IL TESSUTO OSSEO II

(ossificazione)

Ossificazione

- Ossificazione diretta o membranosa
- Ossificazione indiretta

Ossificazione diretta

- Avviene durante la vita embrio-fetale per differenziamento delle cellule mesenchimali in osteoblasti; o durante il rimodellamento dell’osso anche nell’adulto a partire da cellule osteoprogenitrici

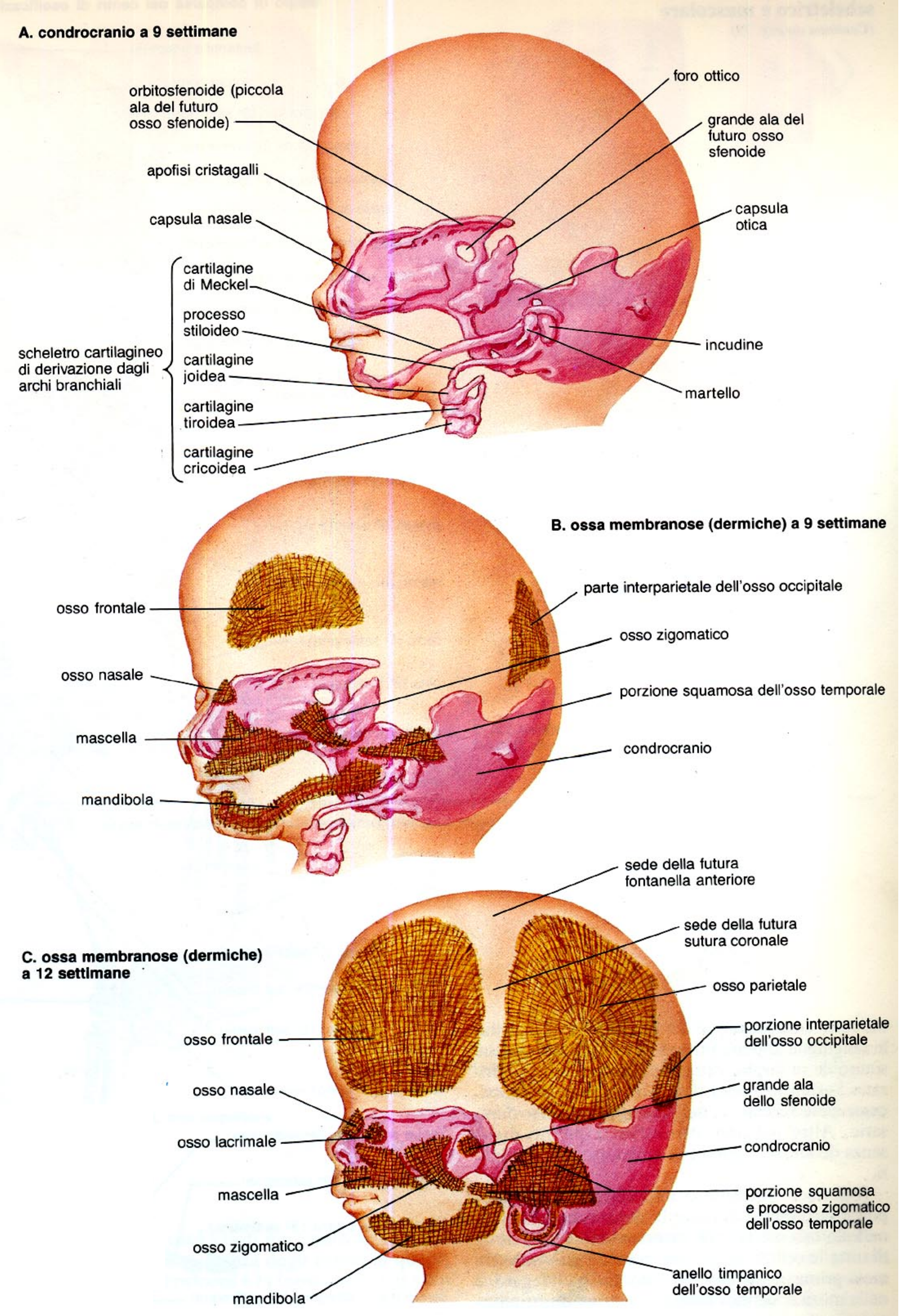
- Nell’embrione, le ossa che si formano con questo tipo di ossificazione sono le ossa piatte della volta cranica (porzione interparietale dell’occipitale, parietali, frontale, la porzione squamosa dei temporali), lamina mediale dei processi pterigoidei dello sfenoide, ossa nasali, lacrimali, palatine, osso zigomatico, la mascella e la mandibola, clavicola

Ossificazione indiretta

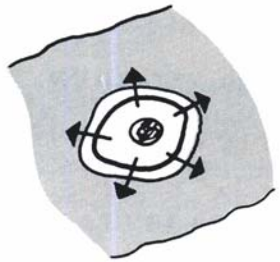
- Le ossa si formano come cartilagine ialina e vengono sostituite da tessuto osseo
- Questo tipo di ossificazione avviene per alcune ossa del cranio (etmoide, quasi tutto lo sfenoide, vomere, squama occipitale, osso ioide, ossicini dell’orecchio, porzione timpanica e petrosa ossa temporali) e tutte le ossa dello scheletro assile
- Richiede la presenza di cellule osteoprogenitrici
- Avviene sia dalla periferia dell’osso (ossificazione pericondrale) sia dall’interno dell’osso (ossificazione endocondrale)

Una parte dello scheletro della faccia e della base del cranio si abbozza sottoforma di cartilagine (condrocranio) (ossificazione indiretta), tuttavia la maggior parte delle ossa della faccia inclusa la mascella e la mandibola si formano per ossificazione diretta.

Dopo il condrocranio si formano le ossa membranose della volta del cranio (frontale, parietali, parte dell'occipitale) la mandibola, la mascella, le ossa nasali, lacrimali, zigomatico e la porzione squamosa dei temporali.



ossificazione diretta

(1) Differenziamento delle cellule mesenchimatose in osteoblasti	
(2) Secrezione della matrice organica del tessuto osseo (fibre collagene + sostanza fondamentale) da parte degli osteoblasti (l'osteoblasta, quando è completamente circondato dalla matrice, prende il nome di osteocita)	
(3) Mineralizzazione della matrice organica (deposito di cristali di apatite) Osso primario immaturo (non lamellare a fibre intrecciate)	
(4) Comparsa degli osteoclasti Rimozione t. osseo primario e deposizione di tessuto osseo maturo (lamellare)	

Formazione di tessuto osteoide
(tessuto osseo non mineralizzato)

↓

Mineralizzazione con formazione di tessuto
osseo non lamellare a fibre intrecciate
trabecolato simile allo spugnoso

↓

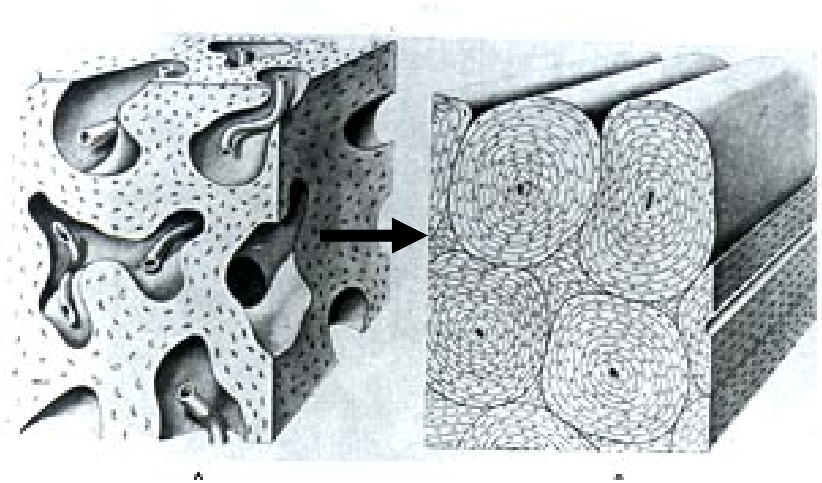
Riassorbimento di questo tessuto osseo
(osteoclasti) e nuova deposizione di
tessuto osseo non mineralizzato
(osteoblasti)

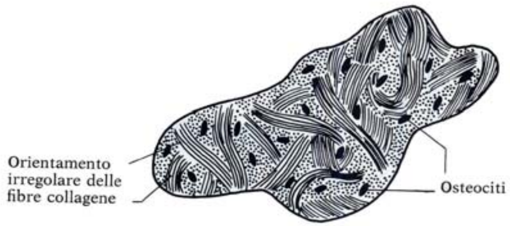
↓

Mineralizzazione del tessuto in lamelle che
formano trabecole nelle regioni di tessuto
spugnoso e osteoni primari irregolari e secondari
regolari nelle regioni di tessuto osseo compatto

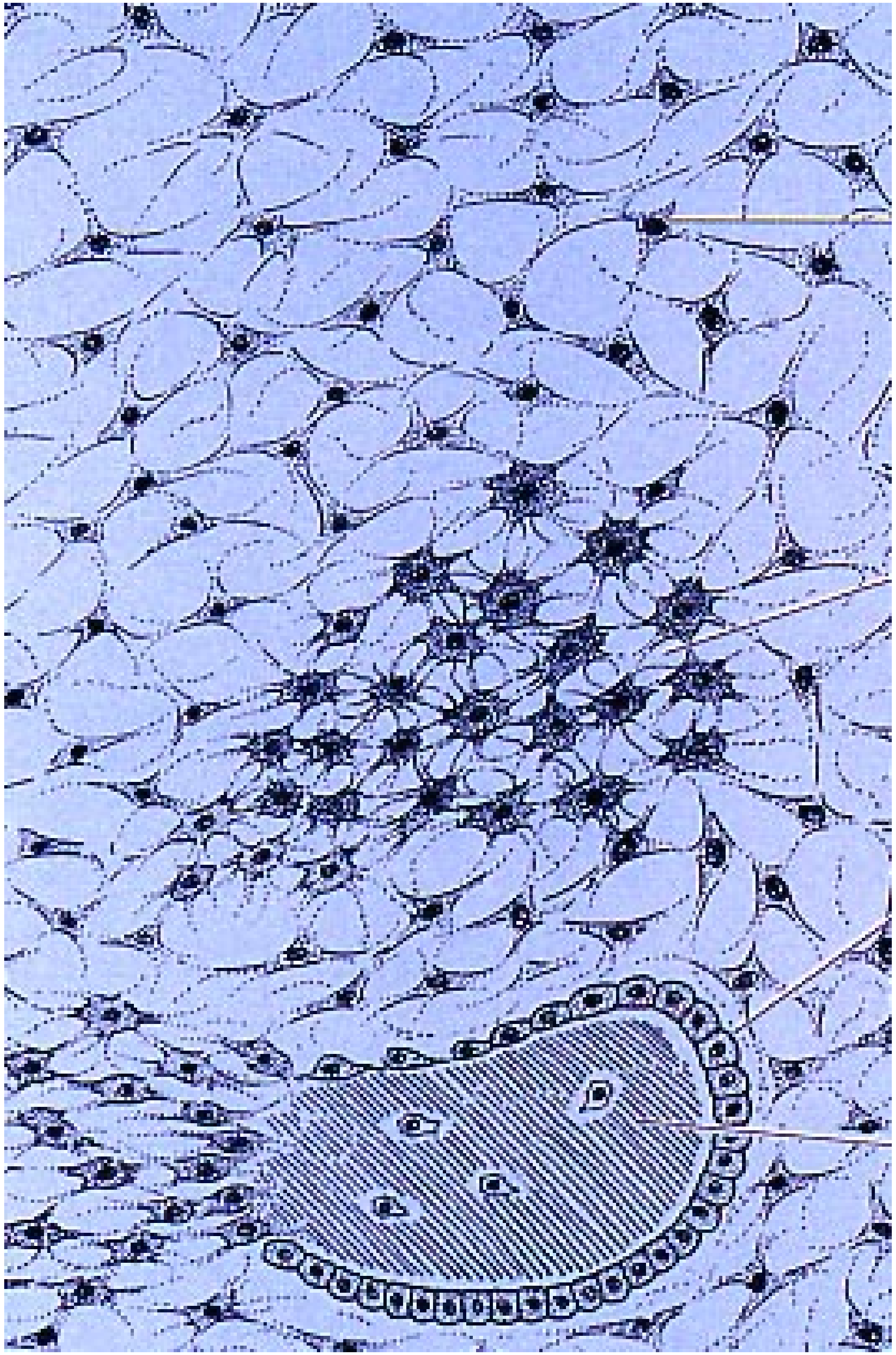
↓

Continui processi di
rimodellamento dell'osso

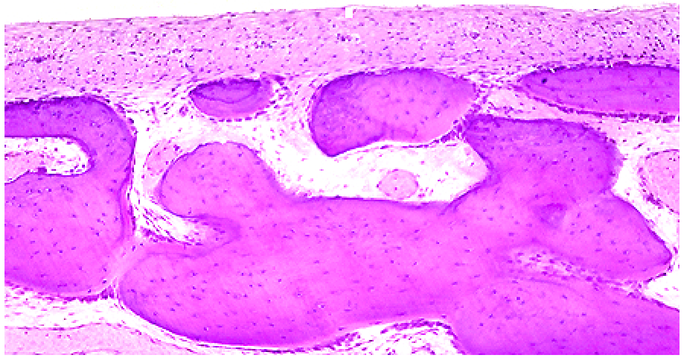




Il primo tessuto osseo che si forma è non lamellare a fibre intrecciate trabecolato: esso viene gradatamente sostituito da tessuto osseo lamellare spugnoso o compatto a seconda delle regioni dell’osso.



