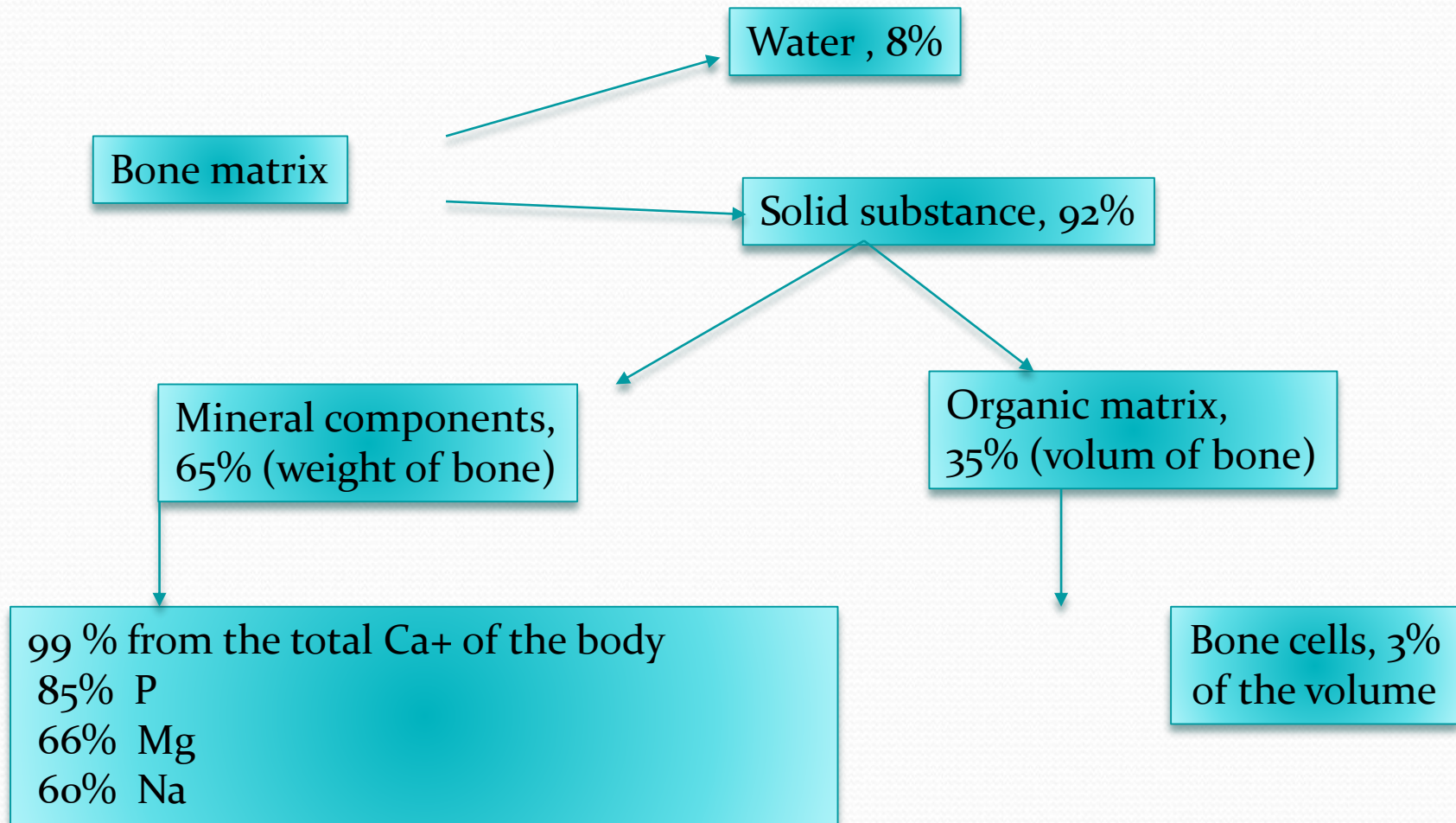




Osteoporosis

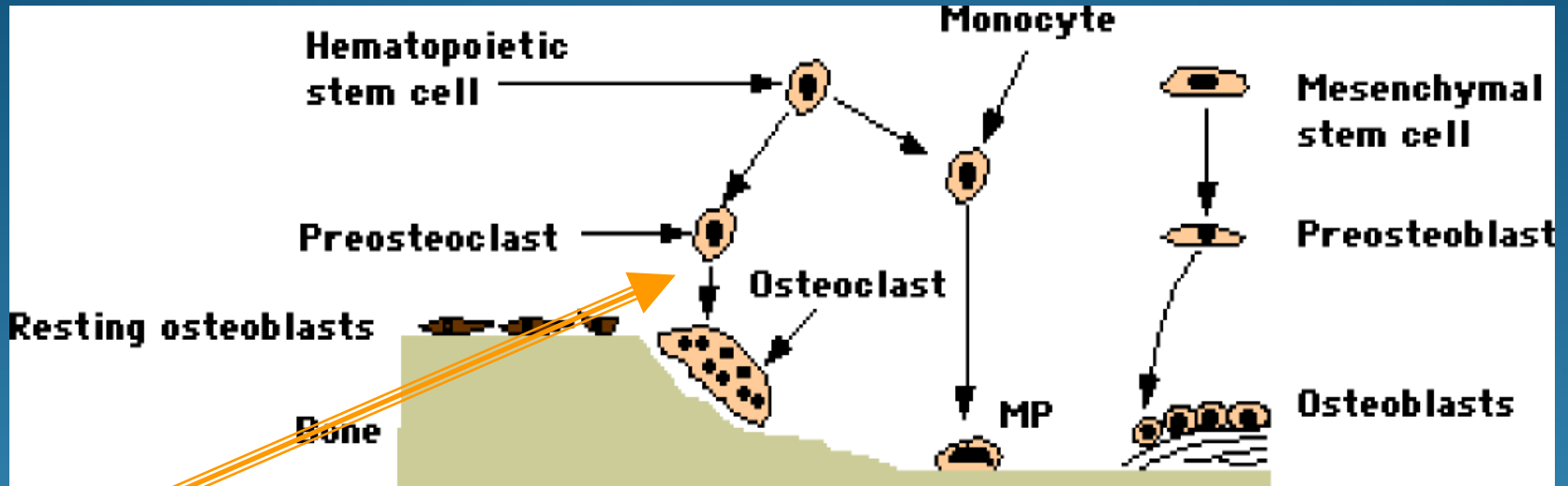
The main components of bone tissue



Bone remodeling

- Bone remodeling is the processes of resorption and continuous formation of bone, which takes place permanently at any time in the skeleton
- The summary effect of these processes and their balance creates a healthy bone.
- The bone remodeling takes place in basic multicellular centers (BMC).
- In the human body, at any moment there is approximately 1 million BMC.

Bone remodeling

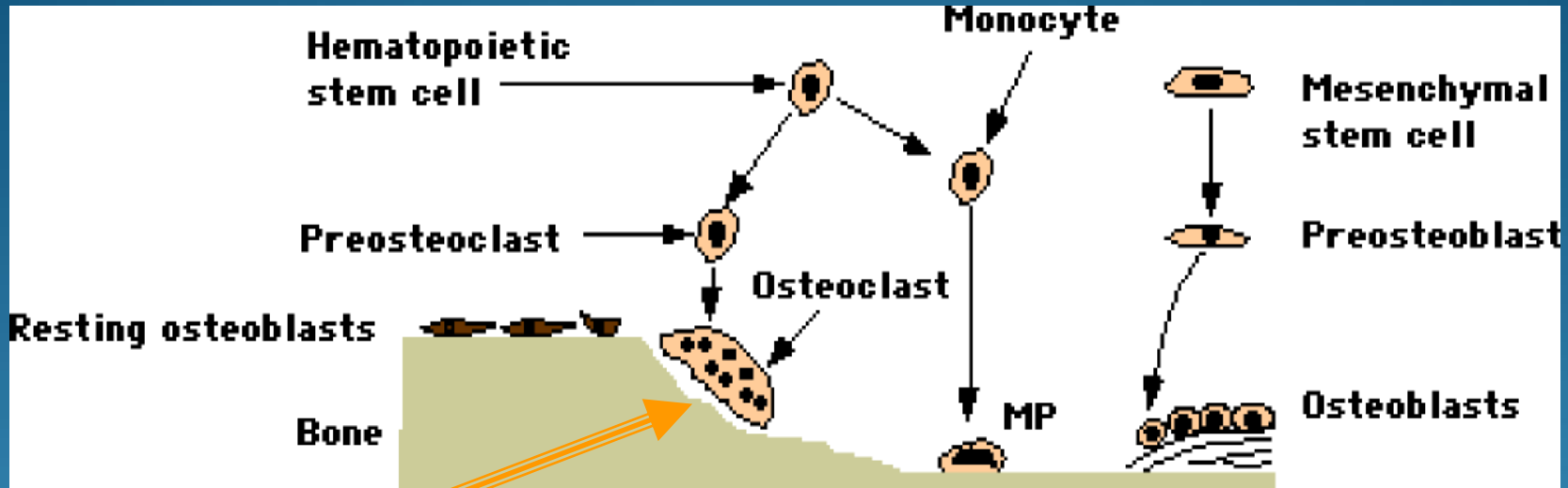


Activation 1 Resorption 2 Reversal 3 Bone formation 4 Resting 5

1. Activation phase:

- It starts by migration of the partially differentiated mononuclear cells (preosteoclastic) to the bone surface
- The fusion of preosteoclasts into osteoclast (large, multinucleated cells).

Bone remodeling

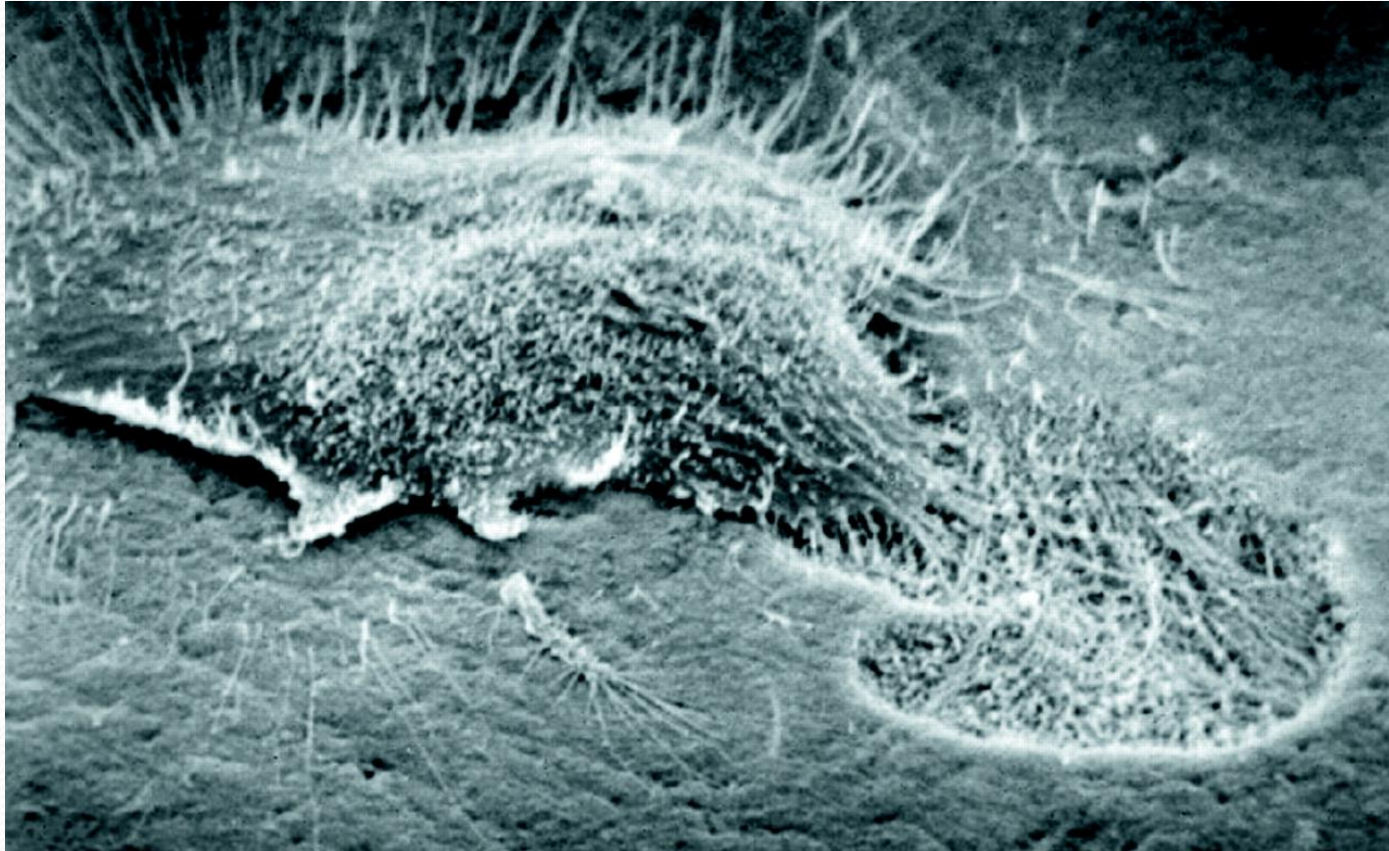


Activation 1 **Resorption** 2 Reversal 3 Bone formation 4 Rest 5

2. Resorption : osteoclasts attached to the bone surface cause limited reabsorption of minerals and bone matrix from the trabecular surface or in the cortex of the bone

