Aging under the microscop
Workshop SMSC
Dr Franck Girard, faculté des sciences et de Médecine, Fribourg
Octobre 2025

AGING is associated with:

- Tissue / organ structural changes
- Cell morphological / functional changes
- Wear and tear
- Increased cellular senescence

- Increased susceptibility to diseases
- Decreased resilience / abilty to cope with diseases
- Increased inflammation
- Decreased cell/organ function
- Disturbed extracellular matrix composition and functions

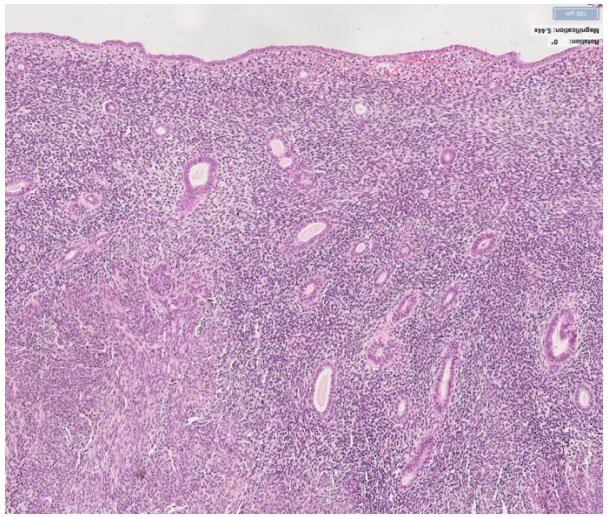
Utérus

Comparer les coupes : 195 (phase de prolifération)
196 (phase de sécrétion)
194 (phase inactive)

Involution progressive / aplasie de l'endomètre
Pas de figures mitotiques dans l'épithélium glandulaire
Stroma de l'endomètre plus compact
Myomètre moins épais et plus fibreux

Progressive Involution / Aplasie des Endometriums
Keine mitotischen Figuren im Drüsenepithel
Stroma des Endometriums kompakter
Myometrium weniger dick und faseriger

194



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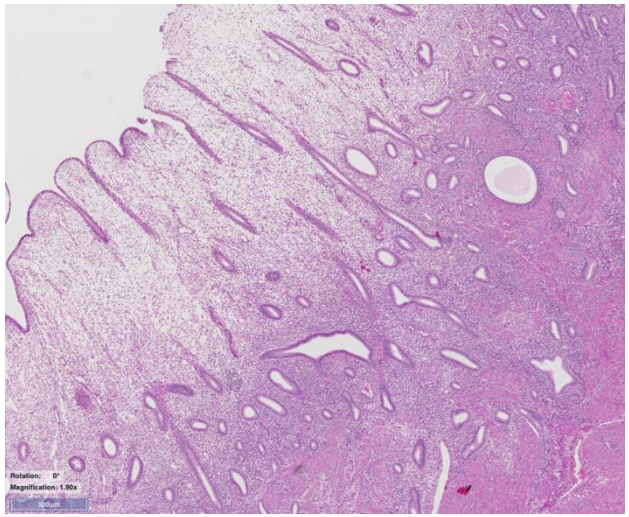

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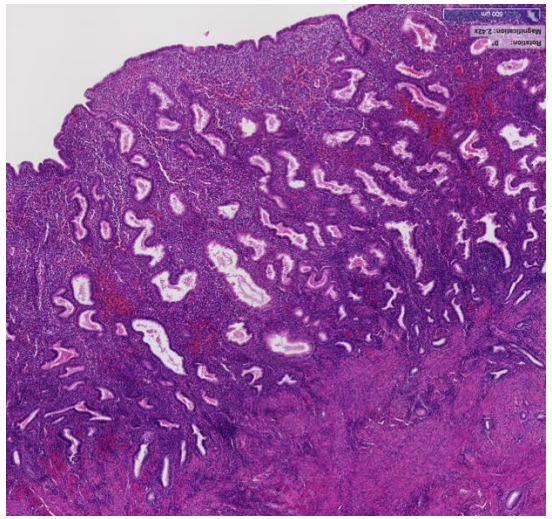

Images: Microscopie virtuelle, Unifr

Marti-Garcia et al.
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Reproductive Biology and Endocrinology

REVIEW Open Access

Age-related uterine changes and its association with poor reproductive outcomes: a systematic review and meta-analysis

