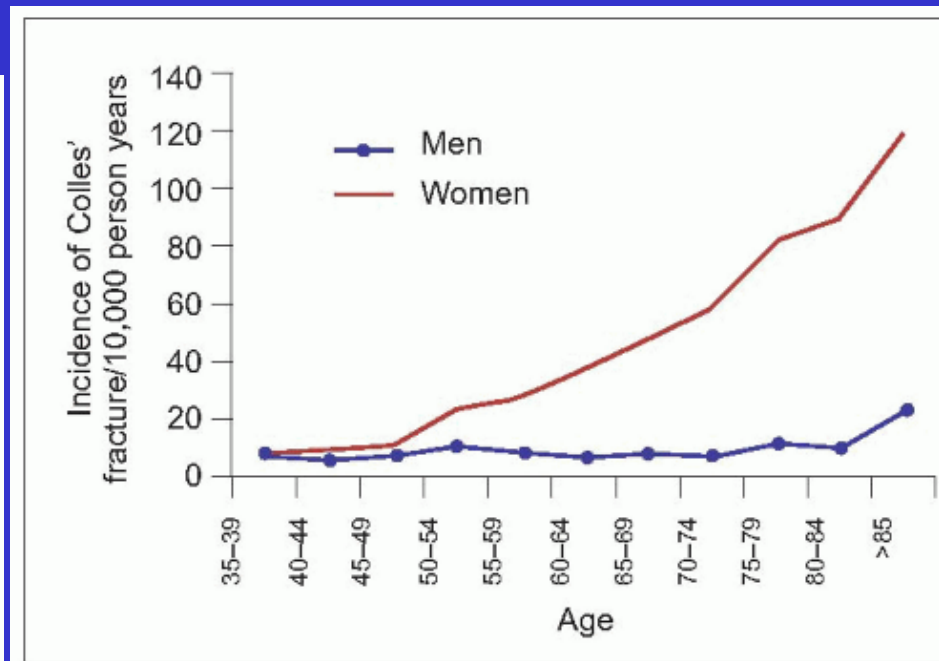
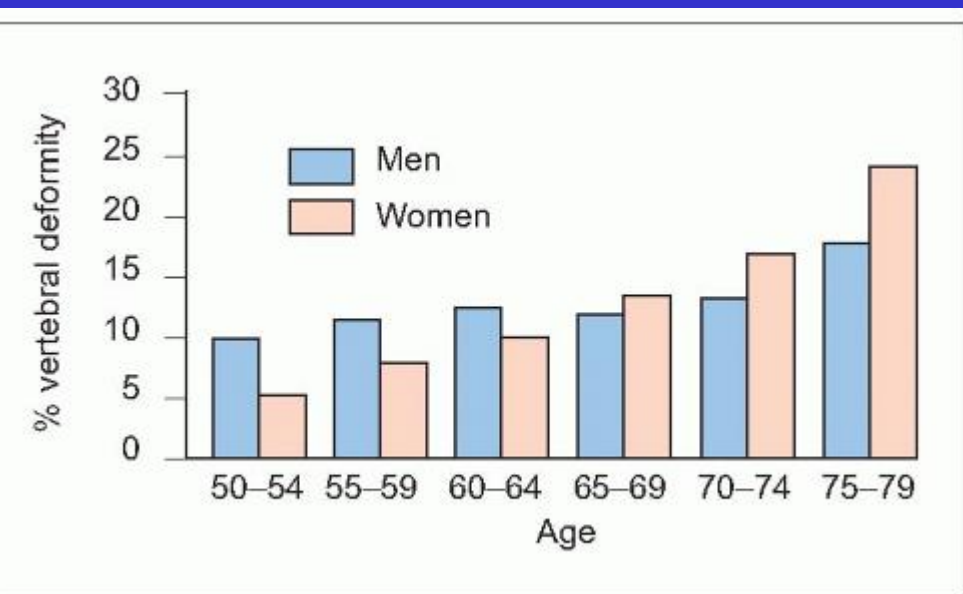


Drugs for osteoporosis

Across the world

Osteoporosis is a most common bone disease affecting **one in three women and one in five men over the age of 50 worldwide**



Scanning electron micrograph (SEM) of normal bone. The image shows a dense, interconnected network of bone trabeculae with a relatively smooth surface. The trabeculae are thick and form a continuous, porous structure. A semi-transparent grey box with the text "Normal bone" is overlaid on the upper right portion of the image.