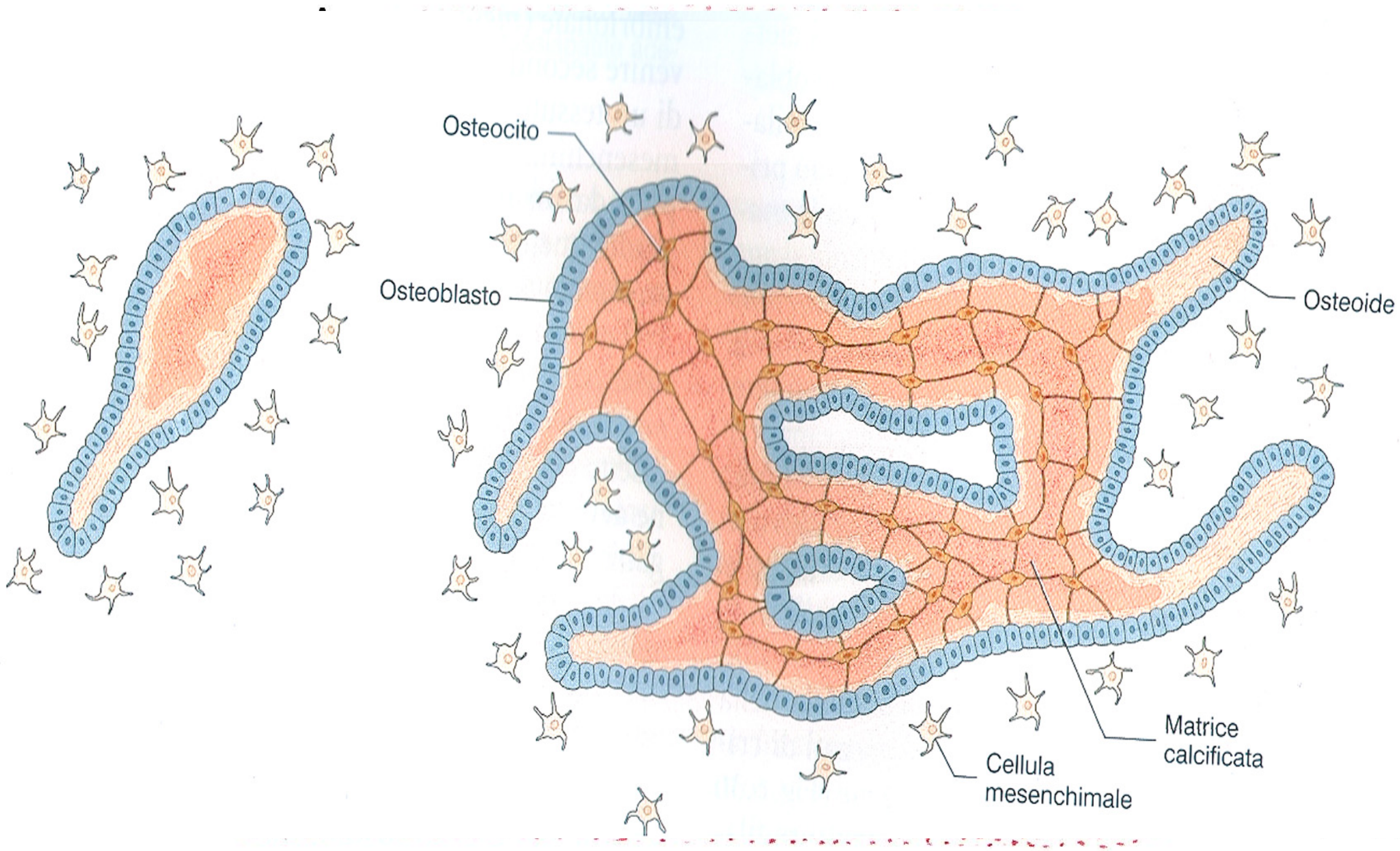
Formazione di trabecole ossee da cellule mesenchimali che differenziano in osteoblasti

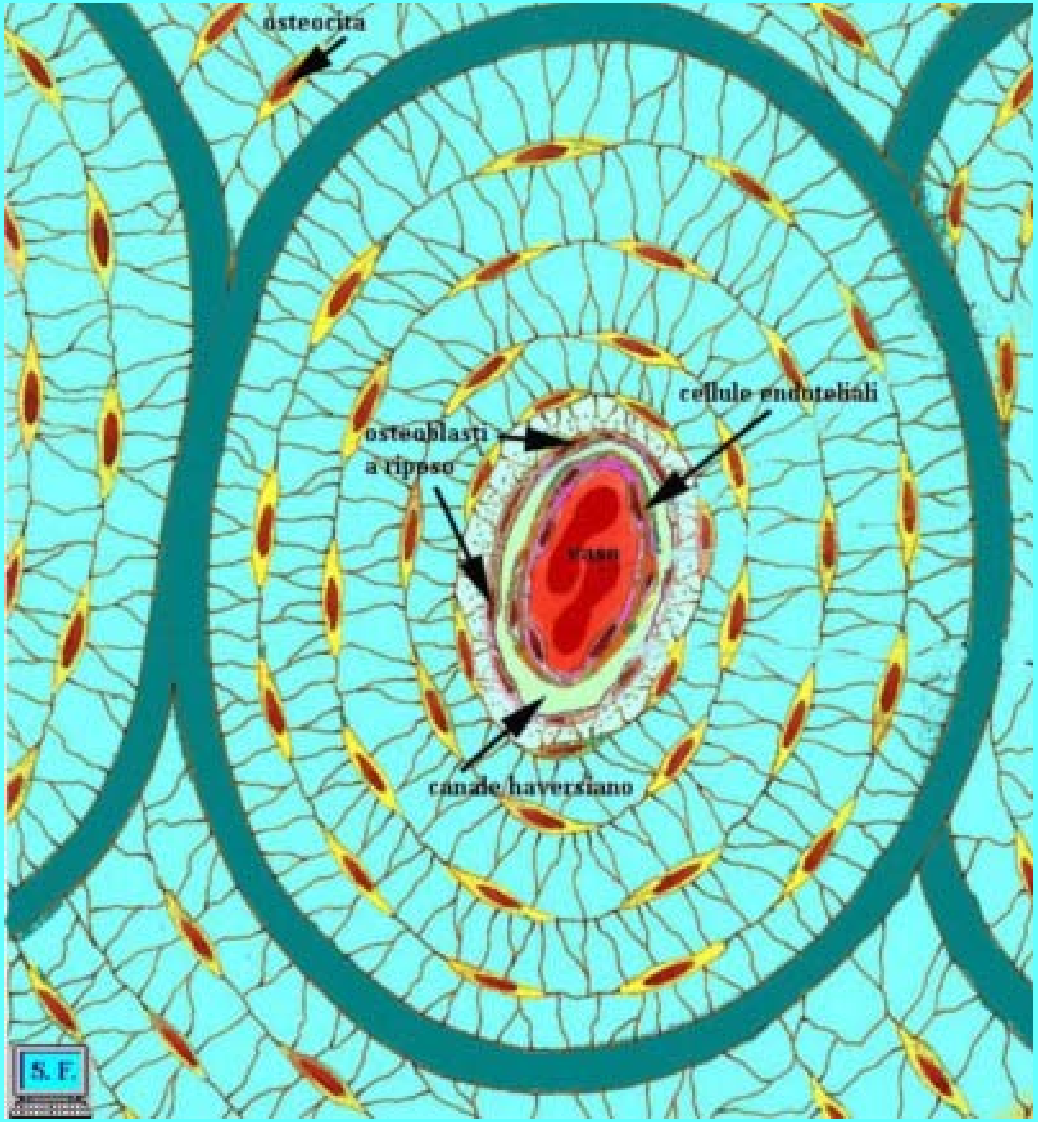


osteoblasti

trabecola

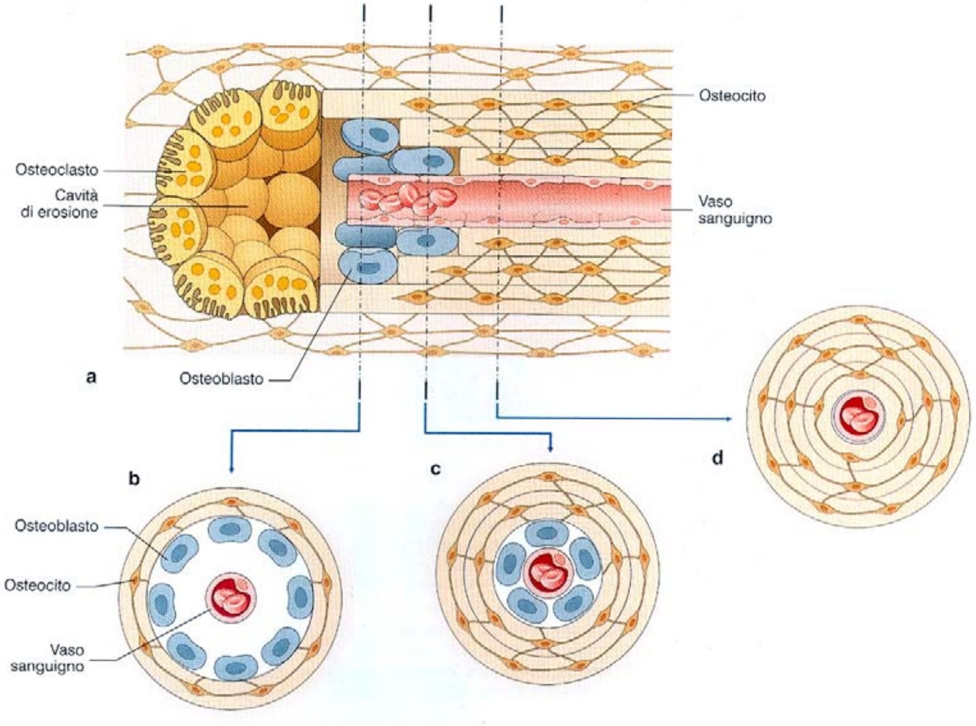
Ossificazione diretta di un osso piatto



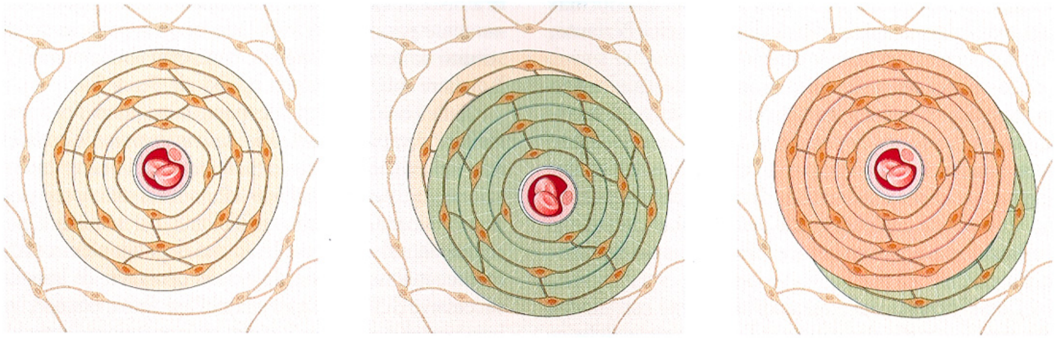

osteocita
cellule endoteliali
osteoblasti
a riposo
vaso
canale haversiano
S. F.