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UTERUS

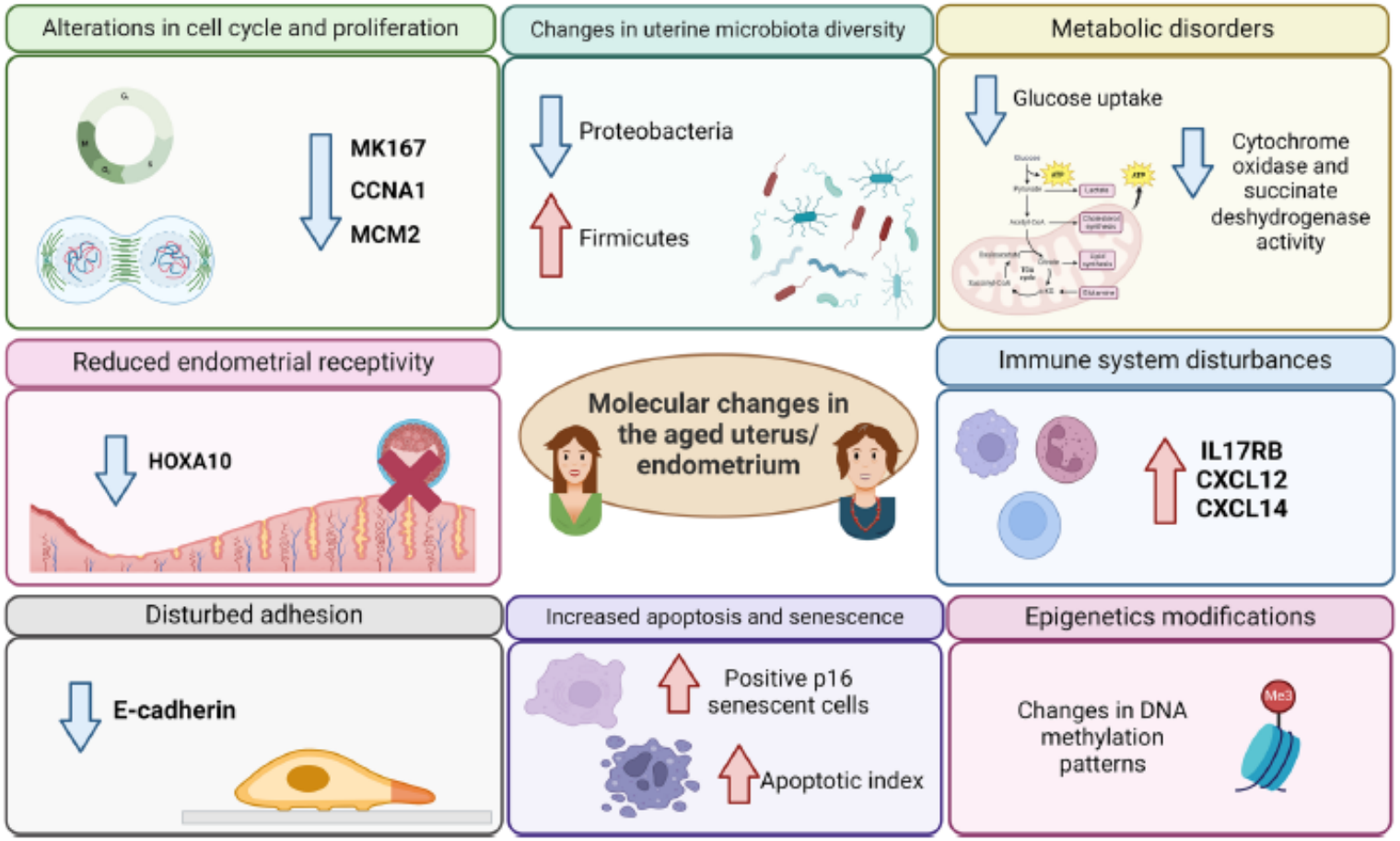


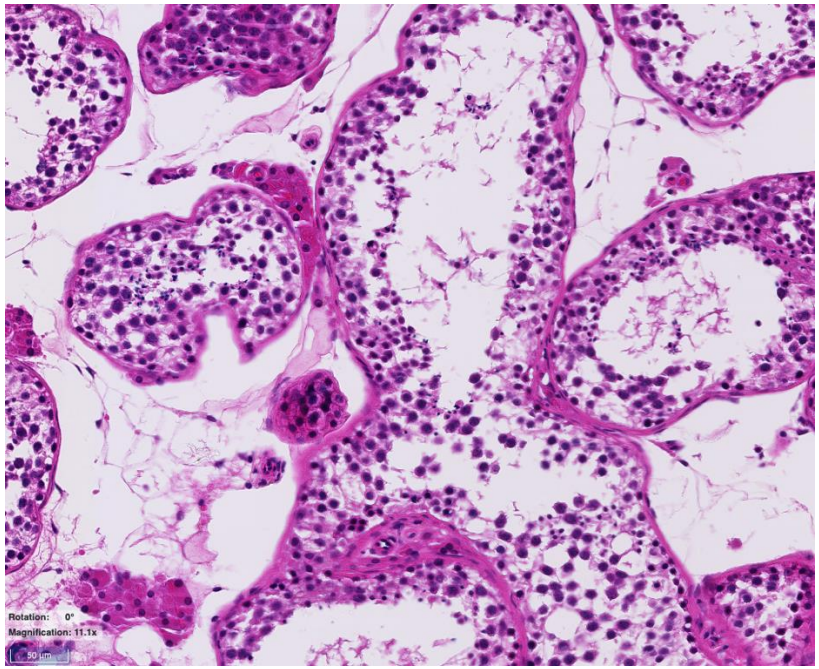
Fig. 3 Main findings of studies evaluating the effect of age on molecular mechanisms and functions of the endometrium. Summary of the main findings of studies evaluating age-related functions disruptions of the uterus or endometrium, including those reported by single and high throughput experimental approaches. MKI67 is related to regulation of chromosome segregation and mitotic nuclear division, CNNA1 is related to control of meiosis, and MCM2 is related to initiation of genome replication. CCNA1, cyclin-A1; CXCL12, CXC motif chemokine ligand 12; CXCL14, CXC motif chemokine ligand 14; HOXA10, homeobox A10 DNA-binding transcription factor; IL17RB, interleukin-17 receptor B; IL8, interleukin-8; LIF, leukemia inhibitory factor cytokine; MCM2, minichromosome maintenance complex component 2; MKI67, marker of proliferation Ki-67; MUC1, mucin 1; NS, not significant; PGR, progesterone receptor. Created with BioRender.com

Testicule

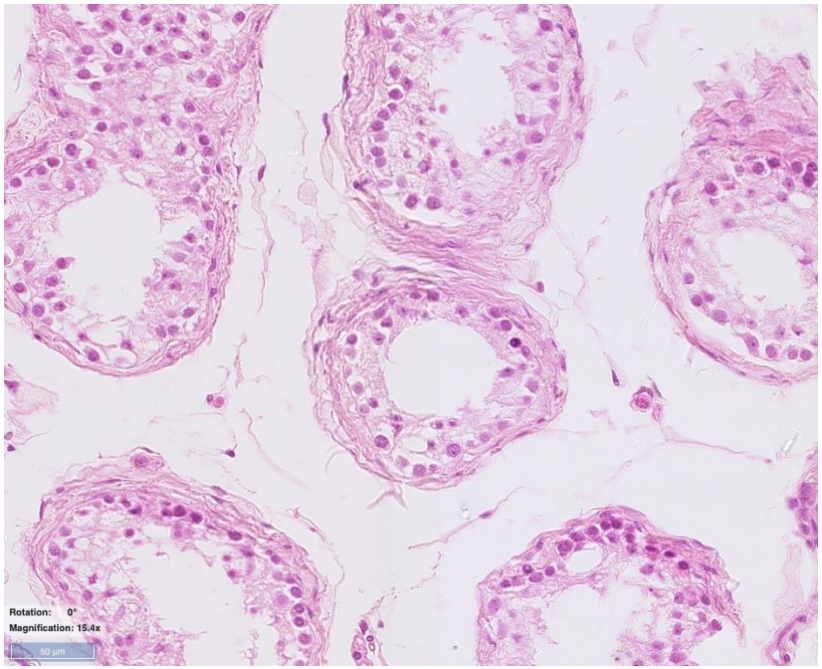
Comparer les coupes : 180, 181 (actif)
182 (sénile)

