

Arterial aging: Manifestations and clinical consequences

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“A man is as old as his arteries”

Dr. Thomas Sydenham

Objectives of the course

Some preliminary questions...

1- Arteriosclerosis (stiffness) vs. Atheroma

2- How to assess arterial stiffness?

3- Arterial stiffness and age-related diseases

4- Accelerators of arterial stiffness

Question 1: The arterial aging induces a:

1. Decrease in the length and the diameter of the large arteries
2. Increase in the Systolic Blood Pressure
3. Increase in both Systolic and Diastolic BP
4. Increase in arterial thickness

Question 2: Atherosclerosis (atheroma) and arteriosclerosis (stiffness) are both influenced by:

1. Aging
2. High cholesterol
3. Cigarette smoking
4. High salt diet
5. Diabetes

Question 3: Hypertension (HTn) and Atherosclerosis (ATH) and Arteriosclerosis (STIFF)

1. HTn can induce ATH
2. ATH can induce HTn
3. STIF can induce HTn
4. HTn can induce STIF

Question 4: Clinical consequences of Arteriosclerosis

1. Systolic Hypertension
2. Left Ventr. Hypertrophy
3. Cor. Heart Disease
4. Renal Failure
5. Cognitive decline and dementia
6. CV mortality

Objectives of the course

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- 2- How to assess arterial stiffness?
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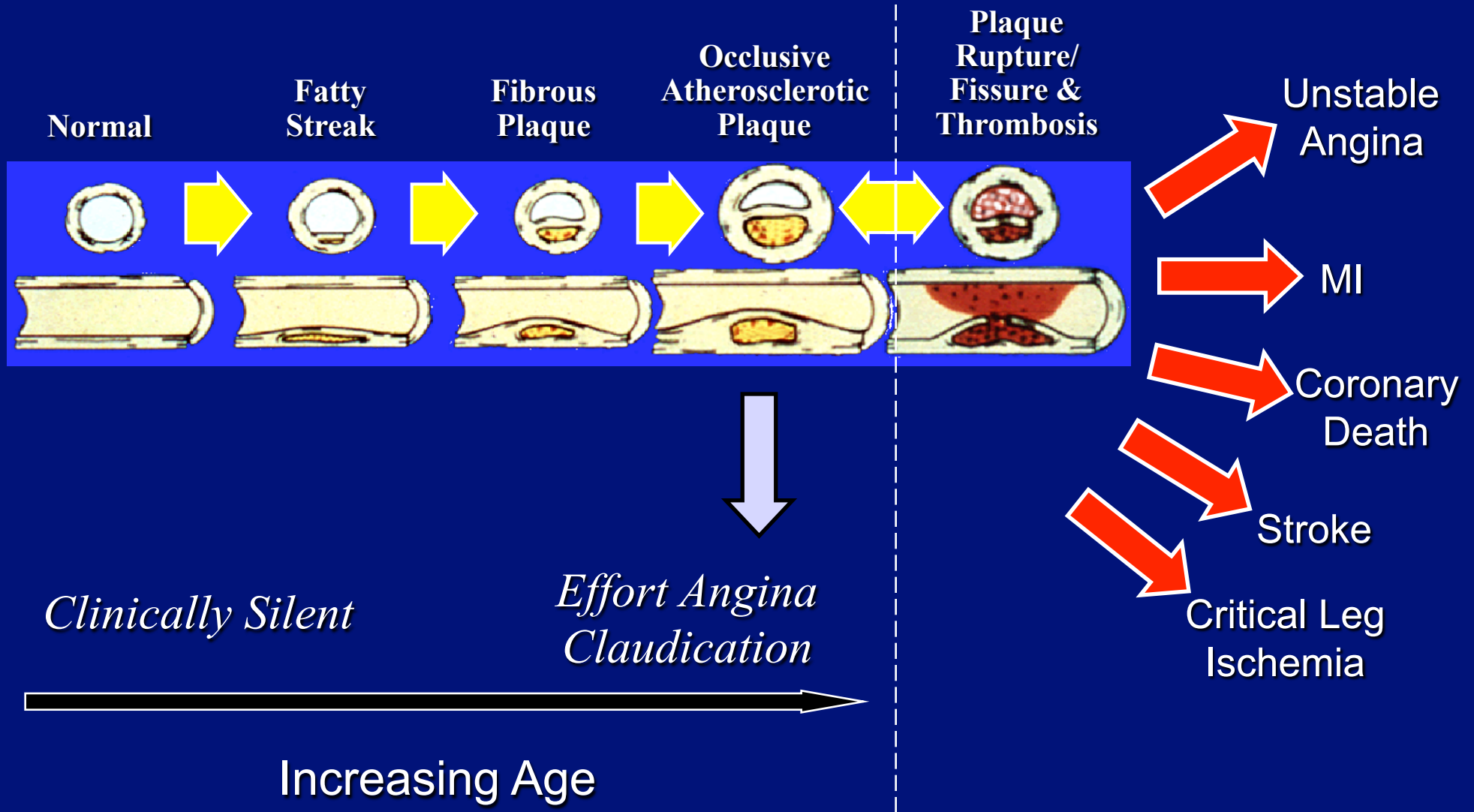
Effects of age on the arterial system



ATHEROMATOSIS

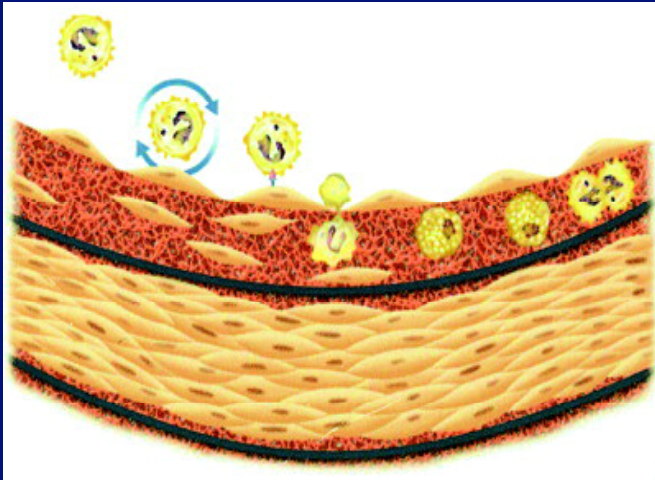
STIFFNESS

Atheroma: A Progressive Process



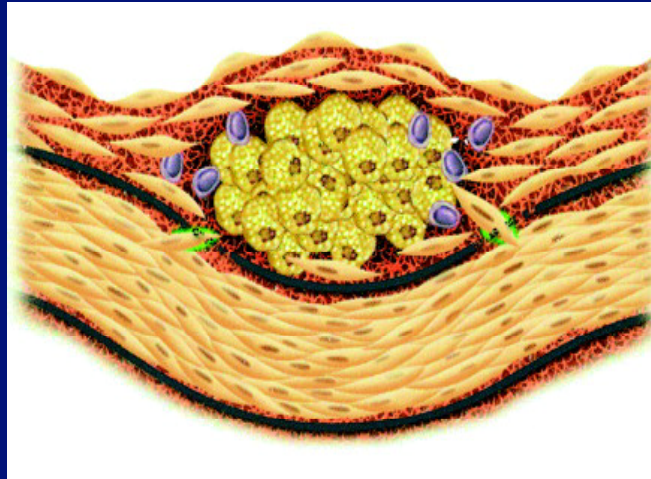
The inflamed coronary artery

Step 1



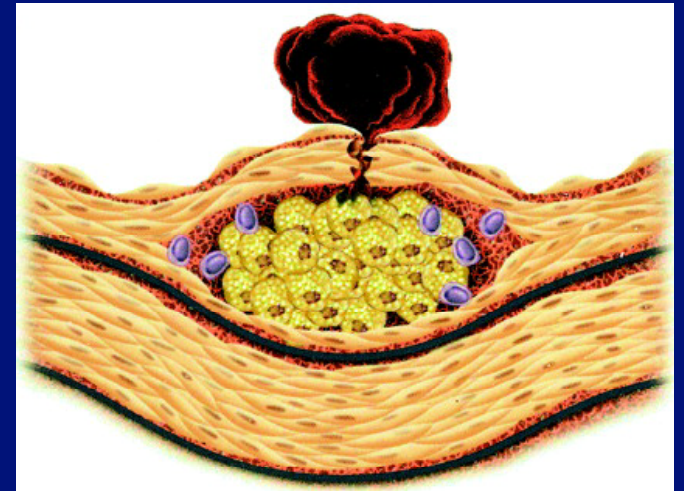
Adhesion and Infiltration
of Leucocytes

Step 2



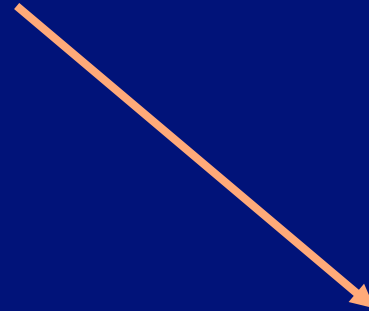
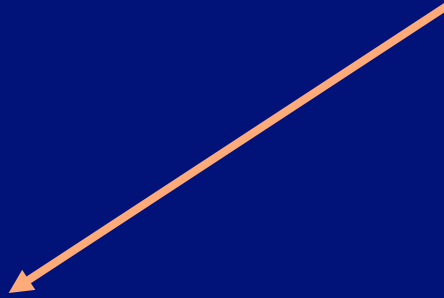
Plaque formation and
Proliferation