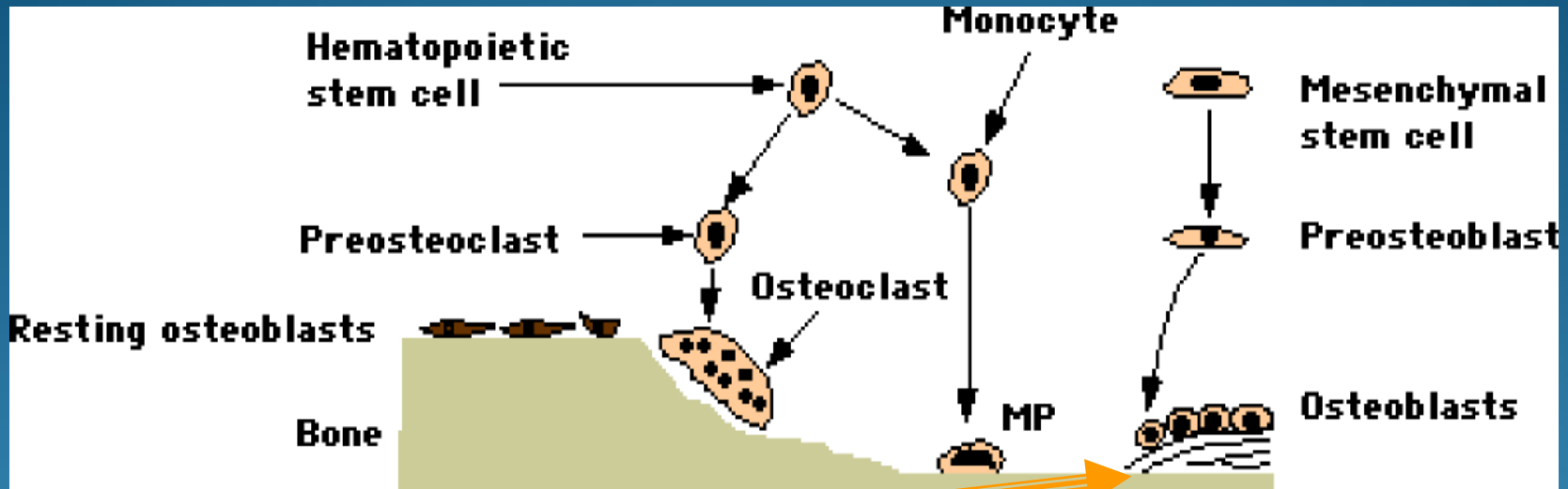
cortex

Electronic microphotograph of the osteoclast



Poole, K. E S et al. BMJ 2006;333:1251-1256

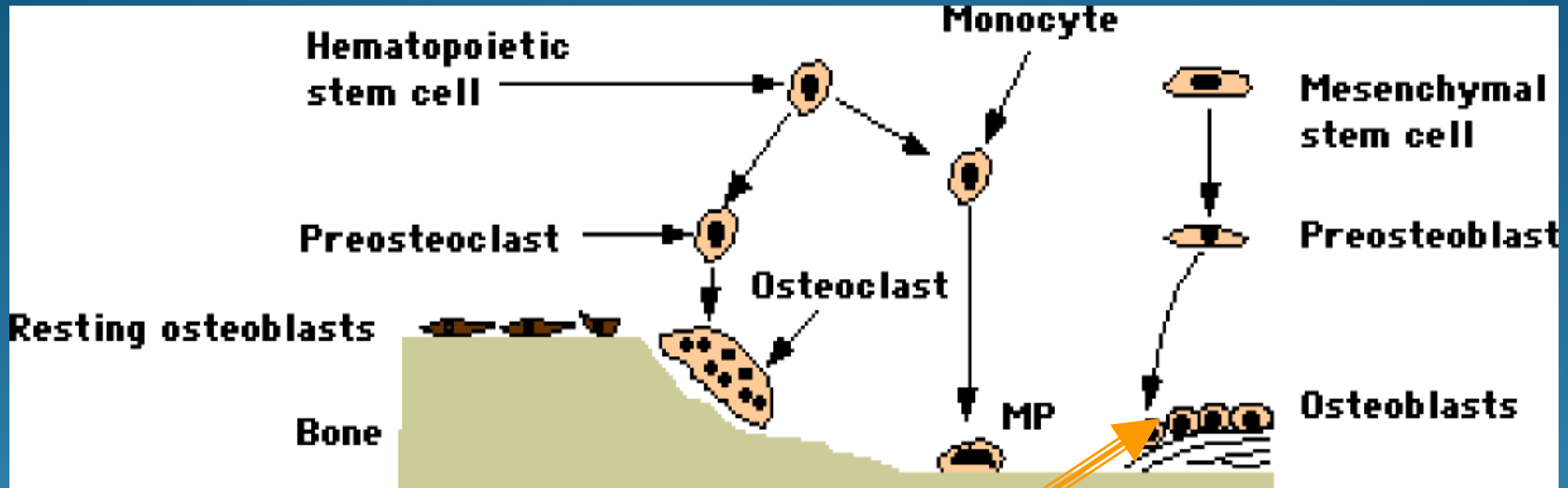
Bone remodeling



Activation 1 Resorption 2 **Reversal 3** Bone formation 4 Rest 5

3. Reversal phase: The mononuclear cells (monocytes + macrophages) are linearly arranged at the bone surface to form a rich glycoprotein layer over the resorbed surface (the "cement line") to which the osteoblasts will adhere, preparing the surface for the formation of the new bone by the osteoblasts.

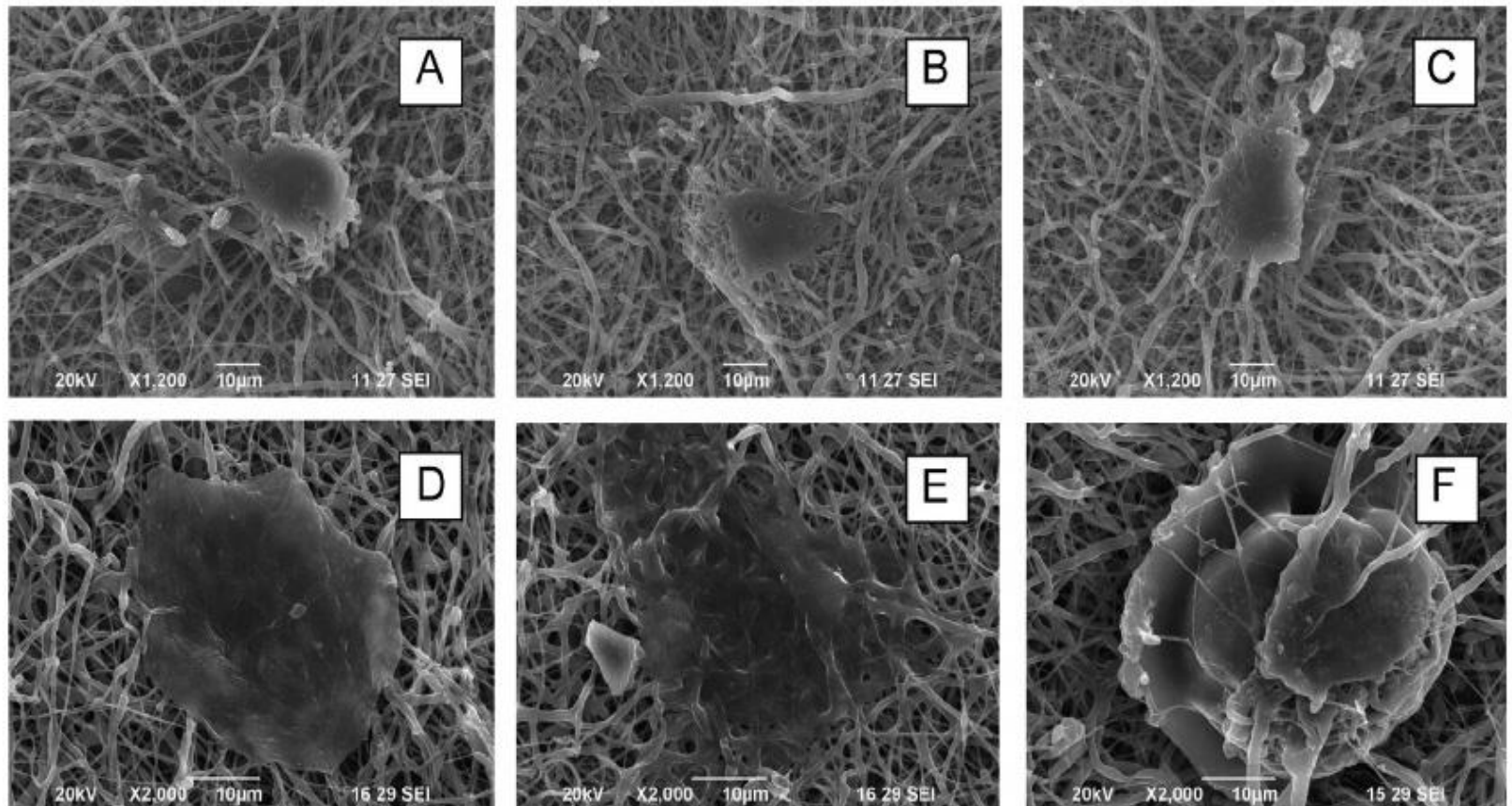
Bone remodeling



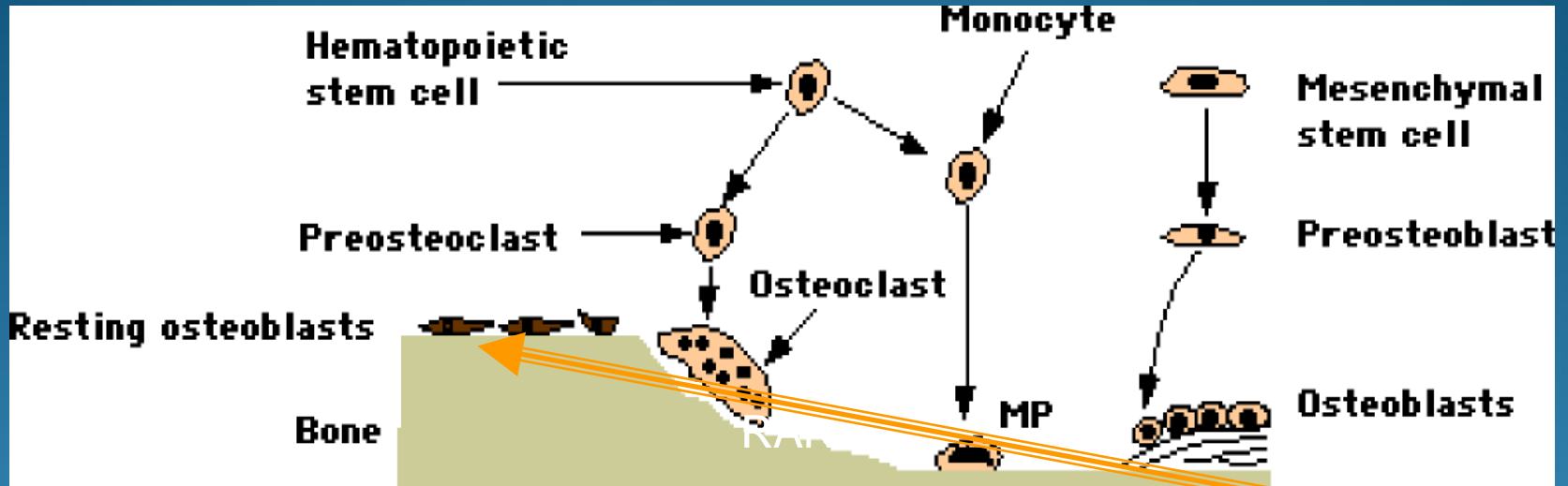
Activation Resorption Reversal **Bone formation** Rest
 1 2 3 4 5

4. Bone formation: new bone structural unit: the osteoblasts and their products are deposited in successive waves over each other, until the resorbed bone surface is completely replaced

Electronic microphotograph of osteoblasts



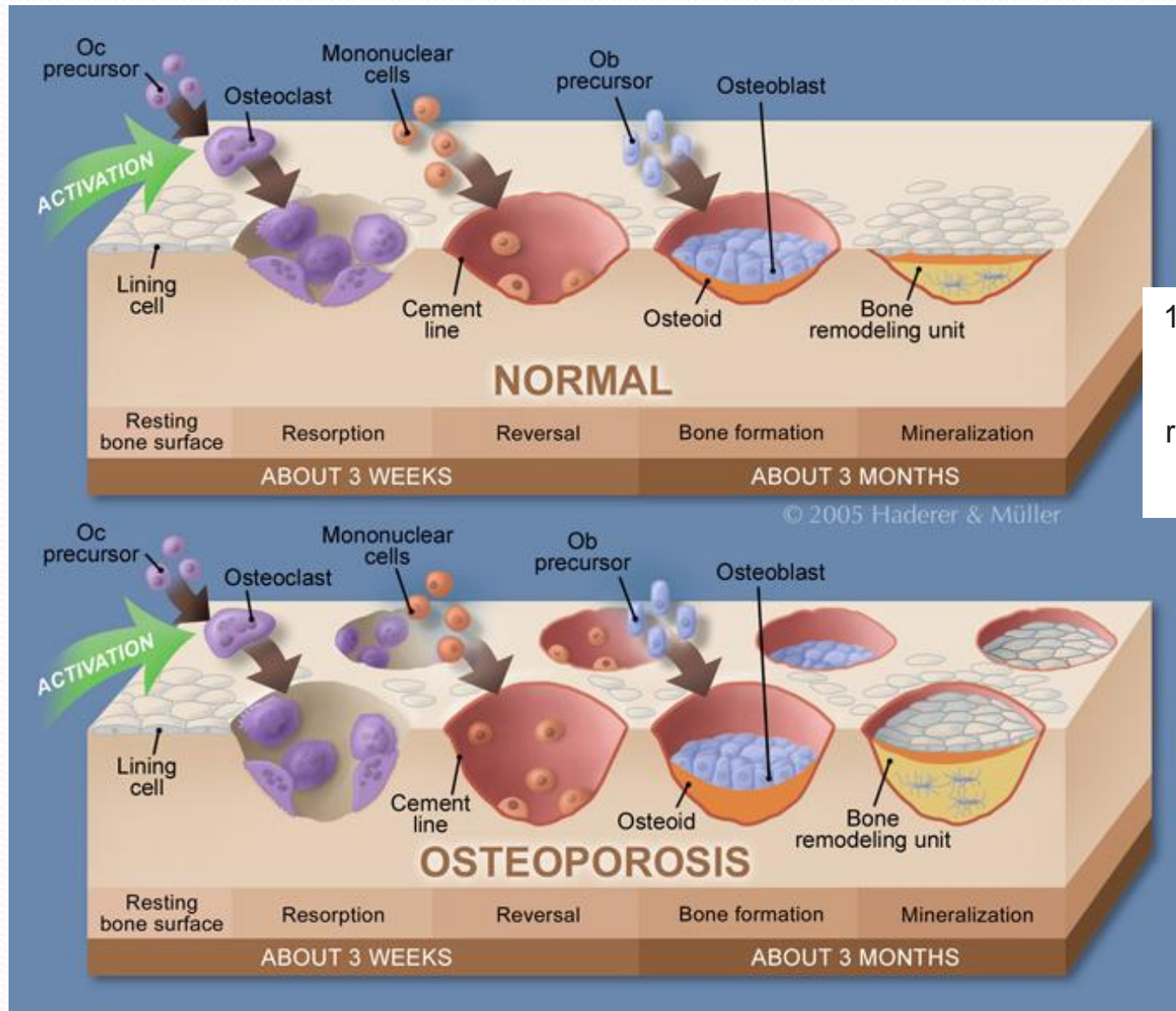
Bone remodeling



Activation Resorption Reversal Bone formation Rest
1 2 3 4 5

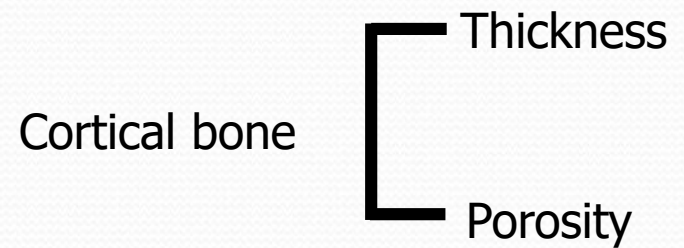
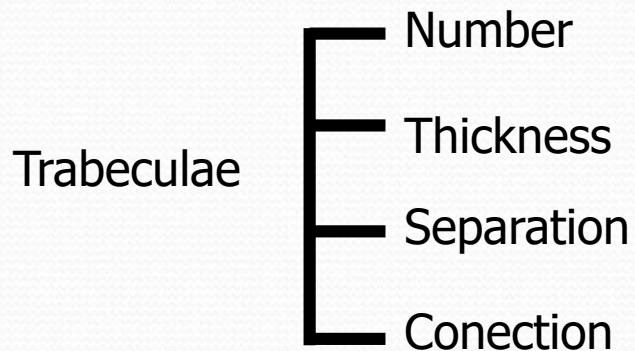
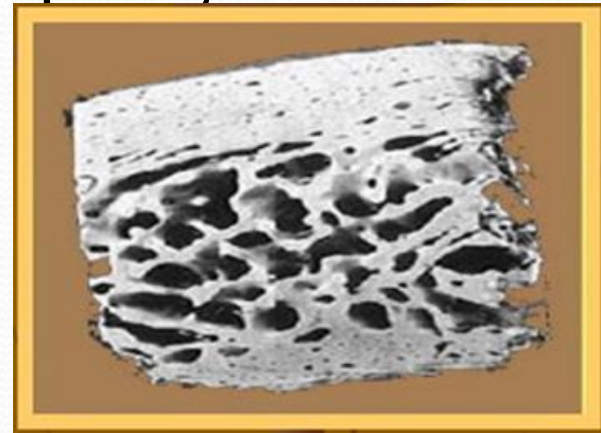
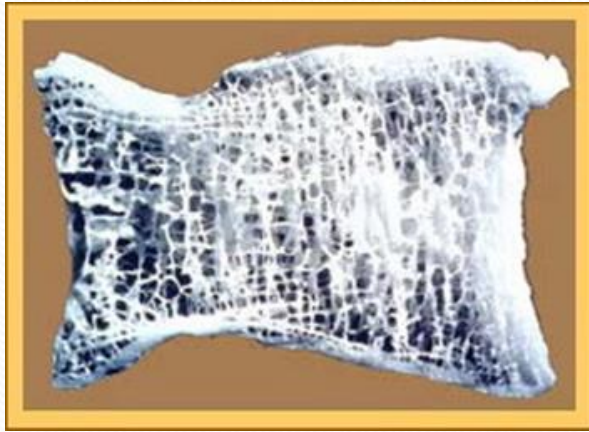
5. Rest phase: at the end of the formation phase, the surface is covered with a layer of flattened, slightly active osteoblasts, till a new remodeling cycle.