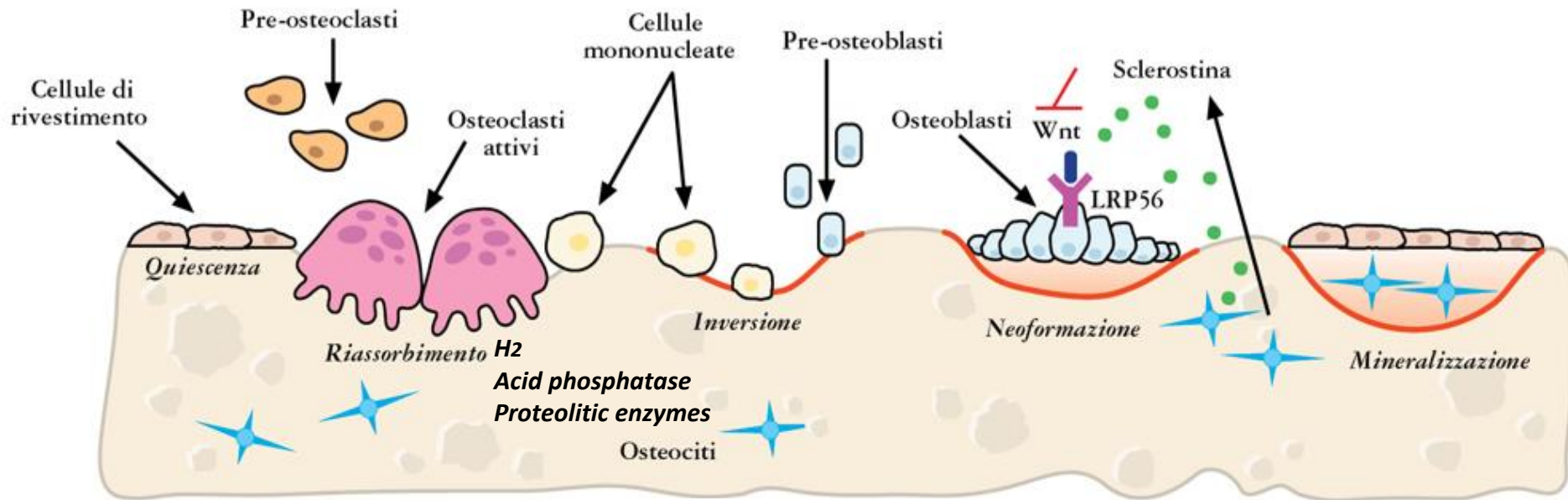
Normal bone

Scanning electron micrograph (SEM) of osteoporotic bone. The image shows a significantly altered bone structure compared to the normal bone. The trabeculae are much thinner, more fragmented, and highly porous, with many small, irregular holes and gaps throughout the structure. A semi-transparent grey box with the text "Osteoporotic bone" is overlaid on the upper left portion of the image.

Osteoporotic bone

Modifications of
bone morphology
by osteoporosis

Osteoclast and Osteoblast



Bone remodeling

Osteoclast precursors fuse to form brush border cells that resorb bone matrix. These cells are replaced by **osteoblasts** which deposit new bone. Wnt-beta catenin

Osteoclast action

Adhesion to the bone matrix to be resorpted

Creation of an acid environment that solubilizes the mineral matrix

Enzymatic digestion of the organic matrix

Biphosphonates

Reduce bone resorption by osteoclasts:

- Osteoclastic proton pump inhibition
- Reduction of osteoclast formation / activation
- Increased apoptosis of osteoclasts