Step 3



Plaque rupture and
Thrombosis

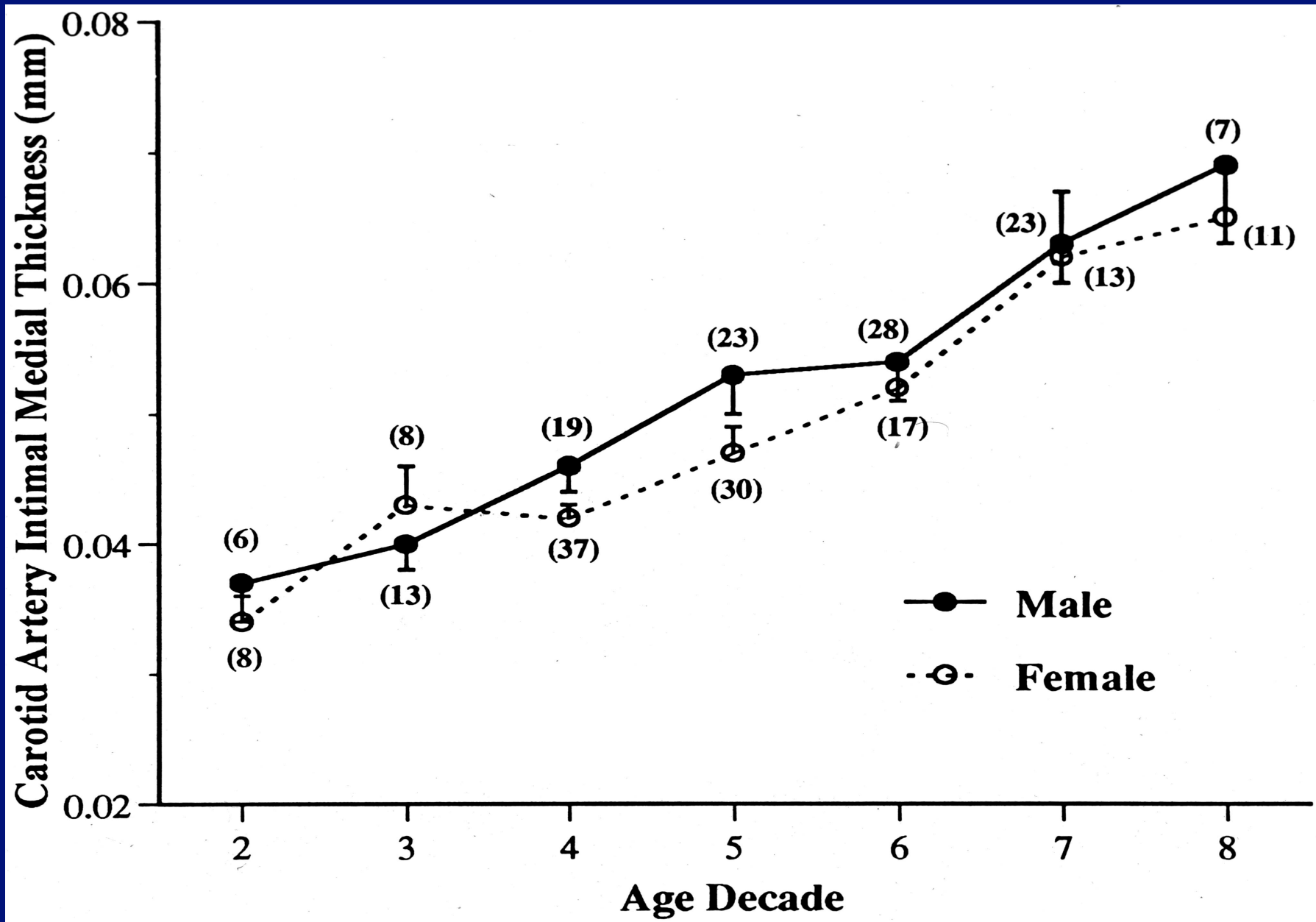
Effects of age on the arterial system



**Pred.
ATHEROMATOSIS**

STIFFNESS

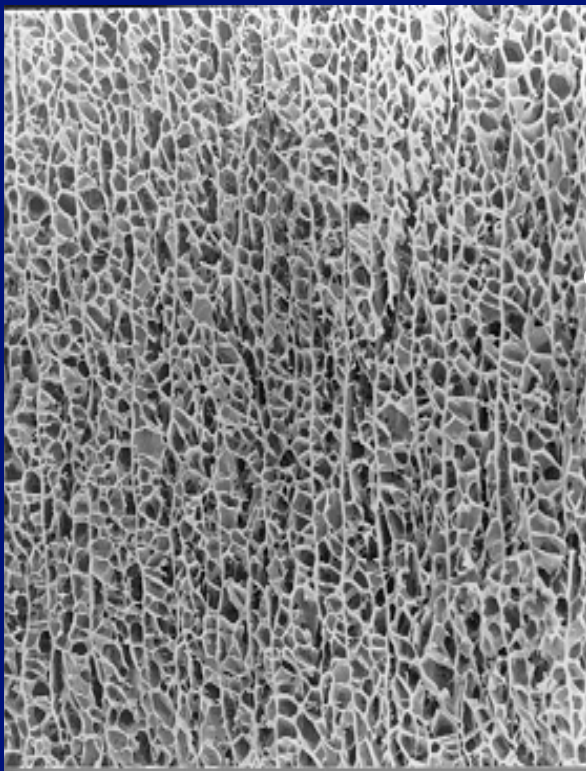
Increase in arterial thickness with age



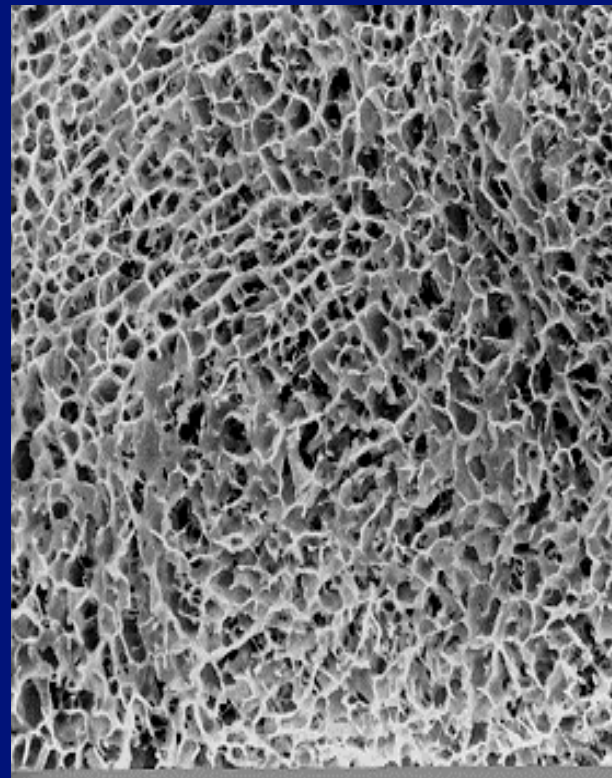
Human thoracic aorta

Structural Changes with aging

Avolio et al, 1998



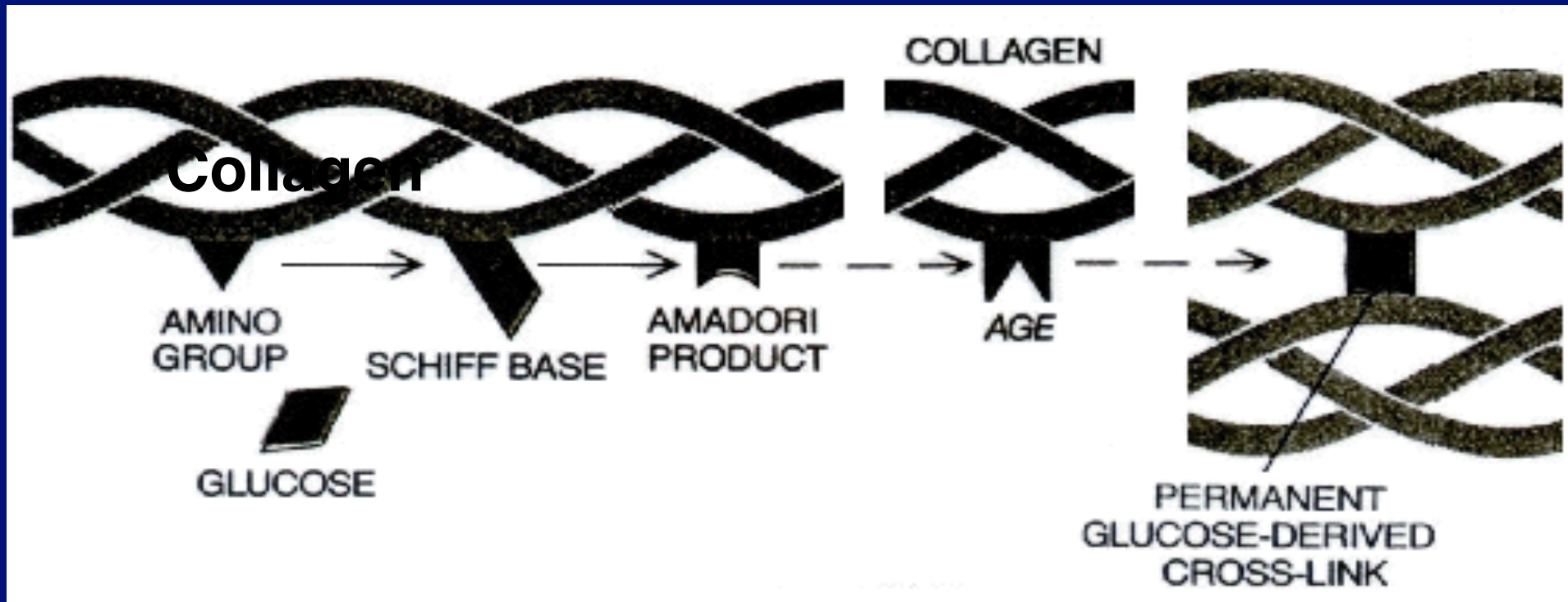
25 y.o.



75 y.o.

Elastin network

AGE Cross-Linking of Collagen



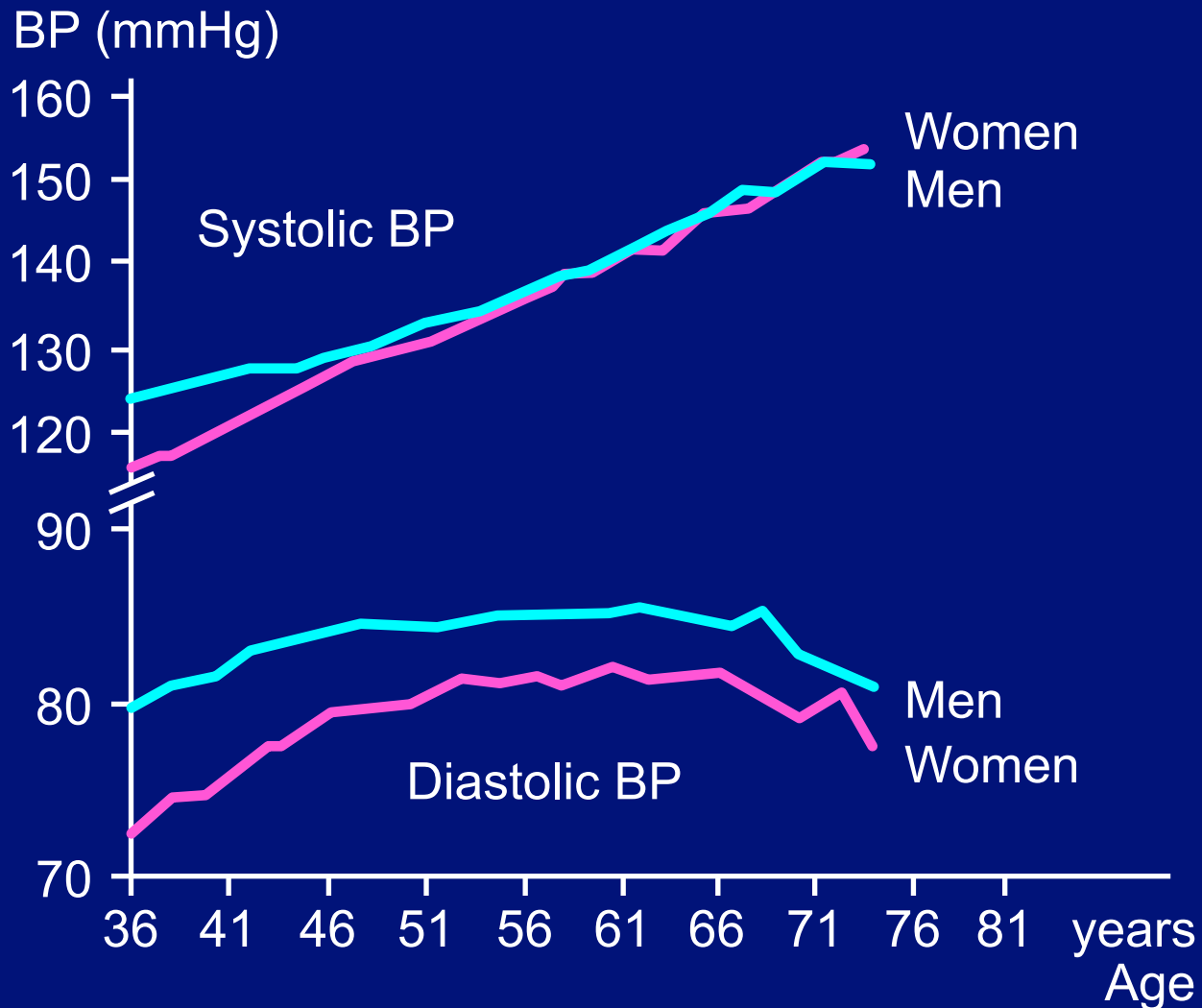
Glycation of collagen
Production of **Advanced Glycation End products (AGEs)**
=
Cross links, fibrosis, decrease in collagen degradation
=
Myocardial stiffness: diastolic dysfunction
Arterial stiffness : increased afterload

Age-related arterial alterations...

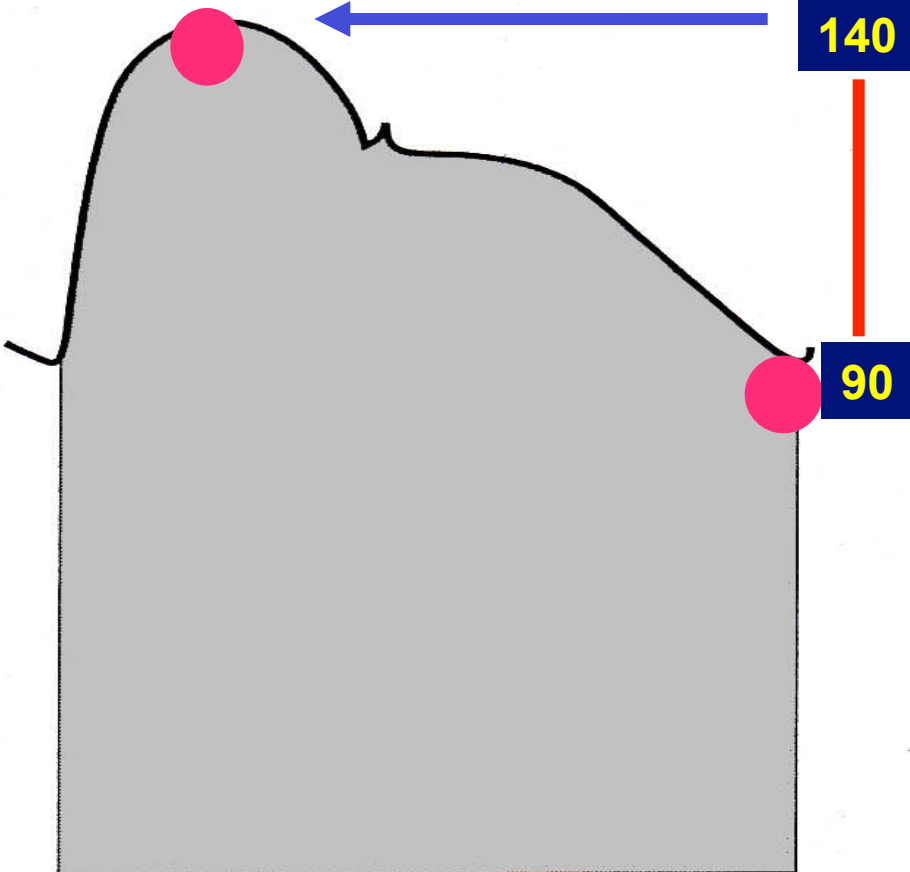
- Increase in arterial diameter and in IMT
- Arterial fibrosis (collagen I and III, fibronectin)
- Destruction of the elastin network
- Non-enzymatic collagen glycation
- Arterial calcifications
- Endothelial dysfunction
- Activation of inflammatory process

leading to...

