Physiology 435 team

AGING AND CHANGES IN THE BRAIN

Objectives:

- **Definition** of Aging.
- **Theories** and **terms** Used.
- **Body** Changes in Aging.
- **Brain** Changes in Aging.
- **Memory** Changes in Aging.
- **Carotid Hypersensitivity.**

سلايدات الطلاب والطالبات موجودة بهالمحاضرة :)!

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Color index: Important - Further explanation - Doctors Notes - Numbers.

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Aging :

The science of aging (Duration 2:05)

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.

الكبر موب مرض ولكن احتمالية ان الشخص يصاب بالأمراض بتزيد مع زيادة العمر.

"A Developmental issue. Healthy older persons are a resource for their families, their communities and economy"- WHO brasilia declaration on aging, July 1996.

كبار السن ثروة لأنهم ممكن يسوون بعض الأعمال اللي صغار السن مايقدرون يسوونها.. مثل الزراعة والعناية بالأطفال وبعض الحرف التراثية.

Successful aging : happens if there was :

Active engagement with life. — **Low probability of a disease or disability.** — **High cognitive and physical function capacity.**

التقدم بالعمر لا يعتبر مرض طبعًا , وإنما حالة فسيولوجية طبيعية لابد من حدوثها .. لكن كبار السن يختلفون في صحتهم وقوتهم وهذا ما نسميه بـ successful ageing بحيث إن الكبير بالسن يعيش بشكل صحي وأفضل.

Aging terms :

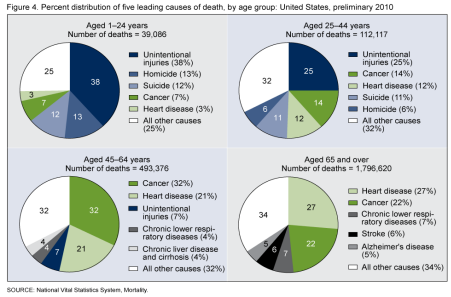
- **Universal Aging :** Changes **everybody** shares.(e.g. Grey hair and wrinkles)
- **Probabilistic Aging :** Changes that **may** happen to some. (eg type two diabetes).
- **Chronological Aging : Degrees** of aging. (eg 50 decades different from 80).
- **Social Aging : Society's expectations** of a person's behavior as they grow older.

يعني تأثير المجتمع , مثلاً في المجتمعات العربية ممكن الوحدة تصير جدة وعمرها لم يتجاوز الـ35 فتحس نفسها عجزت , مع لو أنها أجنبية ممكن تكون ما تزوجت للحين.

- **Biological Aging : Physical state** of a person when he ages.

Leading causes of death age 65+(Medical Diagnoses):

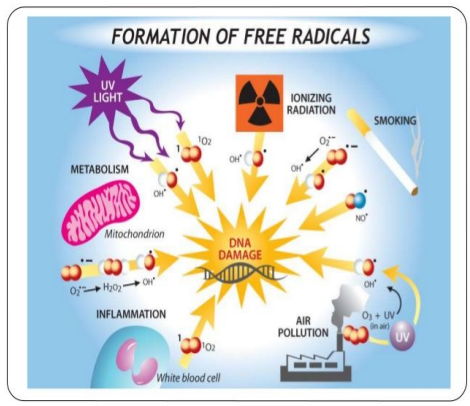
- Heart diseases 32%
- **Cancer 22%**
- **Stroke 8%**
- Chronic respiratory 6%
- Flu/Pneumonia 3%
- Diabetes 3%
- Alzheimer's 3%



Aging theories :