Formazione di osteoni primari e secondari

Il numero degli osteoni e i frammnenti di osteoni nelle regioni interstiziali aumentano con l'età dell'individuo; anche l'aumento del numero delle lamelle/osteone e la diminuzione della grandezza del canale di Havers sono indici di invecchiamento



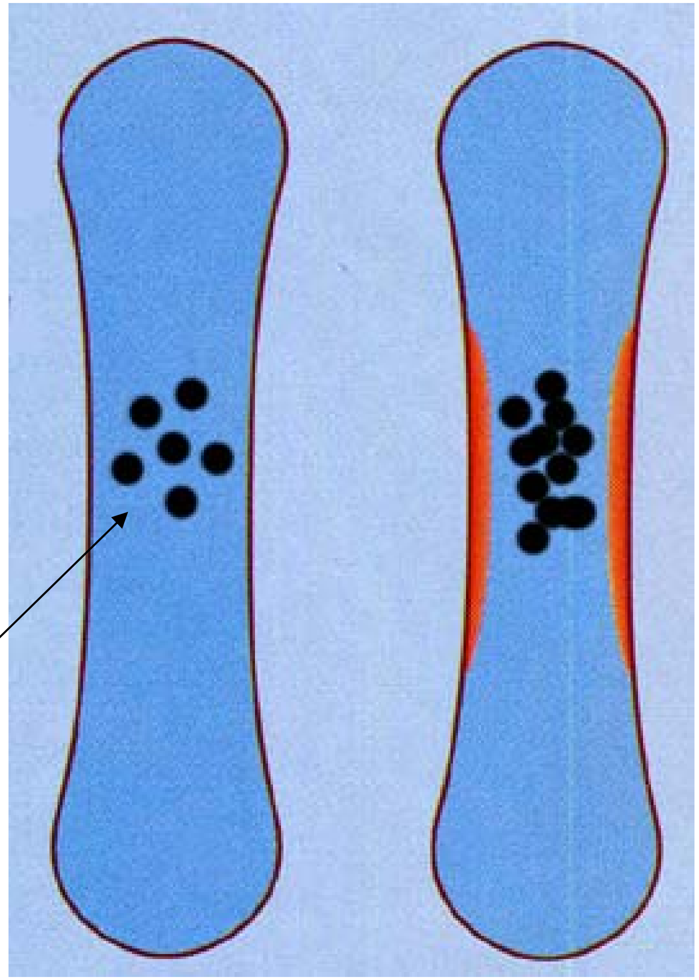
Rimodellamento dell'osso con formazione di osteoni di generazioni successive

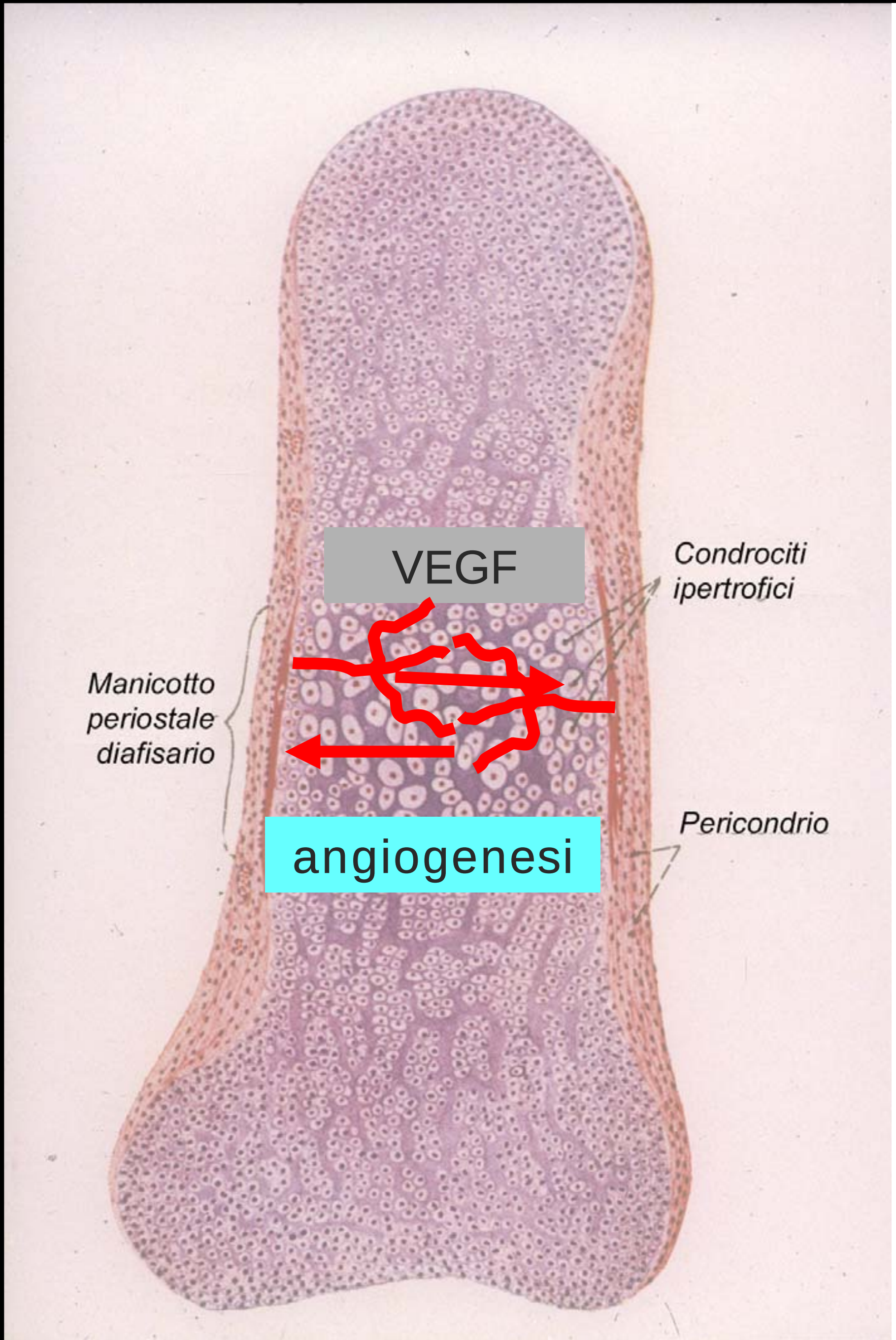


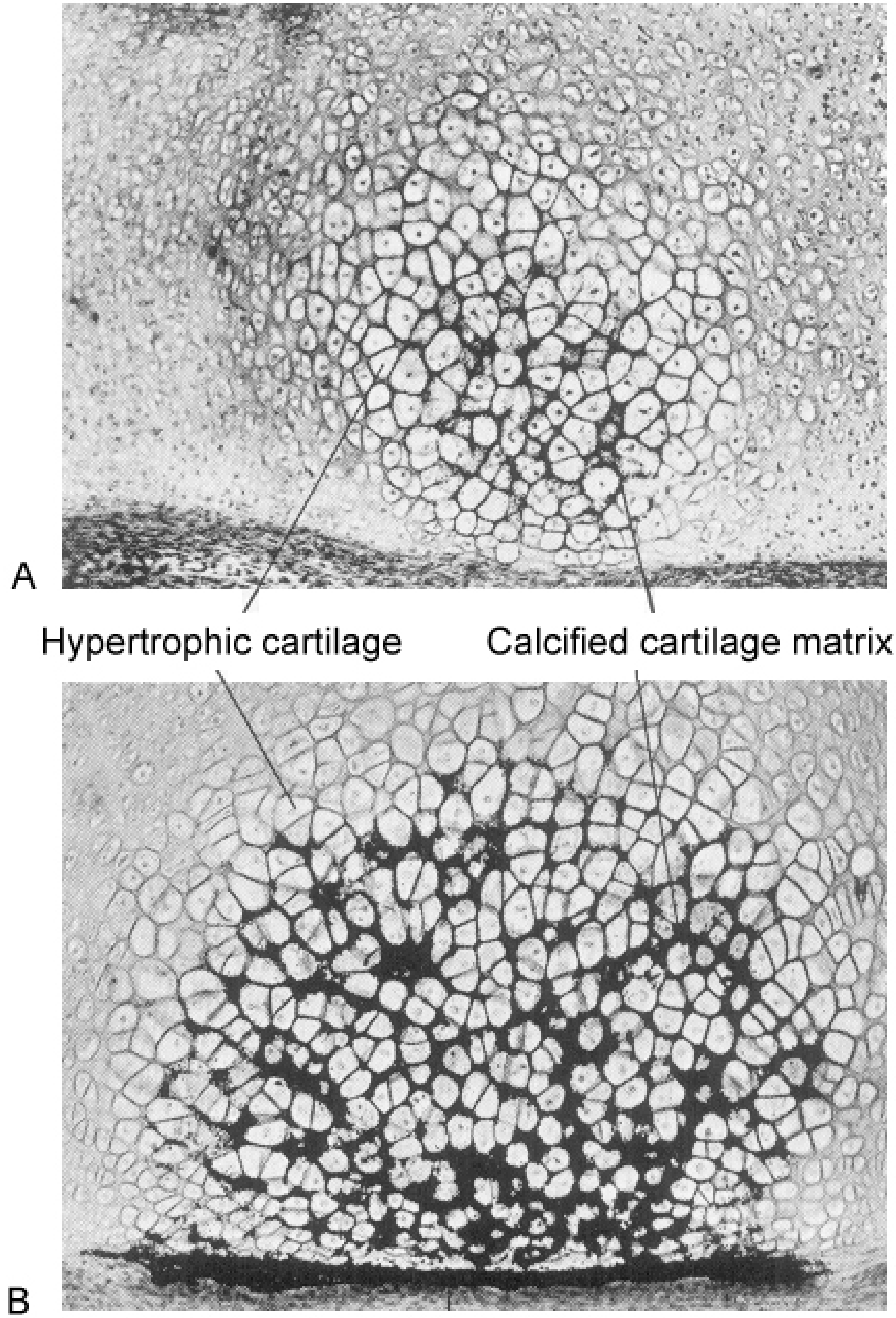
Tappe principali dell'ossificazione indiretta di un osso lungo (periodo embrio-fetale)

- Comparsa di un centro di ossificazione primario nella cartilagine (condroblasti ipertrofici, la matrice calcifica e degenera) nella regione diafisaria

- Nel pericondrio allo stesso livello cellule osteoprogenitrici si differenziano in osteoblasti che iniziano a secernere tessuto osteoide che mineralizza in tessuto osseo primario (non lamellare a fibre intrecciate) (manicotto periostale); questo viene progressivamente sostituito da tessuto osseo maturo (lamellare)

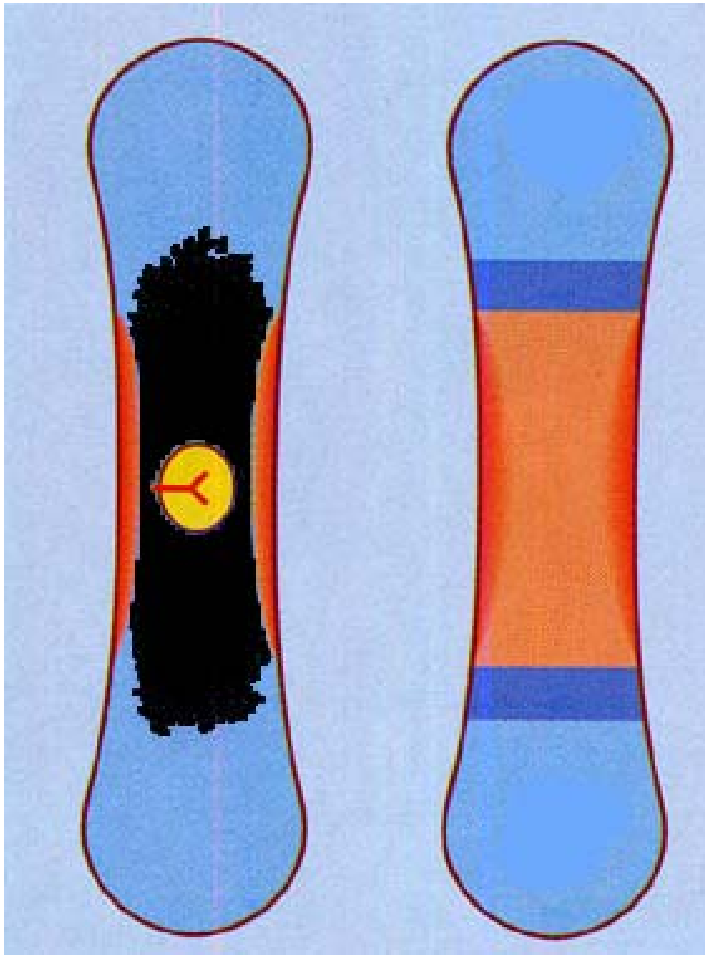



VEGF
Condrociti
ipertrofici
Manicotto
periostale
diafisario
Pericondrio
angiogenesi