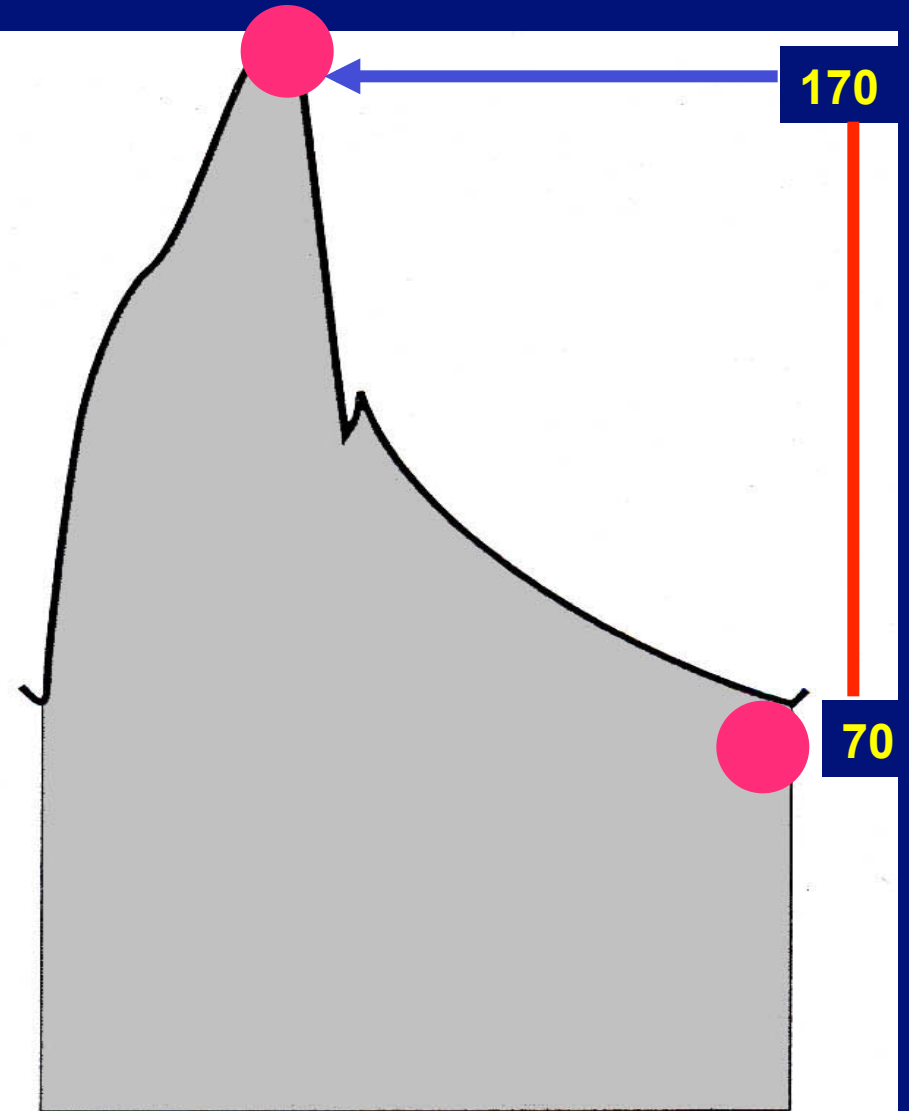
Evolution in blood pressure with age. The Framingham study

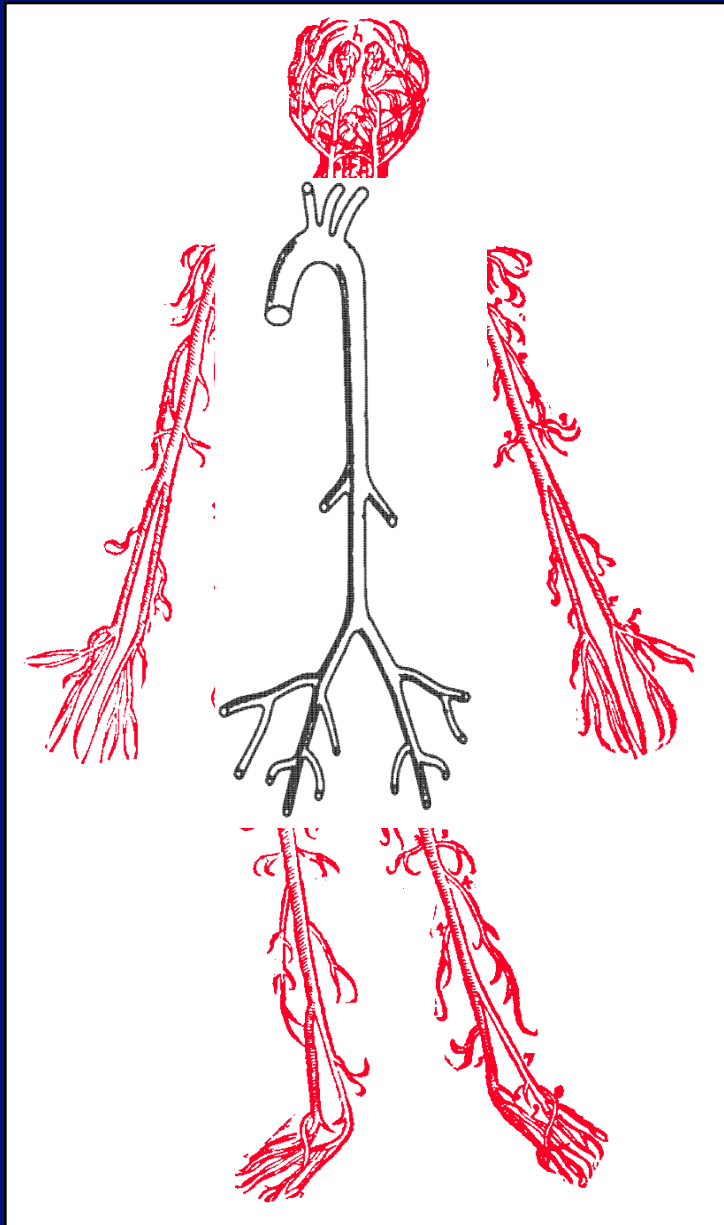


45 years



75 years





Objectives of the course

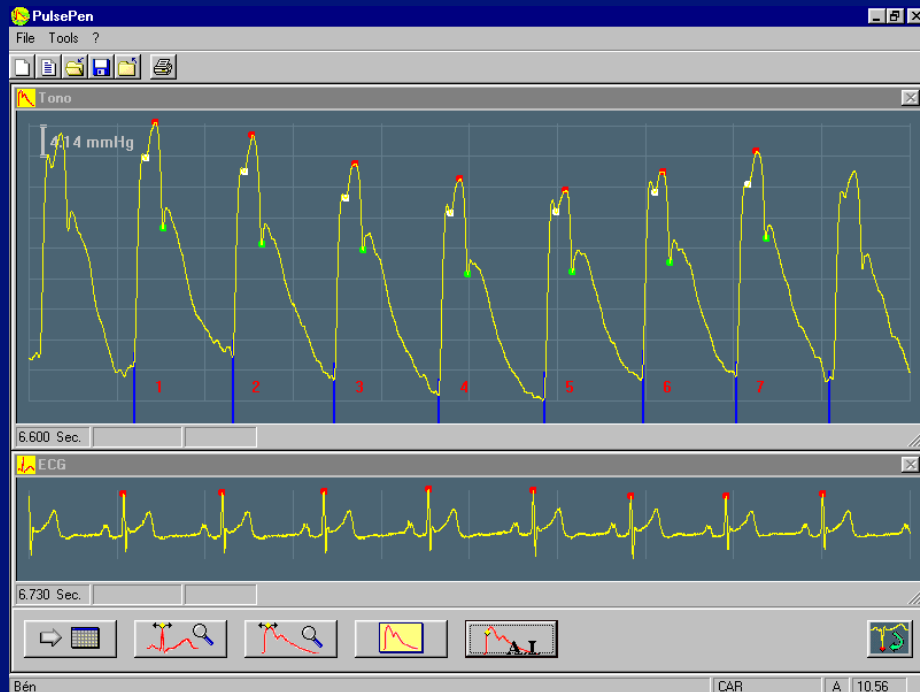
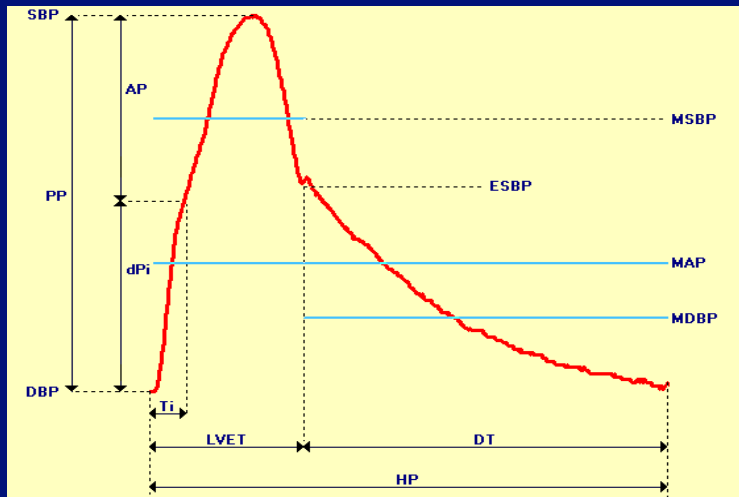
- 1- Arteriosclerosis (stiffness) vs. Atheroma**
- 2- How to assess arterial stiffness?**
- 3- Arterial stiffness and age-related diseases**
- 4- Accelerators of arterial stiffness**

Complior®



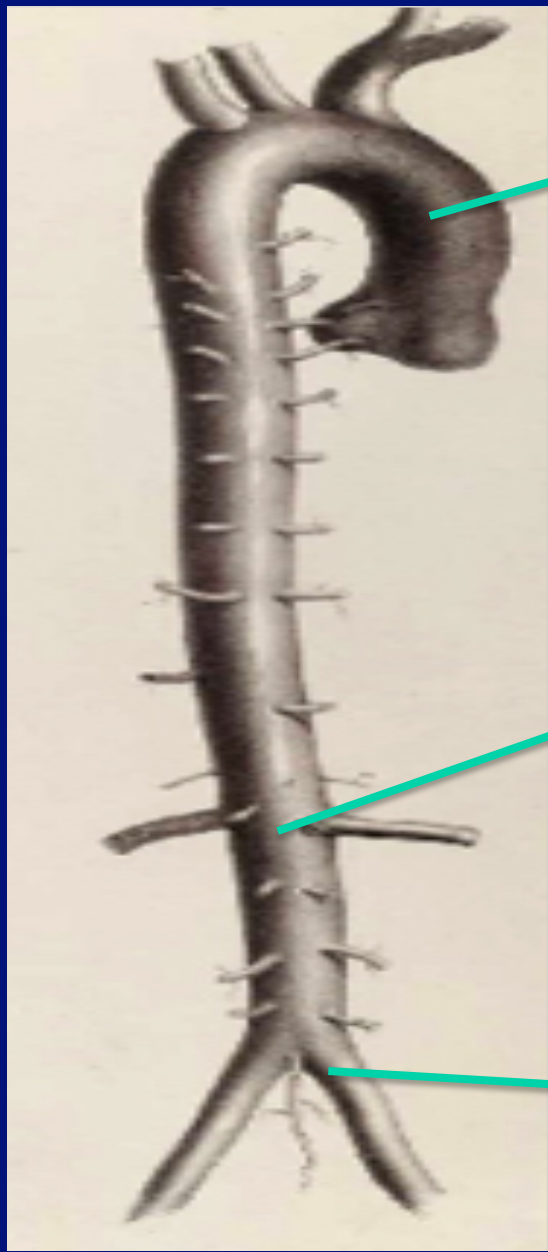
PulsePen®



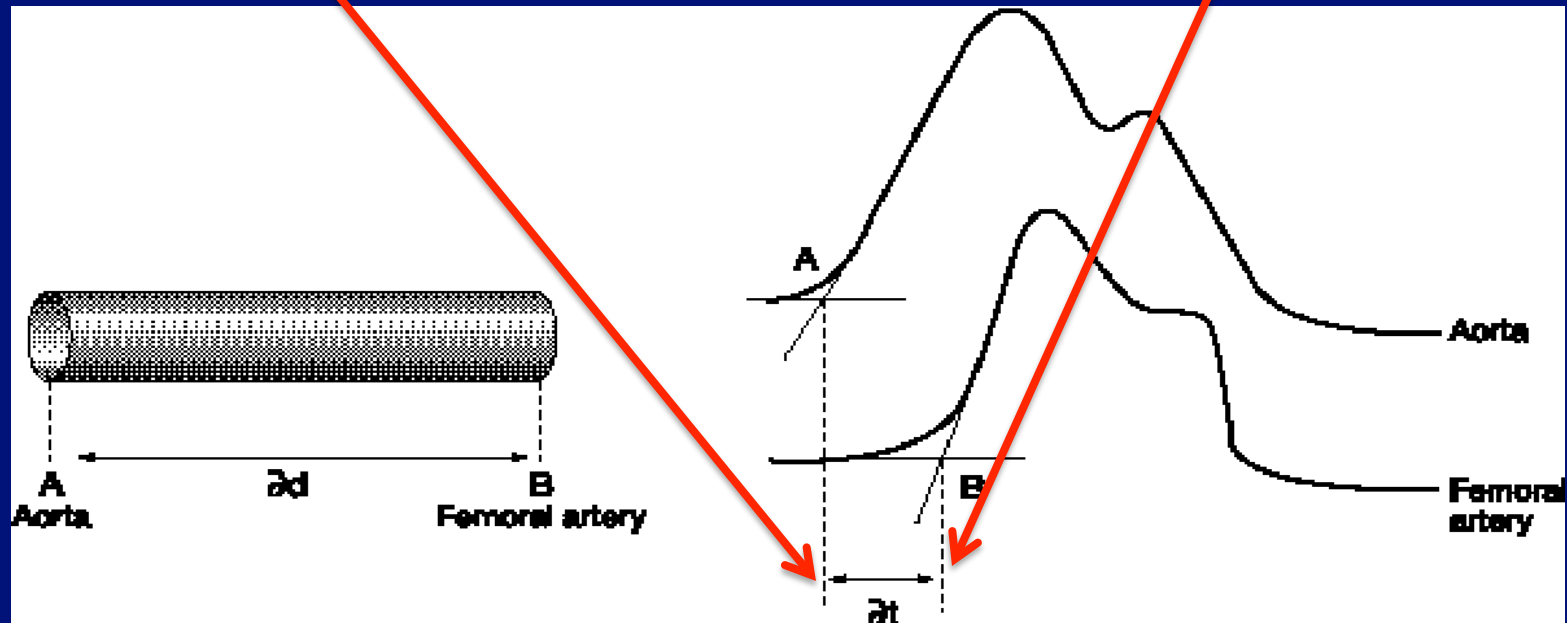
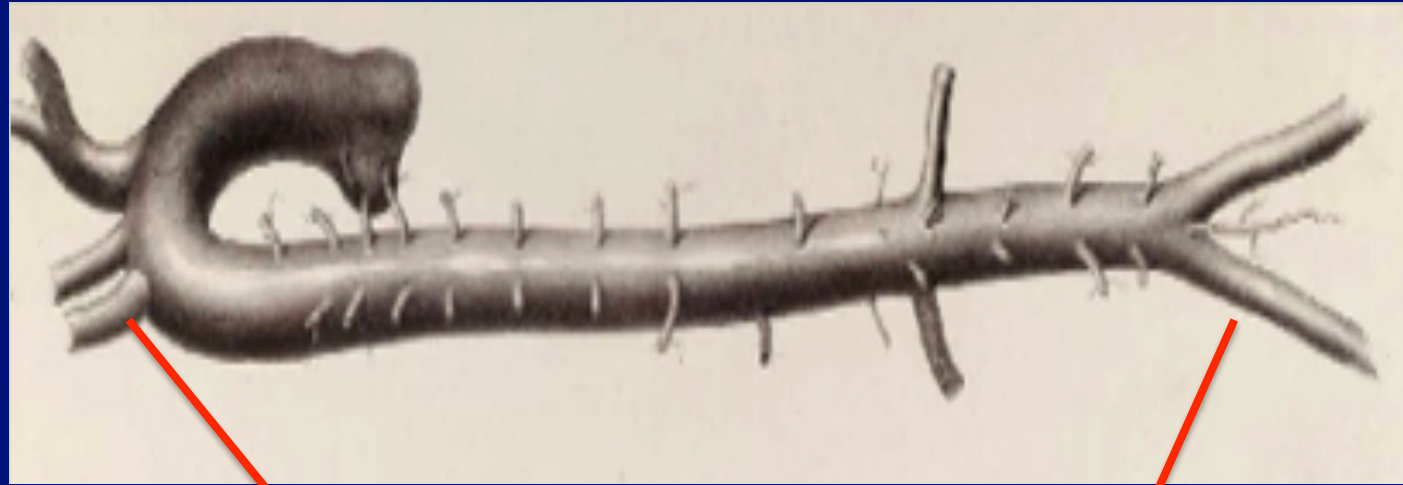