In osteoporosis the bone remodeling is increased, the resorption is more intense than formation



1 BMU cycle = 0.05 cu. mm bone replacement

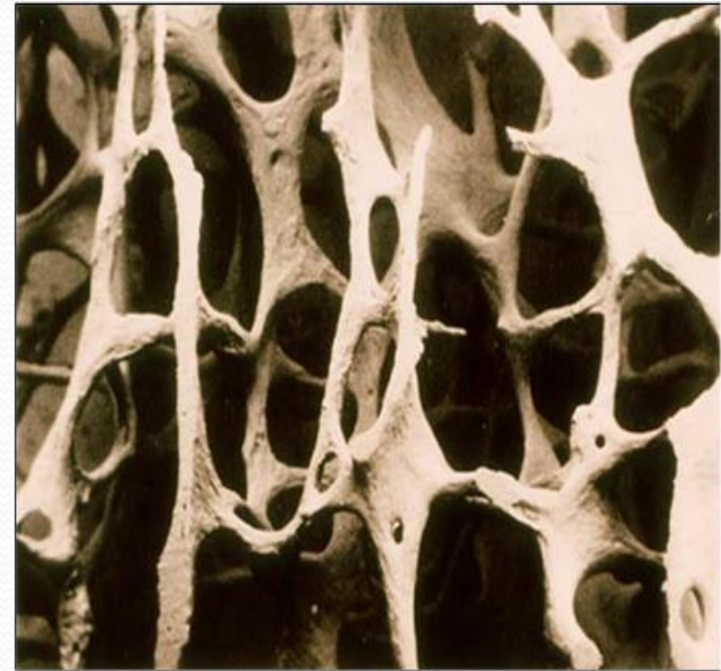
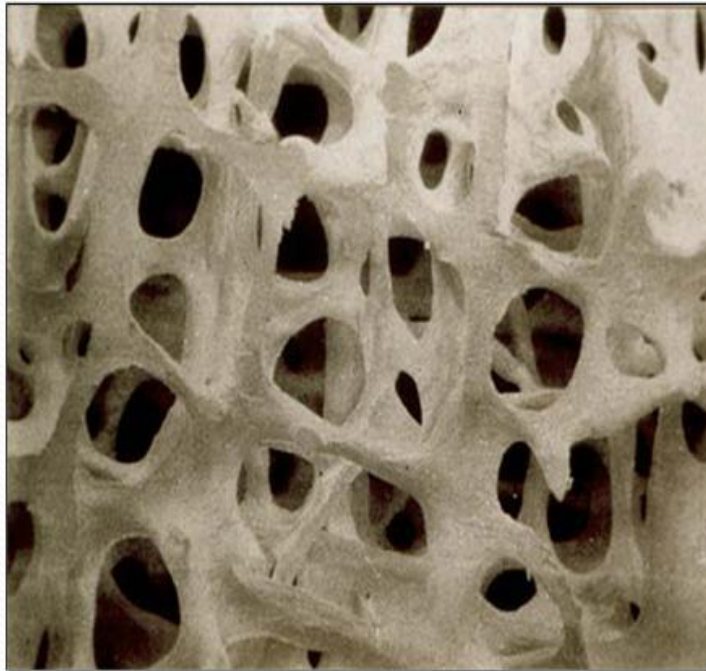
Elements of bone architecture that influence bone strength / quality



Critical role of trabeculae connectivity (micro CT)

Normal bone

Osteoporosis

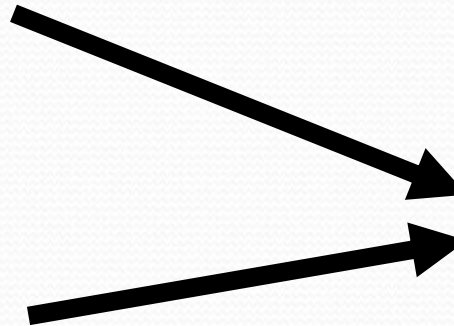


*Thin slits, few in number, with
horizontal defects*

Why the bones are broken?

Maximum load

Strength (Maximum load without fracture occurrence)



Maximum load

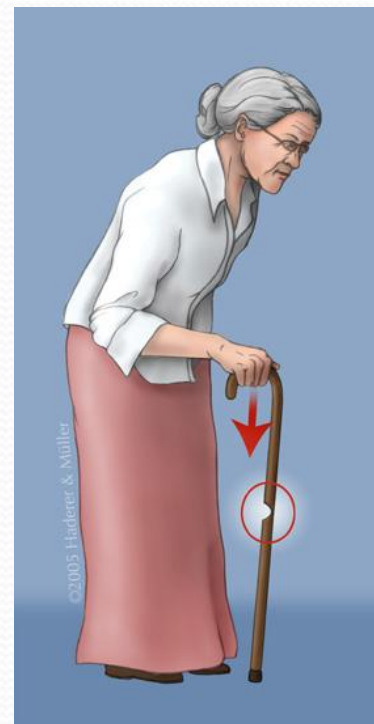
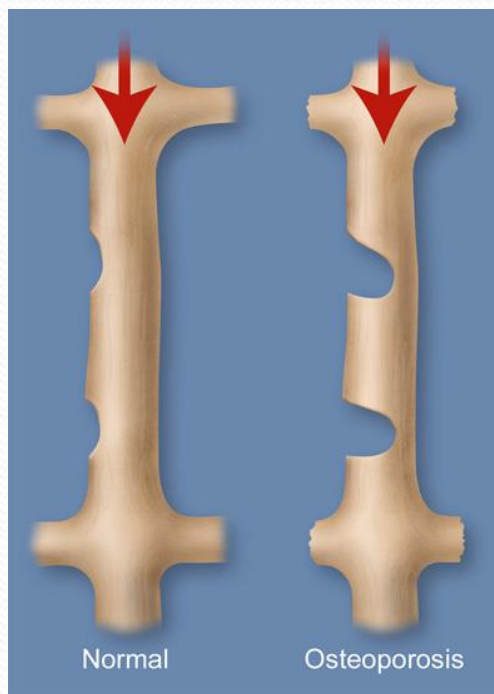
>1



Fracture

Strength

The resorbed cavities concentrate the mechanical load



Definition

- Osteoporosis is a multifactorial bone metabolic disease, characterized by decreased bone mass and deterioration of bone tissue microarchitecture, with decreased resistance and increased bone fragility, thus increasing the risk of fracture.

NIH Consensus Development Panel on Osteoporosis,
JAMA 2001, 285: 785-795

Definition

- Osteoporosis is established when the bone mineral density (BMD) in the patient is $-2.5DS$ or below the mean BMD level in healthy young Caucasian women.

WHO definition

Background

- It is the most common metabolic disease in several countries, such as USA, UK, Canada.
- It is asymptomatic until complications occur.
- The most common complications are osteoporotic fractures.
- In healthy people fractures occur under the influence of an extreme load.
- In the case of osteoporosis the fractures appear at minimal influences, related to the person's daily activity.

Classification of systemic osteoporosis

- **Primary**

Damage of the bone mass is related to aging or low gonadal function. It is usually found in postmenopausal women or men after 70 years.

- **Secondary**

It results as a complication of chronic conditions or the administration of certain medications, for example, corticosteroids, which accelerate bone loss.

Classification of systemic osteoporosis

- **Primary**

1. Involution
- Type I (postmenopausal)
- Type II (senile)
2. Juvenile idiopathy
3. Idiopathic middle age

- **Secondary**

1. Drugs induced
2. In endocrine diseases
3. In rheumatic diseases
4. In kidney diseases (in renal failure)
5. In gastrointestinal tract diseases
6. In the diseases of the blood
7. Others

Secondary osteoporosis, causes

1. **Drugs induced**
 - Glucocorticosteroid drugs
 - Heparine
 - Thyroid replacement therapy
 - Methotrexat
 - Antacids
2. **Endocrine**
 - Hyperthyroidism
 - Diabetes mellitus
 - Hypercorticism (Cushing syndrome)
 - Hypogonadism
 - Hyperparathyroidism
 - Pituitary disorders
 - acromegaly
 - hypopituitarism
3. **Rheumatic diseases**
 - LES
 - RA
4. **Renal diseases**
 - Chronic kidney disease
 - Renal acidosis
 - Fanconi syndrome
5. **Nutritional and gastrointestinal disorders**
 - Gastrectomy
 - Coeliac disease
 - Malabsorption syndrome
 - Liver disease
 - Primary biliary cirrhosis
 - Chronic hepatitis
 - Alcoholic hepatitis
6. **Hematologic disorder**
 - Lymphoma, leukemia
 - Hemophilia
 - Multiple myeloma
 - Thalassemia
 - Anemie
7. **Others**
 - Osteogenesis imperfecta
 - Marfan syndrome
 - Pregnancy and lactation

Epidemiology

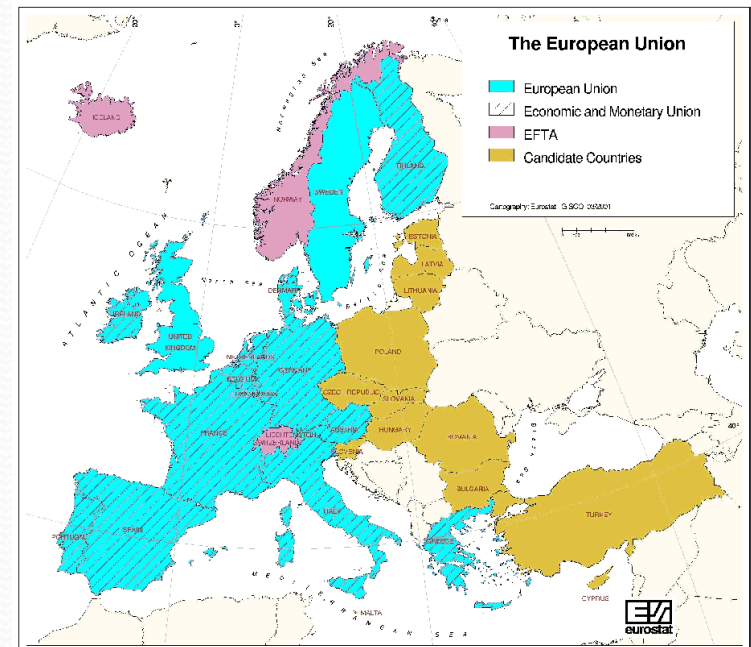
Osteoporosis is considered a disease of old age:

- The data from the last years show a significant increase in the number of the population over 65 years.
- In the European countries the population over 65 years::

12-17 % in 2002

14 -19% in 2014

20-25 % to 2025



Epidemiology

- In the United States about 10 million people suffer from osteoporosis. Additionally, 34 million people have low BMD.
- In the USA, 1.5 million osteoporotic fractures are registered annually.
- The direct costs treatment of these fractures constitutes \$ 18 billion.

Epidemiology

- After the age of 50, OP fractures show an exponential growth:
 - 30% of women and 5% of men will have an osteoporotic fracture ever in their life
 - A woman over 60 years doubles her risk of a fracture in every decade of her life

Epidemiology

Fractures caused by OP lead to different degrees of disability (eg vertebral, forearm) or even death (eg hip-fracture):

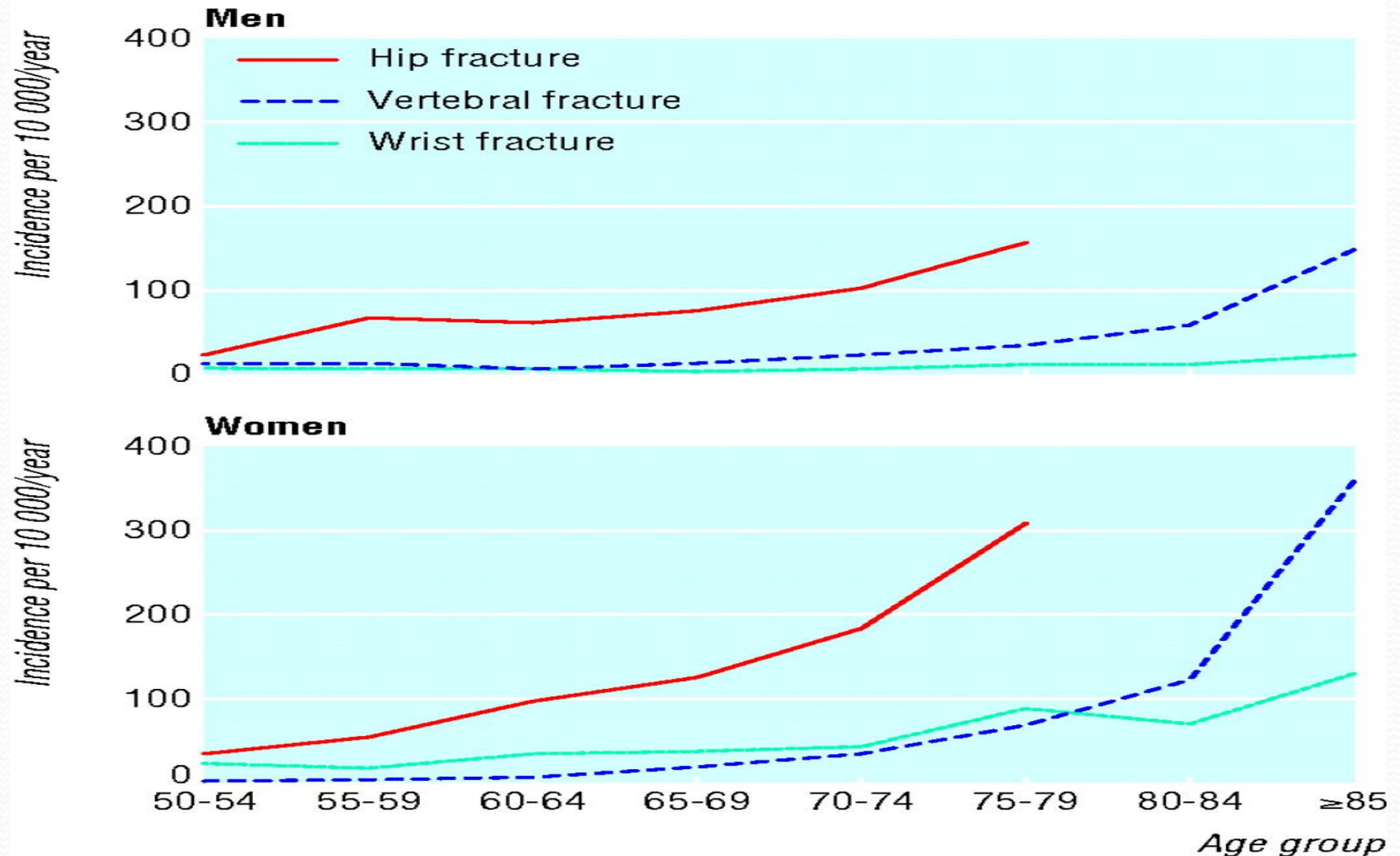
- One year mortality from hip fracture is between 20-30%
- Only 20-50% of patients with hip fractures regain pre-accident motor function
- In the USA, the direct costs for the care of a patient with an osteoporotic fracture range from \$ 4000-5400, plus the expected recovery costs

