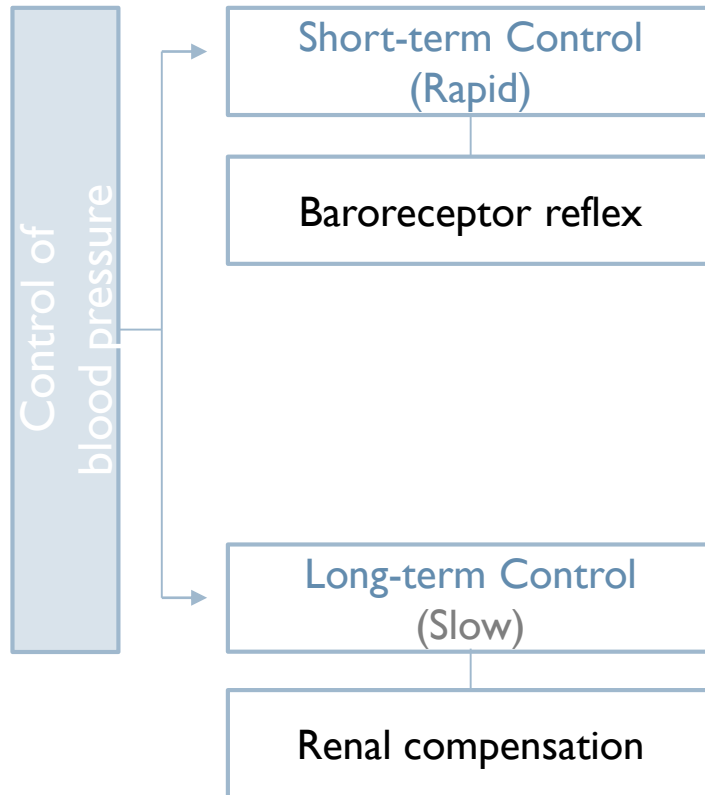
Neurofibrillary tangles

- ▶ 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.

يعني تشابكات بين النيوروفايبرز

Control of blood pressure

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Baroreceptor reflex Cont.

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- ▶ Quick operation (within few second).
- ▶ Mediated through autonomic nerves.
- ▶ Adjusts CO & TPR to restore BP to normal.
- ▶ Influence heart & blood vessels.

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

- ▶ Vasodilatation
- ▶ Marked bradycardia
- ▶ Fainting or syncope

Carotid sinus hypersensitivity

- ▶ **The "Carotid sinus syncope" occurs:** when there is an exaggerated vagal response to **carotid sinus stimulation**.
- ▶ **Carotid sinus hypersensitivity is provoked by:**
 1. wearing a tight collar,
 2. looking upwards or turning the head.
- ▶ **Carotid sinus syndrome** occurs in the elderly and mainly results in **bradycardia**. (Vasodilation)
- ▶ Most common etiologies of **atrioventricular block**.
- ▶ **Do not massage** both carotids simultaneously.

يصير فيه ديفيكت في الباروري سيبتر لذلك يتكون كاروتيد ساينس

- ▶ ***FROM 435**
 - ▶ Carotid sinus hypersensitivity (CSH) is an exaggerated response to carotid sinus baroreceptor stimulation. It results in dizziness or syncope from transient diminished cerebral perfusion. Although baroreceptor function usually diminishes with age, some people experience hypersensitive carotid baroreflexes. For these individuals, even mild stimulation to the neck results in marked bradycardia and a drop in blood pressure.

Vision

- ▶ **Loss of ability** to see items that are close up begins in the 40's (Presbyopia).
- ▶ Size of pupil grows **smaller** with age: focusing becomes less accurate.
- ▶ Pupil less sensitive to light.
- ▶ Opacification of lens (Cataract).
- ▶ Lens of eye **yellow**s making it more difficult to see **red** and **green** colors.
- ▶ Sensitivity to glare **increases**.
- ▶ Night vision not as acute.
- ▶ Arcus Senilis.