Methods for evaluating Arterial Stiffness

- Pulse Wave Velocity (PWV) is the easiest and the most validated method



PWV = Distance (dD) / propagation time (dt) (m/sec)



Pulse wave velocity (PWV)

Reference method for measuring arterial stiffness

1. Precise, rapid, low cost
2. Reference values established
3. Well correlated with morbidity and mortality in several populations

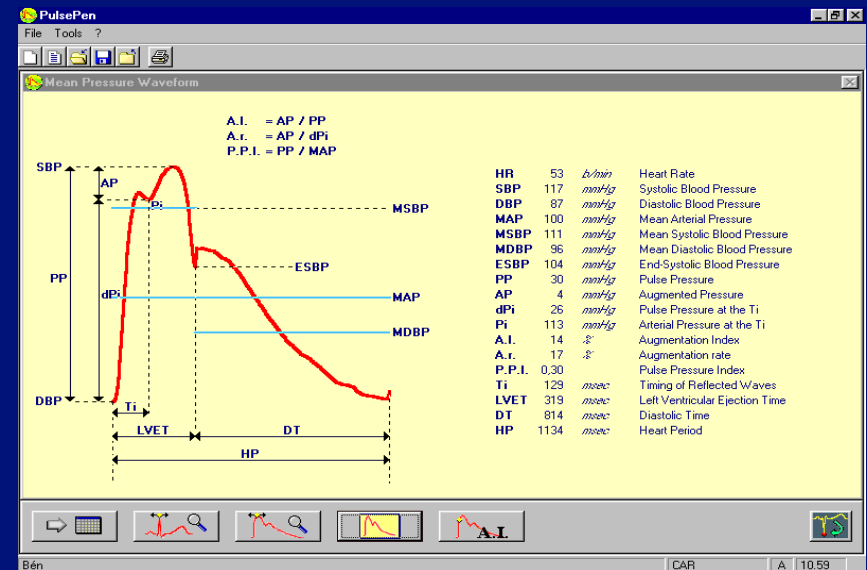
Complior®



PulsePen®



Sphygmocor®





Determinants of pulse wave velocity in healthy people and in the presence of cardiovascular risk factors: 'establishing normal and reference values'

The Reference Values for Arterial Stiffness' Collaboration[†]

Received 21 September 2009; revised 30 March 2010; accepted 21 April 2010

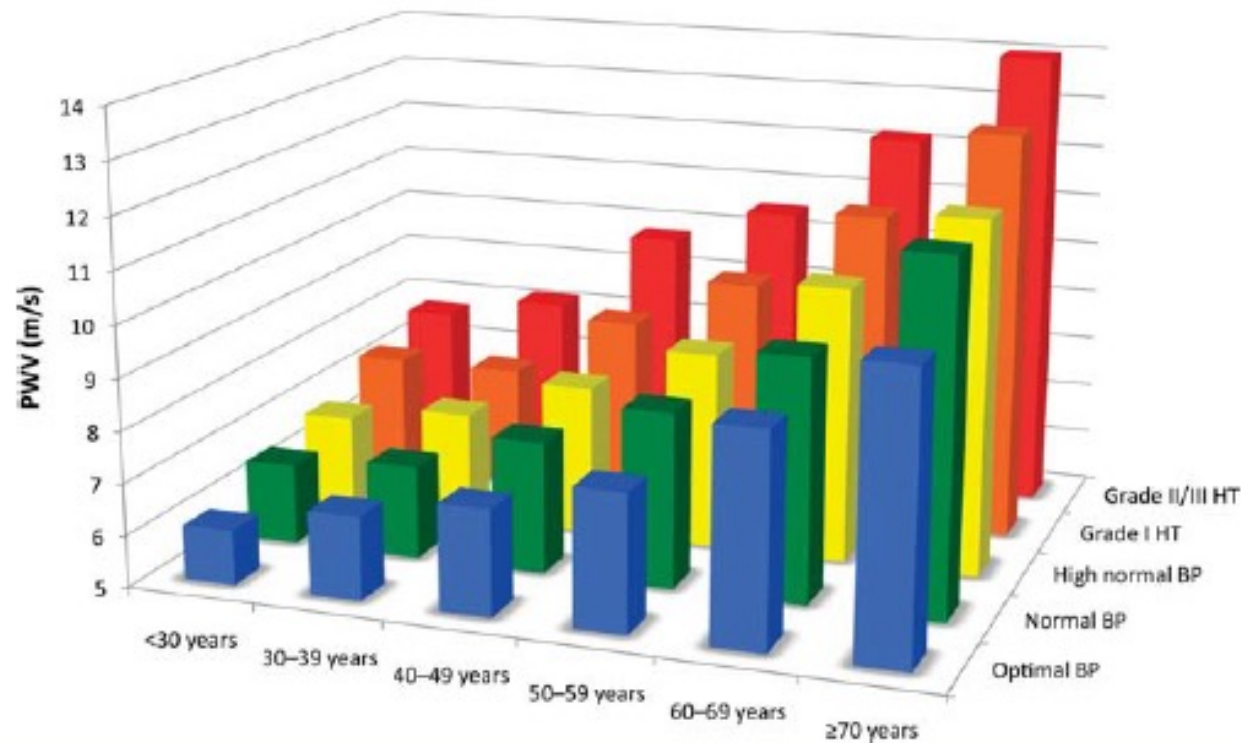
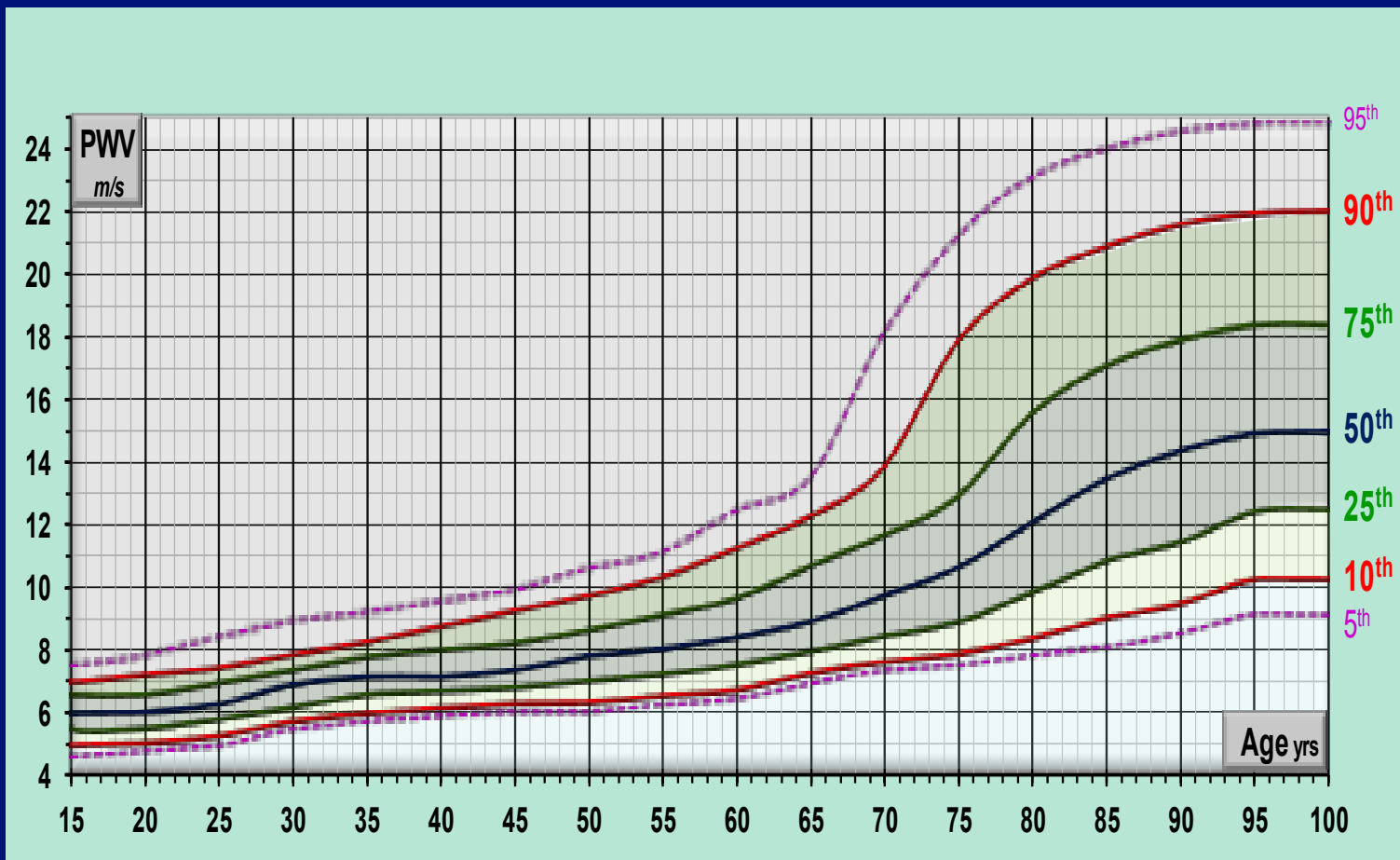


Figure 3 Reference values for pulse wave velocity (PWV): mean values according to age and blood pressure (BP) categories (11 092 subjects). HT, hypertension.

Relation Age/VOP dans une population française

Données Salvi-Bénéto



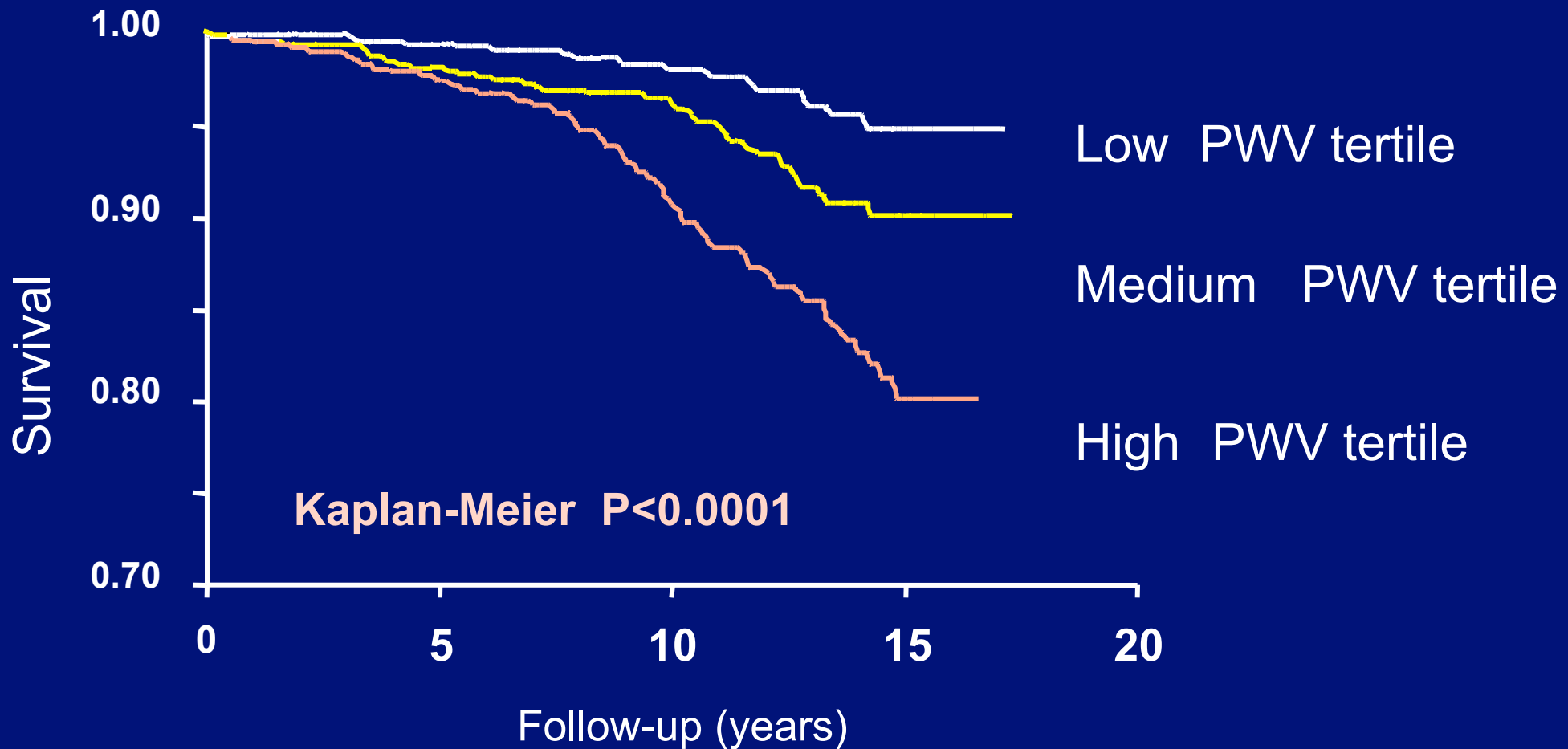
1- Arteriosclerosis (stiffness) vs. Atheroma