Aplasie de l'épithélium germinal
Atrophie des cellules de Leydig
Epaississement de la gaine péritubulaire
Atrophie des tubes séminifères
Aplasie des Keimepithels
Atrophie der Leydig-Zellen
Verdickung der Peritubulusscheide
Atrophie der Tubuli seminiferi

180



182



Images: Microscopie virtuelle, Unifr

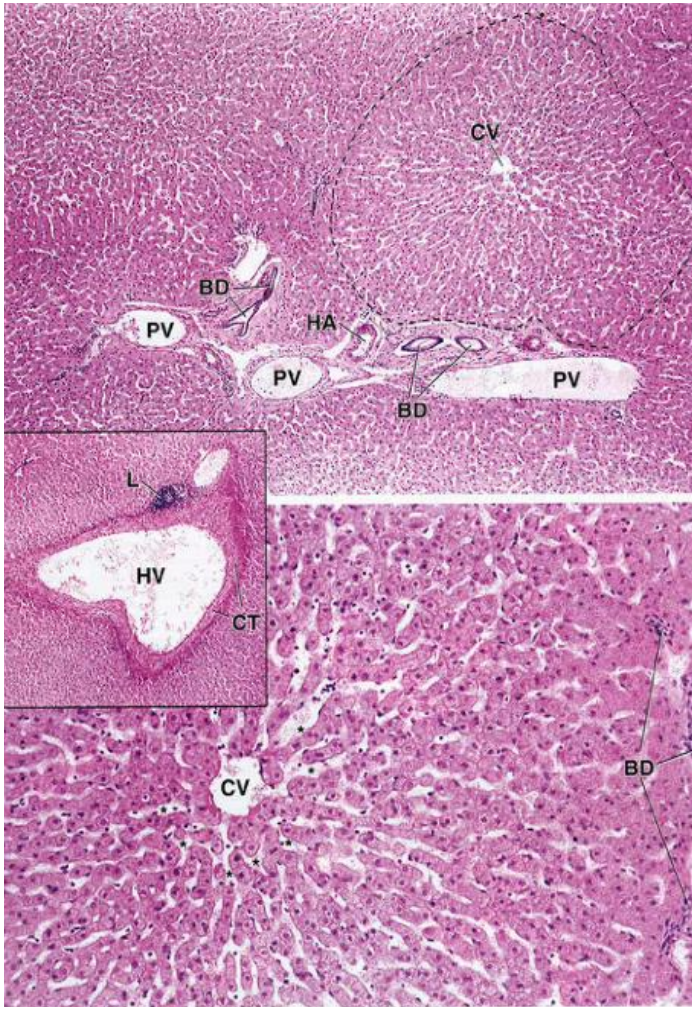
Foie

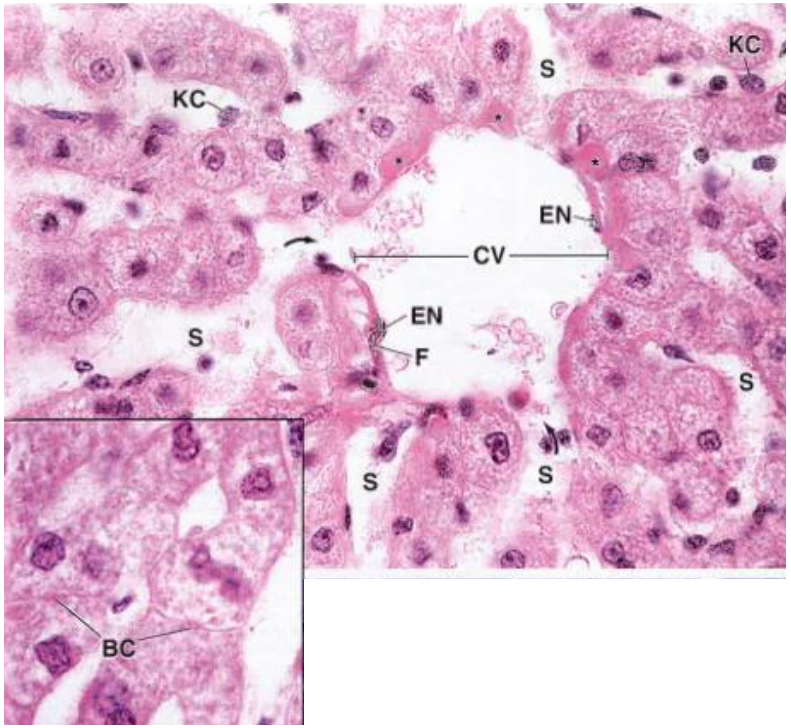
Organisation en lobules

Hépatocytes arrangés radialement autour d'une veine centrale

Espaces porte (Triade de Glisson: A.hepatique, V.porte, canal biliaire)

Tissu conjonctif lâche (collagène type I) dans espace porte; collagène type III (réticuline) dans le parenchyme