Epidemiology

	EU6	France	Germany	Italy	Spain	Sweden	UK
Estimated number of individuals aged 50+ with osteoporosis in 2015	20 million	3.8 million	5.3 million	4 million	2.8 million	500 000	3.5 million
Prevalence of osteoporosis among men (♂) and women (♀) aged 50+ in 2015	N.A.	♂ 22.7 % ♀ 6.9 %	♂ 22.5 % ♀ 6.7 %	♂ 23.1 % ♀ 7.0 %	♂ 22.5 % ♀ 6.8 %	♂ 22.5 % ♀ 6.9 %	♂ 21.8 % ♀ 6.8 %
Estimated lifetime risk of hip fracture for men (♂) and women (♀) aged 50	♂ 6.1 – 13.7 % ♀ 9.8 – 22.8 %	♂ 6.0 % ♀ 11.0 %	♂ 9.8 % ♀ 17.1 %	♂ 7.9 % ♀ 16.7 %	♂ 9.0 % ♀ 10.0 %	♂ 13.7 % ♀ 22.8 %	♂ 8.3 % ♀ 17.2 %
Incidence of fragility fractures per year in 2017	2.7 million	382 000	765 000	563 000	330 000	120 000	520 000
Estimated increase in fragility fracture incidence 2017 - 2030	+23.0 %	+24.4 %	+18.5 %	+22.4 %	+28.8 %	+26.6 %	+26.2 %
Fracture-related costs in 2017 (€)	37.5 billion	5.4 billion	11.3 billion	9.4 billion	4.2 billion	2 billion	5.3 billion (€4.5 billion)
Estimated cost increase 2017 - 2030	+27.0 %	+26.0 %	+23.2 %	+26.2 %	+30.6 %	+29.4 %	+30.2 %
Sick days taken by working individuals due to fragility fractures	7.6 million	1.5 million	1.4 million	717 000	355 000	1.1 million	2.6 million
Hours of care after a hip fracture , per 1000 individuals, per year	370 h	138 h	N.A.	882 h	756 h	191 h	248 h
Treatment gap (women who do not receive treatment after a fracture)	60 – 85 %	85 %	60 %	77 %	72 %	83 %	49 %
Fracture liaison services (FLS) improves outcomes		+24 % BMD testing	+22 % treatment adherence	+20 % treatment initiation			
			-5 % re-fracture rate	-3 % mortality			

N.A. = not available

Epidemiology of osteoporotic fractures



Pathogenesis

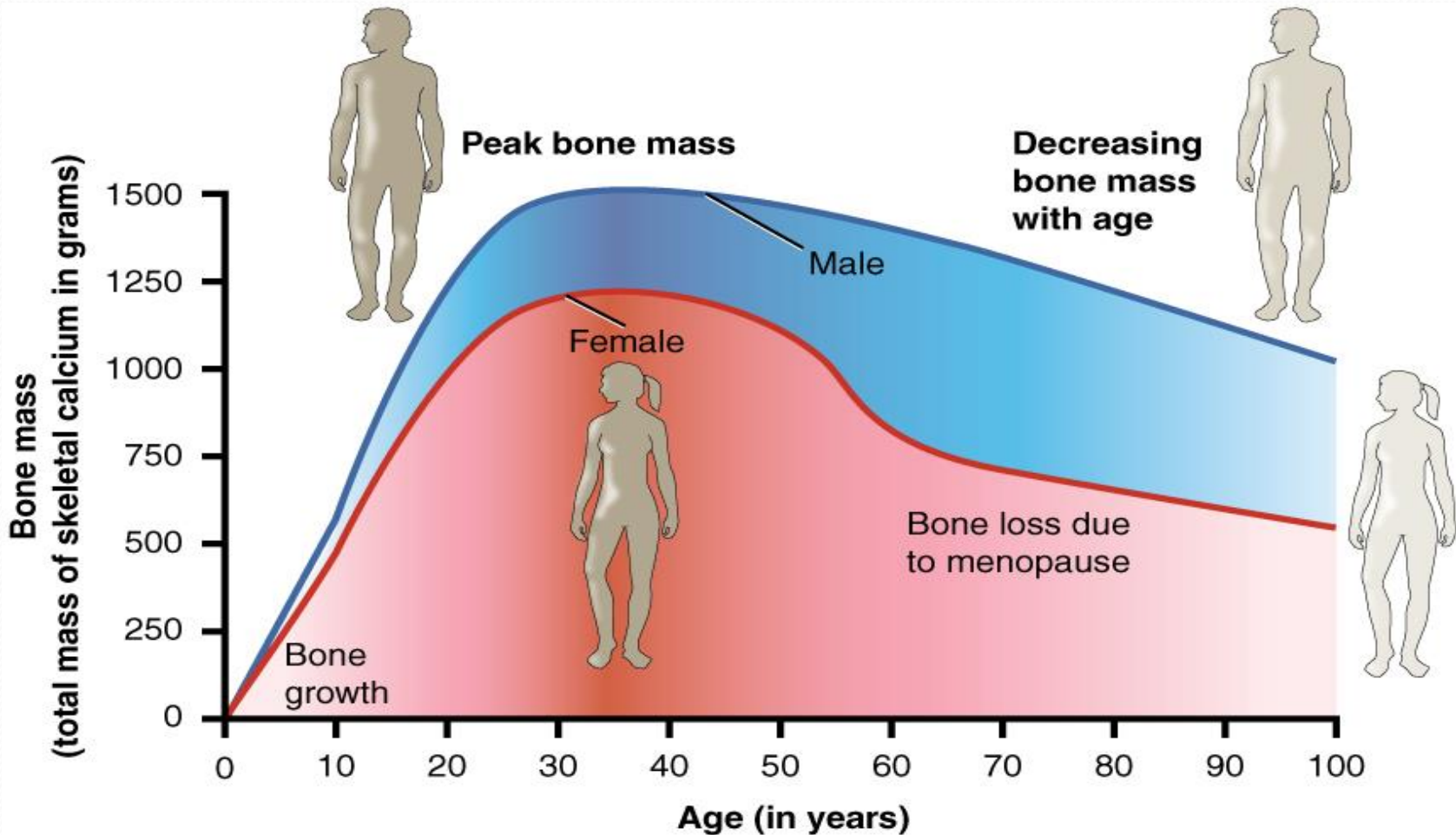
Osteoporosis occurs on the background of natural loss of bone mass, which begins at the age of skeletal maturation (between 35-40 years) and continues more or less, throughout all the life ("physiological osteopenia").

The two sexes loose bone mass differently:

- **Men** almost linearly, with a single increase in loss after the age of 70 .
- **Women**, with two accents of loss, one at the age of menopause (50-55 years) and another after the age of 70 years.

Evolution of bone mass with age

Throughout their lives men lose 30% of their spongy bone and 10% of their cortical bone, while women lose 50% of the spongy bone and 30% of the cortical bone



Pathogenesis

- These "accidents" of the bone loss curve represent the times when risk factors for osteoporosis find the bone more vulnerable and correspond to the installation of the two main forms of primary osteoporosis:
 1. type I (postmenopausal) OP
 2. type II (senile) OP.

Key moments in postmenopausal OP pathogenesis

- Increased cell response to parathormon with increased bone resorption.
- Decrease in calcitonin levels (a hormone of the thyroid gland that inhibits the reabsorption of calcium from the bones with a decrease in its level in the blood).
- Increased calcium excretion with urine.
- Decrease in intestinal calcium absorption.
- Decrease in vitamin D hydroxylation in kidneys

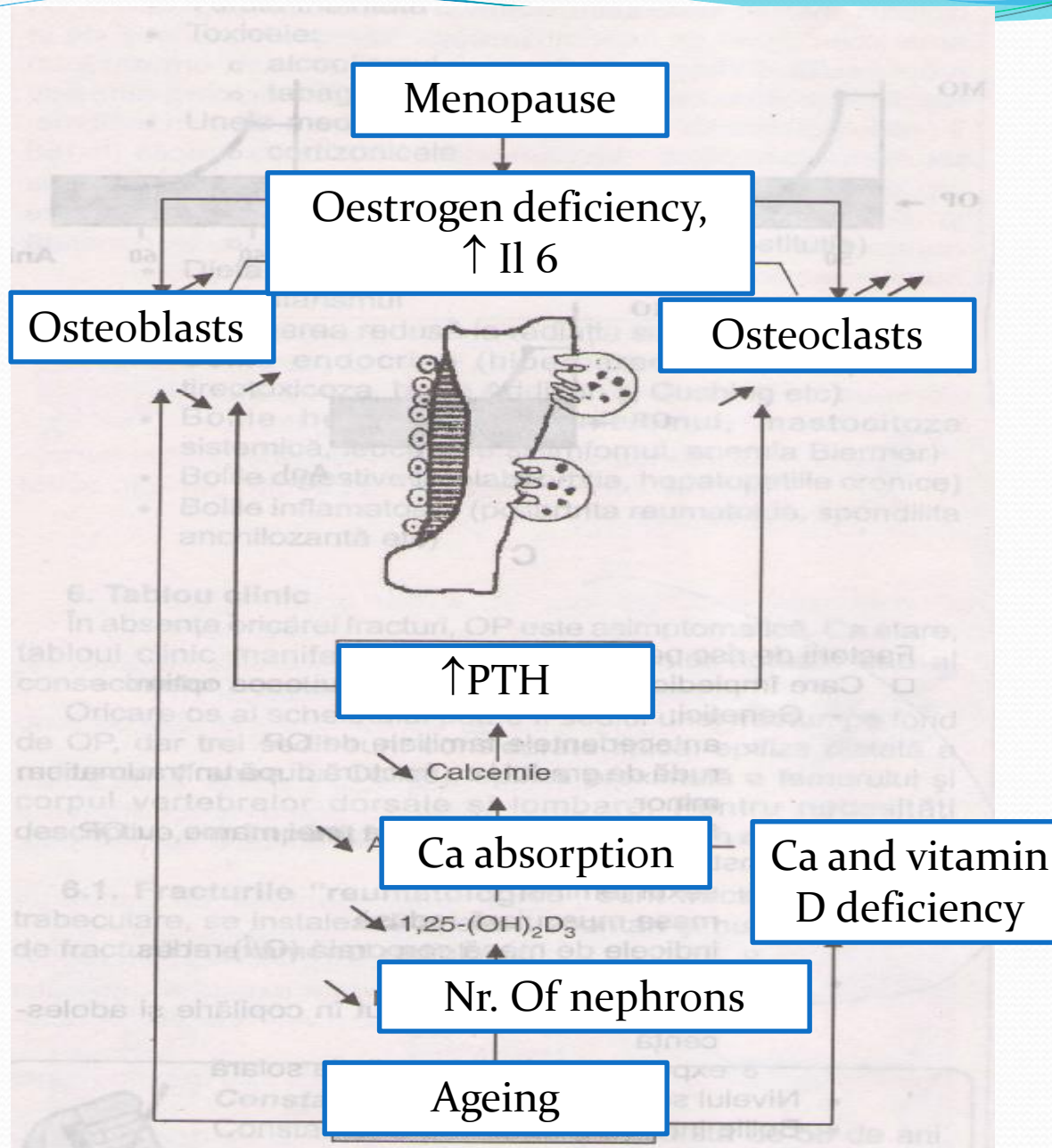
Key moments in postmenopausal OP etiology

- On the background of oestrogen deficiency occurs major resorption of the bone associated with an increased number of osteoclasts and their activity.
- Osteoblasts possess estrogen receptors, while osteoclasts do not have them.
- In the absence of estrogens, osteoclasts produce IL-6, which increases the recruitment and differentiation of osteoclasts.

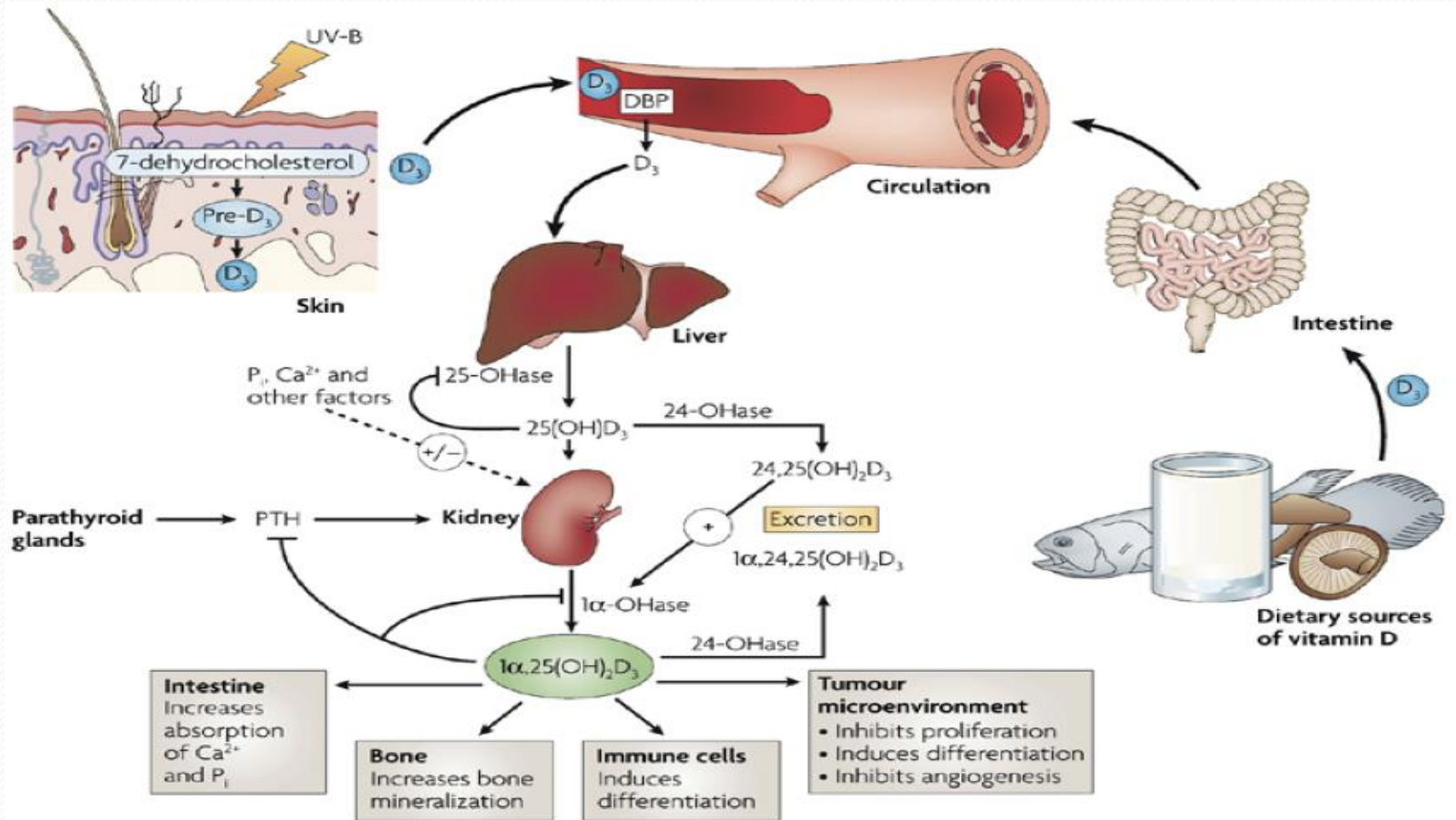
Key moments in senile OP etiopathy

- ❖ Occurs 20-30 years after the onset of menopause
- ❖ To the effects of hypoestrogenism are added those caused by aging :
 - Decrease in the number of functional nephrons
 - Reduction of the synthesis of the active metabolite of vitamin D, which is the hormone $1,25-(\text{OH})_2\text{-D}_3$
 - Hypocalcemia (including due to food deficiency)
 - Decrease in intestinal absorption of calcium
 - Secondary hyperparathyroidism
 - Increase bone turn-over
 - Imbalance between resorption and bone formation, in the favour of resorption

Mechanisms of production in common osteoporosis (by Kuntz, 2010)