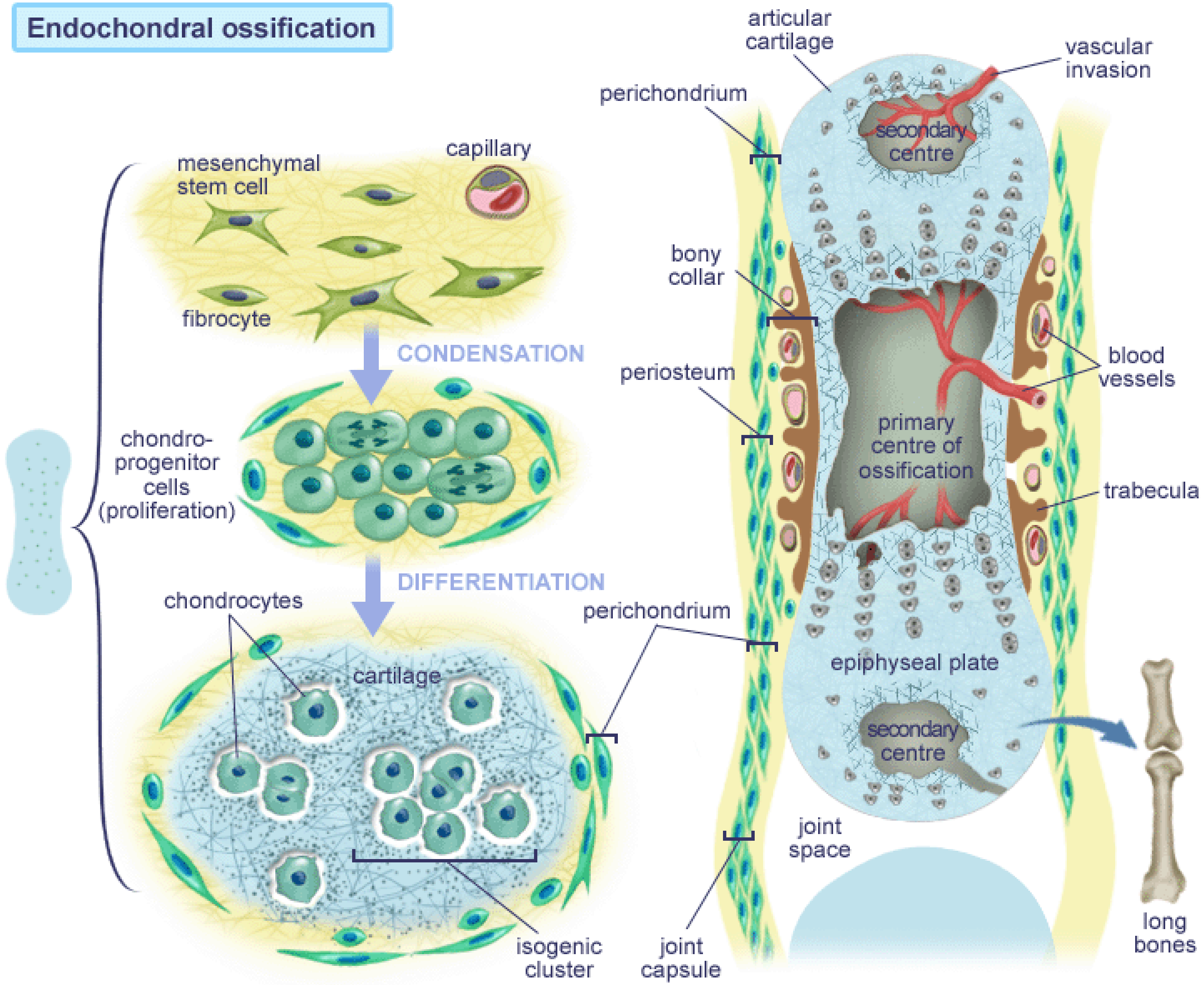

A
Hypertrophic cartilage
Calcified cartilage matrix
B

Tappe principali dell'ossificazione indiretta di un osso lungo (periodo embrio/fetale)

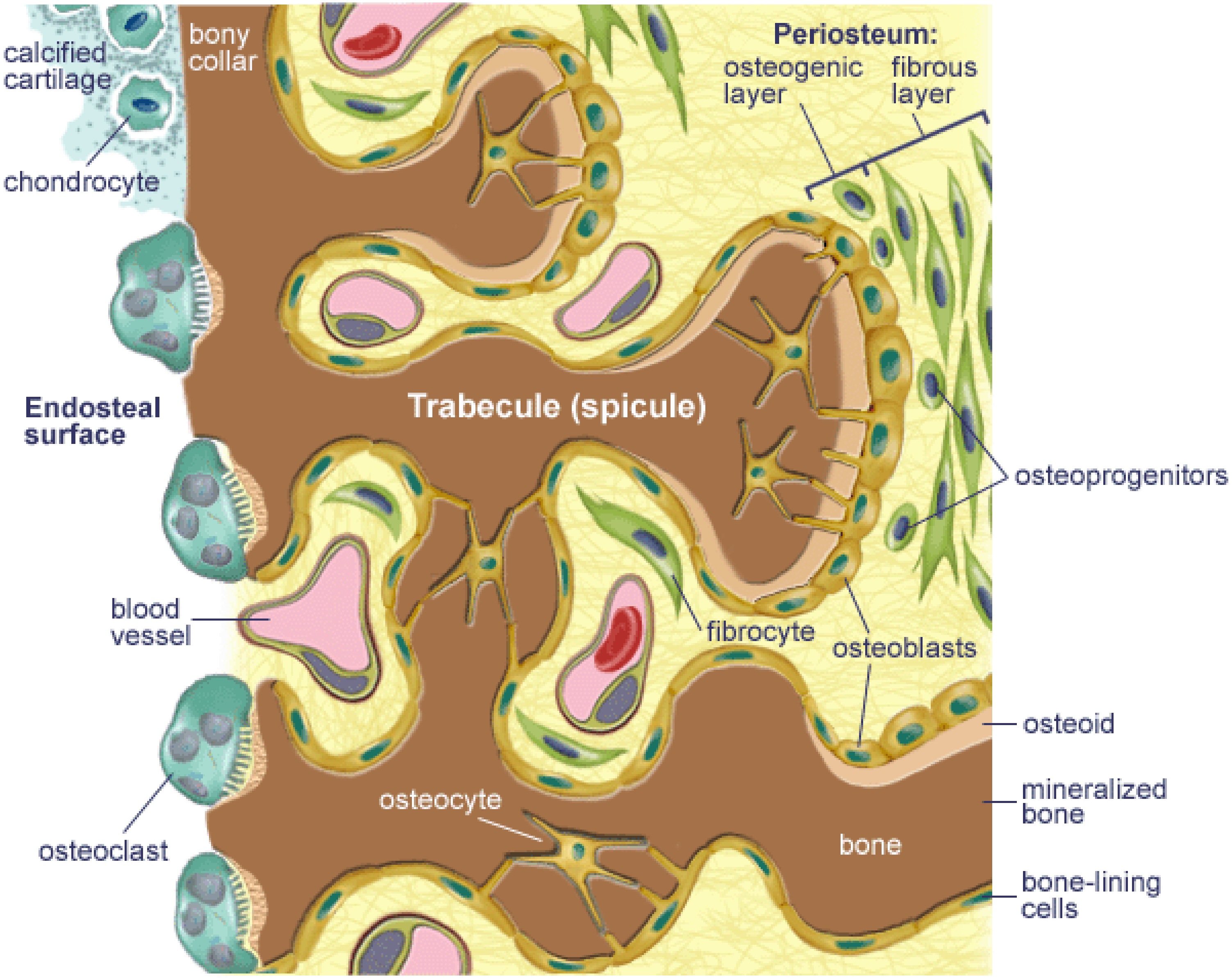
- Capillari del periostio vengono attratti nel centro di ossificazione primario (VEGF) portando osteoblasti
- Gli osteoblasti secernono tessuto osteoide che ricopre la cartilagine in degenerazione; mineralizzazione in tessuto osseo primario e sua progressiva sostituzione con t.osseo maturo
- Tali fenomeni si spostano gradatamente verso le epifisi mentre le regioni di cartilagine limitrofe al centro di ossificazione si organizzano in cartilagine di coniugazione
- Processi di riassorbimento e deposizione di nuovo tessuto osseo si verificano nelle regioni ossificate



Endochondral ossification



Bony collar



calcified cartilage
bony collar
chondrocyte
Periosteum:
osteogenic layer
fibrous layer
Endosteal surface
Trabecule (spicule)
osteoprogenitors
blood vessel
fibrocyte
osteoblasts
osteoid
mineralized bone
osteocyte
bone
bone-lining cells
osteoclast

Formazione di tessuto osteoide
(tessuto osseo non mineralizzato)

↓

Mineralizzazione con formazione di tessuto
osseo non lamellare a fibre intrecciate
trabecolato simile allo spugnoso

↓

Riassorbimento di questo tessuto osseo
(osteoclasti) e nuova deposizione di
tessuto osseo non mineralizzato
(osteoblasti)

↓

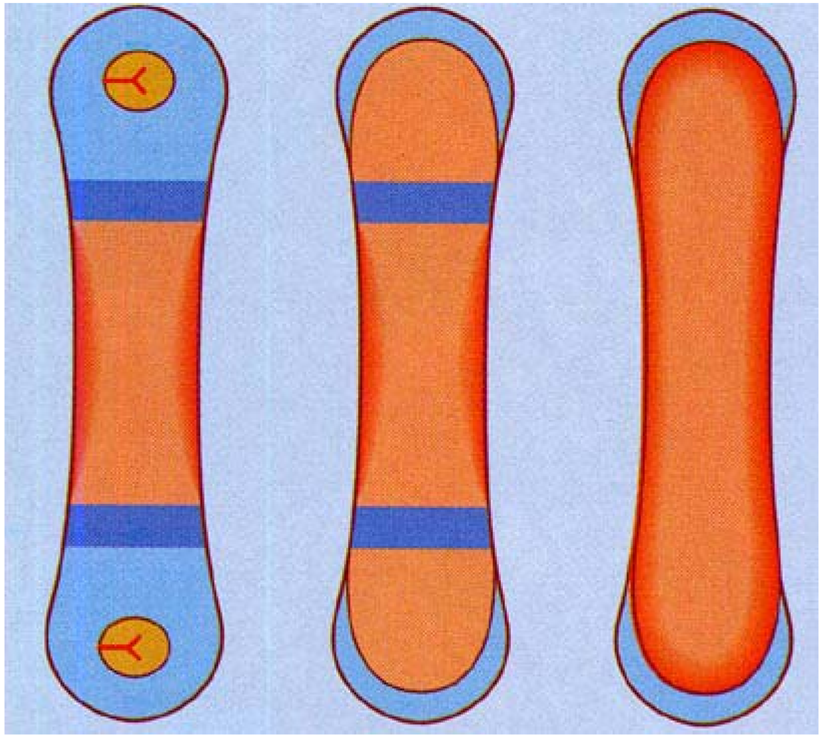
Mineralizzazione del tessuto in lamelle che
formano trabecole nelle regioni di tessuto
spugnoso e osteoni primari irregolari e
secondari regolari nelle regioni di tessuto
osseo compatto