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PWV and all-cause mortality in hypertensive subjects



Vascular stiffness :

A major determinant of age-related diseases

- Heart Failure
- Stroke
- Coronary heart disease
- Renal failure
- Vascular dementia
- **But also...**

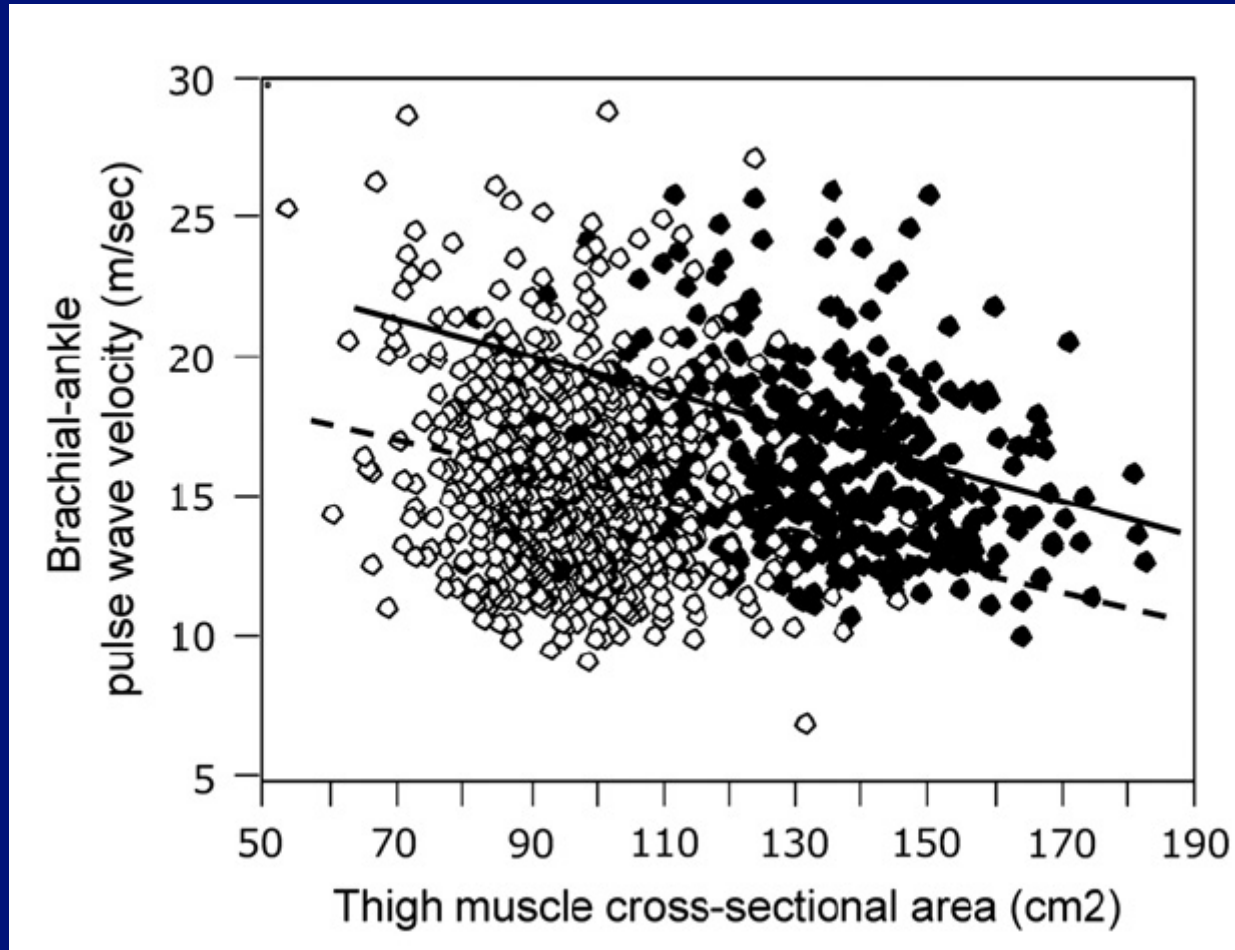
Possible relationships between arterial stiffness, age-related diseases and functional status in older individuals

- Sarcopenia
- Osteoporosis
- Gait disorders
- Slow walk speed

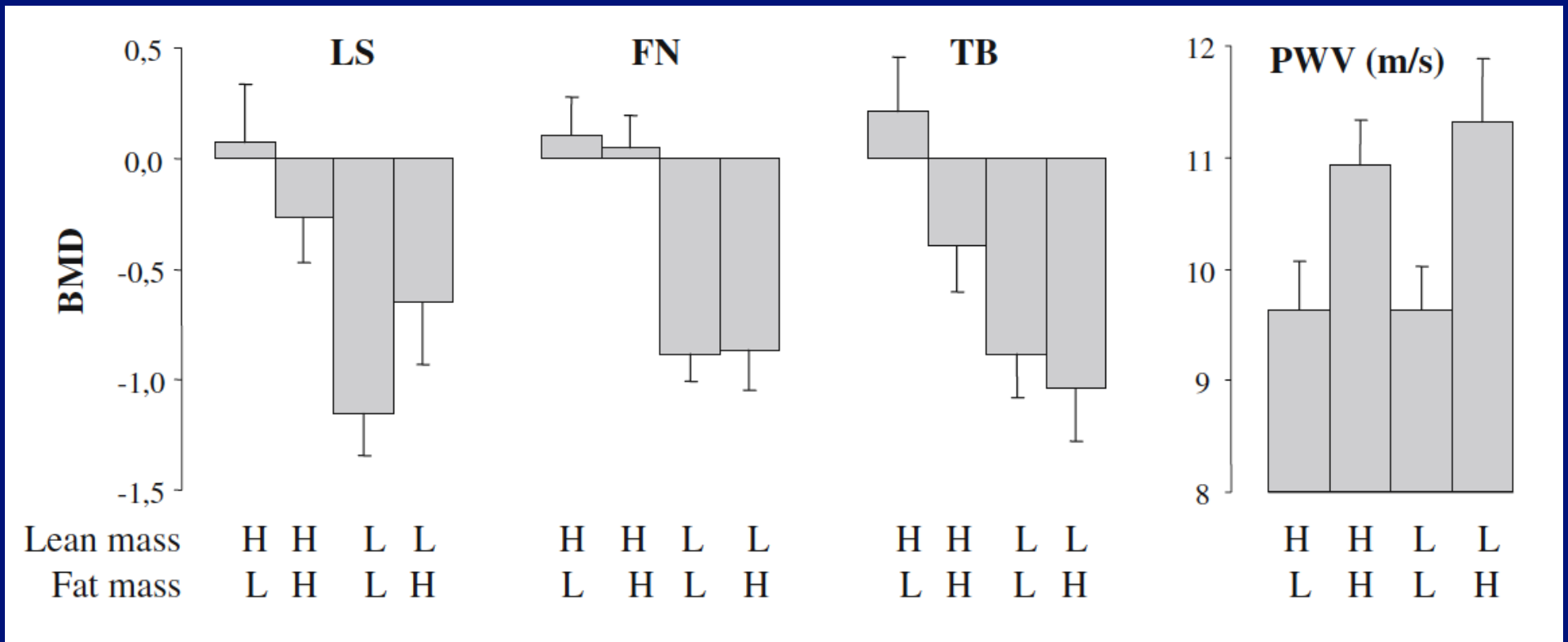


Falls
Fractures
Frailty
Loss of autonomy

High arterial stiffness is associated with sarcopenia



Bone mineral density and PWV values in men



Blood Vessels

Arterial Stiffness, Physical Function, and Functional Limitation

The Whitehall II Study

Eric J. Brunner, Martin J. Shipley, Daniel R. Witte, Archana Singh-Manoux, Annie R. Britton,
Adam G. Tabak, Carmel M. McEniery, Ian B. Wilkinson, Mika Kivimaki

Study performed in 5392 individuals

Hypertension 2011;57:1003-1009

Association of PWV with functional limitation

Independent Measures	ADL (N=5380)		IADL (N=5380)	
	Odds Ratio (95% CI)*	<i>P</i>	Odds Ratio (95% CI)*	<i>P</i>
Pulse wave velocity	1.23 (1.12 to 1.35)	<0.001	1.18 (1.07 to 1.31)	0.002
Pulse pressure	0.93 (0.84 to 1.02)	0.12	0.94 (0.84 to 1.05)	0.28
Mean arterial pressure	0.95 (0.87 to 1.04)	0.30	0.90 (0.81 to 0.99)	0.04
Antihypertensive treatment (yes vs no)	1.58 (1.32 to 1.88)	<0.001	1.29 (1.05 to 1.59)	0.01
Chronic disease†	1.42 (1.15 to 1.74)	<0.001	1.48 (1.17 to 1.87)	<0.001
Pulse wave velocity, fully adjusted‡	1.20 (1.08 to 1.34)	<0.001	1.21 (1.06 to 1.37)	<0.003

Association of PWV with functional limitation

- ...In conclusion, the concept of vascular aging is reinforced by the observation that arterial stiffness is a robust correlate of physical functioning and functional limitation in early old age. The nature of the link between arterial stiffness and quality of life in older people merits attention.

Vascular stiffness

A major determinant of age-related diseases

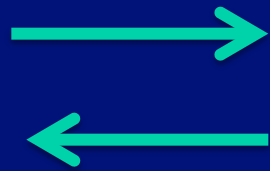
- Heart Failure
- Stroke
- Coronary heart disease
- Renal Impairment
- Vascular dementia

...But also

- Sarcopenia
- Walk speed
- Functional limitations
- Osteoporosis

Arterial stiffness and functional status in the elderly

**Arterial
stiffness**



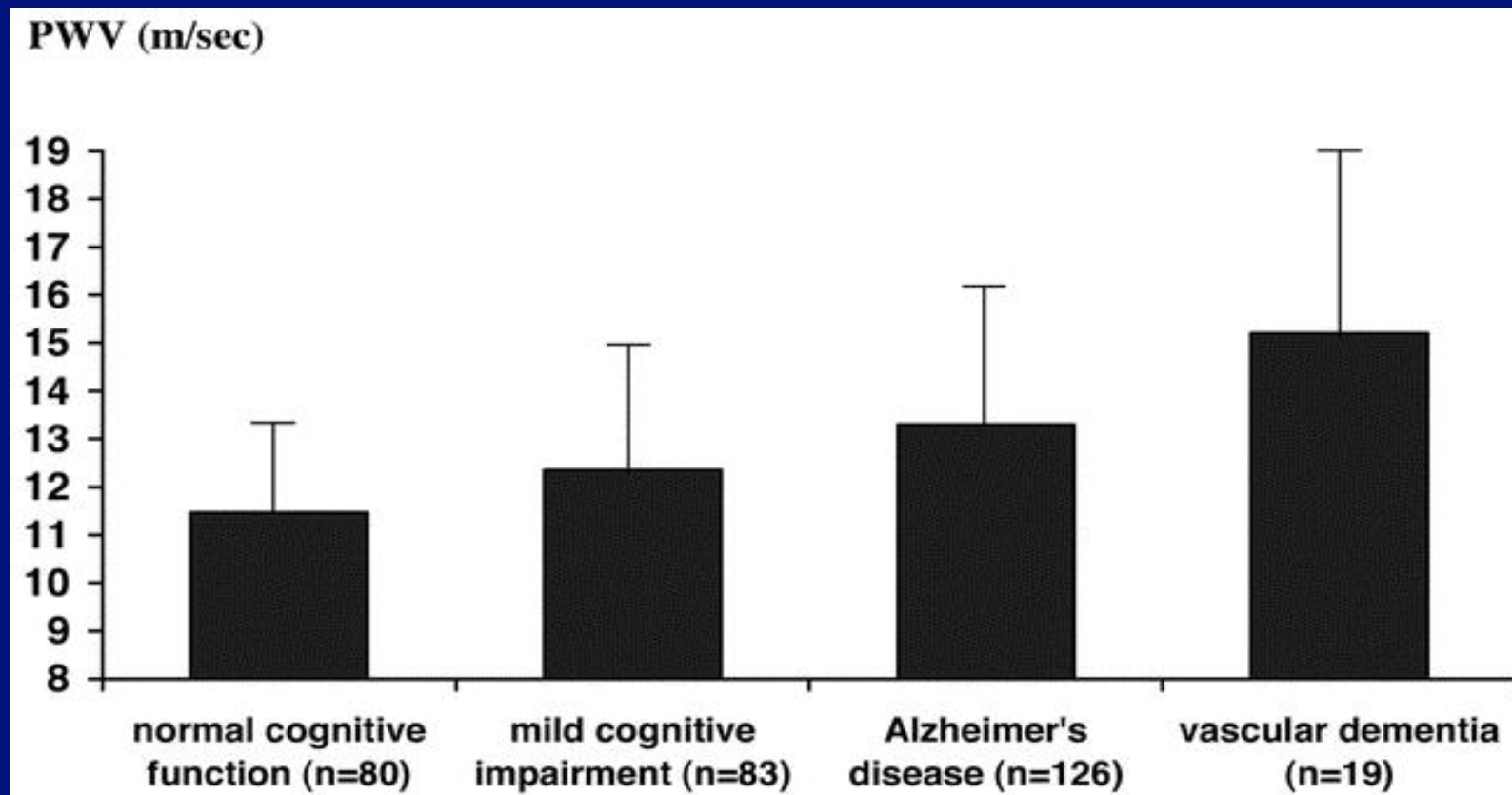
- **Sarcopenia**
- **Osteoporosis**
- **Gait disorders**
- **Functional limitations**