Images: Pawlina, Histology, a text and atlas

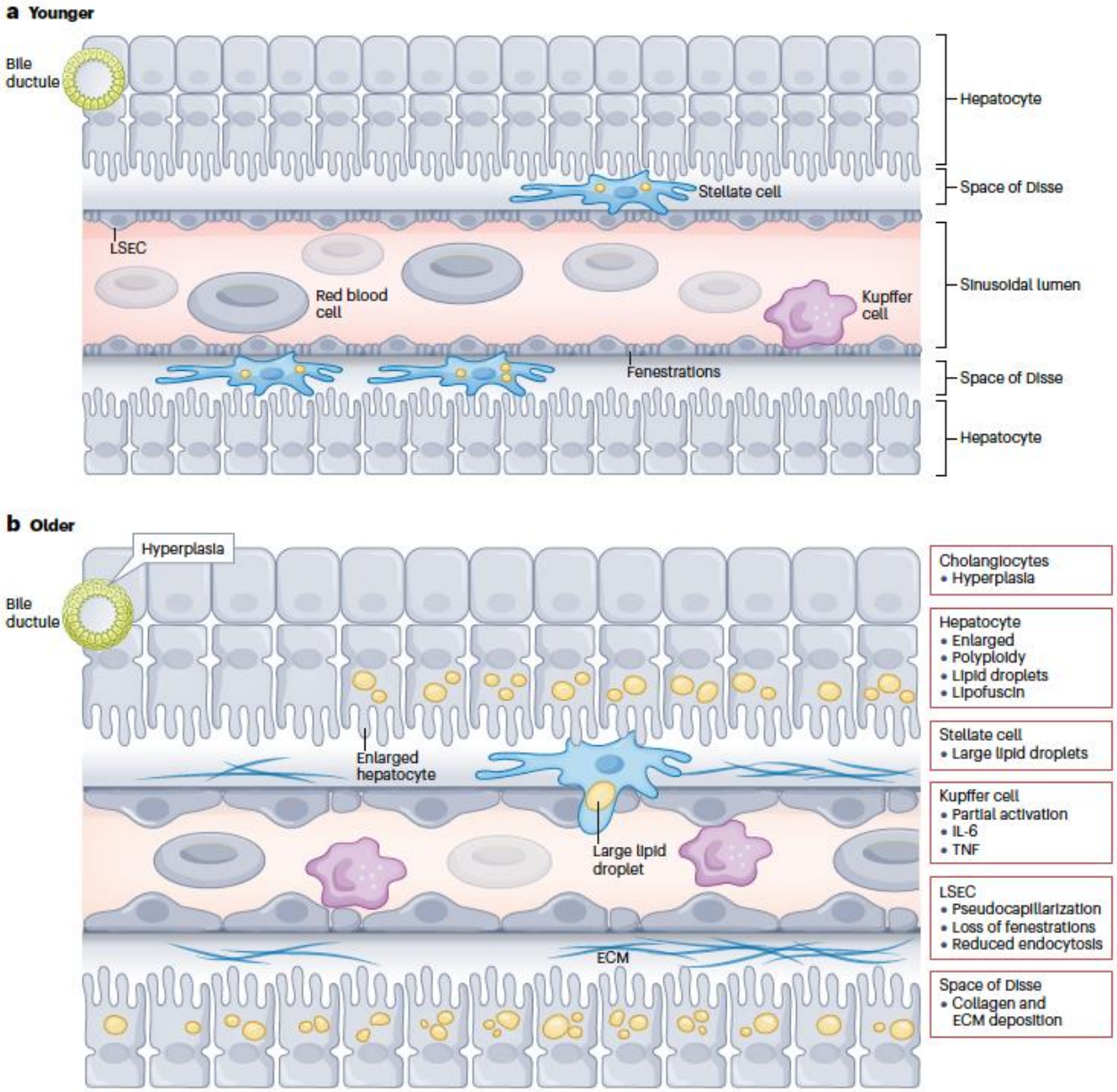


Fig. 1 | Structural changes in the ageing liver. Some of the major morphological changes in ageing from younger ages (part **a**) to older ages (part **b**) in the parenchymal cells of the liver (hepatocytes) and the non-parenchymal cells (liver sinusoidal endothelial cells, Kupffer cells, cholangiocytes and hepatic stellate cells). ECM, extracellular matrix; LSEC, liver sinusoidal endothelial cell.

Foie: Comparer les coupes coupes 146a; « foie humain » »

Changements morphologiques et fonctionnels des hépatocytes (variation dans la taille, polyploïdie, accumulation de lipofuscine…).

Stéatose (accumulation de graisses dans les hépatocytes).

Espace portal: fibrose (fibres de collagène plus denses); artérioles hépatiques plus épaisses.

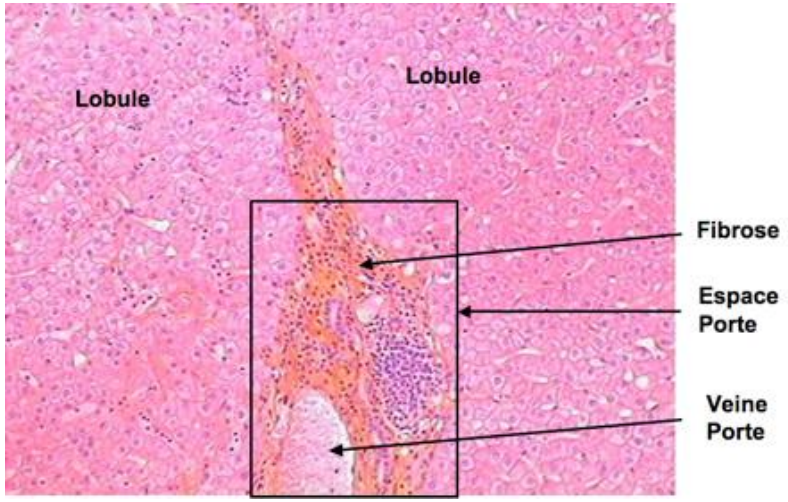
Fibrose (stroma; périsinusoïdale; veine centrale).