ليش نكبر ؟ هالسؤال الخطير خلا العلماء يطلعون بأكثر من نظرية تجاوب على هالسؤال

Hypothesis :	How it may work :
Genetic	Aging is a **genetic program** activated in post-reproductive life when an individual's evolutionary mission is accomplished. يعني فيه علماء قالوا إن التقدم في العمر وسبب فقدان الكثير من وظائف الجسم الطبيعية يعتبر شيء متوارث وموجود بالجينات كمصير للإنسان.
Oxidative stress	Accumulation of **oxidative damage** to DNA, proteins, and lipids **interferes** with normal function and produces **a decrease** in stress responses. الأدوية والكريمات المستخدمة للتجاعيد وعلامات التقدم بالسن قاعدة تشتغل على هذي النظرية.
Mitochondrial dysfunction	A common deletion in **mitochondrial DNA** with age **compromises** function and **alters** cell metabolic processes and adaptability to environmental change. المايتوكوندريا هي مصنع الطاقة بالخلية، فحدوث أي مشكلة بالحمض النووي الخاص فيها ممكن انه يؤثر على وظائف الخلية ويغير فيها ويساهم في عملية الـaging
Hormonal changes	The decline and loss of **circadian rhythm** in secretion of some hormones produces a **functional hormone deficiency state**. بعض الهرمونات لهم circadian rhythm بحيث ان بعضهم ما ينتج الا الصباح وباوقات بدري (مثل الكوتريكوستيرودز) وبعضهم ما يفرز إلا بأوقات متأخرة.. فلو صارت لخبطة بهال circadian rhythm ممكن انه يؤدي الى مشاكل بالهرمونات.
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 *overactivity of the natural immunity* create vulnerability to Infection.
Accumulation of senescent cells	Renewing tissues become **dysfunctional** through loss of ability to renew. الخلايا العجوزة "اللي تشيخ" المفروض ان الشخص يتخلص منها علشان ماتكون عبء على الـtissue اللي هي فيه بحيث انها تاخذ من طاقة الخلية وتشكل جزء منها.. هذي النظرية تقول ان الـaging ماهو الا نتيجة ناتجة عن تراكم هالخلايا



OXYGEN free radicals (FR) and reactive oxygen species (ROS) resources :

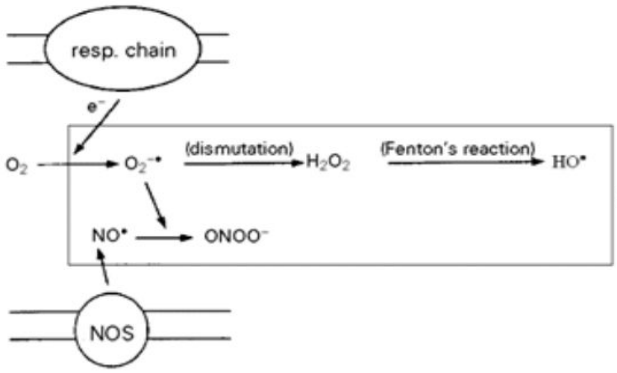
1. **Cell metabolism.**
2. **Environment. (Radiation)**
3. **Lifestyle. (Smoking)**
4. **Pollution.**
5. **Diet.**
6. **Infection.**

Mitochondria produce ROS:

[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.

In Respiratory chain: → Production → **Superoxide radical (o2-)** → To generate → **Hydrogen peroxide (H2O2) & Hydrogen radicals (OH-)**

Nitric oxide synthesis (NOS) → Production → **Nitric oxide (NO)** → Combines with → **Superoxide radical (o2-)** → To generate → **Proxinitrrite (ONOO-)**



Molecules damaged

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

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.

Aging related changes :

In general :

Decreased	**Height** - **Lean** body mass "muscle and bone mass" - **Body water** - **Metabolic** rate[2] - certain **memory** functions - **sexual activity** and in women menopause - **kidney**, **pulmonary**, and **immune** functions, declines in **exercise** performance, and multiple **endocrine** changes - Functional decline **audition**, **olfaction**, and **vision.**
Increased	**Body fat - Reaction times** "response time"
Consequence Changes in **pharmacokinetics** "due to decrease in the body muscles, bones, and water"	

Nervous system changes :

What happens to the nervous system when we get older?

- Neuronal loss is **normal** in the aging brain but the ability to learn remains generally **unchanged.**

تذكروا "اطلبوا العلم من المهد للحد" يعني الشخص قادر على انه يتعلم حتى وهو كبير.

[2] علشان كذا نشوف كبار السن ياكلون وممكن يزيدون بالوزن.

- There is loss of dendritic arborization the communication between the different neurons will decrease
- Recall memory is **affected more** than cognitive function in normal aging.