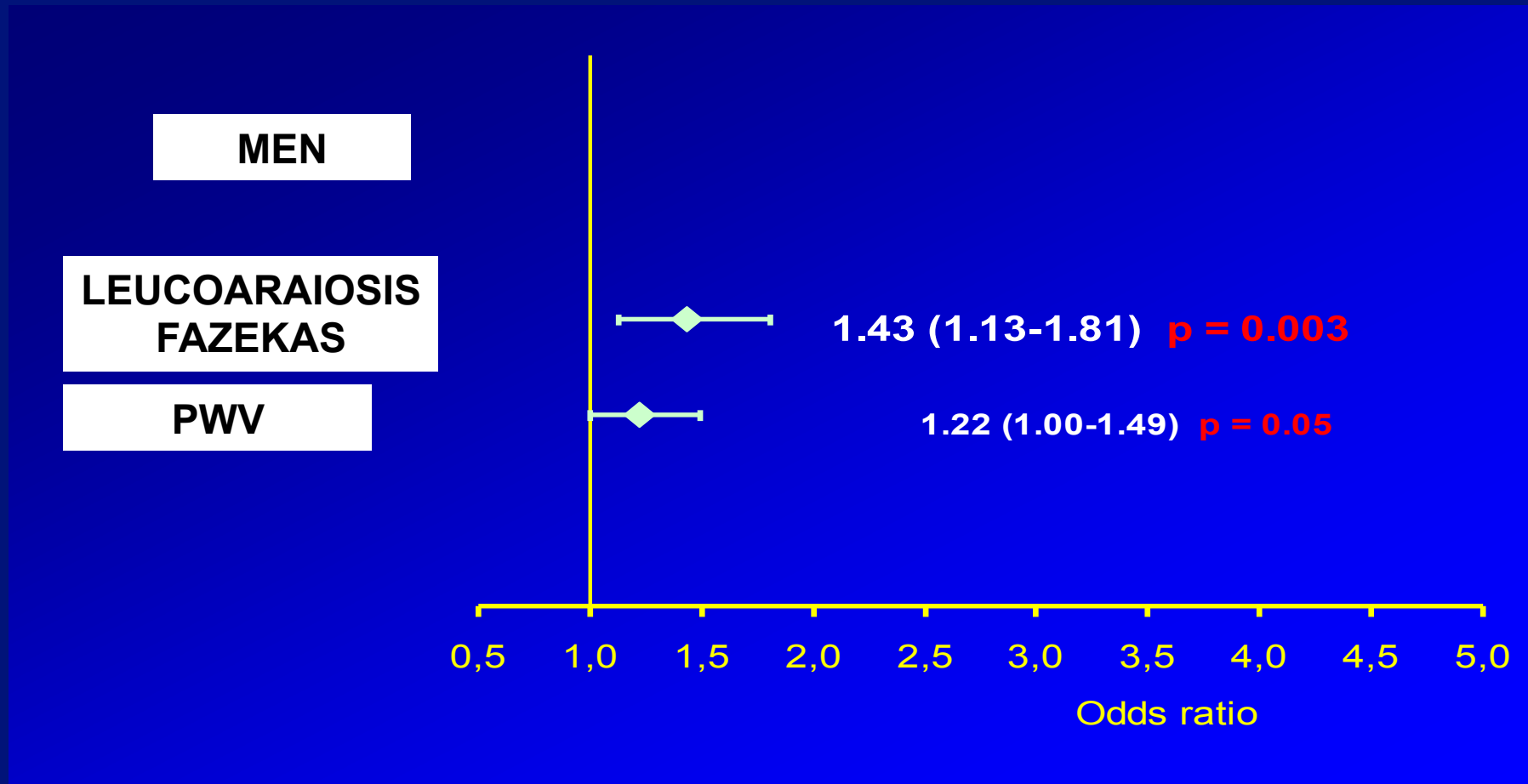
Falls and Fractures
Frailty, Loss of autonomy

**Arterial stiffness and cognitive
status in older adults**

Arterial stiffness is increased in patients with neurocognitive diseases



Aortic stiffness, and leucoaraïosis are independent determinants of cognitive impairment in hypertensive subjects over 60 yo : The ADELAHYDE study



Baseline values of arterial stiffness and BP in « decliners » and « non-decliners » over a 2-year follow-up period. The PARTAGE study (>80 yo living in NHs)

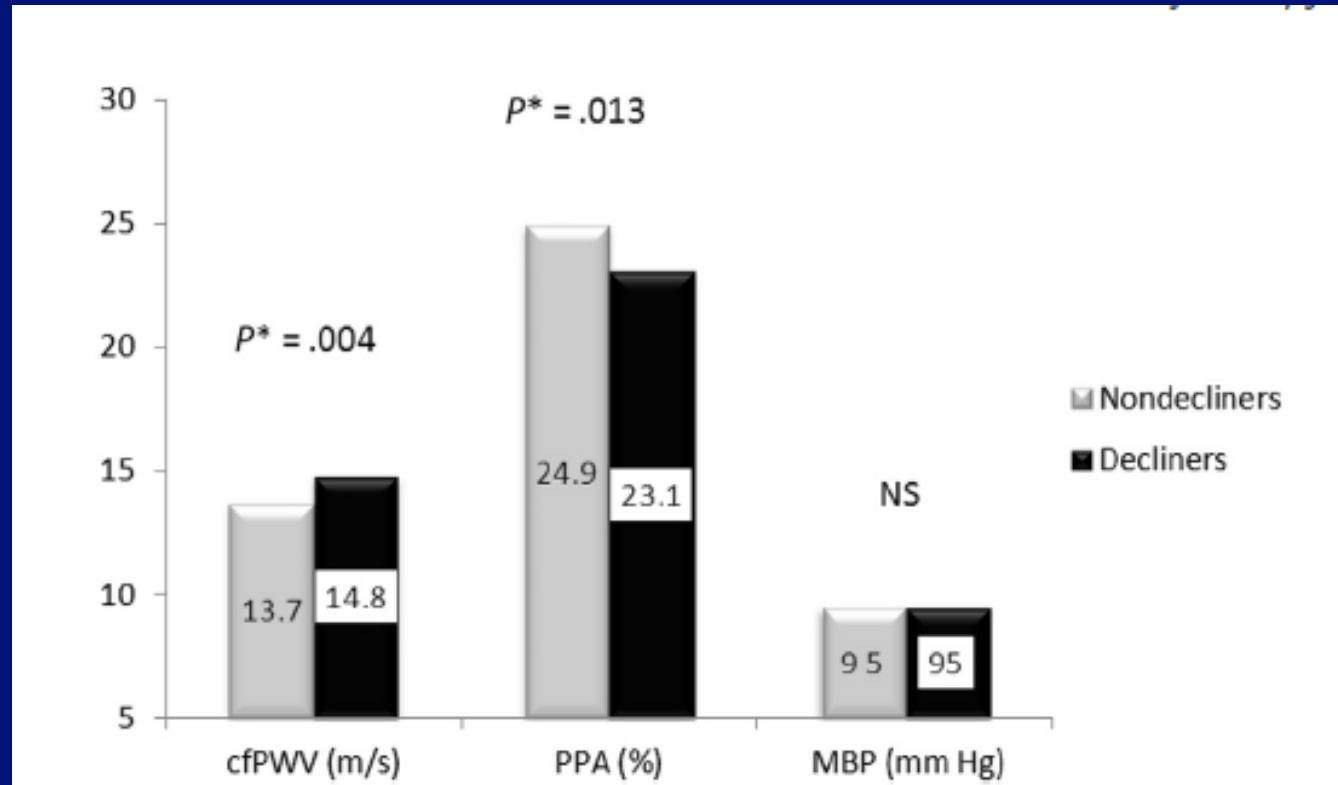


Fig. 2. Adjusted arterial stiffness and mean BP values according to MMSE decline. *Comparisons were performed using trend ANOVA. Data were adjusted for MBP (except for MBP comparison), age, education level, HR, BMI, and baseline MMSE and ADLs.