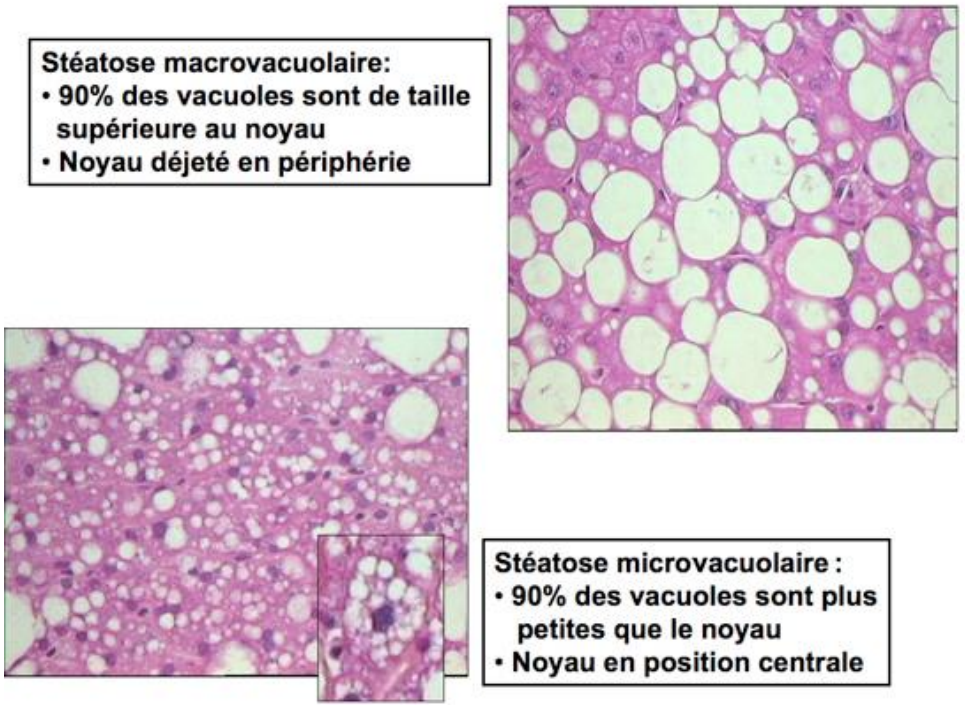
Morphologische und funktionelle Veränderungen der Hepatozyten (Variation in der Grösse, Polyploidie, Ansammlungvon Lipofuszin…).

Steatose (Ansammlung von Fetten in den Hepatozyten).

Portalraum: Fibrose (dichtere Kollagenfasern); dickere Leberarteriolen.

Fibrose (Stroma, Perisinusoid, Zentralvene).





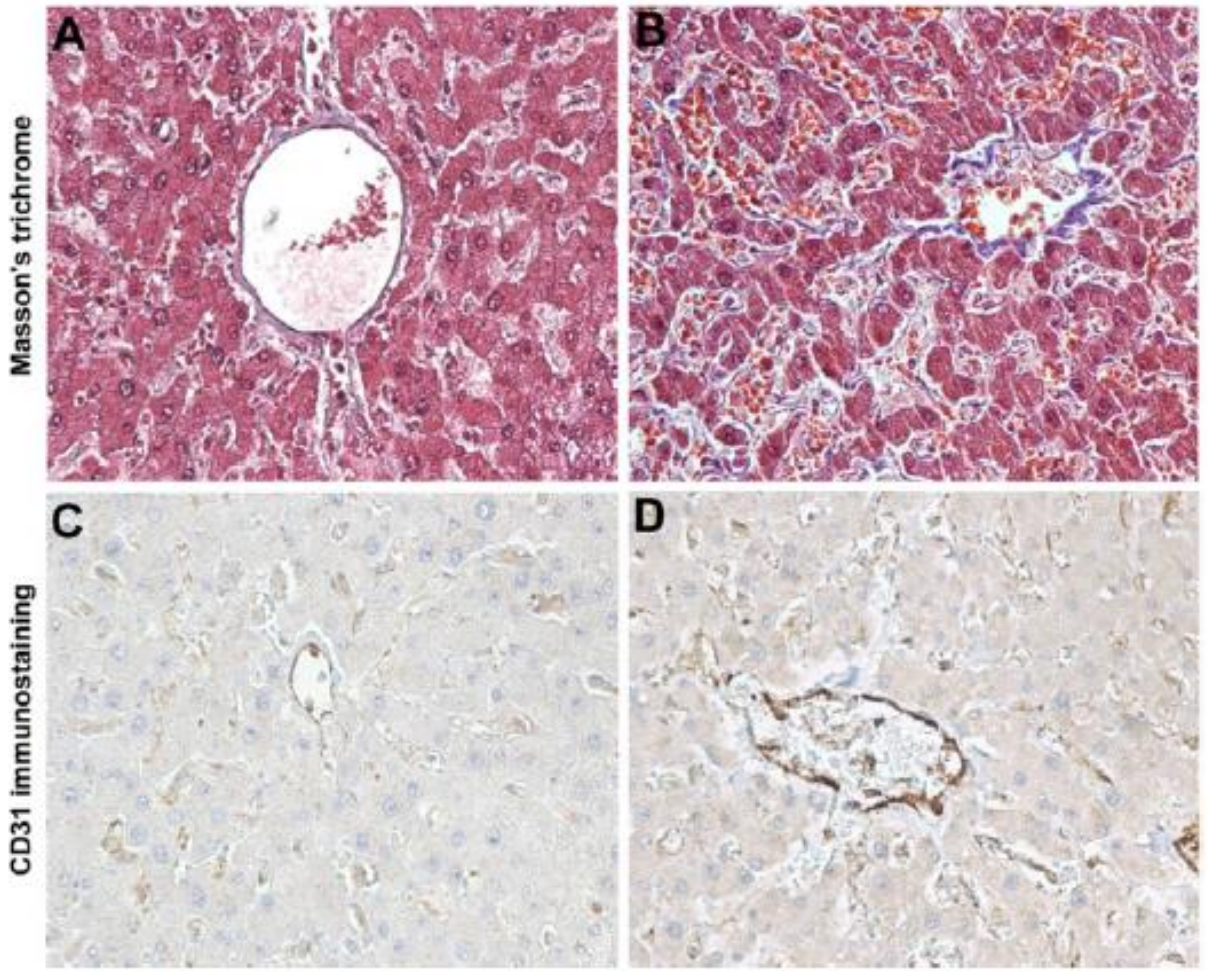
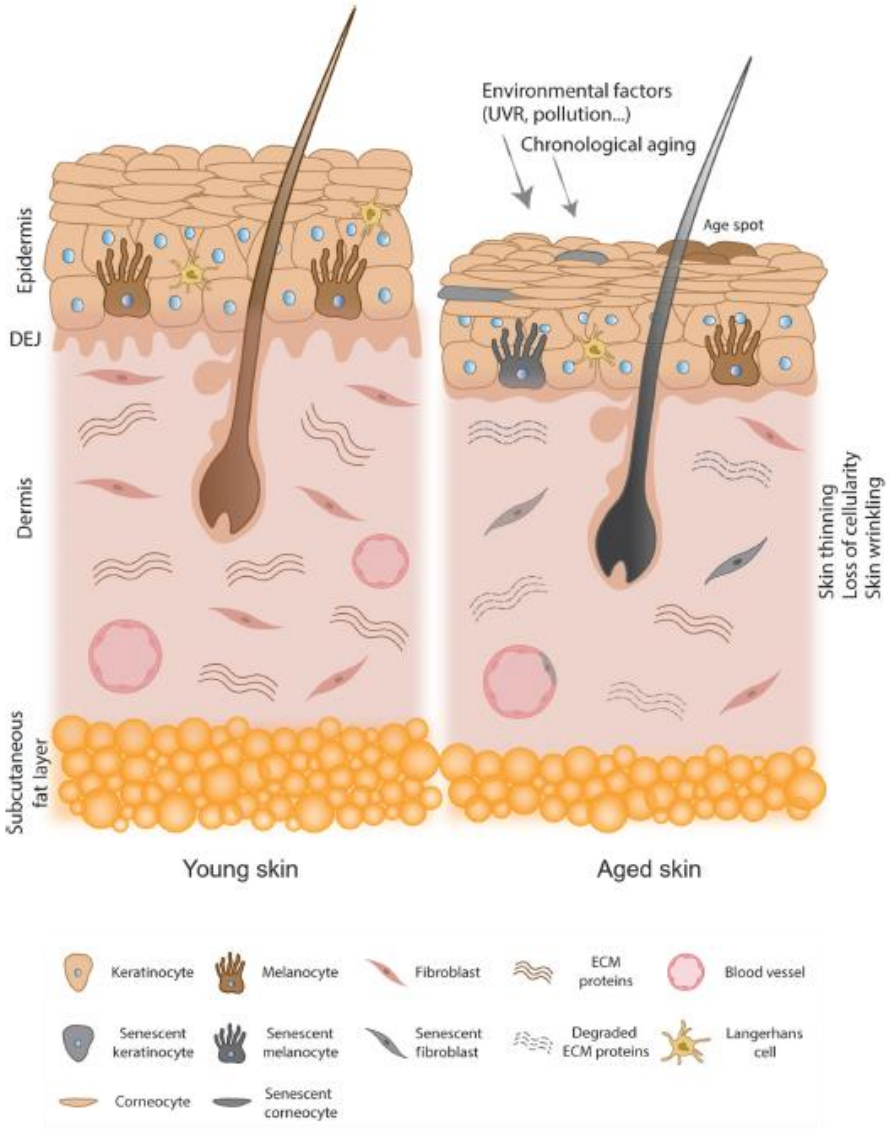