يعني فهم الشخص واستيعابه راح يكون قريب من الطبيعي يعني لا يزال قادر يفهمك ويعطيك رأي وقرار ، اللي راح تتأثر أكثر هي الذاكرة وقدرته على التذكر راح تقل بشكل ملحوظ.

- Cerebral **atrophy** shows up on CTs and MRI scans.
- **Lowered** seizure threshold يكون الشخص معرض للتشنجات بصورة أكبر
- **Reduced Sympathetic** nervous system activity.
- **Reduced Neurotransmitter** levels.
- Changes in sleep patterns.
- Abnormalities in EEG tracings.
- **Increased** risk of stroke.
- **increased cerebral amyloid.** Amyloid = protein fragments, the normal body should get rid of it but there is shortage in enzymes and proteins synthesis so it will remain.
- 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) ⟶ "lead to the loss of proteins" but **not** DNA
- **Loss** of lipids, and lipid turnover rate, and a **decrease** in catabolism and synthesis.

In nervous system:

Changes	Consequences
Decreased brain weight	Drug toxicities
	Delirium = هذيان
Decreased Cerebral blood flow	Altered mood مزاجه ملخبط ممكن أشياء بسيطة تسعده وممكن أشياء بسيطة تضيق صدره :)
Decreased Memory	Decreased IQ scores
Alteration in CNS neurotransmitters	"Benign senile forgetfulness"
Decreased vibratory sense إحساسه بال vibration	Increased postural instability
	Altered gait
	Falls, accidents

In nervous system (structure-function related) :

Structure	Regional function	Due to:
Basal ganglia	Becomes **bright** in appearance	Iron accumulation.

Subarachnoid space	**Increase** in size	Brain shrinkage.
Hippocampus	**Reduction** in size	Cell loss in the structure.
Ventricles	**Increase** in size	Brain shrinkage.
White Matter	**Reduction** in size	Neuronal atrophy in the deep brain.

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.

يعني ممكن تتكلم معه وقاعد تأخذ رأيه في شيء , هو بيفهمك وعارف ومتذكر كل حاجة لكن مو قادر يستوعب بسرعة زي قبل ويقرر ايش يسوي لكن بإمكانه يعطيك قرارات ممتازة , وممكن ما يكون شيء مُلاحظ لكن فعلاً التقدم في العمر يؤثر على اتخاذ القرارات وسرعة الادراك والاستيعاب.

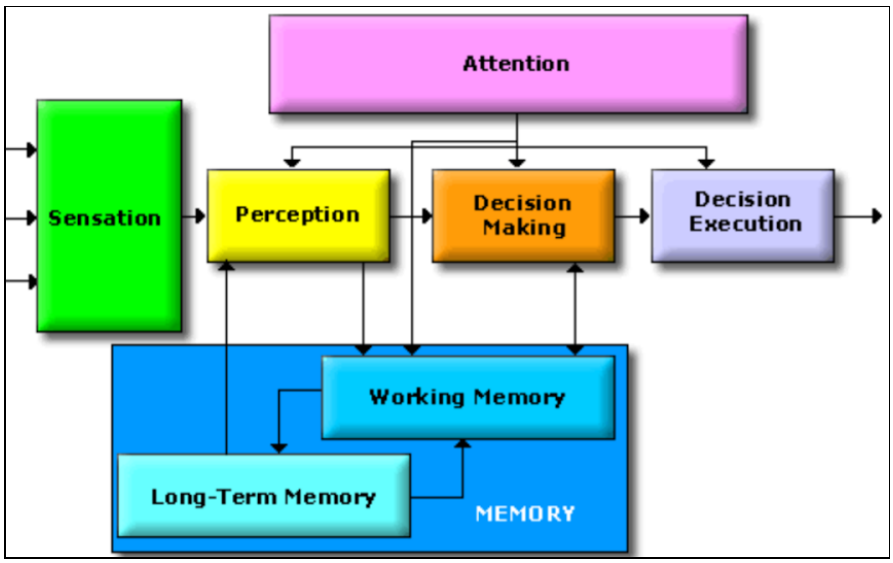
- Also the memories which is known as :

  1) long term memory.