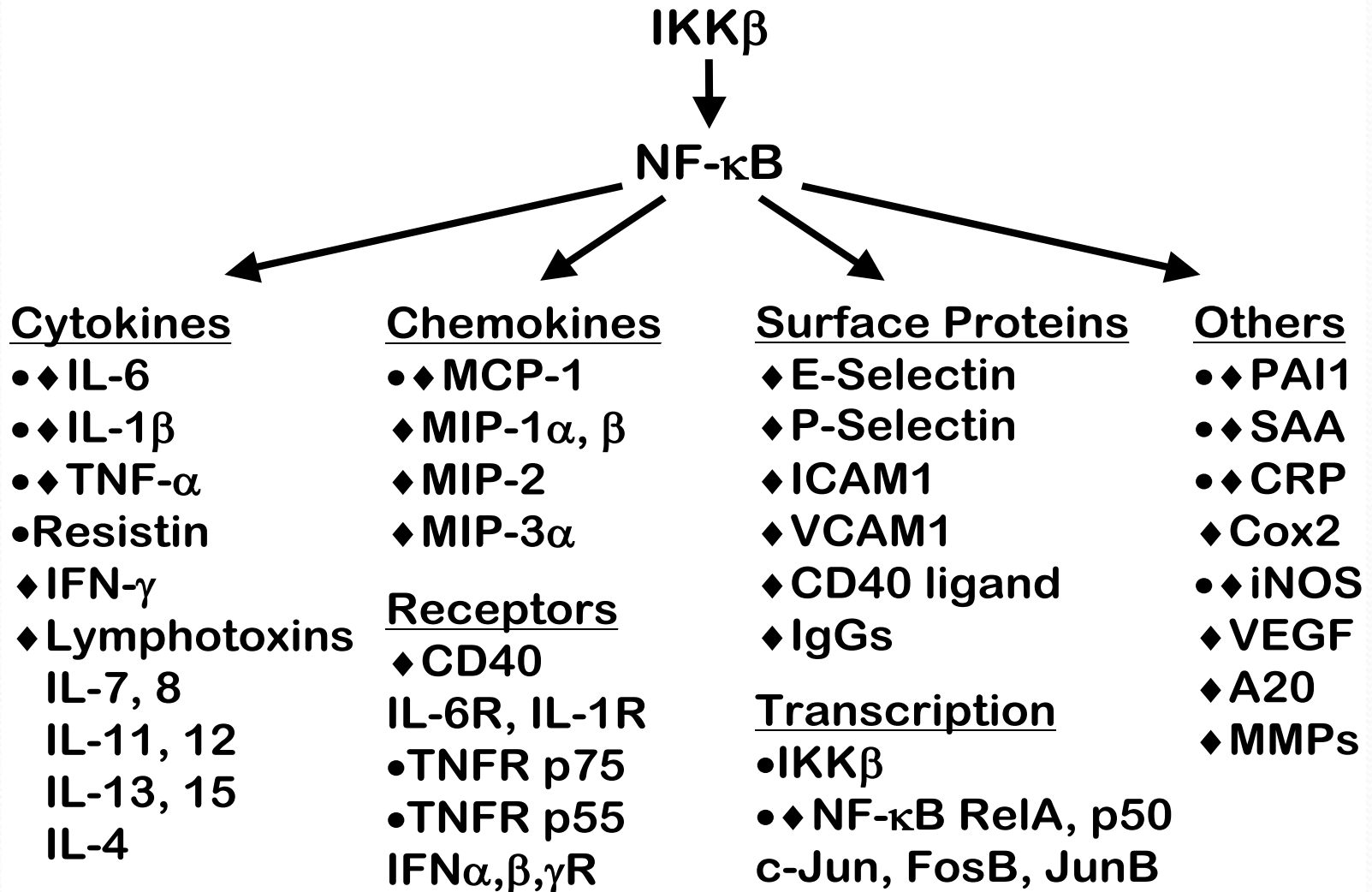
Formation and circulation of vit. D



Pathogenesis

- Combination of bone resorption and bone formation makes the basis of bone metabolism.
- Bone reshaping is controlled by a system consisting of 3 proteins: N kappa B factor activator receptor (Receptor Activator of Nuclear Factor Kappa beta - RANK) and its ligands: osteoprotegerin (osteoprotegerin - OPG) and ligand RANK (RANK Ligand - RANKL), the two cytokines (OPG and RANKL) being competitors for the same receiver, RANK.

NF-κB



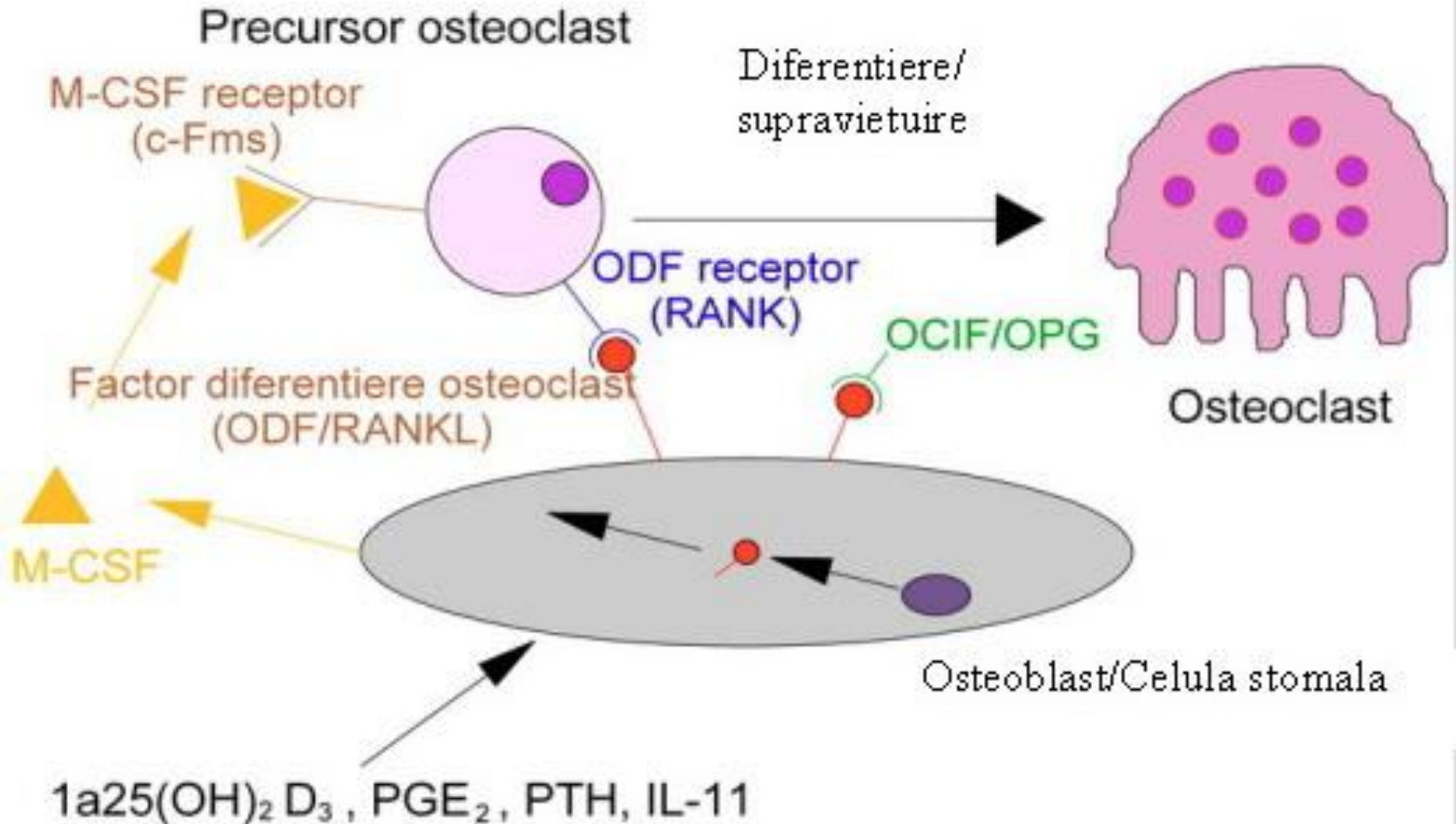
Pathogenesis

- RANK is a transmembrane protein with osteoclastic receptor role.
- OPG is a member of the tumor necrosis factor (TNF) superfamily.
- RANKL is a TNF-related cytokine, a member of the same superfamily, synthesized and secreted by osteoblasts, T lymphocytes, B lymphocytes and megakaryocytes.

Pathogenesis

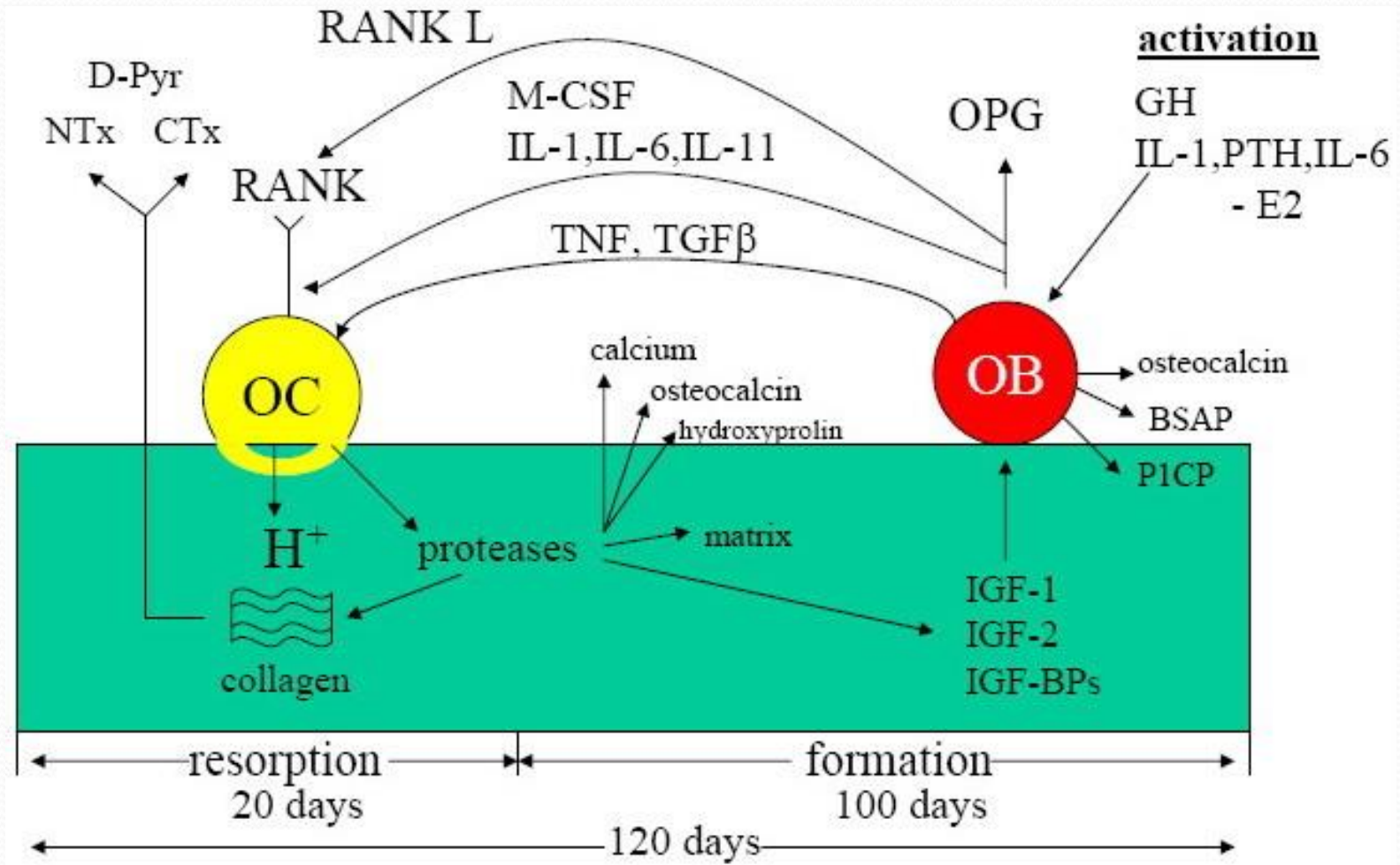
- The action of RANKL consists in promoting the differentiation and activation of osteoclasts, causing increased bone resorption.
- The increase in RANKL secretion is stimulated by various cytokines (IL-1, IL-11 and TNF- α), calciotropic hormones (PTH, 1.25 Vitamin D₃) and PGE₂.
- Physiologically, OPG participates in bone remodeling by attaching it to the osteoclast receptor, RANK and prevents its interaction with RANKL, thus inhibiting the differentiation and activation of osteoclasts.

In OP balance the rank-RANKL-OPG system is damaged in favor of RANK-RANKL and stimulation of osteoclastic resorption



Difference of osteoclasts (after ERISTO, www.medes.fr, 2004).

Bone remodeling



The risk factors for OP are :

Prevent the realization of optimal bone capital:

- **Genetic:**

- Family history of OP
- First-degree relative with a fracture after minor trauma
- Descending woman of a mother with OP

- **Constitutionali:**

- Female Sex
- Reduced Muscle Mass
- Reduced Body Mass Index (G/H)

- **Carens:**

- Low calcium intake in childhood and adolescence
- Reduced exposure to sun

- **Low Level of Physical Effort**

- **Intercurrent Diseases**

- **Delayed Puberty**


Accelerate the loss of BM after reaching its maximum value:

- **Hypoestrogenism:**
- Menopause, especially when it is early (before 45 years)
- Amenorrhea in history (anorexia nervosa, hyperprolactinemia, excessive physical exertion, etc.)
- Ovaryectomy and hysterectomy
- Old age
- **Toxics:**
- **Alcoholism**
- **Smoking**
- **Some medicines:**
- Cortisonic
- Antiepileptics (phenytoin)
- Anticoagulants
- Thyroid hormones (excess substitution)

Accelerate the loss of BM after reaching its maximum value:

- Diet low in calcium
- Sedentaryism
- Reduced exposure to sun
- Endocrine diseases (primary hyperparathyroidism, thyrotoxicosis, Addison and Cushing diseases, etc.)
- Hematological diseases (myeloma, systemic mastocytosis, leukaemia and lymphoma, Biermer anemia)
- Digestive diseases (malabsorption, chronic hepatitis)
- Inflammatory diseases (rheumatoid arthritis, ankylosing spondylitis, etc.)

FRAX

Country : **UK** Name / ID : About the risk factors 

Questionnaire:

1. Age (between 40-90 years) or Date of birth
Age: Date of birth: Y: M: D:

2. Sex Male Female

3. Weight (kg)

4. Height (cm)

5. Previous fracture No Yes

6. Parent fractured hip No Yes

7. Current smoking No Yes


8. Glucocorticoids No Yes

9. Rheumatoid arthritis No Yes

10. Secondary osteoporosis No Yes

11. Alcohol 3 or more units per day No Yes

12. Femoral neck BMD (g/cm²)

BMI 33.5 

The ten year probability of fracture (%)

without BMD

<input checked="" type="checkbox"/> Major osteoporotic	20
<input checked="" type="checkbox"/> Hip fracture	4.8

FRAX tool

- FRAX can be calculated with or without the use of BMD data.
- It helps in making therapeutic decision in patients with osteopenia (to be treated or not)
- In the case of the risk of osteoporosis fracture in the next 10 years of 8-10% or more, it is recommended to take preventive antiosteoporotic treatment.