Figure 4 Microscopic aspects of human liver pseudocapillarisation. Post-mortem (myocardial acute infarction) histology studies on paraffin-embedded sections (5 μm thick) of formalin-fixed liver tissue. Masson's trichrome staining shows the central vein and pericentral hepatocytes of young **(A)** and old liver **(B)** with perisinusoidal collagen deposition (blue staining). CD31 immunostaining of young **(C)** and old liver **(D)** with an increased sinusoidal protein expression. Magnification 20×.

Trends in
Molecular Medicine
Series: Dermatology
Opinion

Skin senescence: mechanisms and impact on whole-body aging

Ana Catarina Franco,[1,2,3] Célia Aveleira,[1,2] and Cláudia Cavadas[1,2,3,*]



Vieillissement de la peau
Alterung der Haut

L'âge compromet les 4 phases de la cicatrisation (hémostase, inflammation, prolifération, remodelage)
Das Alter beeinträchtigt die 4 Phasen der Wundheilung. (Hämostase, Entzündung, Proliferation, Remodellierung)

Activité proliférative réduite au niveau épithélial et conjonctif: épiderme plus fin
Verminderte proliferative Aktivität

Activité réduite des fibroblastes; Dégradation des fibres de la MEC
Abbau der EZM

Aplatissement de la jonction Epi/Der
Abflachung der Epi/Der-Verbindung

Altération de la pigmentation (altération de l'activité des mélanocytes)
Veränderung der Pigmentierung (Veränderung der Aktivität der Melanozyten)

Baisse des défenses immunitaires
Senkung der Immunabwehr

Changement de la composition du microbiote
Veränderung der Mikrobiota-Zusammensetzung