Osteoblasts are not inhibited

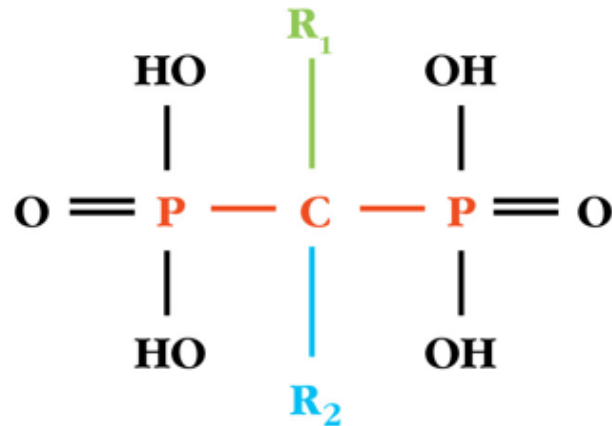
Alendronato
Etidronato
Ibandronato
Pamidronato
Risedronato

Biphosphonate DRUGS

Side Effects:

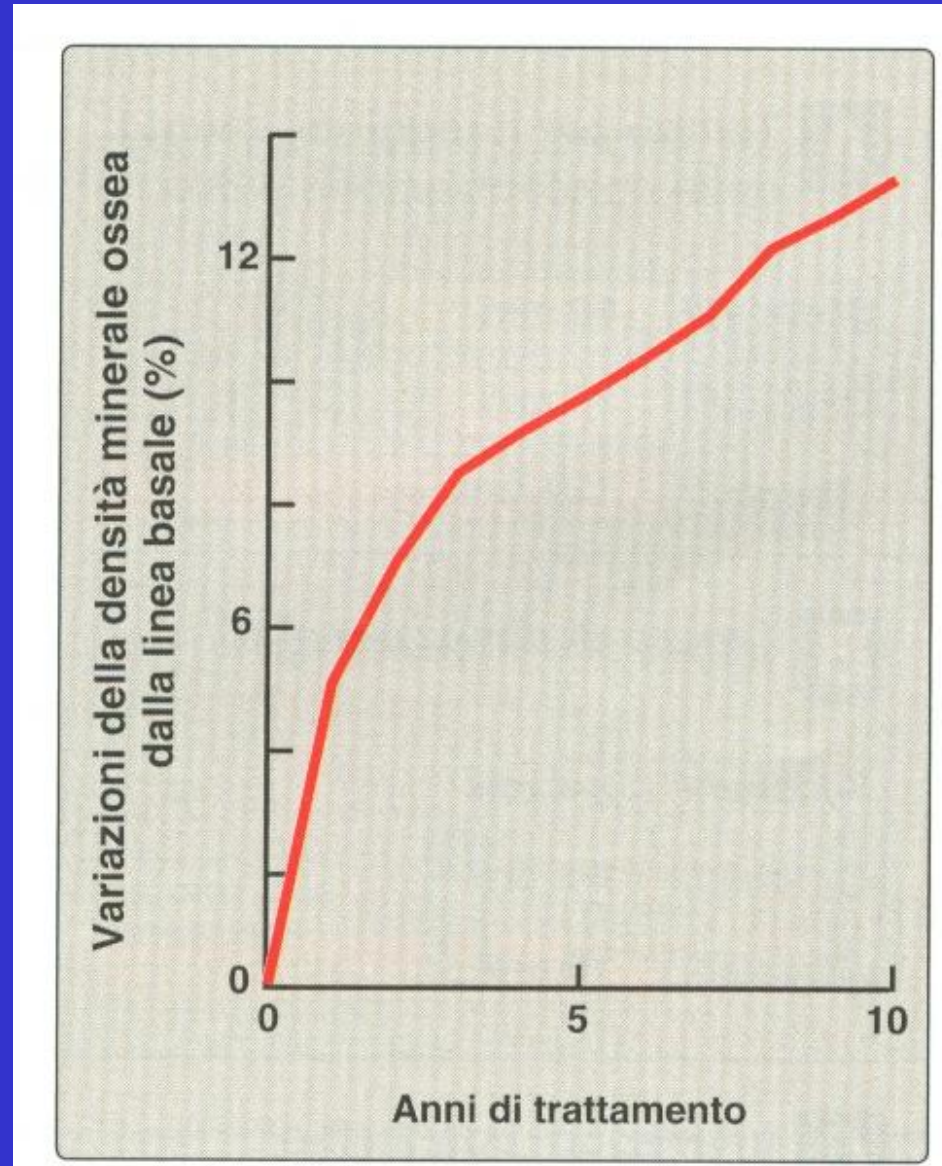
diarrhea, nausea, abdominal pain, oesophageal ulcers, atypical fractures