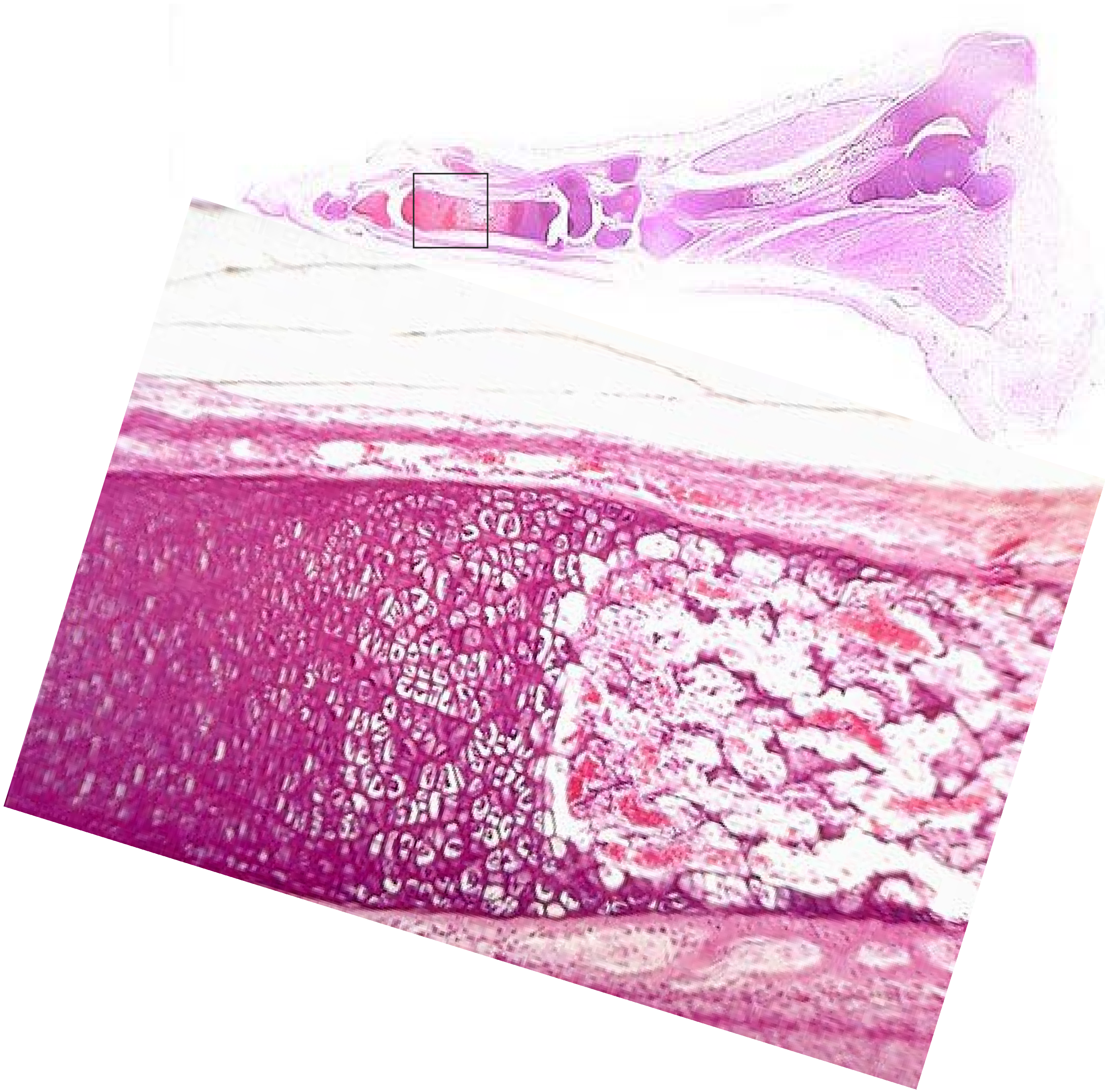
↓

Continui processi di
rimodellamento dell'osso

Tappe fondamentali dell'ossificazione indiretta (post-nascita)

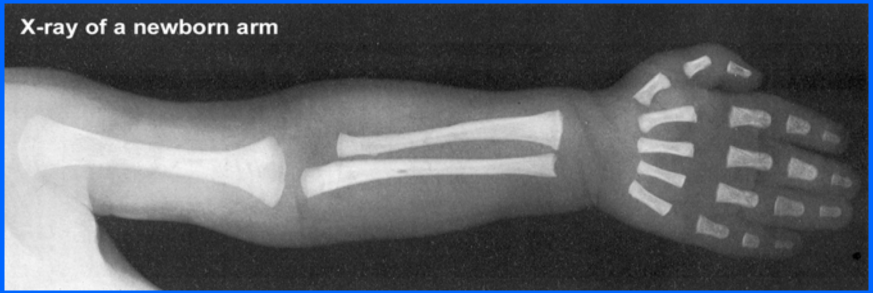
- Comparsa dei centri di ossificazione secondari nelle epifisi
- Osteoblasti portati da capillari provenienti dal pericondrio delle epifisi formano tessuto osteoide primario e maturo con le modalità già descritte
- Il processo si espande dai centri di ossificazione alla periferia
- Al termine della crescita anche le cartilagini di coniugazione verranno ossificate





OSSA LUNGHE

Tutti i centri primari (diafisari) di ossificazione compaiono entro il 3° mese di vita intrauterina, a partire dalla clavicola (5^a-6^a sett.).



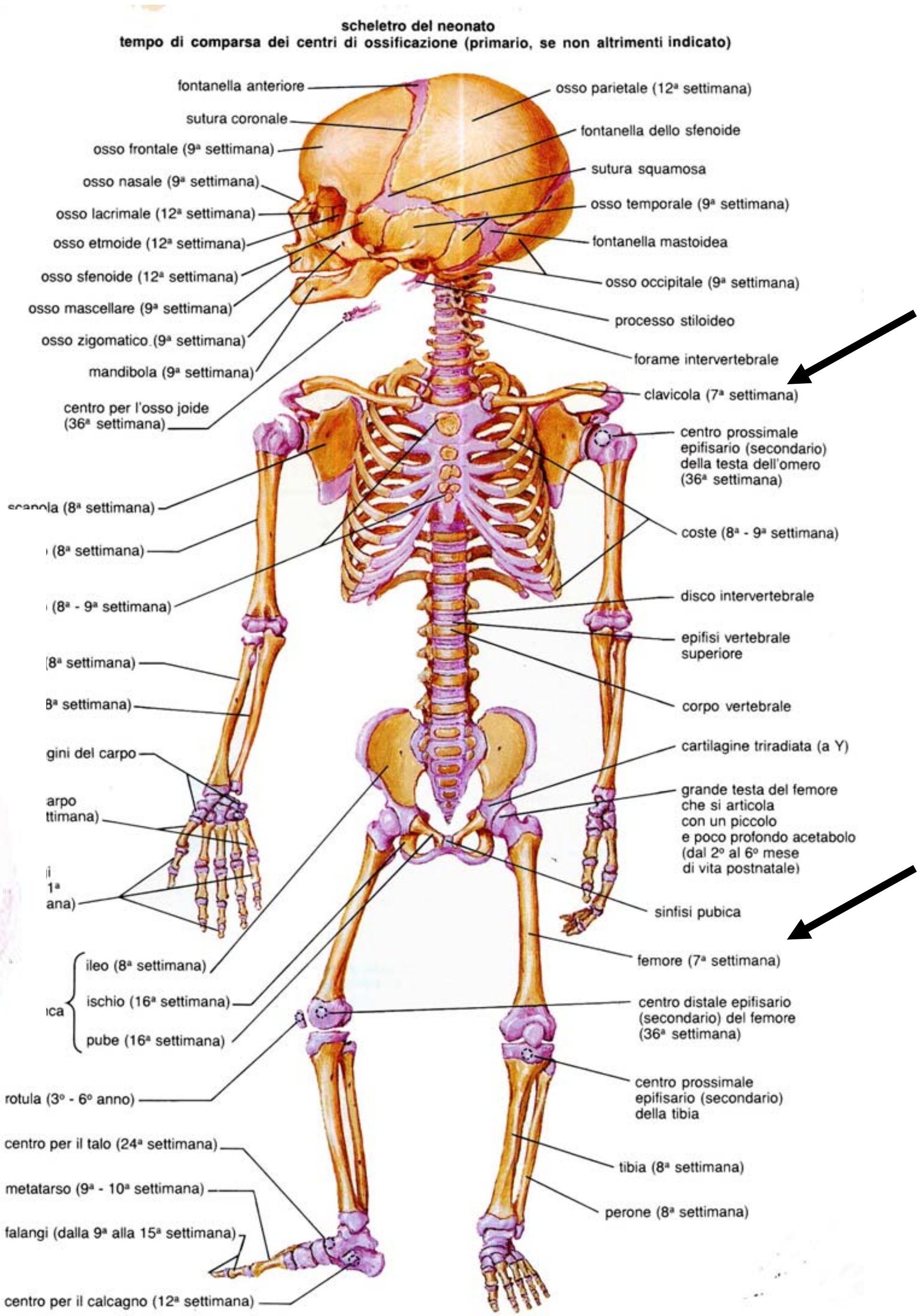
I centri secondari (epifisari) cominciano a comparire nelle ultime due-tre settimane di gravidanza, a partire dalle epifisi distale del femore e prossimale della tibia

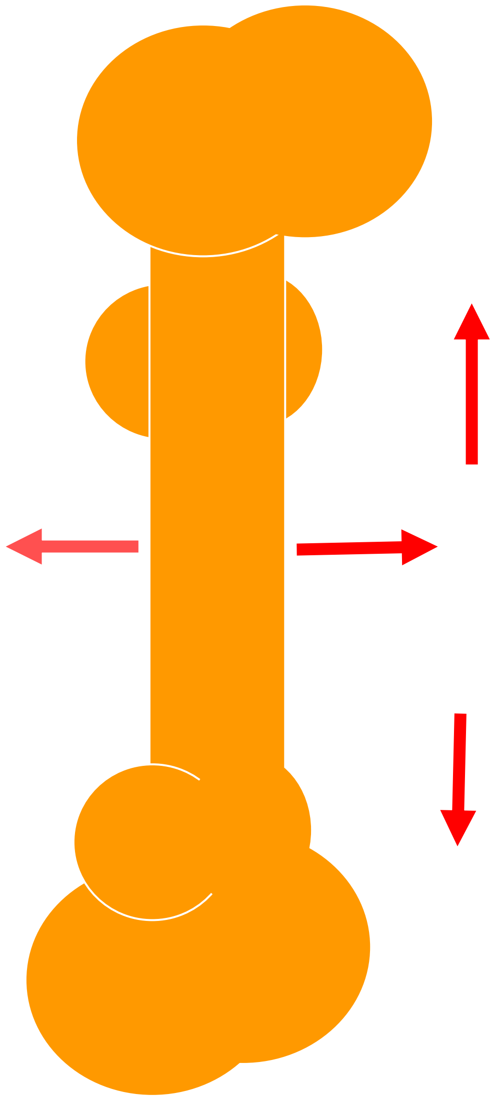
Il primo osso
che mineralizza
è la clavicola
(ossificazione
membranosa);
il primo centro
di ossificazione
indiretta è nel
femore

Embrione di 36-40 g
colorazione alizarina

Centri di ossificazione primaria (comparsa temporale)

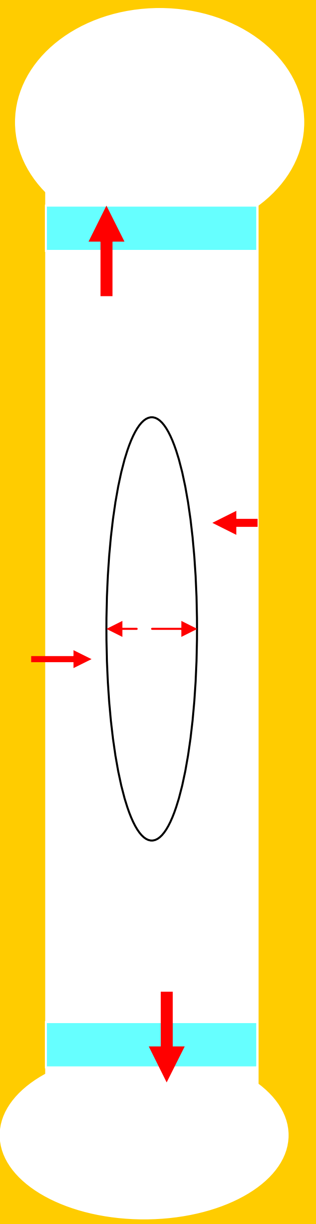
Ossificazione delle ossa del piede di un feto: notare il centro di ossificazione primario nella falange