Hypoderme moins épais
Weniger dicke subcutis

Angiogénèse réduite
Verringerte Angiogenese

https://doi.org/10.1038/s41556-025-01739-1

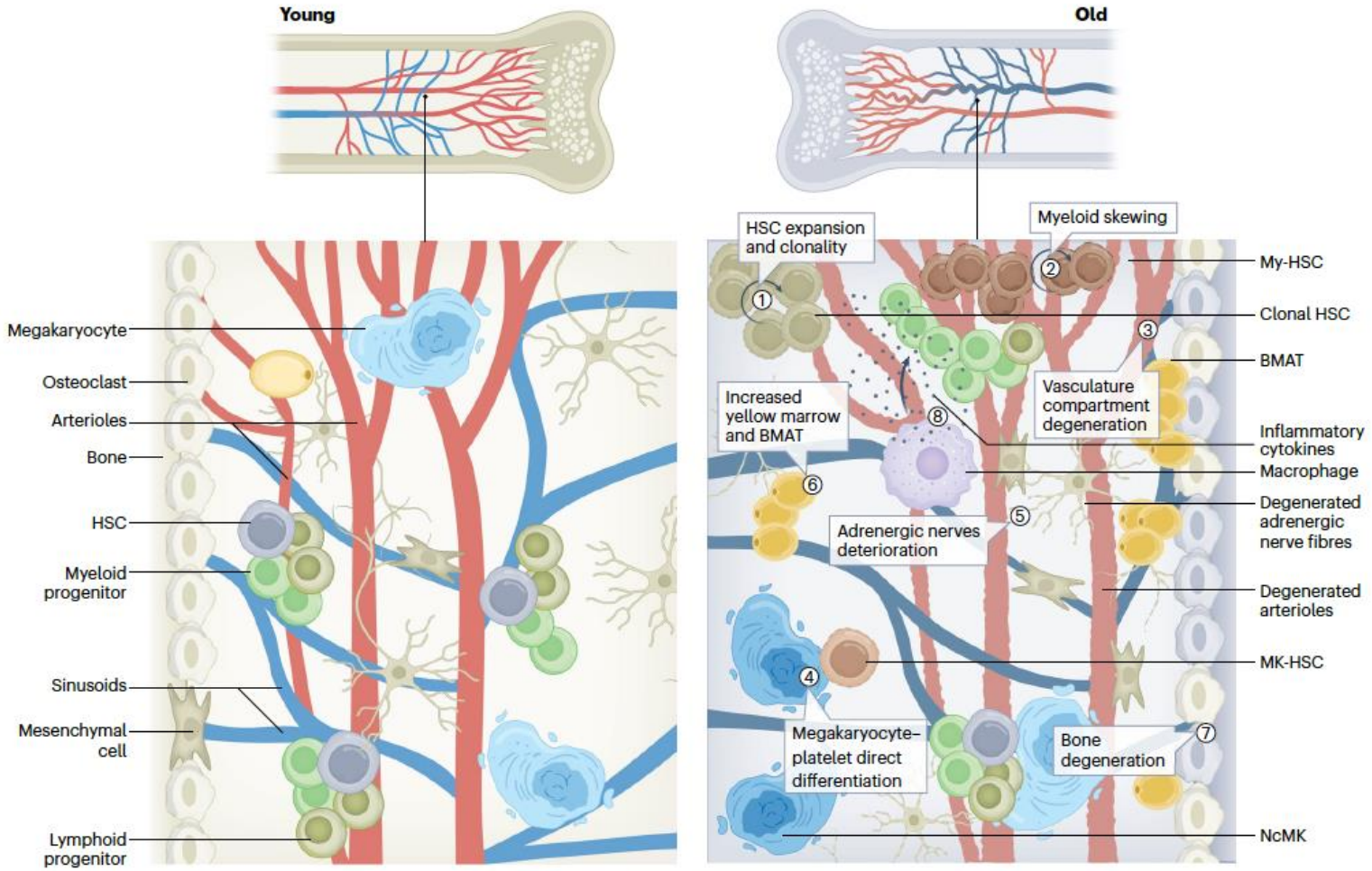


Fig. 2 | Ageing of the BM niche in long bones. The haematopoietic niche remodels upon ageing. Both intrinsic and extrinsic ageing features coexist, leading to a less functional haematopoietic system. Remodelling includes: (1) HSC expansion and clonality, (2) myeloid skewing, (3) vasculature compartment degeneration, (4) megakaryocyte–platelet direct differentiation, (5) adrenergic nerves deterioration, (6) increased yellow marrow and bone marrow adipose tissue (BMAT), (7) bone degeneration, and (8) pro-inflammatory cytokine release.

AGING AND MICROVASCULATURE

BRAIN

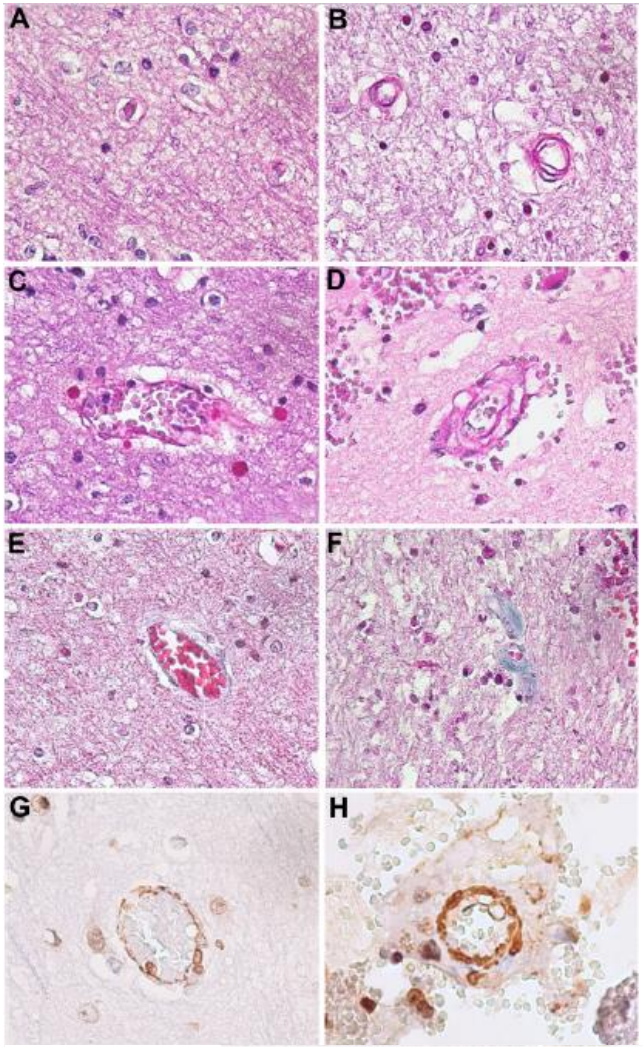


Figure 3 Age-related changes of brain microvasculature. Post-mortem (myocardial acute infarction) histology studies on paraffin-embedded sections (5 μm thick) of formalin-fixed cerebral tissue. PAS staining of human brain gray matter, showing normal capillaries and arterioles in a young **(A,C)** compared to concentrically thickened microvessels in an aged man **(B,D)** mostly due to hyalinization (pink staining). Masson's trichrome staining shows normal microvessel in a young **(E)** and perivascular deposition of collagen (blue staining) around capillaries in an aged man **(F)**. Immunohistochimical analysis for α-SMA shows normal arteriole in a young **(G)** and concentrically thickened arteriole due to an altered proliferation of smooth muscle cells in an aged man **(H)**. Magnification 40×.