Hearing

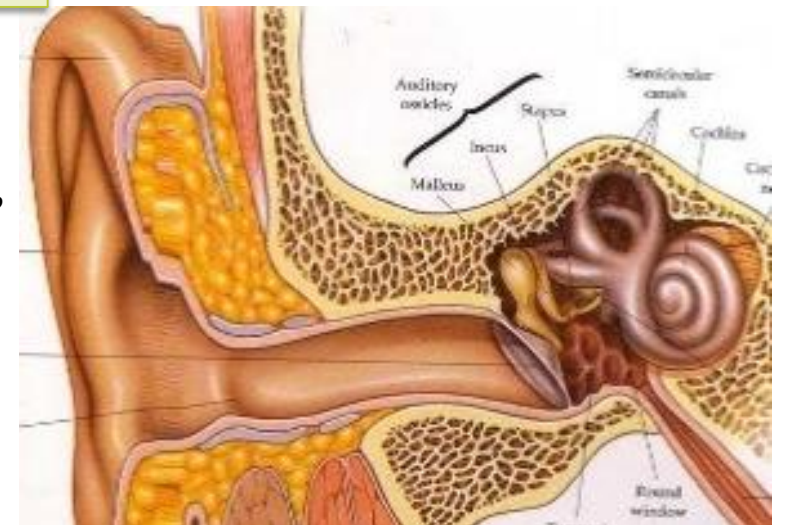
- ▶ **Presbycusis:** Part of normal aging (35% people over 60 years of age have bilateral, symmetric & progressive impairment for high pitched sounds sensorineural hearing loss).
- ▶ **Cerumen impaction:** is one of the most common reversible cause of conductive hearing loss in elderly.