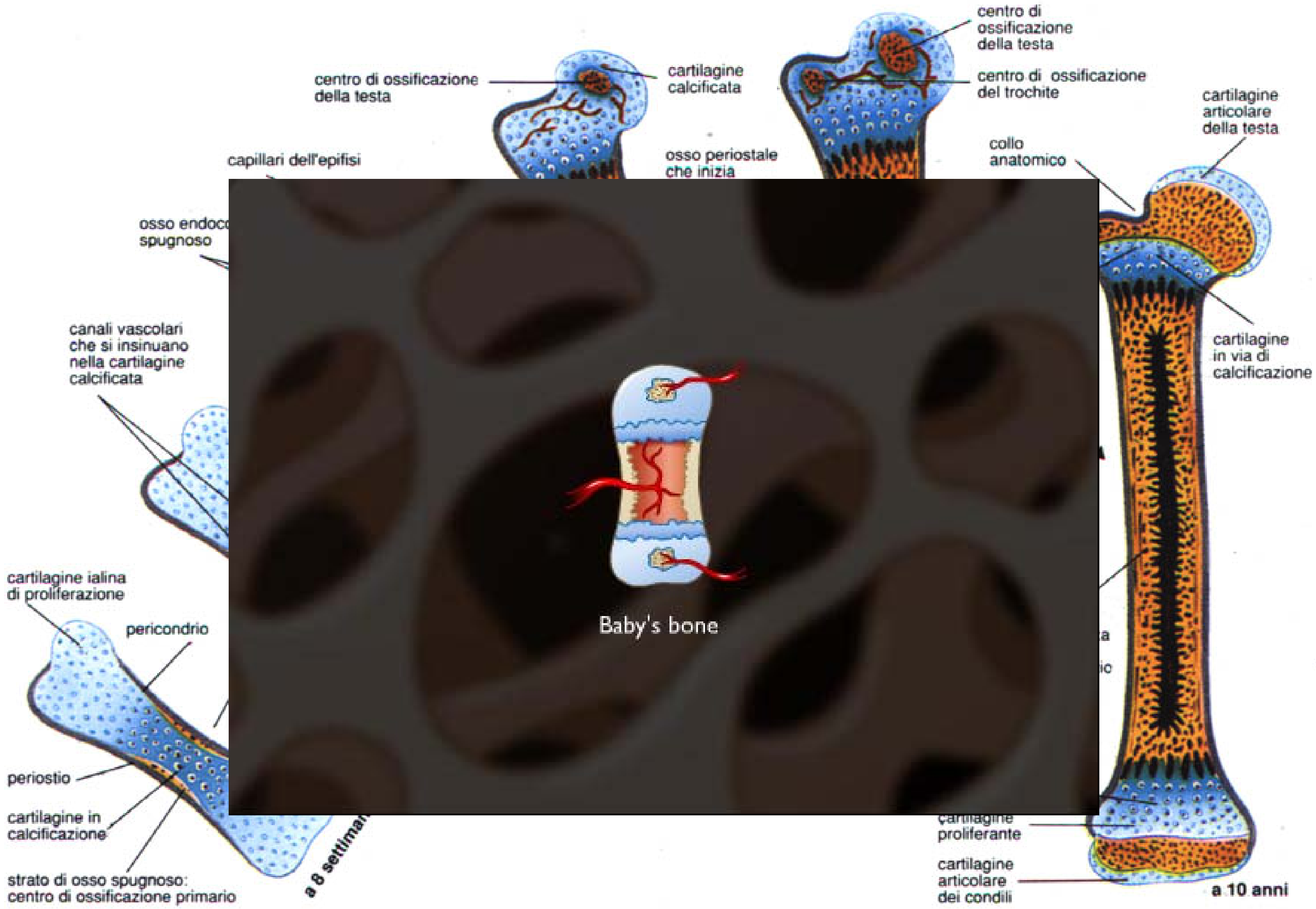


Rimodellamento e accrescimento in lunghezza e spessore delle ossa:
mentre procede l’ossificazione l’ osso si accresce in lunghezza e spessore.

- L’accresciemento in lunghezza è dovuto all’attività proliferativa della **cartilagine di coniugazione** e all’avanzamento del processo di ossificazione dalla regione diafisaria verso l’epifisi
- L’accrescimento in spessore è dovuto **all’attività osteogenica del periostio** dall’esterno all’interno dell’osso ed erosiva degli osteoclasti dall’interno all’esterno.
- L’attività degli osteoclasti è responsabile anche della formazione della cavità midollare e di quelle dell’osso spugnoso.



FASI DI ACCRESCIMENTO E OSSIFICAZIONE DELL'OMERO
(dalla vita fetale a 10 anni)

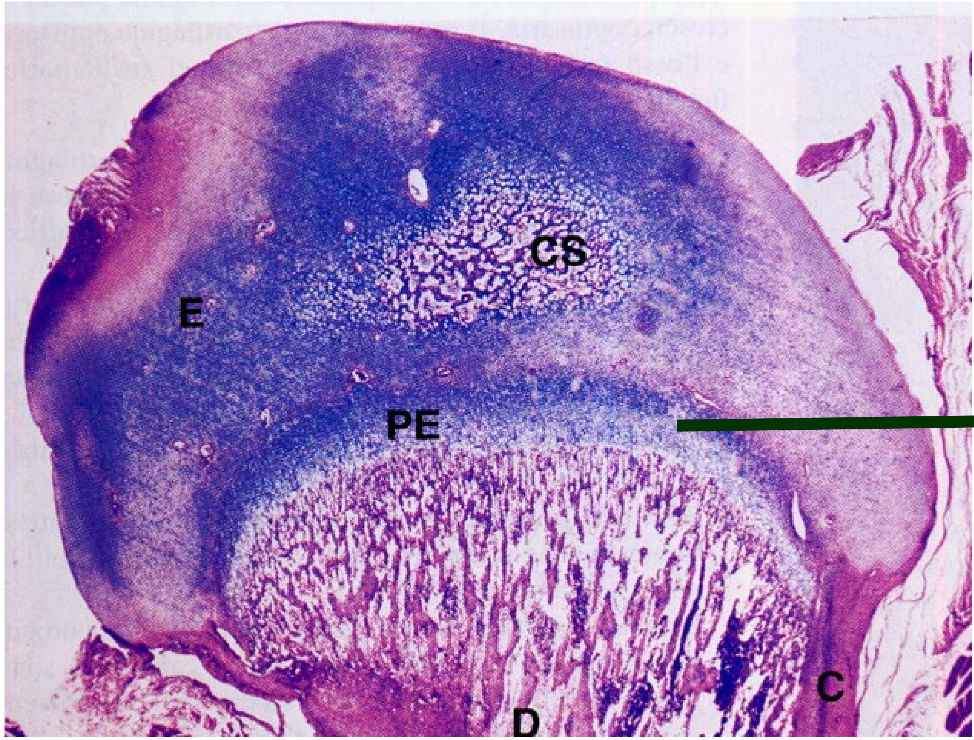


- Accrescimento in lunghezza di un osso

$\downarrow$

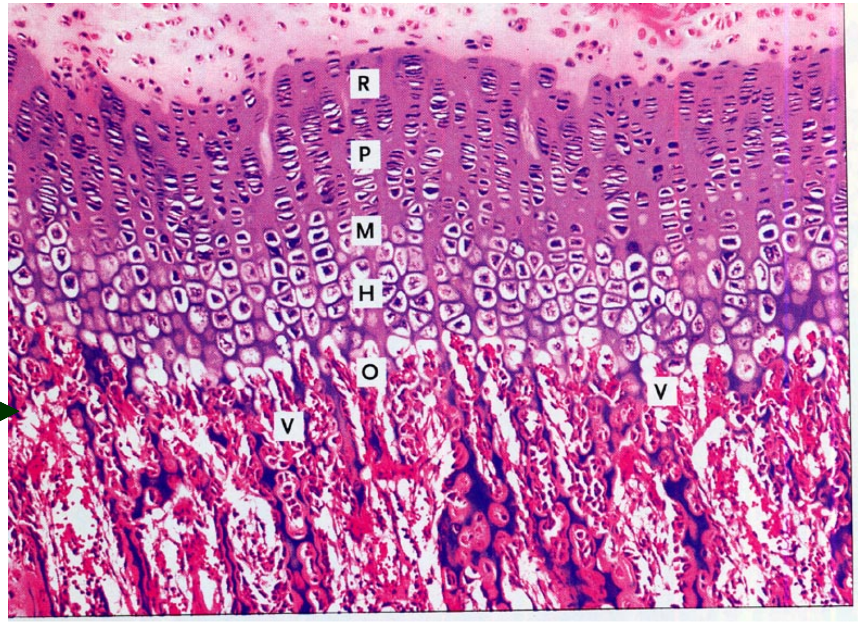
Cartilagine metafisaria

Cartilagine metafisaria (o di coniugazione o seriata: i gruppi isogeni di condrociti formano file di cellule parallele)