Scioli et al; 2014, Vascular Cell 6:19

DERMIS

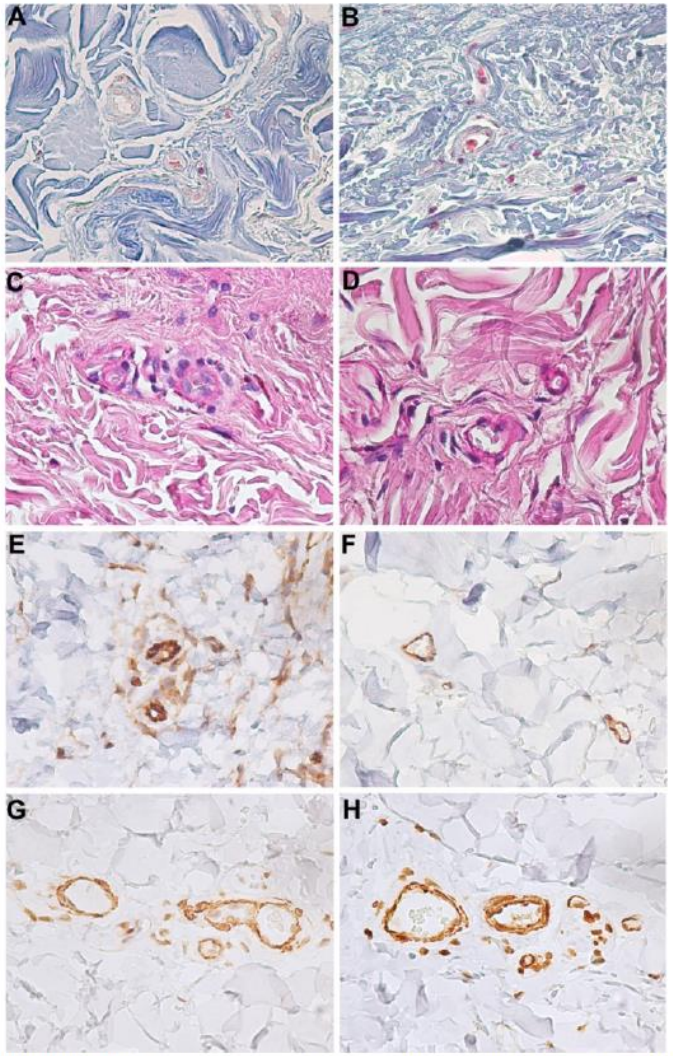


Figure 6 Ageing in skin microcirculation. Histology studies on paraffin-embedded sections (5 μm thick) of formalin-fixed skin of healthy subjects. Masson's trichrome staining shows collagen distribution (blue staining), around microvessels, in young **(A)** and old dermal skin **(B)**. PAS staining shows hyaline deposits (pink staining), around microvessels, in young **(C)** and old dermal skin **(D)**. CD31 immunostaining of young **(E)** and old dermal skin **(F)** showing the descrease of capillaries associated with ageing process. α-SMA immunostaining of young **(G)** and old dermal skin **(H)** showing the proliferation of VSMCs around aged microvessels. Magnification 40×.

Normal ageing of the brain: Histological and biological aspects

T. Teissier [a,*], E. Boulanger [a,b], V. Deramecourt [c,d]

Revue neurologique 176 (2020) 649-660

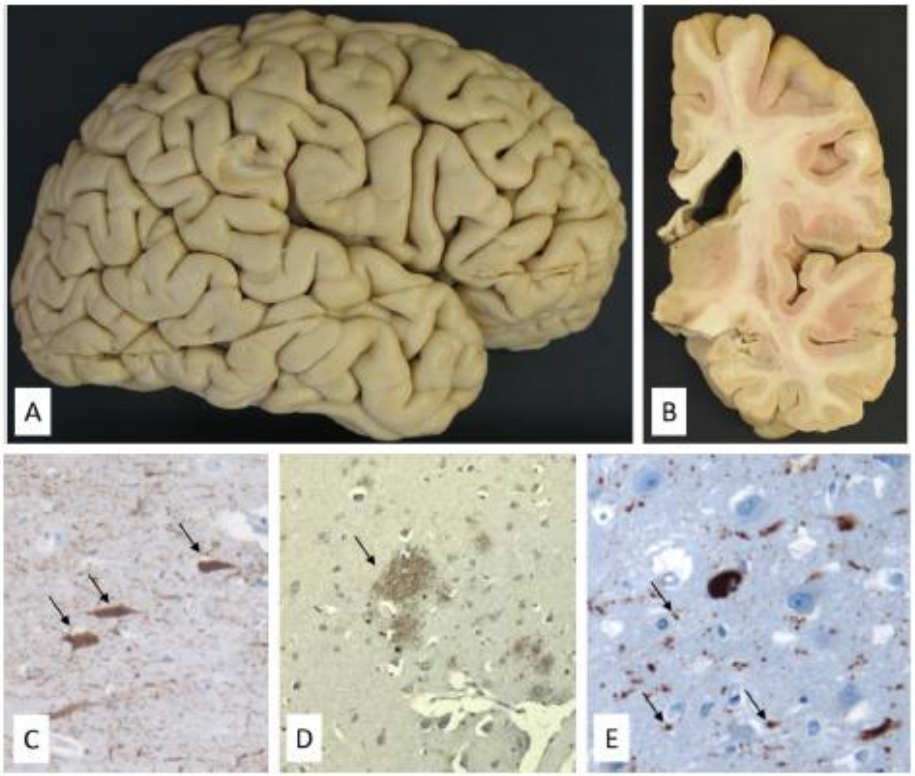


Fig. 1 – Illustration of common histological changes during normal brain ageing. A. Gross morphology of a formalin-fixed post mortem brain hemisphere from an 85-year old man without any cognitive decline. Note the very subtle and diffuse cortical atrophy and the preservation of most associative cortical areas. B. Coronal view from the same brain specimen. Note the absence of significant atrophy of the hippocampus. C. Sparse neurofibrillary tangles (arrows) in the hippocampus of the same patient (Tau protein immunohistochemistry). D. Diffuse cortical amyloid deposits in the same case (arrow). Note the absence of senile plaque (β-amyloid immunohistochemistry). D: Isolated argyrophilic grains (arrows) in the hippocampus of an 86-year old cognitively normal woman (Tau protein immunohistochemistry).

Table 1 – Gene expression changes over time in the ageing human brain.

Gene category	Expression
Mitochondrial function	↘
Neural plasticity/Synapes	↘
Inhibitory interneurons	↘
Ubiquitin-proteasome system	↘
Stress response	↗
Immune/inflammatory response	↗
Metal ion homeostasis	↗
Myelin-related functions	↗
Glia	↗