**Possible mechanisms of these
associations**

Hypoperfusion et Maladie d'Alzheimer

R.N. Kalaria / *Neurobiology of Aging* 21 (2000) 321–330

325

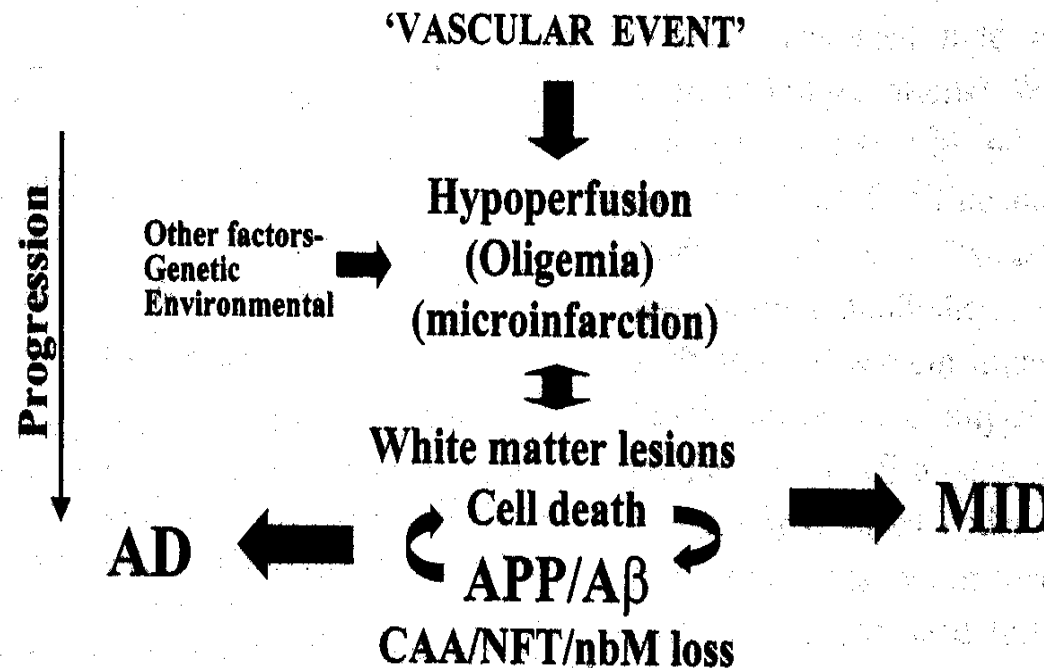
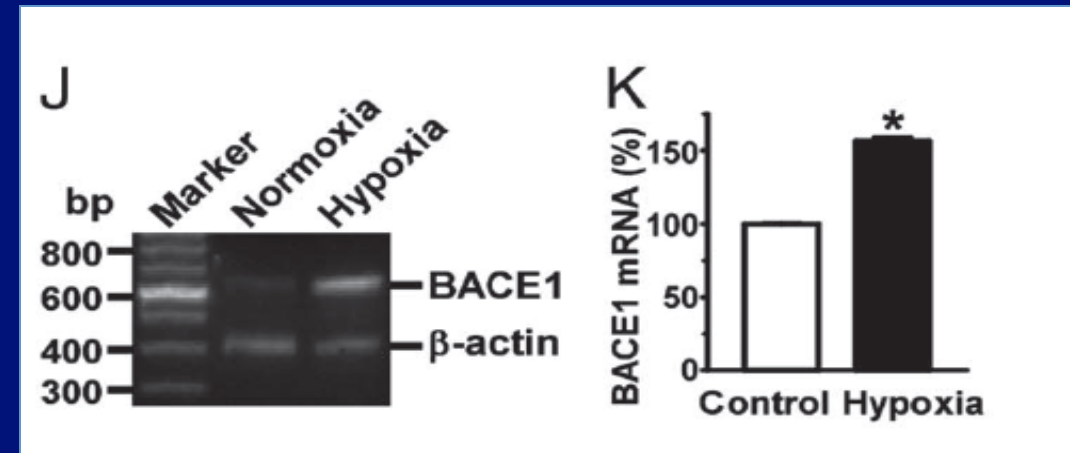
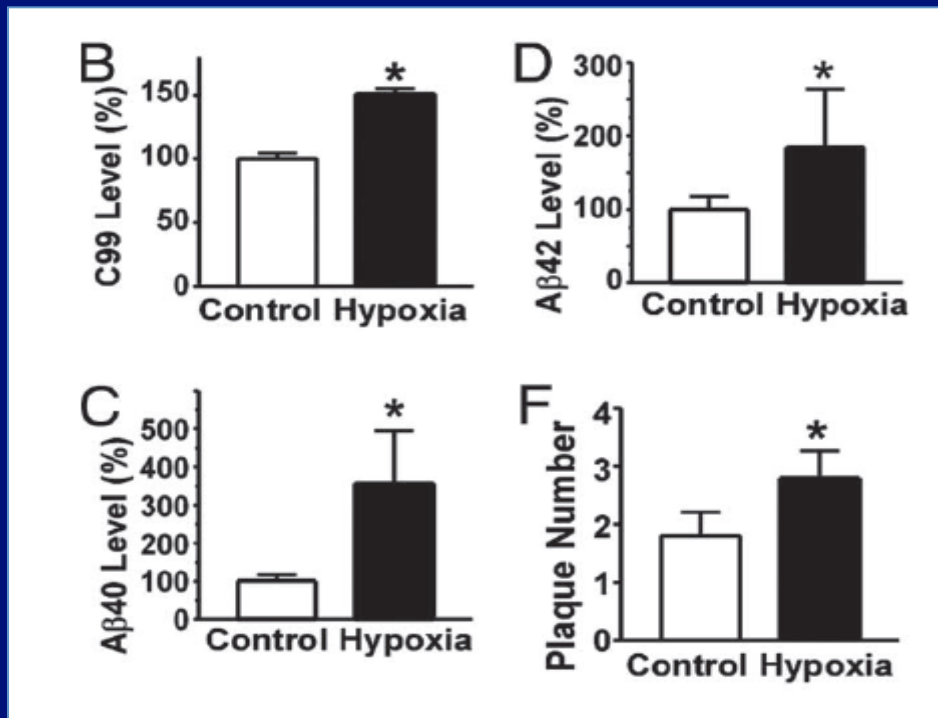
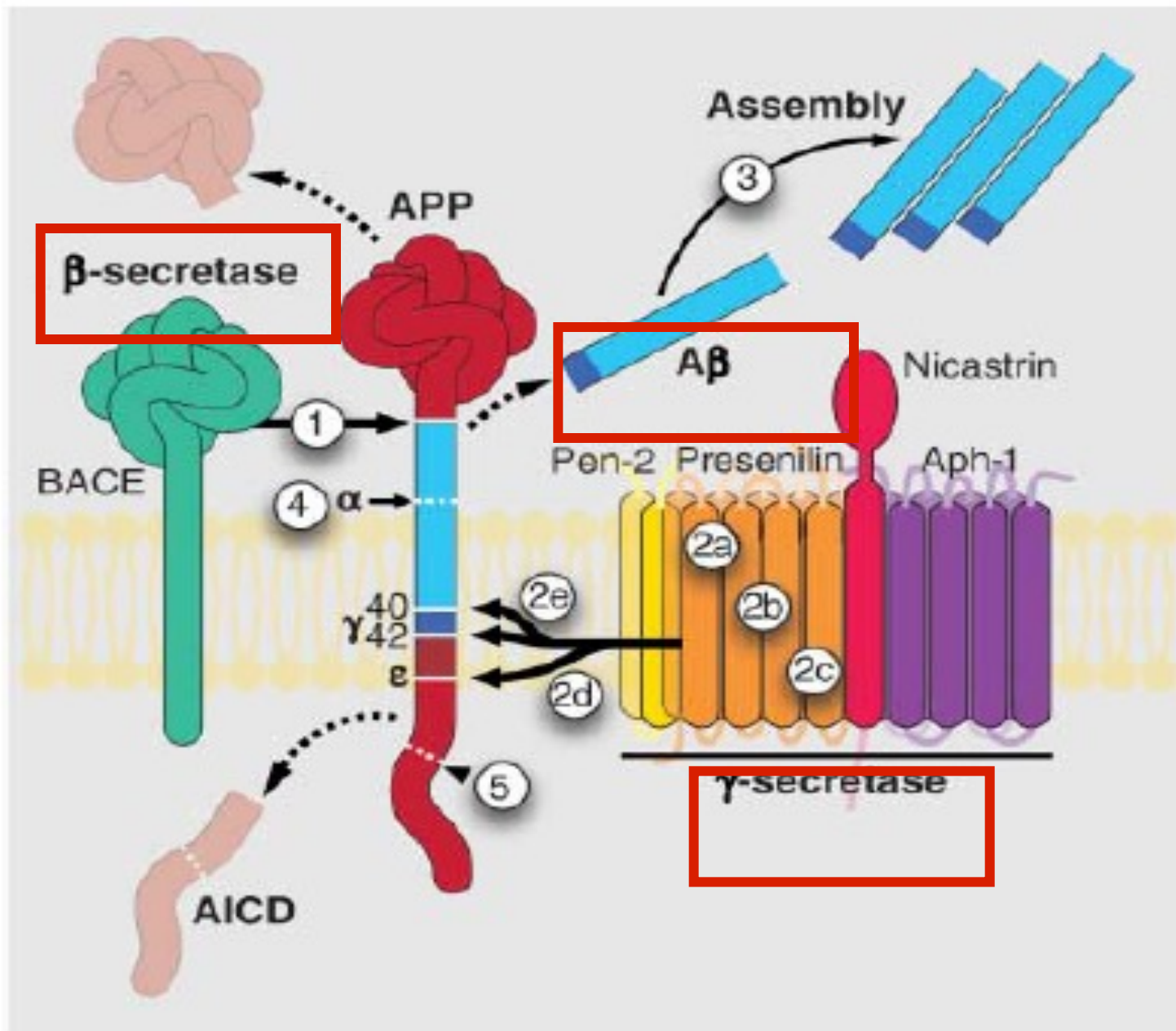


Fig. 2. Hypothetical scheme showing the ultimate effects of sustained vascular influences during aging that lead to AD type of changes. Genetic factors and the degree and severity with which initial insults occur may modify eventual outcome. "Vascular event" may occur as either peripheral vascular disease, e.g. hypertension, heart disease or cerebrovascular disease or both. A β , amyloid beta; CAA, cerebral amyloid angiopathy; MID, multi-infarct dementia; NFT, neurofibrillary tangles.

Hypoxia increases - secretase cleavage of APP and Amyloid deposition in APP23 transgenic mice.





Vascular stiffness: A major determinant of age-related diseases

- Heart Failure
- Stroke
- Coronary heart disease
- Renal failure
- Vascular dementia

...**But also**

- Sarcopenia
- Slow walk speed
- Osteoporosis
- Decrease in functional status
- Alzheimer Disease



- Iterative hospit.
- Frailty
- Loss of autonomy
- Death

1- Arteriosclerosis (stiffness) vs. Atheroma

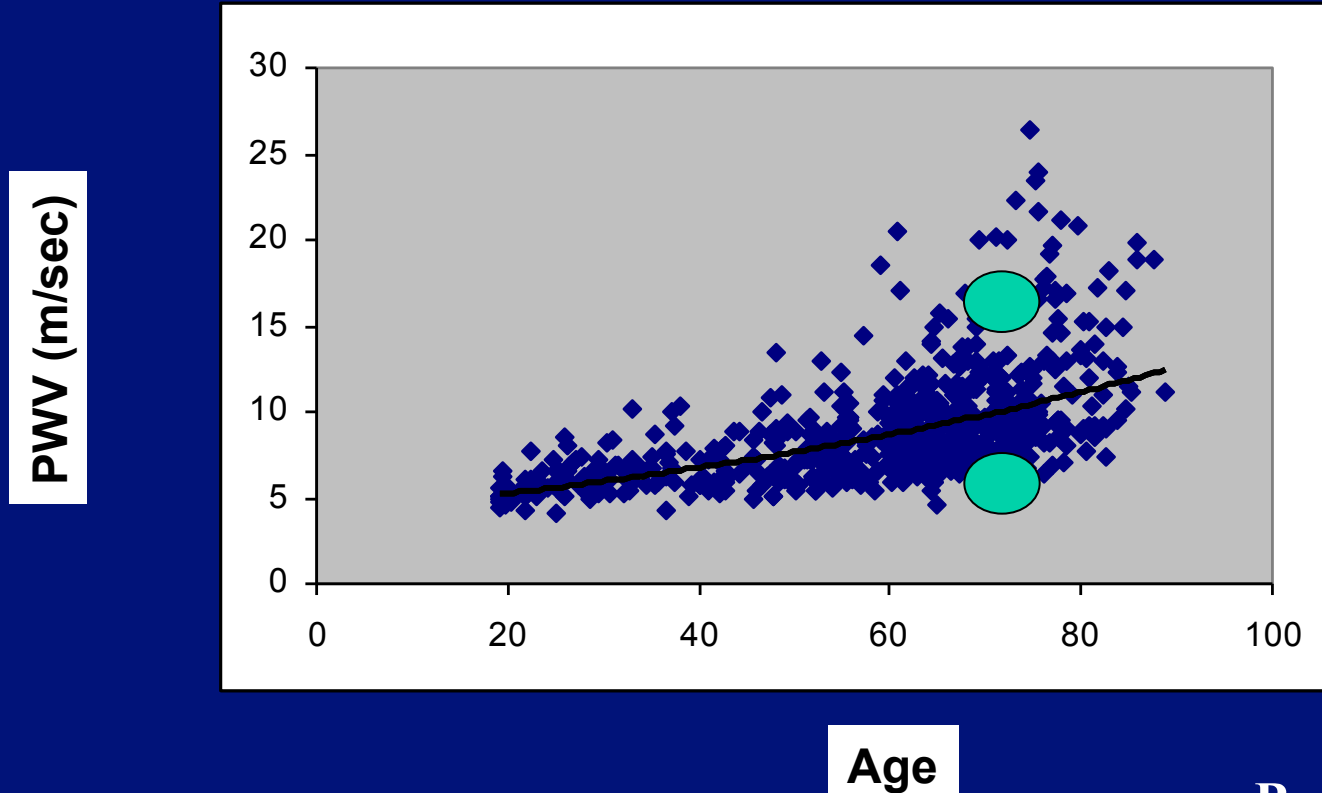
2- How to assess arterial stiffness?