ONLY IN MALES' SLIDES

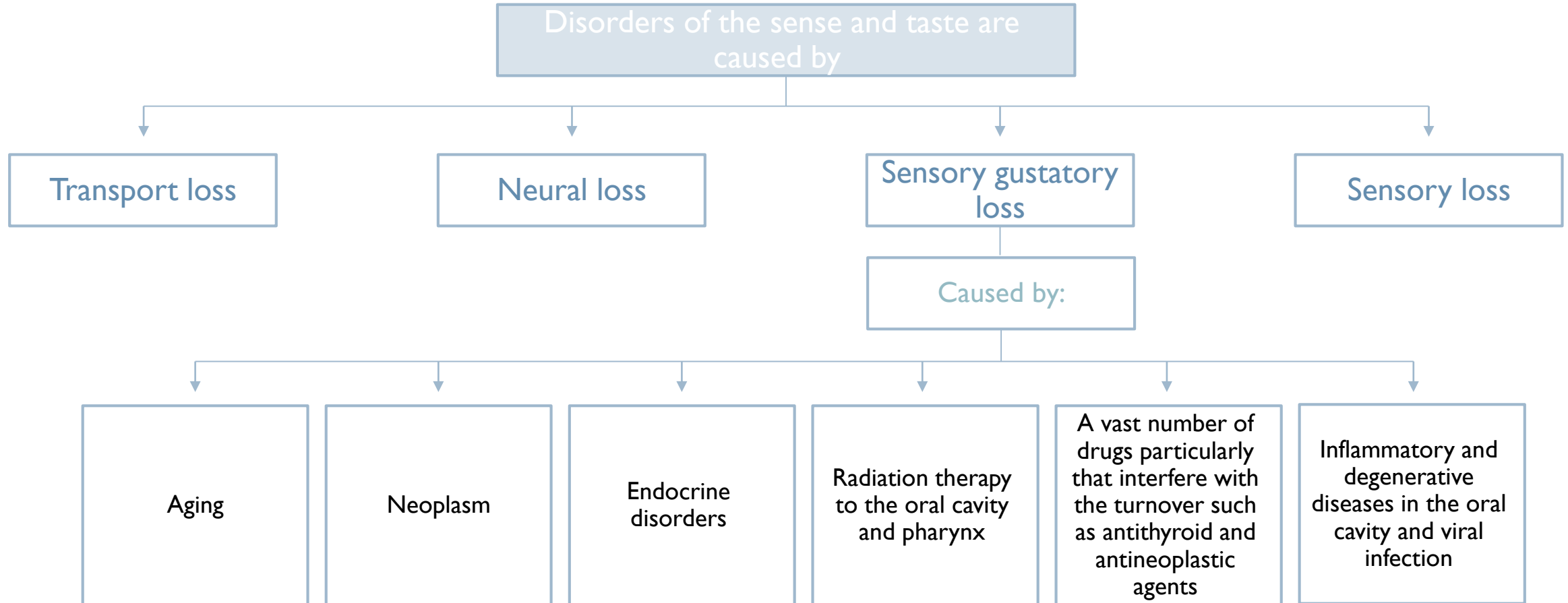


- ▶ **Sensorineural hearing loss:**

Damage to the hair cells of the organ of Corti may be caused by intense noise, viral infections, ototoxic drugs (e.g., salicylates, aminoglycoside antibiotics, furosemide and chemotherapeutic agents such as cisplatin), fractures of the temporal bone, meningitis, cochlear otosclerosis, Ménière's disease and Aging.



Disorders of the sense and taste



Pain and sense of touch

- ▶ With age, skin is not as sensitive as in youth.

- ▶ **Contributing factors include:**
 1. Loss of elasticity
 2. Loss of pigment
 3. Reduced fat layer

- ▶ **Safety Implications:**
 1. Lessened ability to recognize dangerous levels of heat
 2. Lessened ability of body to maintain temperature
 3. Tendency to develop bruises, skin tears more easily

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 between the ages of **40** and **70**, **52%** of responders reported some degree of ED. Complete ED occurred in **10%** of respondents, moderate ED occurred in **25%**, and minimal ED in **17%**.

Sleep Patterns

- ▶ It tends to become more fragmented, with more awakenings during the night.
- ▶ Total sleep time stays the same or is slightly decreased (6.5 to 7 hours per night).
- ▶ The transition between sleep and waking up is often abrupt, which between sleep and waking up is often abrupt, which makes older people feel like they are a lighter sleeper than when they were younger.

- ▶ Three or four awakenings each night.

- ▶ The proportion of slow wave sleep.



- ▶ Decreases relative to total sleep time, but the proportion of sleep that is REM sleep ↓ or unchanged.

Brief geriatric assessment instruments

مو مطلوب حفظ ال
بس اقرؤها للاحتياط

Domain	Instrument	Comment
Cognition	-	-
Dementia	MMSE ⁶	Widely studied and accepted
	Timed time and change test	Sensitive and quick
Delirium	CAM ⁷	Sensitive and easy to apply
Affective disorder	GDS ⁸ 5-question form	Rapid screen
Visual impairment	Snellen chart	Universally used
Hearing impairment	Whispered voice	No special equipment needed
	Pure tone audiometry	Can be performed by trained office staff

⁶ The Mini–Mental State Examination used extensively in clinical and research settings to measure cognitive impairment.

⁷ The Geriatric depression scale.

⁸ Geriatric depression scale.

Cont.

Domain	Instrument	Comment
Dental health	DENTAL ^C	-
Nutritional status	Weight loss of >4.5 kg (>10 lb) in 6 months or weight	-
Gait and balance	"Timed Get Up and Go" test	Requires no special equipment

Thank you!

اعمل لترسم بسمة، اعمل لتمسح دمة، اعمل و أنت تعلم أن الله لا يضيع أجر من أحسن عملا.

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QUIZ



اقتراحات وشكاوي

References:

- Females' and Males' slides.
- Guyton and Hall Textbook of Medical Physiology (Thirteenth Edition.)