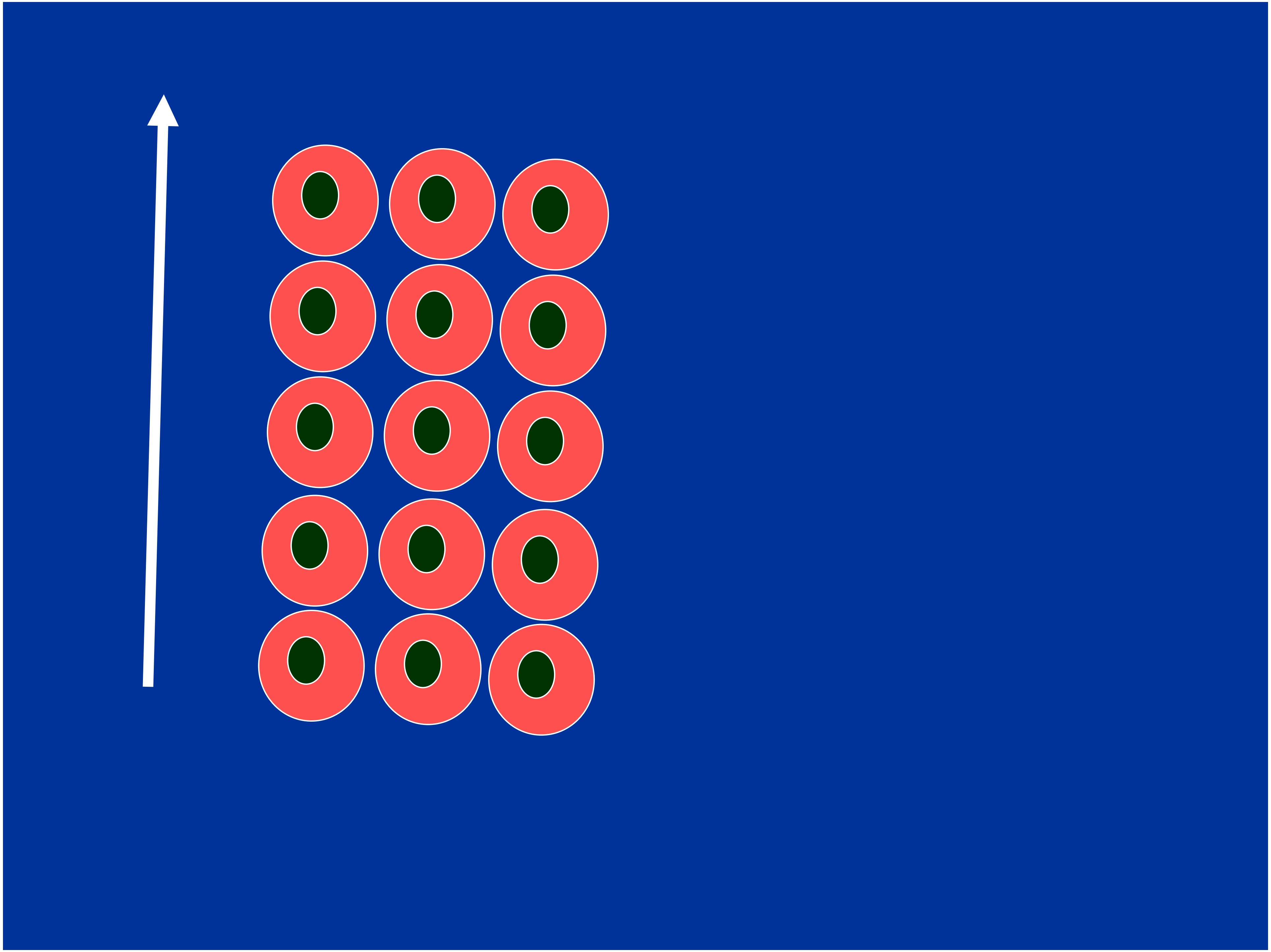


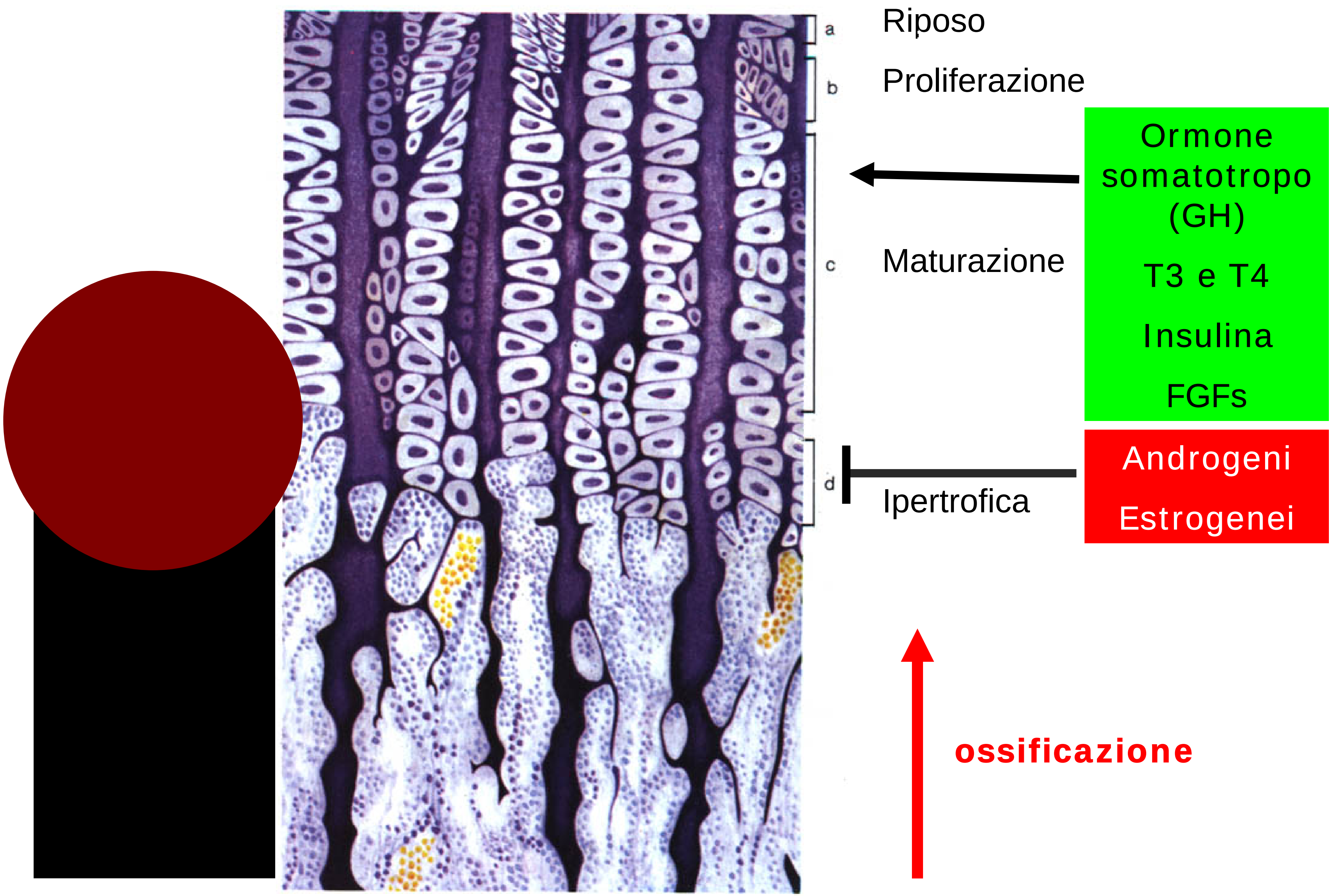
Colorazione con Alcian blu

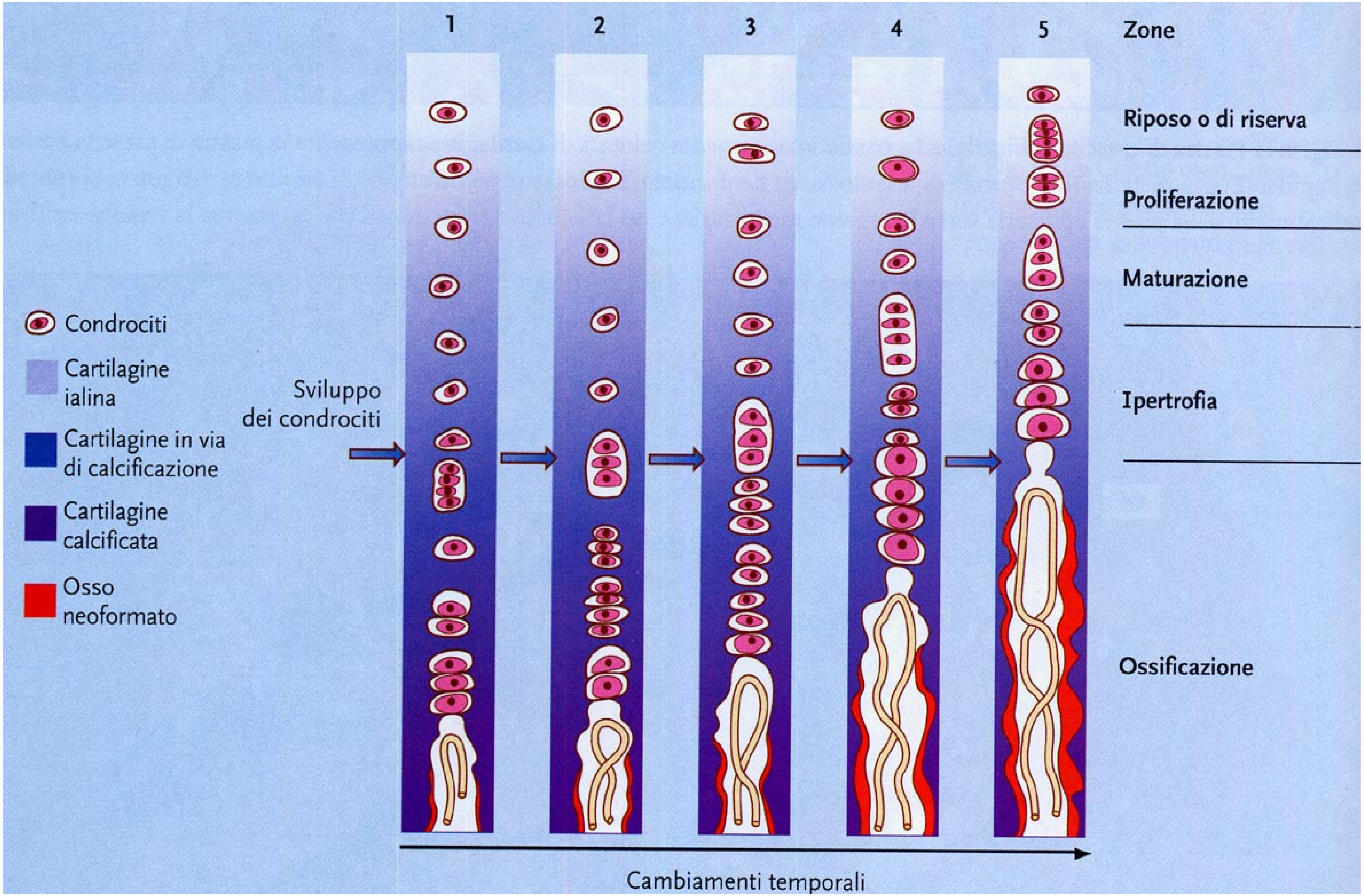
PE= piastra epifisaria o cartilagine metafisaria



V= vasi, O= ossificazione, H= c. ipertrofica, M= c. in maturazione, P= c. in proliferazione, R= c. a riposo




a
b
c
d
Riposo
Proliferazione
Maturazione
Ipertrofica
Ormone somatotropo (GH)
T3 e T4
Insulina
FGFs
Androgeni
Estrogenei
ossificazione

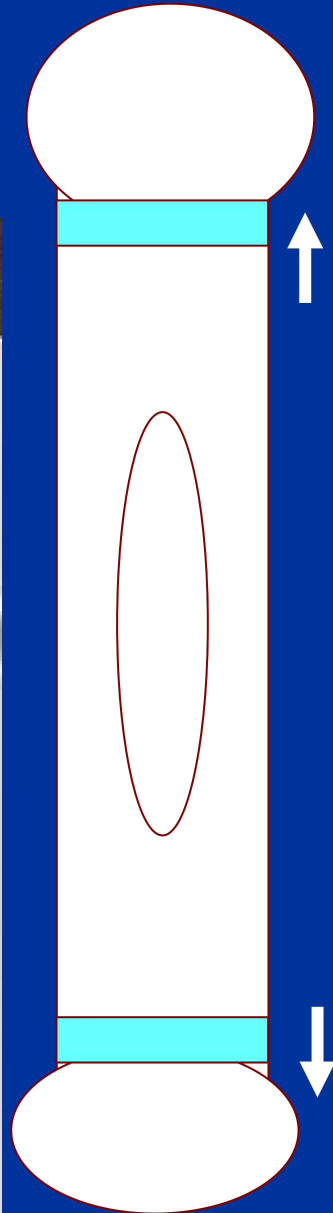


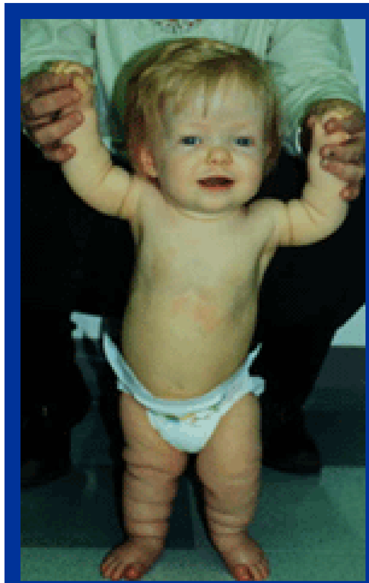
Modificazioni di un gruppo isogeno della cartilagine metafisaria nel corso dell'ossificazione

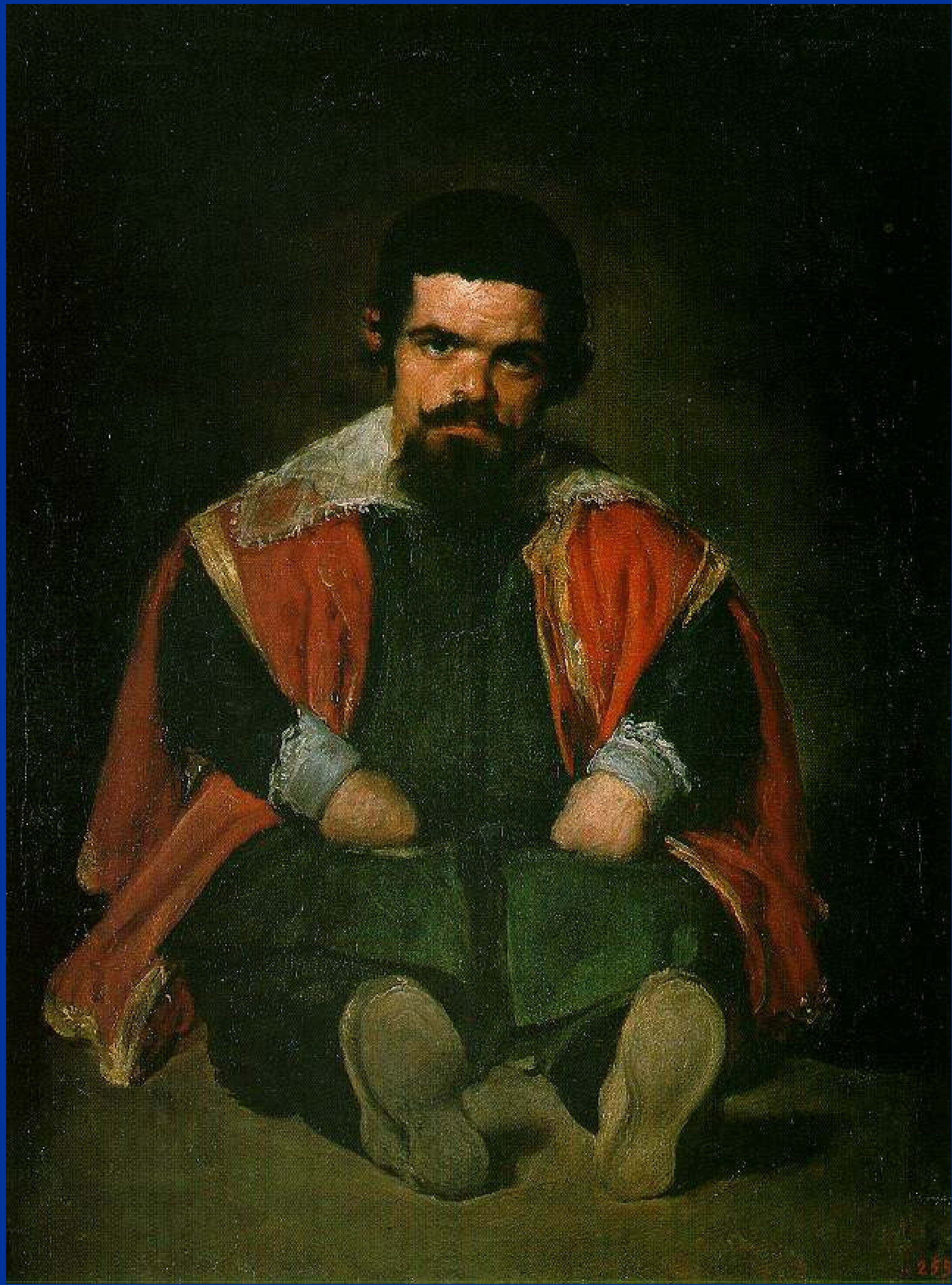
Cartilagine metafisaria
(o di coniugazione o seriata):