THE CLINICAL USE OF THE FRAX® ALGORITHM

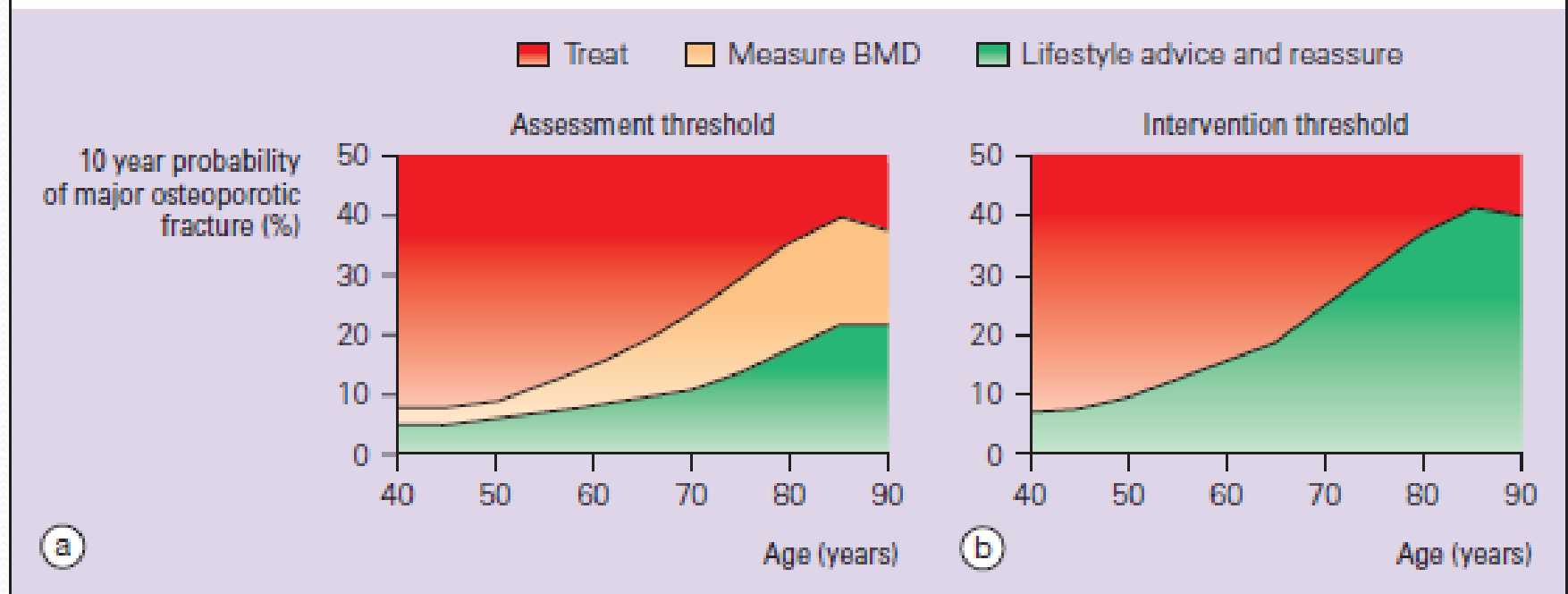


Fig. 194.5 The clinical use of the FRAX algorithm. (a) After the assessment of fracture risk using clinical risks factors of the FRAX in the absence of BMD, the patient may be classified to be at low, intermediate, or high risk. (b) After the recalculation of fracture probability with the additional input of femoral neck BMD, the individual's risk may lie above or below the intervention thresholds for major osteoporotic fracture and/or hip fracture. (Data from World Health Organization. WHO Risk Fracture Assessment Tool. Available at <http://www.shef.ac.uk/FRAX>.)

Diagnosis:

- In the absence of any fracture, OP is asymptomatic.
- Physical examination can detect sensitivity along the spine, scoliosis, kyphosis.
- Causes, leading to secondary osteoporosis (hypogonadism, signs of thyroid diseases, cushingoid)
- The clinical picture of OP is that of current fractures or their consequences.
- The most common compression vertebral fractures occur in Th11-L2.
- Other common places for fractures are those of the distal radius (Colles fracture), femoral neck (most serious, disabling and expensive), pelvis.

Diagnosis

In order to establish the early and definite diagnosis of osteoporosis, it is recommended to measure BMD in the following groups:

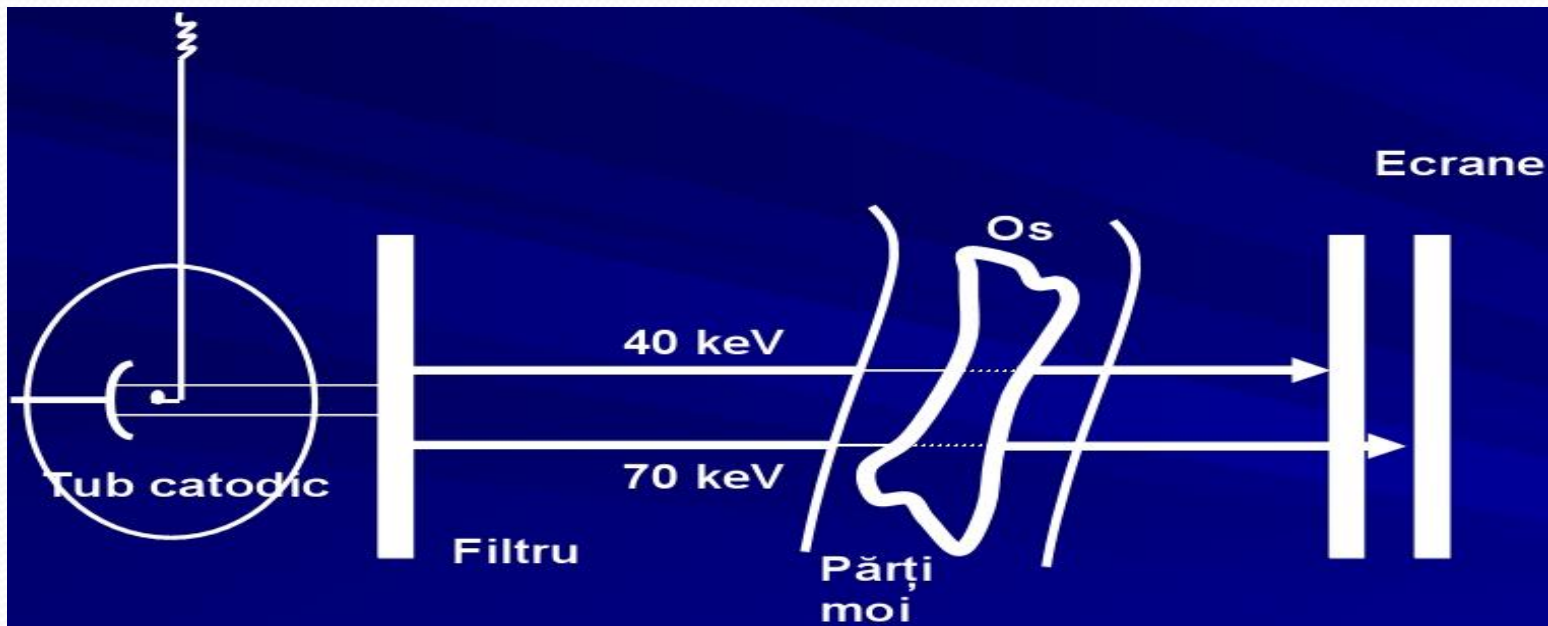
- Women after 65 years
- Men after 70 years
- Women of any age with fractures on the background of minimal trauma
- Any adult person with a disease , which contributes to the appearance of OP or a person, who receives drugs with a risk of development of OP

Diagnosis

- The measurement of BMD (Bone Mineral Density) is performed by the DXA method (dual X-ray absorption) at the femoral neck or lumbar spine, or in both places.
- Simultaneously, anamnesis and the risk factors of the OP should be assessed.

Measuring DMO Osteodensitometry

- Bone density measurement is based on the attenuation of an energy beam when it passes through the bone, which is directly proportional to BMD.



Measuring DMO

Osteodensitometry

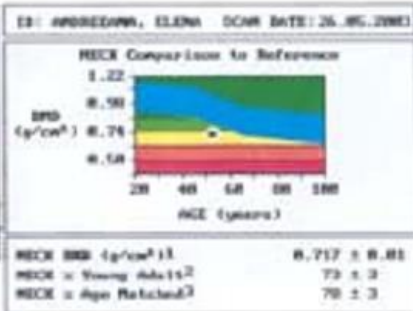
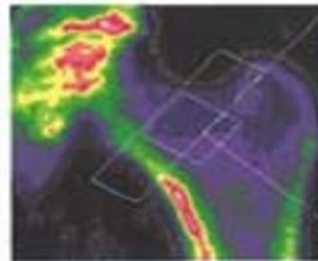
- DXA is the gold standard in the diagnosis of OP
- In the absence of DXA, the diagnosis, as it is made by WHO, cannot be established.
- The measurement of BMD at any level of the skeleton has a predictive value for the assessment of fracture risk.
- Exposure to a very low dose of radiation (1/10 from simple X-ray)



DXA

Center for Osteoporosis
Department of Rheumatology
University Hospital of Cluj-Napoca, Romania

PATIENT ID: ANDREERANA SCAN: 1.15 26.05.2003
NAME: ANDREERANA, ELENA ANALYSIS: 1.15 26.05.2003



Age (years)	53	Large Standard	279.72	Scan Mode	Fast
Sex	Female	Medium Standard	202.36	Scan type	DPX-Alpha
Weight (kg)	75.0	Small Standard	143.96	Collimation (mm)	1.48
Height (cm)	166	Low keV Air (cps)	79042	Sample Size (mm)	1.2x 1.2
Ethnic	White	High keV Air (cps)	46607	Region height (cm)	40.8
System	8722	Resolv (kFat)	1.33(26.6)	Region width (cm)	15.8
View	Left	Current (uA)	3000	Region angle (deg)	55

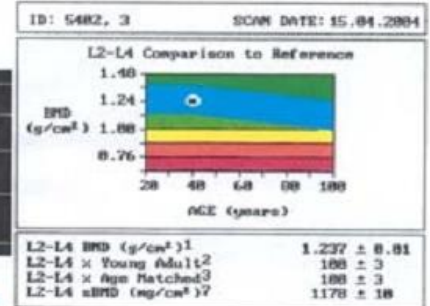
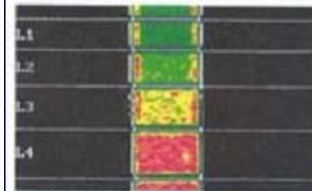
NECK : BMC⁴ (grams) = 4.17 AREA⁵ (cm²) = 5.8;
WARDS : BMC⁴ (grams) = 2.25 AREA⁵ (cm²) = 3.7;
TROCH : BMC⁴ (grams) = 6.51 AREA⁵ (cm²) = 9.8!

REGION	BMD ¹ g/cm ³	Young Adult ²		Age Matched ³	
		T	Z	T	Z
NECK	0.717	73	-2.19	78	-1.66
WARDS	0.597	64	-2.40	75	-1.56
TROCH	0.658	83	-1.20	84	-1.11

1 - See appendix E on precision and accuracy. Statistically 68% of repeat scans will fall within 1 SD.
2 - USA femur Reference Population, Ages 20-45. See Appendixes.
3 - Matched for Age, Weight (Males 25-100kg, Females 25-100kg), Ethnicity.
4 - Results for research purposes, not clinical use.

Center for Osteoporosis
Department of Rheumatology
University Hospital of Cluj-Napoca, Romania

PATIENT ID: 5402 SCAN: 1.15 15.04.2004
NAME: 5402, 3 ANALYSIS: 1.15 15.04.2004



Age (years)	40	Large Standard	270.98	Scan Mode	Medium
Sex	Male	Medium Standard	201.54	Scan type	DPX-Alpha
Weight (kg)	70.0	Small Standard	144.44	Collimation (mm)	1.68
Height (cm)	170	Low keV Air (cps)	78708	Sample Size (mm)	1.2x 1.2
Ethnic	White	High keV Air (cps)	443141	Current (uA)	750
System	8722	Rvalue (kFat)	1.391(4.1)		

REGION	BMD ¹ g/cm ³	Young Adult ²		Age Matched ³	
		T	Z	T	Z
L1	0.897	77	-2.19	77	-2.19
L2	1.065	86	-1.46	86	-1.46
L3	1.213	98	-0.23	98	-0.23
L4	1.384	112	-1.20	112	-1.20
L1-L2	0.989	82	-1.76	82	-1.76
L1-L3	1.078	89	-1.10	89	-1.10
L1-L4	1.173	96	-0.39	96	-0.39
L2-L3	1.146	92	-0.78	92	-0.78
L2-L4	1.237	100	-0.02	100	-0.02
L3-L4	1.304	105	0.53	105	0.53

1 - See appendix E on precision and accuracy. Statistically 68% of repeat scans will fall within 1 SD.
2 - USA AP Spine Reference Population, Ages 20-40. See Appendixes.
3 - Matched for Age.
4 - *BMD (x standardized BMD) See J Bone Miner Res 1994; 9:1503-1514

Measuring DMO

Osteodensitometry

- The results are obtained as the score T and Z.
- **Z score** – is a comparison of the patient's bone mass with that of a normal individual of the same age. It indicates whether the bone mass is true to the patient's age or the action of other factors occurs.
- **T score** – is a comparison of the patient's bone mass with that of a healthy and young individual (30 years old), considered to have peak bone mass. It represents the number of standard deviations of the patient below the peak of bone mass.

Diagnosis

Criteria of Osteoporosis of WHO

- **Normal BMD** - a score $T \geq -1$ DS.
- **Osteopenia** – a T score between: -1 and -2.5 DS
- **Osteoporosis** - a T score < -2.5 DS
- **Established Osteoporosis** a T score < -2.5 DS plus the radiological presence of an osteoporotic fracture.

Measuring DMO

Osteodensitometry

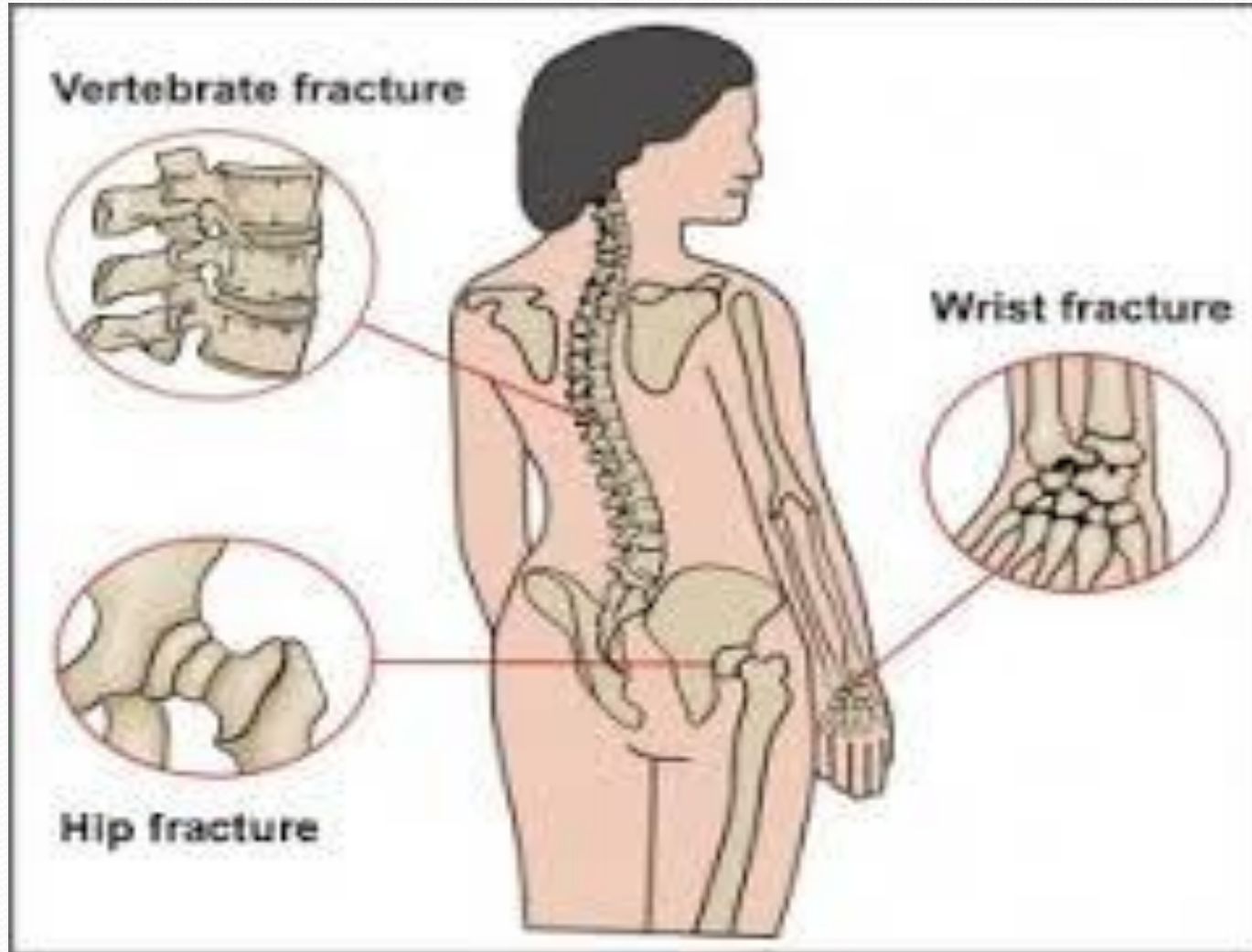
- Usually, central DXA is recommended in the lumbar spine and femoral neck.
- In women younger than 65 years old BMD testing at the lumbar spine may be even more useful, because in the vertebrae there is evidence of a faster loss of bone.
- In women after 65 years , it is recommended to pay attention to the femoral neck, since in the spine can be false negative data (vascular calcinates or spondyloarthrosis)

Measuring DMO

Osteodensitometry

- BMD in the femoral neck best reflects the risk of femoral fracture, but it is also relevant for other localizations.
- In combination with risk factors BMD allows even better prognosis of the risk of osteoporosis fractures.
- To estimate the probability of fracture for 10 years, an electronic instrument has been developed: **The Fracture Risk Assessment Tool (FRAX)**, www.shef.ac.uk/FRAX

Osteoporotic fractures



Diagnosis

Acute Oncet

- Caused by the appearance of a compression fracture
- **Intense pain** occurs in the affected segment
- There may be pain in the projection of the heart, in the lower limbs, leading to difficult differential diagnosis of a heart attack, myocardial infarction, pleurisy or surgical pathology.
- **Any involuntary movement**: coughing, sneezing, changing position from horizontal to vertical leads to increased pain.
- **Movements in the spine are limited**, the spasticity of the paravertebral muscles is observed at palpation, which are sensitive to deep palpation and percussion at the fracture site.