Biphosphonate potency



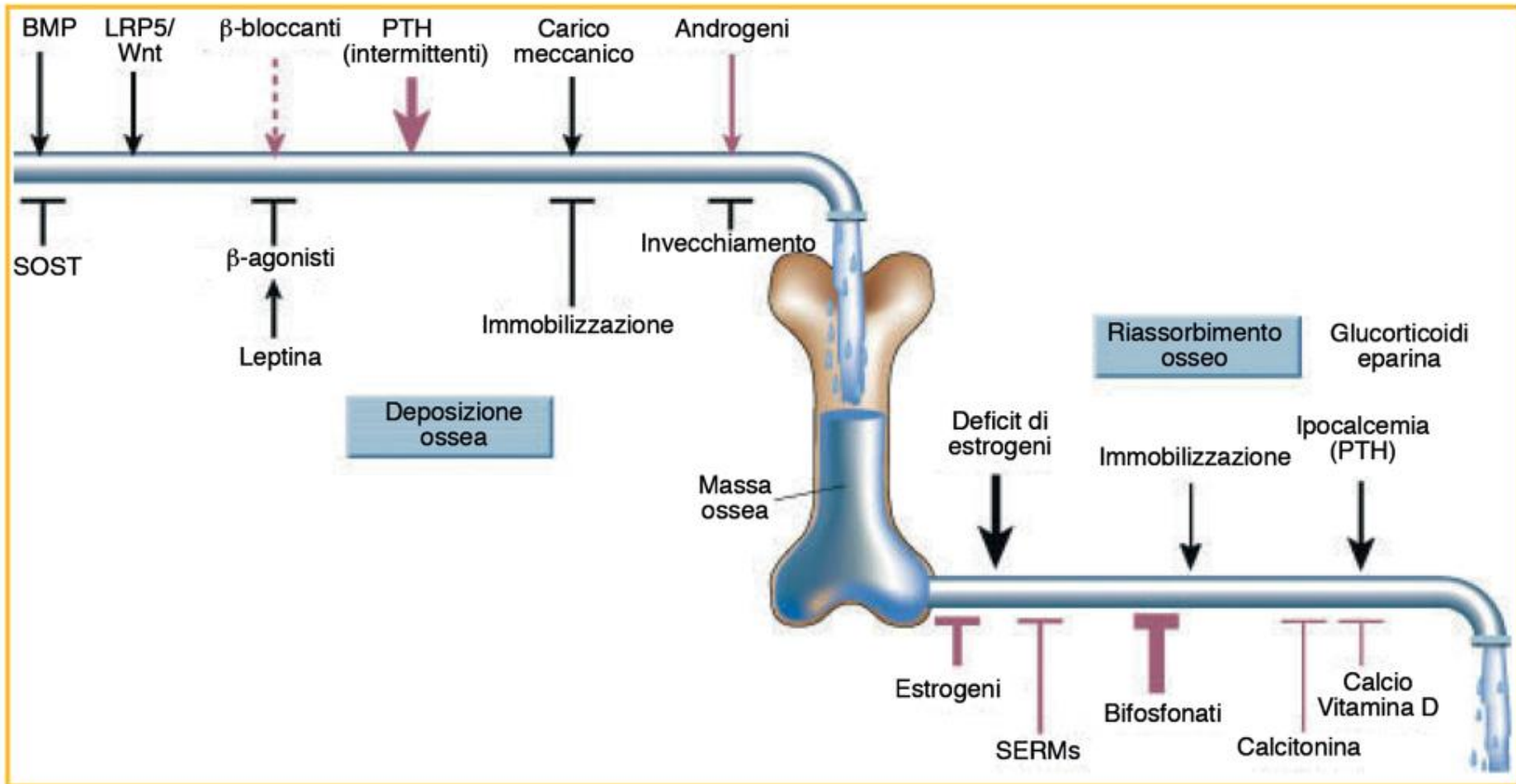
	RADICALE R ₁	RADICALE R ₂	POTENZA
Non amino Bifosfonati			
Etidronato *	OH	CH ₃	1
Clodronato	Cl	Cl	10x
Amino Bifosfonati			
Pamidronato *	OH	CH ₂ CH ₂ NH ₂	100x
Alendronato *	OH	CH ₂ CH ₂ CH ₂ NH ₂	1000x
Risedronato *	OH	CH ₂ -3-piridinile	10000x
Zoledronato	OH	CH ₂ C ₃ N ₂ H ₃	>10000x