وهذي ماشاء الله سليمة , وتلاحظونها في كبار السن ممكن يقولك قصة وهو عمره 10 سنين ويكون متذكرها زين.

  2) working memory = shorter memory.

وهذا النوع اللي يتأثر "تخزين الذكريات الحديثة" ممكن يسألك عن شيء وبعدها يرجع يسألك نفس السؤال.



Geriatric[3] Syndromes :

متلازمة الشيخوخة: أشياء شائعة تحدث لكبار السن.

★ **Dementia[4] and Delirium.[5]**

★ **Falls.**

★ **Urinary Incontinence.**

★ **Pressure Ulcers** التقرحات غالبا تحصل عندما يكون الشخص ملازم للسرير فتتكون من الضغط المستمر للمنطقة (يكون الضغط بين العظم والسرير)..

★ **Functional Decline.**

3 الشيخوخة

4 الخرف

5 هذيان

Dementia and Delirium:

Dementia	Delirium
Syndrome of **progressive decline** in which multiple intellectual abilities deteriorate[6], causing both cognitive and functional impairment. هنا كل وظائف الدماغ تبدأ تقل شوي بحيث كل سنة تقل أكثر من السنة التي قبلها (الخرف)	• An acute state of confusion • It may be the **only manifestation** of a life-threatening illness in the older adult. يصبح لديه في لحظة تو هان فلا يستطيع تمييز أي شيء (الساعة كم ، أين هو ، يتحدث مع شخص ثم فجأة يسأله انت مين؟) لكنه في فترة قليلة (acute) غالبًا يكون بسبب مشكلة في ال cerebral circulation for example cerebral stroke

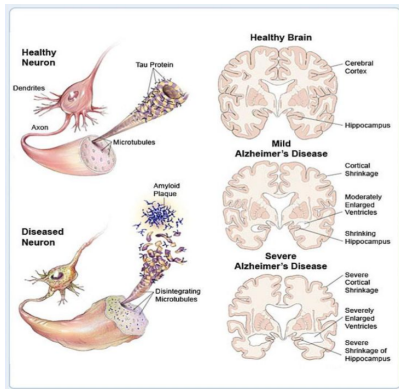
Alzheimer's Disease :

What is alzheimer disease?

- 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.

Incidence increases with age BUT it is not a normal sequence of aging!

Features :



1. **An amnesic type of memory impairment.**
   يبدأ ينسى (ناس، اماكن، عناوين،طرق) الخ
2. **Deterioration of language.** ينسون بعض الكلمات وبعض اللغات ينساها يسمعها بس مايعرف معناها
3. **Visuospatial deficits.** مثلا يطلع من البيت و لا يعرف طريق الرجوع اليه لانه نسى الاتجاهات

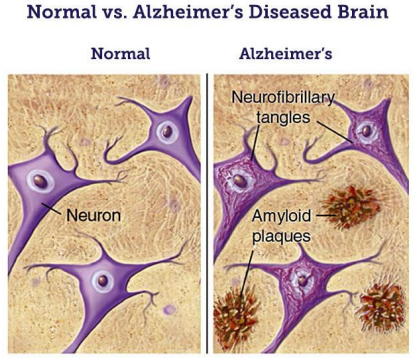
Motor and sensory abnormalities, gait disturbances, and seizures are uncommon until the **late phases of the disease**.

غالبا الزهايمر في بداياته يؤثر على الـsensory والـhigher brain functions ، اما الـmotor functions يؤثر عليهم في المراحل المتقدمة من المرض

Amyloid Plaques:

★ **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. The accumulation is the abnormal thing



6 become progressively worse.

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Cure in Mind. Cure in Sight.

- 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.

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**. Like the picture above

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Baroreceptors reflex and carotid sinus hypersensitivity:

Baroreceptors[7] reflex:

1	Quick operation (within few seconds). if we change our posture and sudden decrease in blood pressure happen the baroreceptors quickly return it to normal
2	Mediated through the autonomic nervous system.
3	Adjust the cardiac output and the peripheral resistance to restore the blood pressure to normal.
4	Influences the heart and the blood vessels.