Diagnosis

Debut Insidious

- **Deaf pain** in the thoracic or cervical region
- Occurs at changes in position, further intensifies and is permanent in the upright position, disappears only in horizontal position
- It is caused by the appearance of **deformities and microfractures in the vertebrae**.
- With the appearance of deformities, muscle weakness increases, **the height decrease occurs**.
- In menopausal women the height decreases in the environment by **2.5 mm/year**, changes the stature and posture, kyphosis occurs, the gait becomes slowed.

Diagnosis

- For the patients, who are suspected for osteoporosis clinical examination includes :
 1. Anamnesis for the detection of risk factors of osteoporosis
 2. Anthropometry

Diagnosis

Anthropometry includes:

1. **Measuring height**
2. **Intensity of cystosis** with the cyphometer, the distance from:
 - a) the neck to the wall in a horizontal position from the 12th vertebra to the iliac crista the angle of inclination of the pelvis, the kyphosis, at which it **increases**, the distance between the patient's neck and the wall
 - b) and the distance between the XII vertebra to the crista iliac + height reduction more than 4 cm – indicates that osteoporosis fracture is present at least in a vertebra.

Diagnosis

Simple Radiological Examination

- Can demonstrate osteopenia, osteoporosis only in case of 20-50% of bone mass loss.
- For these reasons **it is not used** to diagnose osteoporosis.
- It is useful for demonstration of bone fractures, both for long bones and compression vertebral fractures.

Diagnosis

Simple Radiological Examination



- On the left there is a normal bone, that dotted curve called the **Shenton Line** joins the pelvis bones with the neck of the femur. The bone on the left is fractured that line.... You can't see it anymore, the bone is practically "bent" in the neck region. This is the radiological image of the hip fracture. Actually, it's the most common way to make this terrible diagnosis...

Diagnosis

Simple Radiological Examination



Fracture of
the femoral
neck

Diagnosis

Simple Radiological Examination



Fracture of
the femoral
neck

Diagnosis

Simple Radiological Examination



Distal radius
fracture (Colles)



Diagnosis

Simple Radiological Examination

Distal radius
fracture (Colles)



Diagnosis

Simple Radiological Examination

Radiographic signs of OP

- "Impression":
 - ✓ Increased skeletal transparency
 - ✓ Accentuating the shadow of the vertebral plateaus
 - ✓ Loss of horizontal trabecular picture and accentuating vertical drawing of vertebral bodies ("vertebra with bars")
 - ✓ Successive loss of the system of bone trabecula in epiphysis of proximal femur (Singh's index)

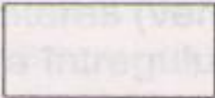



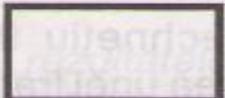
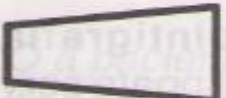
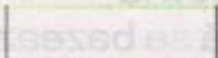
Diagnosis

Simple Radiological Examination

Radiographic signs of OP

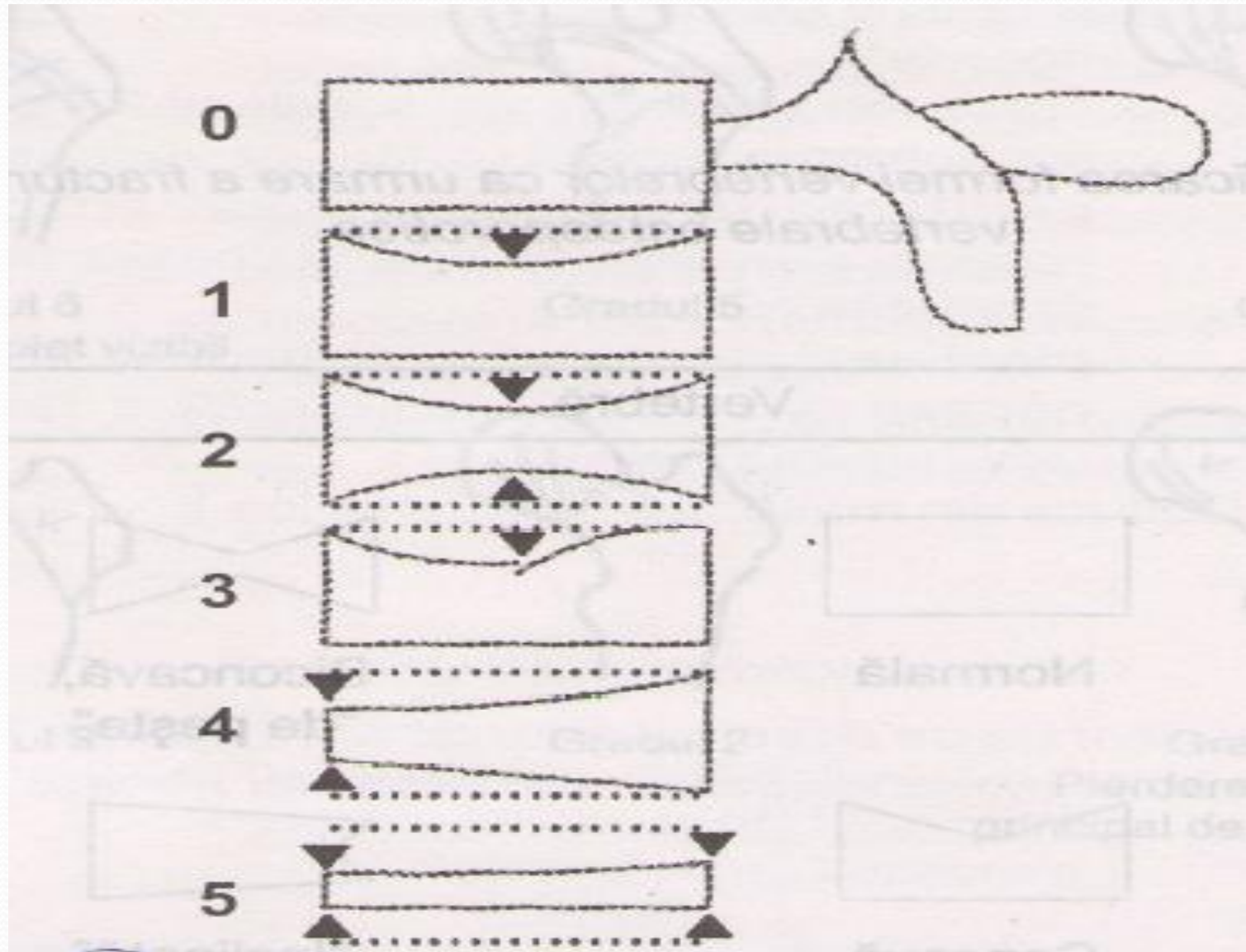
- Qualitative:
 - ✓ Modification of vertebral shape
 - ✓ Interruption of vertebral borderlines
 - ✓ Fracture line at the level of long bones
- Quantitative:
 - ✓ Meunier-Renier Semi quantitative score
 - ✓ Kleerekoper Vertebral Deformation Index, based on measurement of vertebrae height at 3 sites, on lateral X-rays, between D4 and L5

Change in the shape of the vertebrae as a result of osteoporosis vertebral fractures

	Vertebră	
Incidență anteroposterioară	 Normală	 Biconcavă, "de pește"
	 Concavă	 "Înclinată"
Incidență laterală	 Normală	 Cuneiformă, "în ic"
	 Plată	

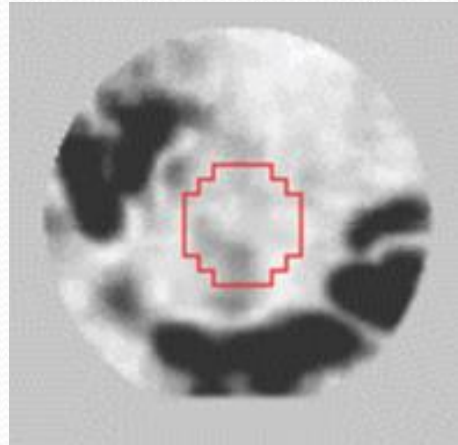


Meunier-Renier score. The score 0 is given to the normal vertebra and one increasingly for the shape changes shown here to all vertebrae from D4 to L5. maximum possible score 70.



Diagnosis of Bone Ultrasonography

- By measuring the modification of some parameters of the ultrasound beam passing through the bone, elements of OP can be identified.
- The most used machines make measurements at the calcane level.
- In case of OP detection by ultrasonography, it is recommended to perform DXA testing for confirmation.



Diagnosis

Quantitative computed tomography



- It has predictive ability for fractures like DXA
- but is more expensive and exposes to a higher dose of radiation
- In everyday practice it is rarely used

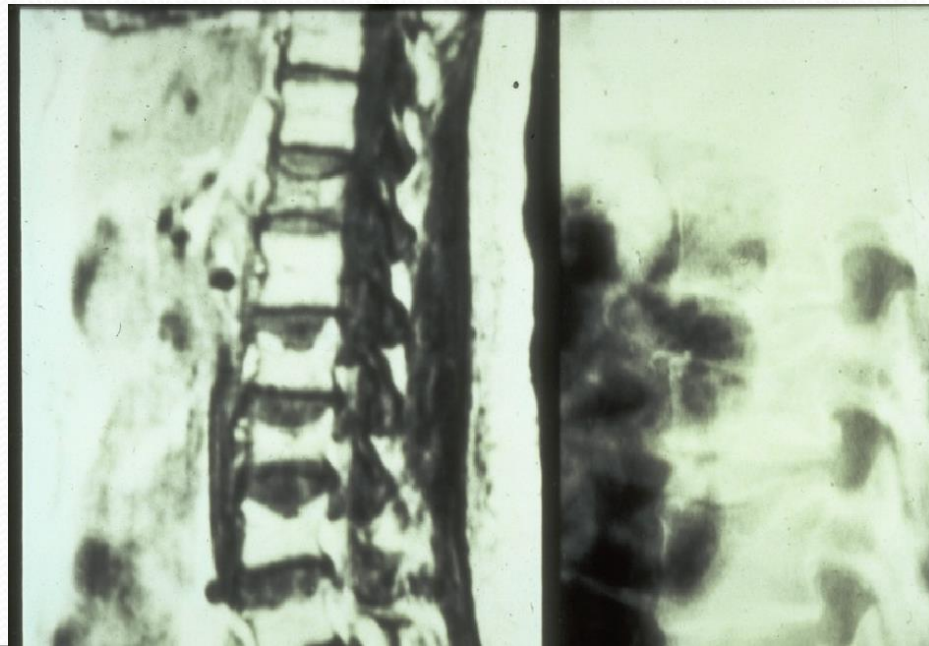
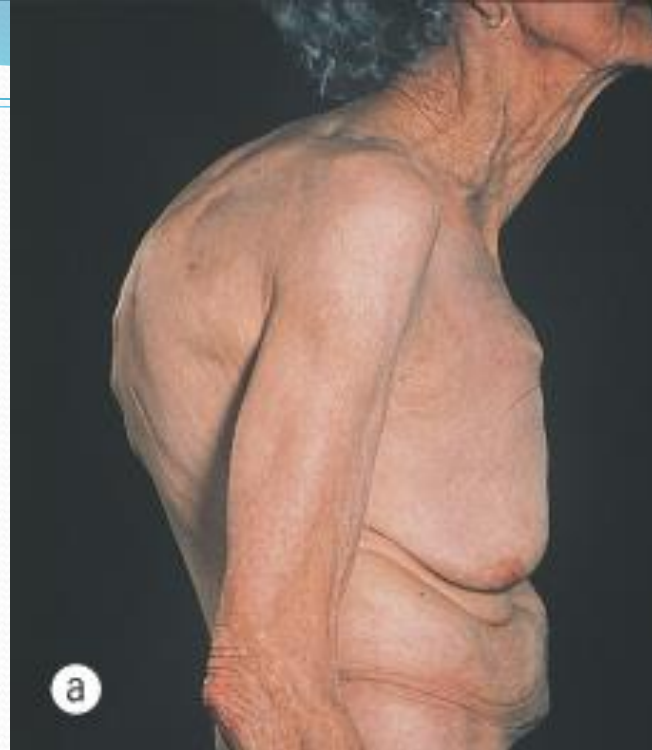
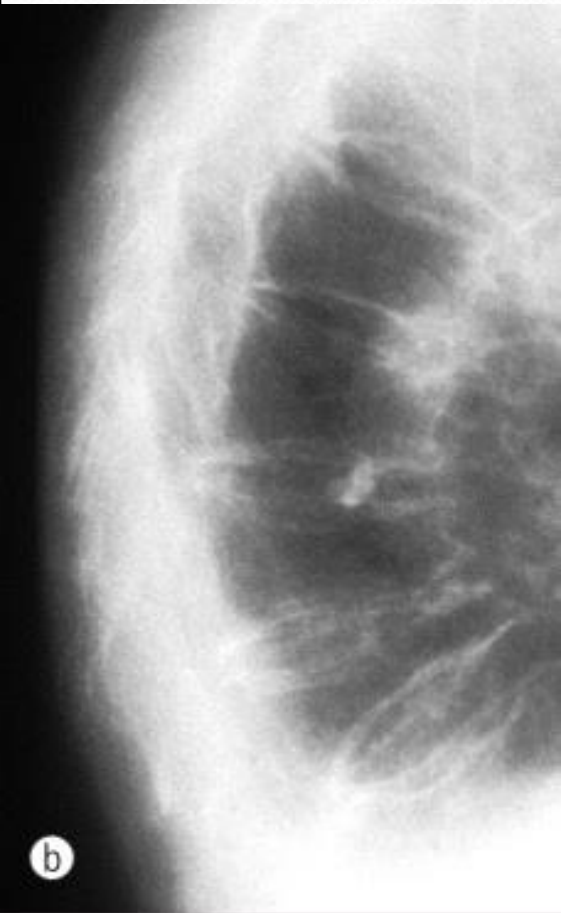
Diagnosis

Bone Scintigraphy

- Bone scintigraphy with technetium 99-m methylenebisfonate may serve to recognize a recent vertebral fracture.