Alendronate therapy: effect on the lumbar spine



- **Calcitonin:** reduces osteoclast activity (reabsorption), tolerance, vertebrae
- **Teriparatide:** fragment of PTH, stimulates bone formation,
 - high cost
- **Strontium ranelate:** Ca +
- **Raloxifene:** SERM (selective estrogen receptor modulators)
- **Vitamin D:** Ca + absorption, affect osteoblast

Deposition and Reabsorption

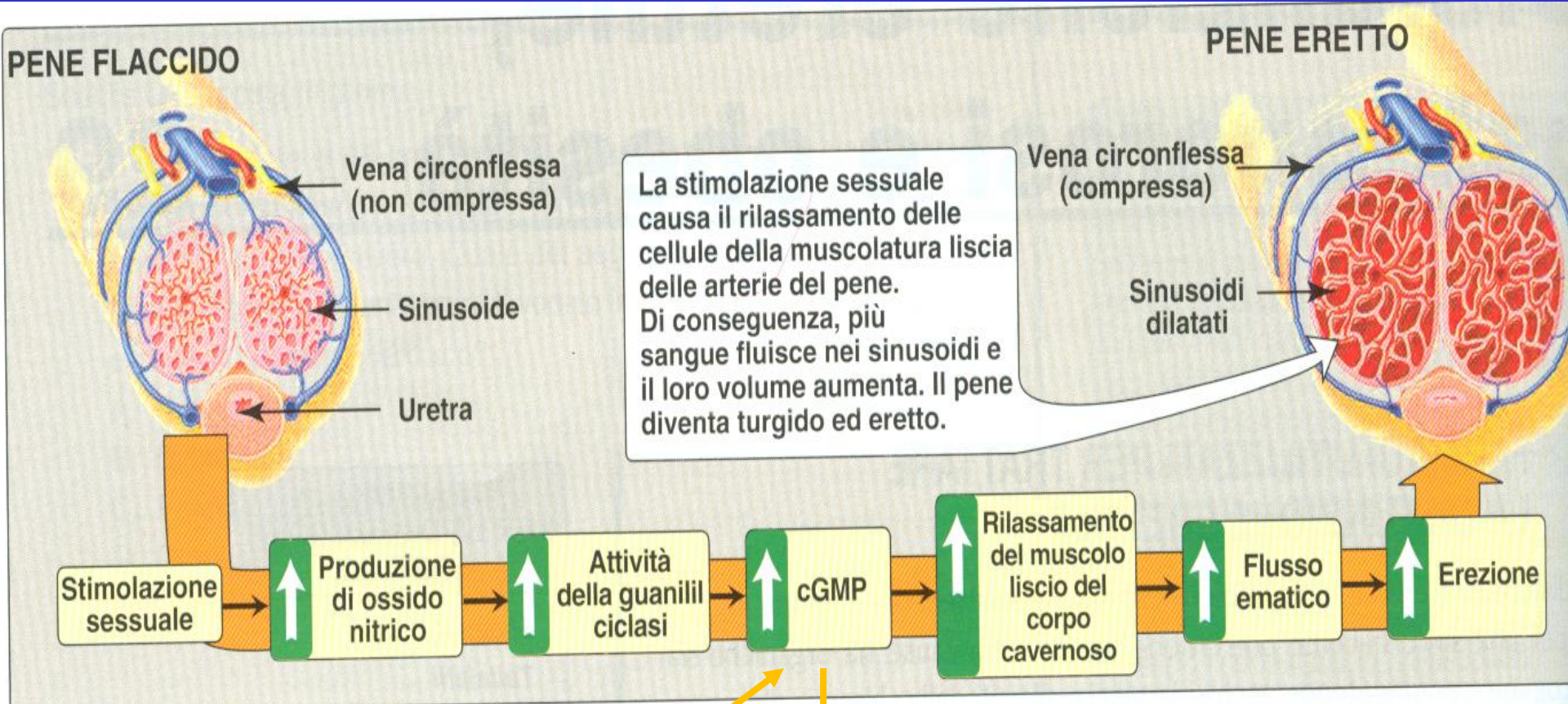


Black: physiological factors. Brown: pharmacological factors

BMP: morphologic bone proteins. SOST: Sclerostine, LRP5: protein 5 correlated to LDL receptor, PTH: parathormon