★ Since the baroreceptors reflex are receptors and the receptors affected by aging so it will develop hypersensitivity or hyposensitivity „ here the problem is hypersensitivity for baroreceptors reflex so, if any pressure happened to the carotid sinus they will develop fall down or severe hypotension (severe vasovagal attack).

Carotid sinus hypersensitivity:

Background:

- 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.

★ **The "carotid sinus syncope" occur :** when there is an exaggerated vagal response to carotid sinus stimulation.

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7 **Baroreceptors** (or archaically, **pressoreceptors**) are sensors located in the blood vessels of all vertebrate animals. They sense the blood pressure and relay the information to the brain, so that a proper blood pressure can be maintained, and is excited by stretch of the blood vessel

★ **the carotid sinus hypersensitivity is Provoked by:**

1. **Wearing a tight collar.**
2. **Turning the head**

★ **Carotid sinus syndrome occurs in** the elderly and mainly results in bradycardia.

★ Most common etiologies of **atrioventricular block** .

★ **Advice**: Do not massage both carotids simultaneously. مثل لمن الرجل يحلق

Pressure on the carotid sinus (produced by the tight collar or carotid massage) lead to → marked bradycardia → vasodilatation → Fainting or syncope

Why bradycardia? As we get older the Sympathetic nervous system activity decreases → the parasympathetic nervous system is unaffected → bradycardia

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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.
- Lens of eye **yellows** making it more difficult to see **red** and **green** colors.
- Sensitivity to glare increases.
- Night vision not as acute.

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,quinine and its synthetic analogues, aminoglycoside antibiotics, loop diuretics such as furosemide and ethacrynic acid, and cancer chemotherapeutic agents such as cisplatin).
- Fractures of the temporal bone.
- Meningitis.
- Cochlear otosclerosis.
- Ménière's disease[8].
- Aging .

Disorders of the Sense of Taste, pain and touch:

Causes of taste disorders:

8 a disease of unknown cause affecting the membranous labyrinth of the ear, causing progressive deafness and attacks of tinnitus and vertigo.

Neural loss	Transport loss	Sensory loss
Causes of sensory gustatory lose:		
Aging	Neoplasms	Endocrine disorders
Radiation therapy to the oral cavity and pharynx	A vast number of drugs, particularly those that interfere with cell turnover such as antithyroid and antineoplastic agents	Inflammatory and degenerative diseases in the oral cavity and viral infections

Pain and Sense of Touch

- **With age, skin is not as sensitive as in youth**
  - **Contributing factors include:**
    1. Loss of elasticity. سبب ظهور التجاعيد
    2. Loss of pigment.
    3. Reduced fat layer.
  - **Safety Implications:**
    1. Lessened ability to recognize dangerous levels of heat.

ممكن انهم يلمسون شي حار ولايحسون بدرجة الحرارة العالية وتحترق اصابعهم

    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%

Brief geriatric assessment instruments:

Domain	Instrument	Comments
Cognition	-	-

Dementia	**MMSE**[9]	Widely studied and accepted
	Timed time and change test	Sensitive and quick
Delirium	**CAM**[10]	Sensitive and easy to apply
Affective disorders	**GDS**[11] **5-question form3**	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
Dental health	DENTAL^c	
Nutritional status	Weight loss of >4.5 kg (>10 lb) in 6 months or weight <45 kg (<100 lb)	
Gait and balance	**"Timed Get Up and Go" test**	Requires no special equipment

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For your own knowledge: What is Geriatrics or geriatric medicine?

- Geriatrics or geriatric medicine is a specialty that focuses on health care of elderly people.
- It aims to promote health by preventing and treating diseases and disabilities in older adults.
- There is no set age at which patients may be under the care of a geriatrician or geriatric physician, a physician who specializes in the care of elderly people. Rather, this decision is determined by the individual patient's needs, and the availability of a specialist.
- It is important to note the difference between geriatrics, the care of aged people, and gerontology, which is the study of the aging process itself.

★ References:

- 435 girls slides and notes.
- WebMD.
- Medscape.
- Wikipedia.

9 The Mini–Mental State Examination (MMSE) or Folstein test is a 30-point questionnaire that is used extensively in clinical and research settings to measure cognitive impairment.

10 The Geriatric Depression Scale .

11 Geriatric Depression Scale .