Pacientă cu fractură/tasare vertebrală la nivel L1. Pe scintigrafia osoasă «whole body» se remarcă aspectul ariei de hipercaptare cu scaderea în înălțime a corpului vertebral; filmul radiografic confirmă colapsul vertebral L1





Compression fractures viewed at MRI – lumbar segment

Diagnosis. Bone markers.

By various biochemical and immunological methods some substances can be revealed in biological liquids during the development of the bone remodeling process:

- **Markers of osteoformation, present in the blood:**
 - ✓ Osteocalcin
 - ✓ Total alkaline phosphatase and bone isoenzymes
 - ✓ Type I collagen propeptide
- **Bone resorption markers, removed in urine:**
 - ✓ Piridinoline and related peptides
 - ✓ Hydroxiprolin

The indications of these determinations are found in the:

- Diagnosis of the physiopathological form of OP
- Monitoring of therapeutic effect
- Scientific research

Differential diagnosis

It should be carried out with:

- Osteomalacia
- Bone Metastases
- Multiple Myeloma
- Hyperthyreosis
- Hyperparathyreosis
- Renal Osteodystrophy
- Malabsorption Syndromes
- Vitamin D deficiency
- Paget Disease

Making a therapeutic decision

- The decision to start treatment should take into account an **overall patient profile** and not just an isolated measurement of bone mineral density.
- The accept by the patient of the **proposed treatment**. The doctor is obliged to inform the patient about all the benefits, but also the risks associated with.
- **Compliance with treatment and monitoring.**
- **Lifestyle and other risk** factors should be taken into account. Risk factors such as smoking, fractures of any type in history after the age of 50, maternal history of hip fracture.
- **Hormone status and age.**

Treatment

Non-pharmacological measures

- Cautious for physical activity in the orthostatic position
- Use of shoes with elastic heel
- Correct lifting and wearing weights
- Properly
- Avoid bending in front and lifting with bending knees
- Carrying loads in next to the body and evenly distributed between the two upper limbs

Treatment

Non-pharmacological measures

- Preventing falls and protecting against fractures:
 - maximum possible correction of hearing and visual problems
 - floors and coverings without irregular surfaces
 - avoiding carpets
 - good but not excessive "nocturnal" light in all rooms
 - available phones
 - short electrical wires , without placing them on the floor
 - the absence of objects on the floor that would prevent the movement
 - domestic animals

Treatment

Adequate intake of Ca and Vitamin D

- Daily consumption of Ca must be appropriate according to age.
- Most Ca pills come in the form of calcium carbonate and calcium citrate, which have a good bioavailability.
- Ca preparations, as a rule, are combined with vitamin D
- The daily dose of vitamin D for adults constitutes 800UI/day

Treatment

Appropriate Intake of Ca



Women

Age	Dose
25-50 years	800 mg
25-50 years (pregnancy/ lactation)	1200 mg
> 50 years	1500 mg
> 50 years with hormone replacement therapy	1000 mg

Men

Age	Dose
25-65 years	800 mg
>65 years	1500 mg

The main sources are:
dairy products, products
fortified with Ca, sardines,
sesame.

Lactate plus

DAIRY-FREE SOURCES OF CALCIUM



White Beans



Dried Figs



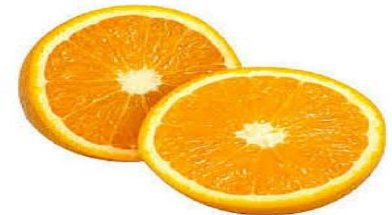
Bok Choy



Black-eyed Peas



Broccoli



Orange



Salmon



Almonds



Kale

Treatment

Adequate intake of vitamin D

- Bronze fills the most easily necessities in vitamin D .
- In to get physiological doses of vitamin D, the rules are:
 - avoid excessive exposure to the sun
 - exposure is 10-15 minutes 3-4 times a week.
- Some amount of vitamin D can be found in egg yolk, beef liver, cod liver.

Treatment

Indications for anti-resorptive treatment

- Adults with osteoporotic fractures of the femoral neck or spine
- Adults with T score ≤ -2.0 DS without specific risk factors OP
- Adults with T score ≤ -1.5 DS specific risk factors OP
- Women after 70 years with several risk factors start treatment without measuring BMD.

Antiresorptive treatment

Front-line

Bisphosphonate

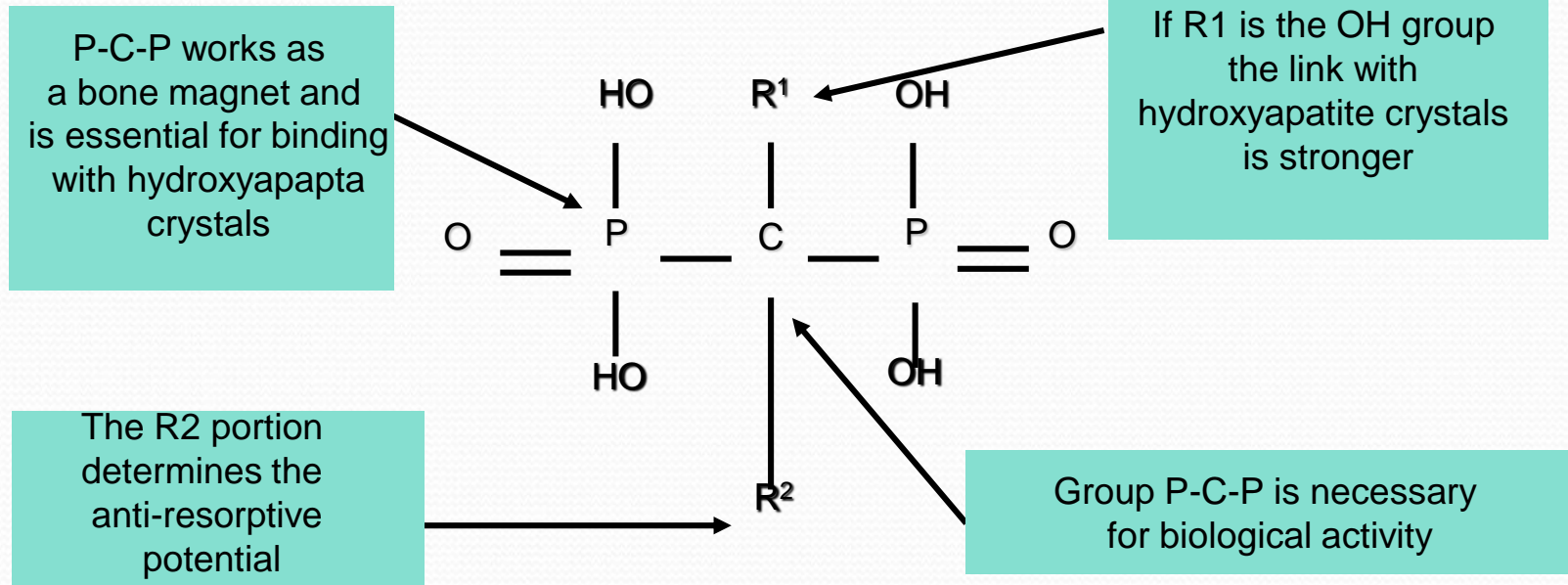
- Alendronate 70 mg/sap
- Risendronate 35 mg/sap
- Ibandronate 150 mg/month; 3 mg, i/v, every 3 months
- Zoledronate 5mg/year

Duration up to 10 years

2nd Line

- **SERM** – Raloxifen 60 mg/day
- **Calcitonin** (intra-nasal) 200 IU/day
- **Teriparatide** (rhPTH 1-34) 20 mcg/day
- **Hormone replacement therapy** – prevention, in persons with indications outside OP
- **Strontium ranelate** – 2 g per bone, daily
- **Denosumab** – anti RANKL a/c, 60 mg s/c, every 6 months

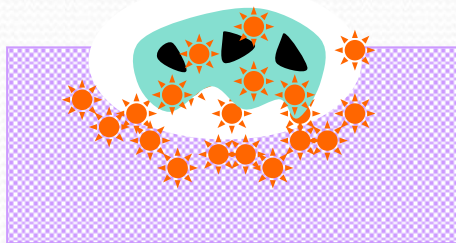
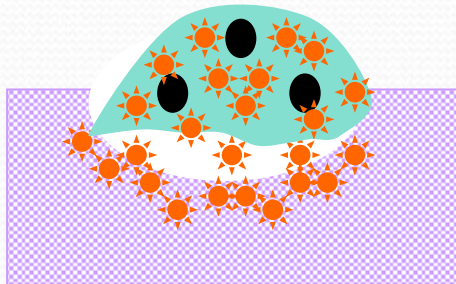
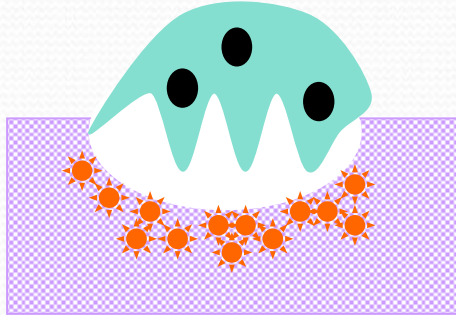
Bifosfonatii



Class of synthetic compounds, preparations of the first line in the treatment of osteoporosis.

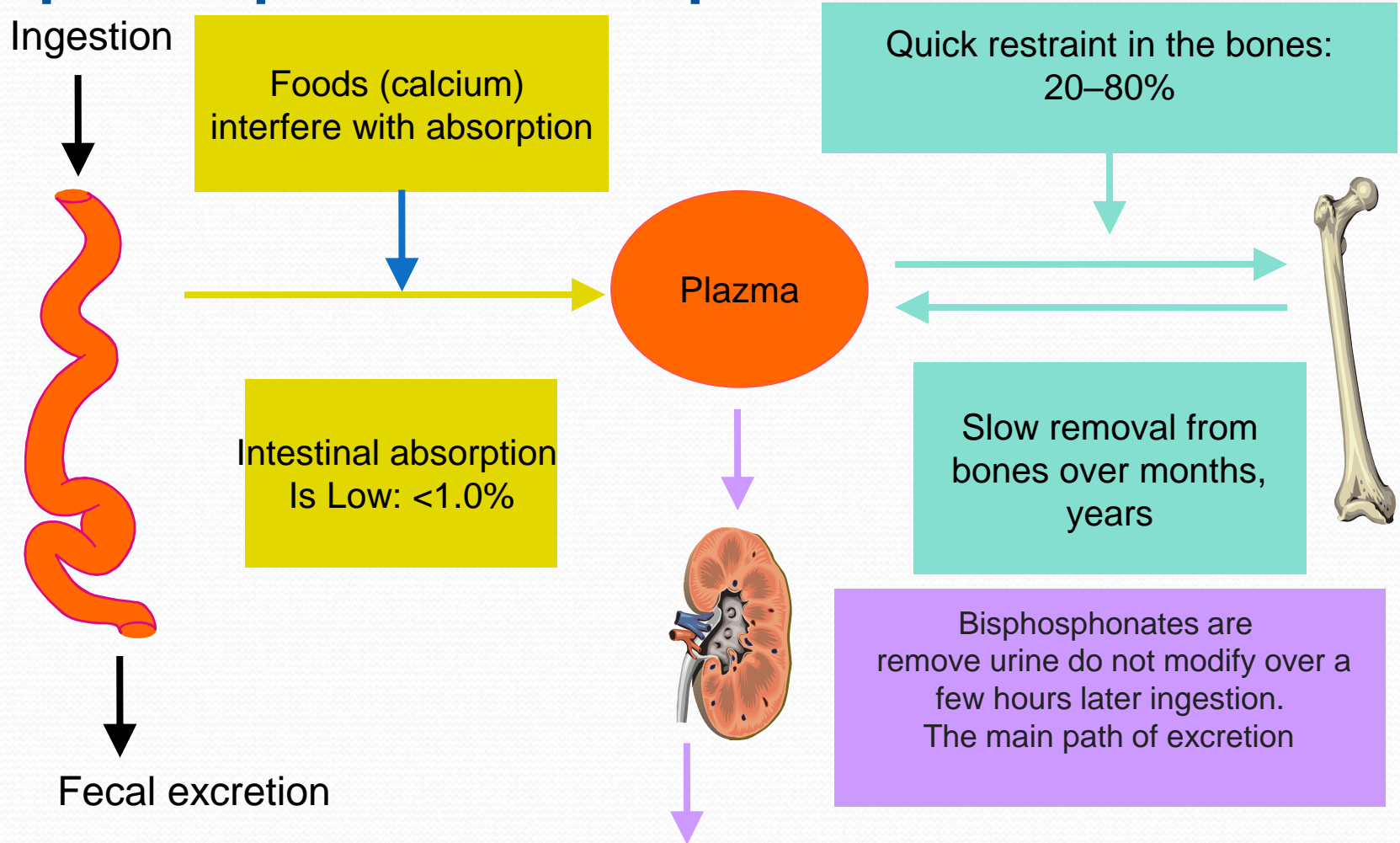
- Strong anti-resorptive drugs.
- They have an affinity to hydroxyapatite crystals and are resistant to metabolic degradation.
- Reduces osteoclasts' ability for bone resorption, accelerates their destruction

Bisphosphonates: mechanism of action



1. The active osteoclast reabsorbs the bone mold
2. BISPHOSPHONATIONS[☀] are deposited on the bone surface
3. BISPHOSPHONATIONS are absorbed by osteoclast
4. Osteoclast is inactivated
5. Osteoclast becomes apoptotic ('suicidal') and dies

Bisphosphonates: pharmacokinetics



Bisphosphonates : side effects, contraindications

Adverse reactions:

Digestive (peroral forms)

**Esophagitis, oesophageal ulcer, dysphagia,
abdominal pain, osteonecrosis of the mandible/maxilla**

Musculoskeletal pain

Flu-like syndrome (parenteral forms)

Contraindications :

Inability to maintain orthostatism minimum 30 min (peroral forms)

Hypersensitivity to bisphosphonates

Hypocalcemia uncorrected ClCr - 35 ml/min

Treatment

- Administration of 2-line preparations should be considered in the case of bisphosphonate intolerance or failure of bisphosphonate therapy over 1 year
- For the evaluation of the effectiveness of treatment DXA over 1 year is performed or markers of resorption (N-telopeptide in urine or carboxy-terminal collagen crosslinks CTX in serum) are done before treatment and 3 and 6 months after initiation of treatment.
- Therapeutic success is considered DXA – the same level or improvement; biochemical markers – 50% decrease in urine or 30% in serum.
- Combination of antiresorptive therapy usually is not indicated

Prophylaxis and treatment

The essence of OP is fracture, therefore any action directed against this disease should aim reduction of the rate of fractures.

What we can do:

- Primary prophylaxis, intended to prevent OP by itself and
- Secondary prophylaxis, means OP treatment, which aims to prevent fractures in osteoporotic subjects

Prophylaxis and treatment

- Hygiene measures for the general population:
 - ✓ Optimal intake of calcium and vitamin D in all periods of life
 - ✓ Optimal intake and even more of vitamin C during skeletal growth
 - ✓ Encouraging sports activities, especially outdoor activities (sun exposure)

Prophylaxis and treatment

- **General measures for persons at risk:**
 - ✓ Combating sedentaryism: early mobilization after therapeutic rest
 - ✓ Cessation of smoking and alcohol consumption
 - ✓ Reasonable limitation of osteoporosis medications, especially corticotherapy (small doses, short duration)
 - ✓ Treatment of diseases likely to induce secondary OP
 - ✓ Hormone Replacement Therapy (HRT) for ovariectomized women and for "target groups" of perimenopause women

Thank you