Drugs for erectile dysfunction

Mechanism of erection



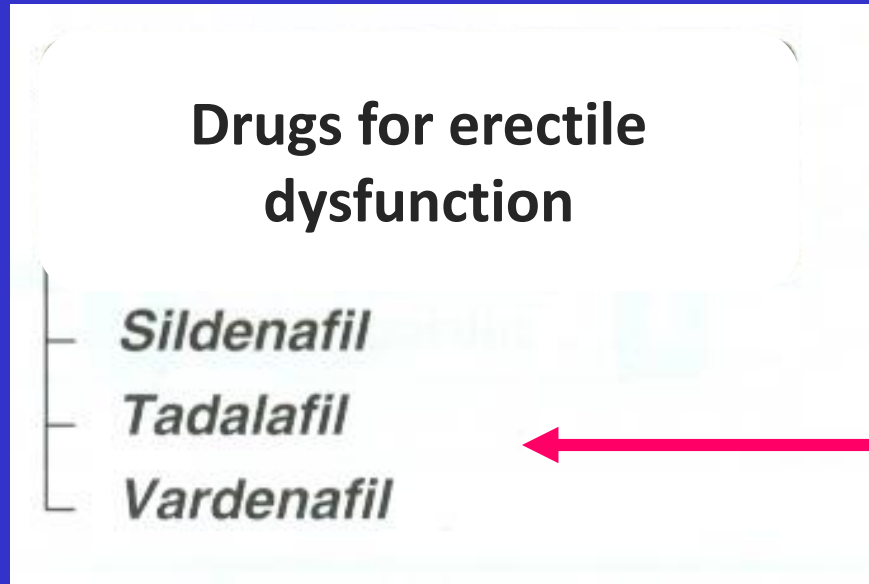
PDE-5 controls half-life of cGMP

↑ activation K^+ ↓ Ca^{2+} intracellular



Effect of inhibitors of phosphodiesterase on cGMP levels in the muscle of cavernous body

Drugs for erectile dysfunction



Inhibitors of
phosphodiesterase
(PDE-5)

Intracavernous administration

Papaverine (cGMP)

Prostaglandin E1 (alprostadil) (cAMP)

Linsidomine (NO)

A**Time to reach peak concentration***Sildenafil*

60 min

Vardenafil

50 min

Tadalafil

120 min

B**Half-life***Sildenafil*

3-4 ore

Vardenafil

4-5 ore

Tadalafil

18 ore

C**Food interactions***Sildenafil*

Si

Vardenafil

Si

Tadalafil

No

Properties of inhibitors
of phosphodiesterases

Interactions

Inhibitors of NO

Antagonists of alfa-adrenergic

Farmaco	Legame Proteine (%)	t _{1/2} min	Somministrazione	Indicazioni	Tossicità	Interazioni
<u>Alprostadil</u>	81 (Albumina)	5-10	Infusione e.v. Intrararteriosa Intrauretrale Intracavernosa	<u>Disfunzione erettile</u>	Dolore genitale o uretrale da lieve a moderato; priapismo; sanguinamento nel sito d'iniezione o formazione di piccoli ematomi; ipotensione; sincope	Aumento dell'attività di farmaci vasodilatatori ed anti-ipertensivi la durata dell'erezione può essere aumentata dalla co-somministrazione di farmaci rilassanti la muscolatura liscia e bloccanti α-adrenergici
	55 (α-globulina)		Infusione e.v. lenta	Pervietà del dotto arterioso	Apnea; iperpiressia; bradicardia; ipotensione	n.r.
			Infusione e.v. lenta Endoarteriosa	Vasculopatie periferiche	Dolore; edema ed eritema nel sito di infusione	n.r.