3- Arterial stiffness and age-related diseases

4- Accelerators of arterial stiffness

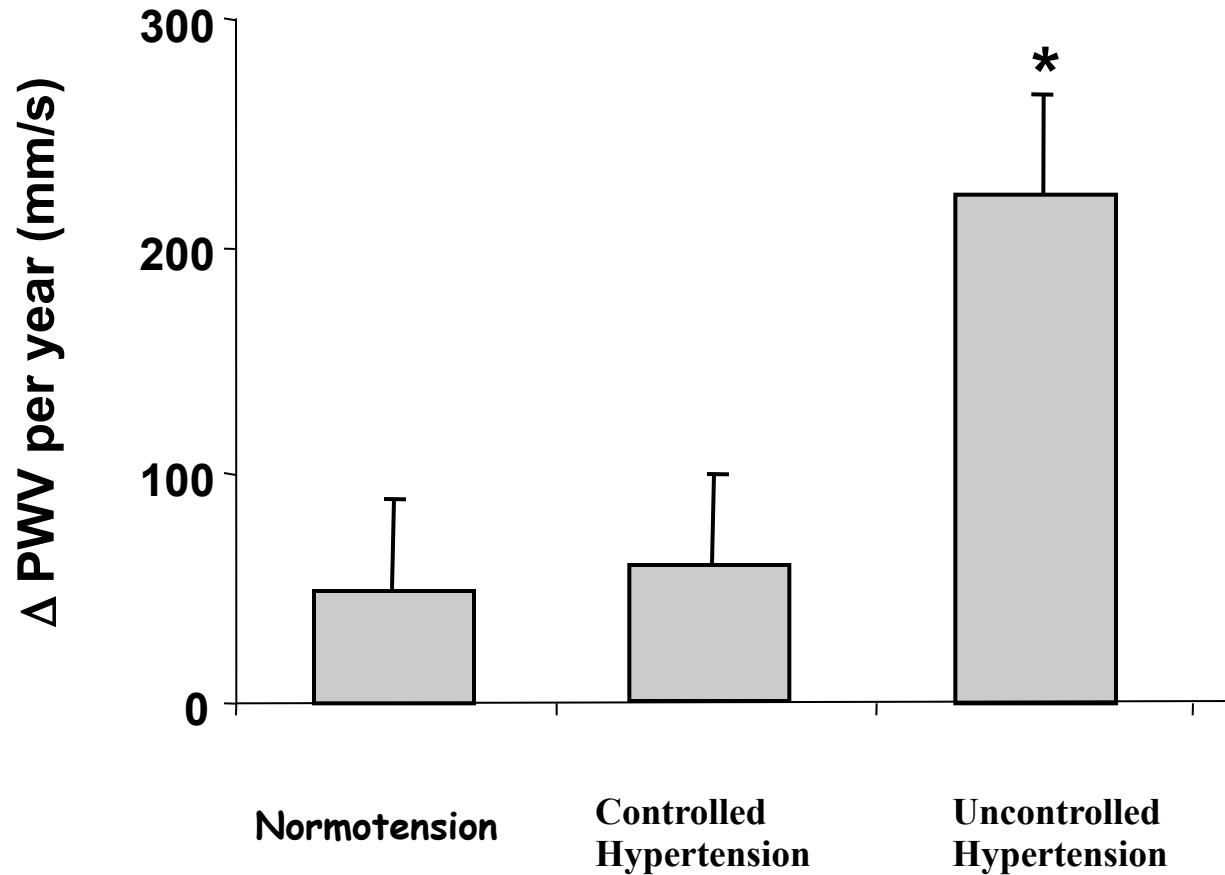
Annual PWV increase

- 50-80 mm/sec (1%) before age of 50-60
- 120-160 mm/sec (2%) after age of 60

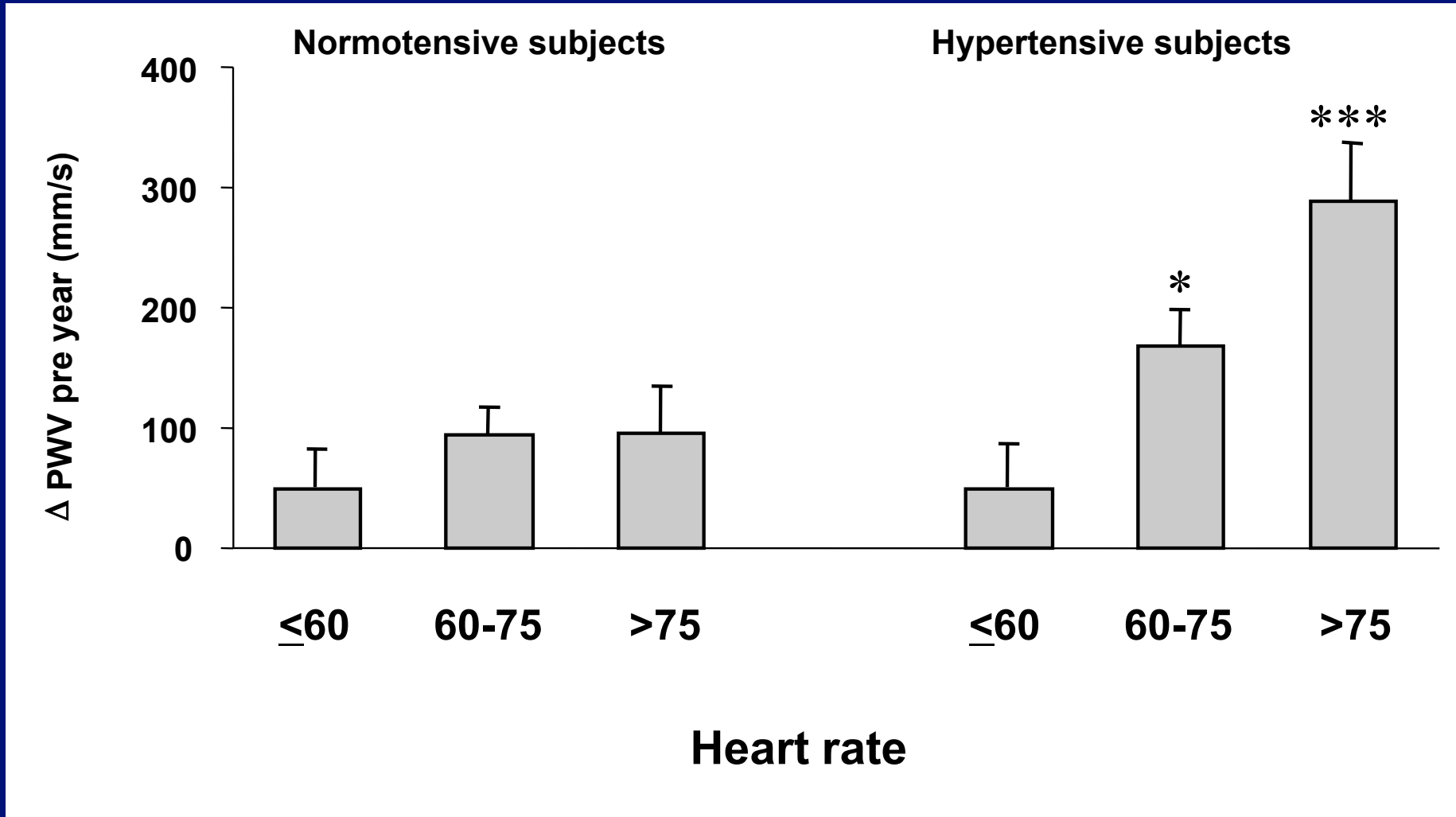


Benetos, Personal data

Progression in aortic stiffness according to the control of hypertension



Progression in aortic stiffness according to the heart rate



Evolution of arterial stiffness over a period of 6 years according to the presence of MetS

Those individuals with metabolic syndrome present a 2-fold more pronounced age-related increase in PWV

Salt diet and progression of arterial stiffness

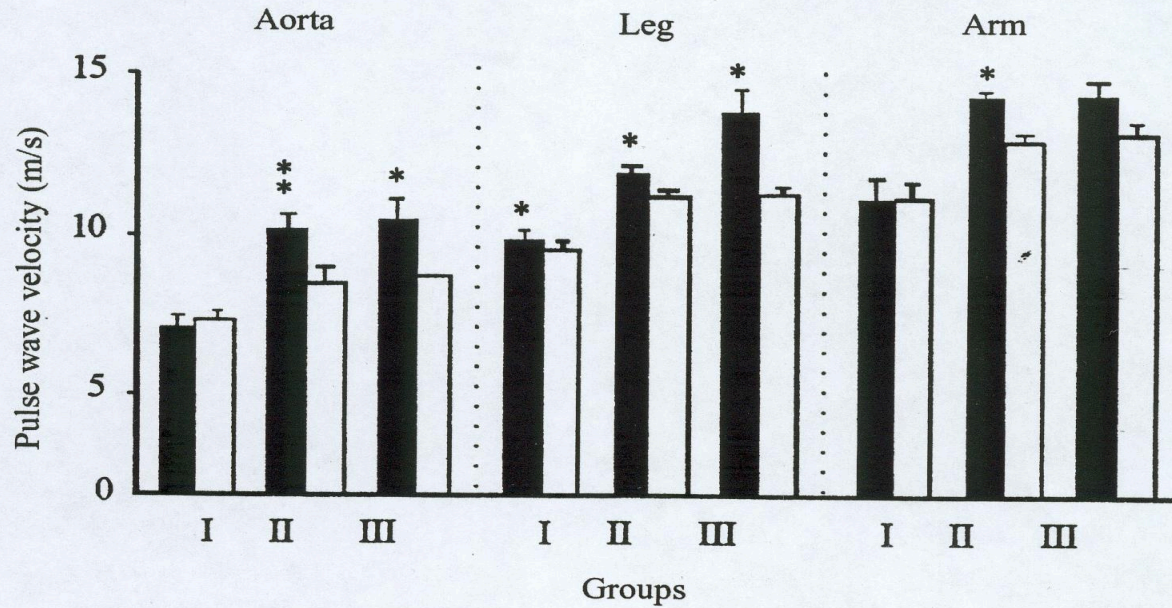
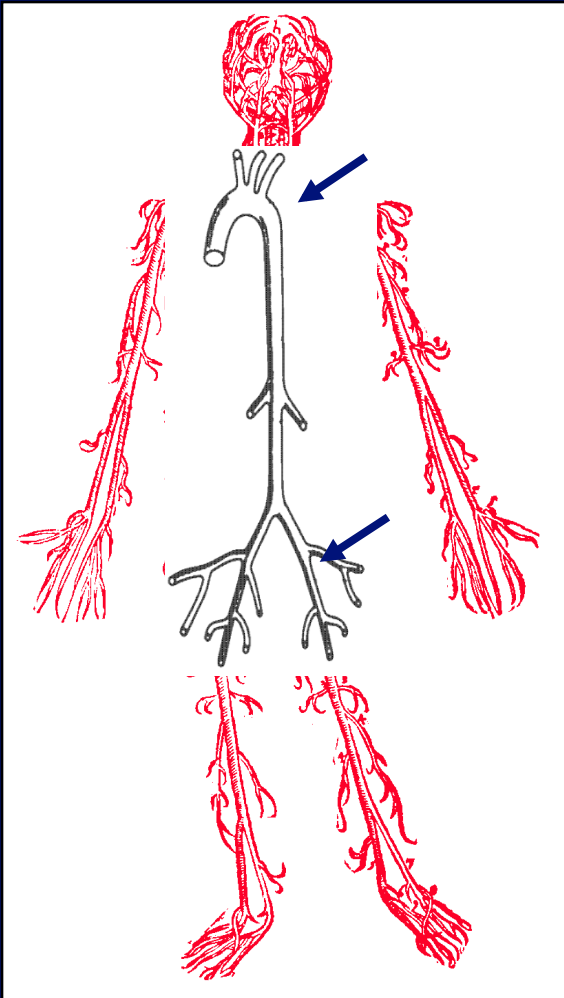


FIGURE 19. PWV at different arterial sites and in different age subgroups: I = 2 to 19 years; II = 29 to 44 years; III = 45 to 66 years in normotensive subjects following normal (■) or low-salt (□) diet. (Adapted from Avolio et al. [41].) * $p < 0.05$ ** $p < 0.01$.

Major diseases/conditions which accelerate arterial aging



Factors

« Added » Arterial Age

Diabetes + Micro Album.	+15
Diabetes type 2	+10
Metabolic Syndrome	+10
High BP (150 vs 130mmHg)	+10
High HR (85 vs 65bpm)	+10
Obesity (isolated)	+5
High salt diet	+5

Effects of CV risk factors on Atheroma and Art. Stiffness

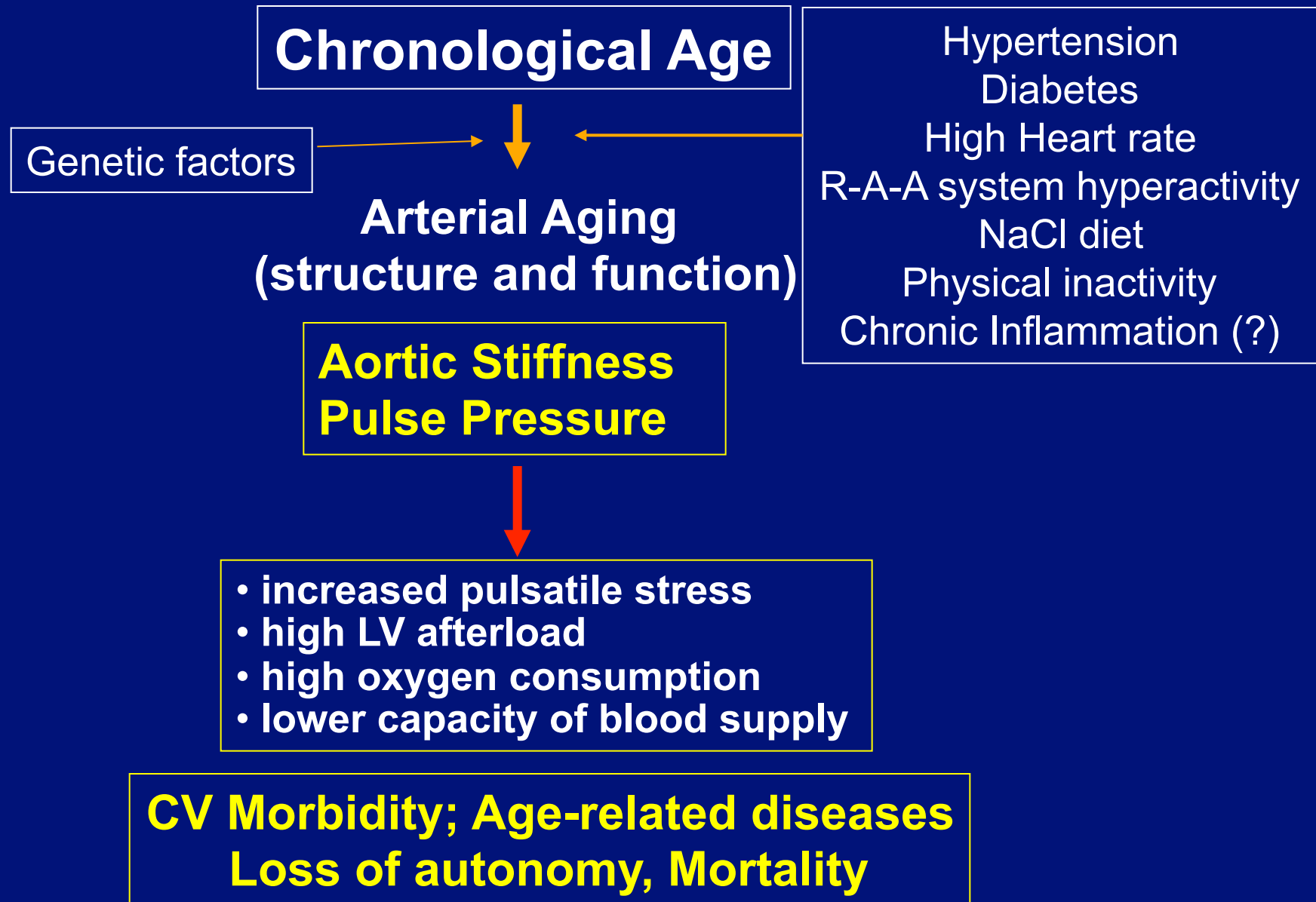


**ATHERO
MATOSIS**

**ARTERIO
SCLEROSIS**

Lipids	+++	+/0
Tobacco	++	+/0
Hypertension	++	+++
Diabetes	++	+++
Tachycardia	0	+
Obesity	+/0	+
High NaCl diet	0	++
No physical activity	+	+

Schematic representation of the development of Arteriosclerosis



CONCLUSIONS

- **Vascular stiffness may accelerate the aging process and several age-related diseases.**
- **Assessment of vascular stiffness in aging subjects could contribute to the preventive geriatrics.**

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2. Increase in the Systolic Blood Pressure
3. Increase in both Systolic and Diastolic BP
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5. Diabetes

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1. HTn can induce ATH
2. ATH can induce HTn
3. STIF can induce HTn
4. HTn can induce STIF

Question 3: Hypertension (HTn) and Atherosclerosis (ATH) and Arteriosclerosis (STIFF)

1. HTn can induce ATH
2. ATH can induce HTn (Renovascular HTn)
3. STIF can induce HTn
4. HTn can induce STIF

Question 4: Clinical consequences of Arteriosclerosis

1. Systolic Hypertension
2. Left Ventr. Hypertrophy
3. Cor. Heart Disease
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