è responsabile della crescita in lunghezza delle ossa lunghe dello scheletro assile

Nanismo ipofisario:
carenza di GH
(nanismo armonico)





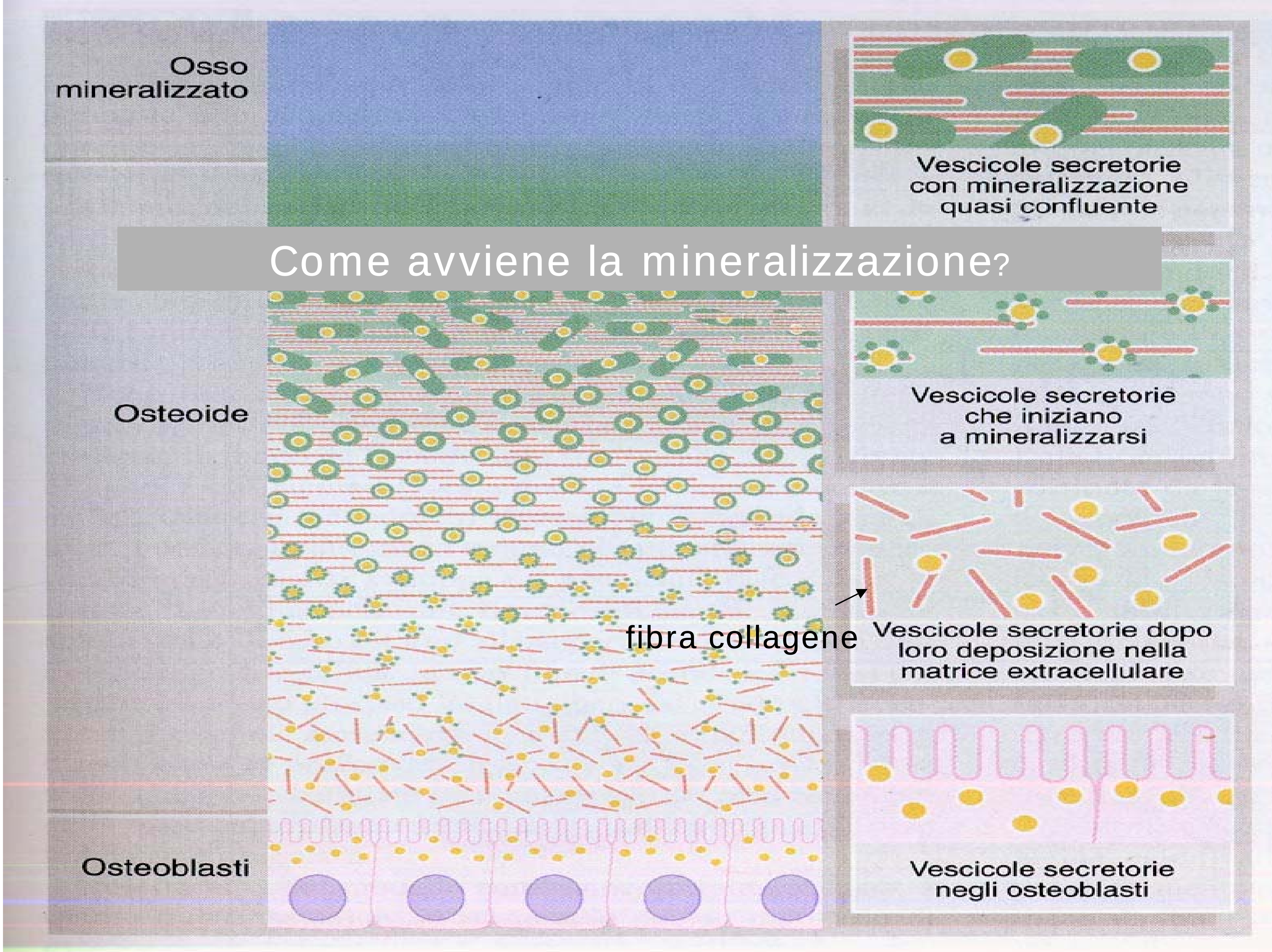


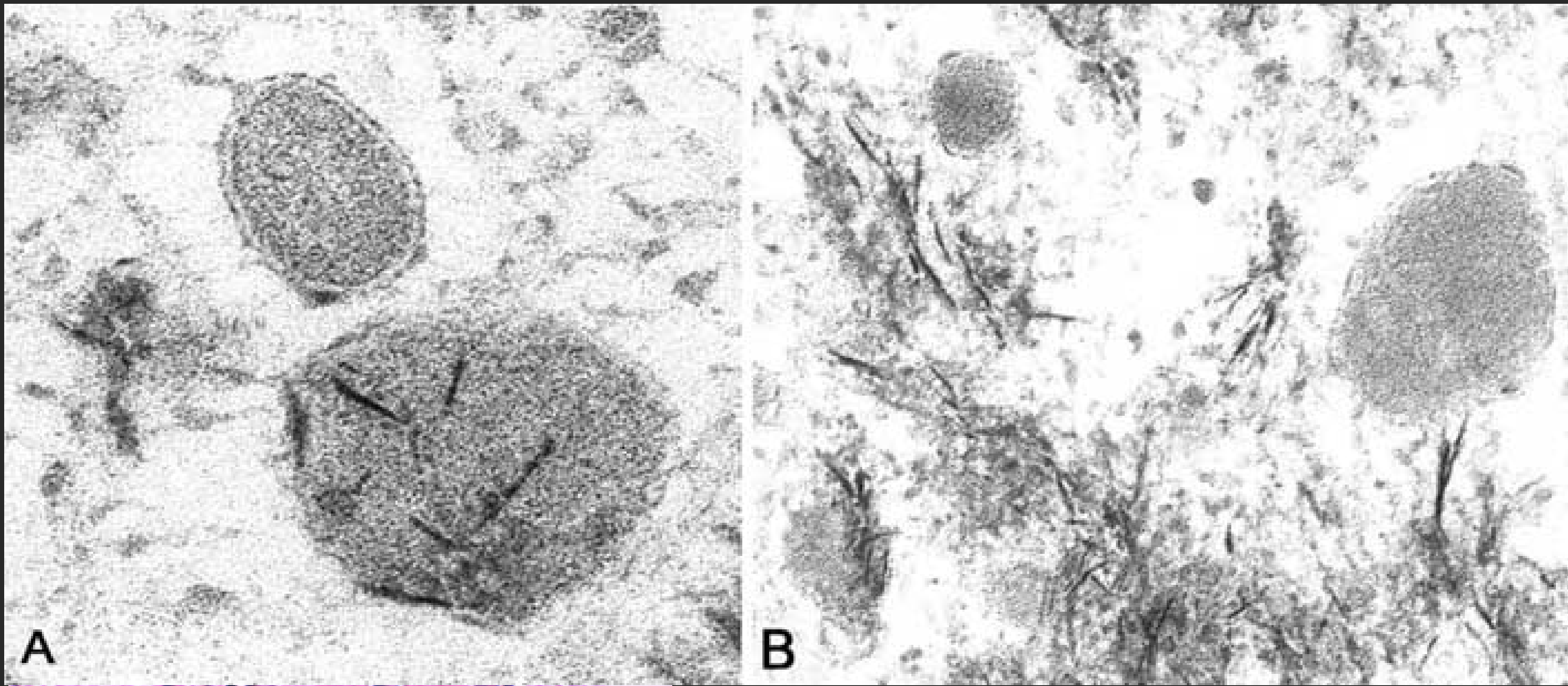
La corretta proliferazione dei condrociti è essenziale per l'ossificazione. La mutazione del gene per un recettore (FGFR3) per uno dei FGF, inibisce la proliferazione dei condrociti e provoca acondroplasia

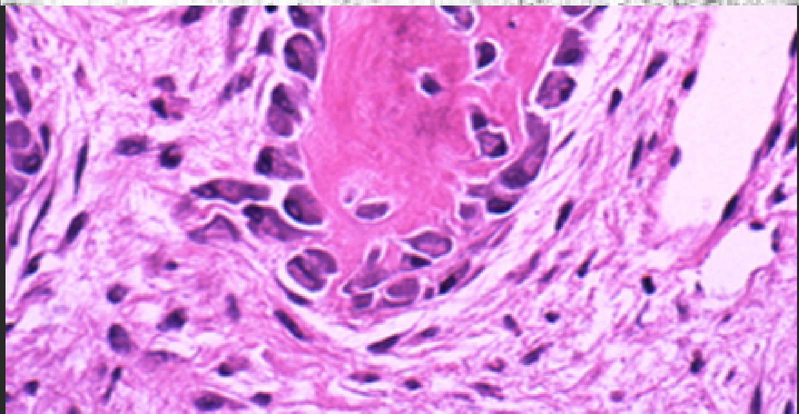
(nanismo disarmonico)

Velazques, Sebastian de Morra

Come avviene la mineralizzazione?



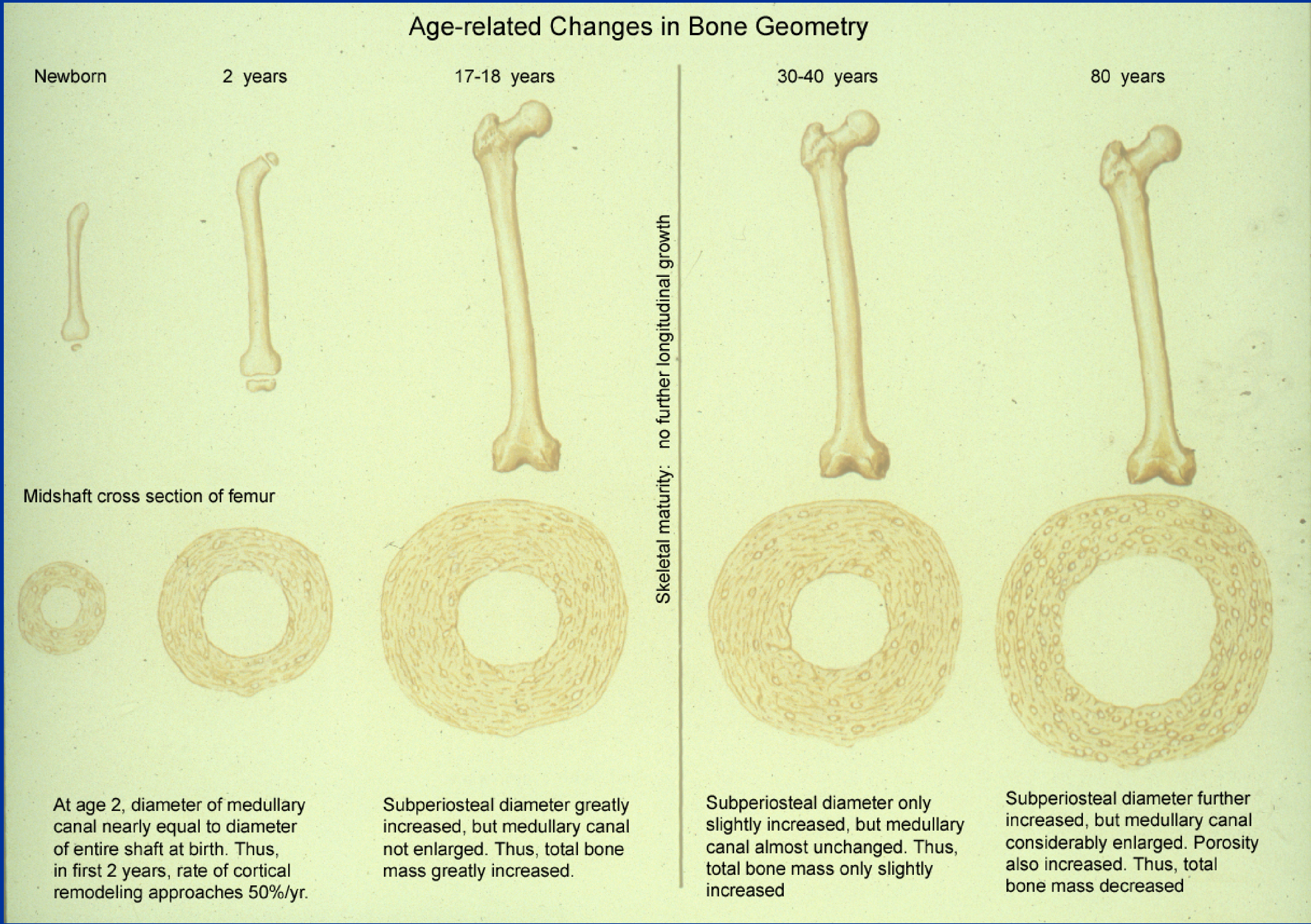


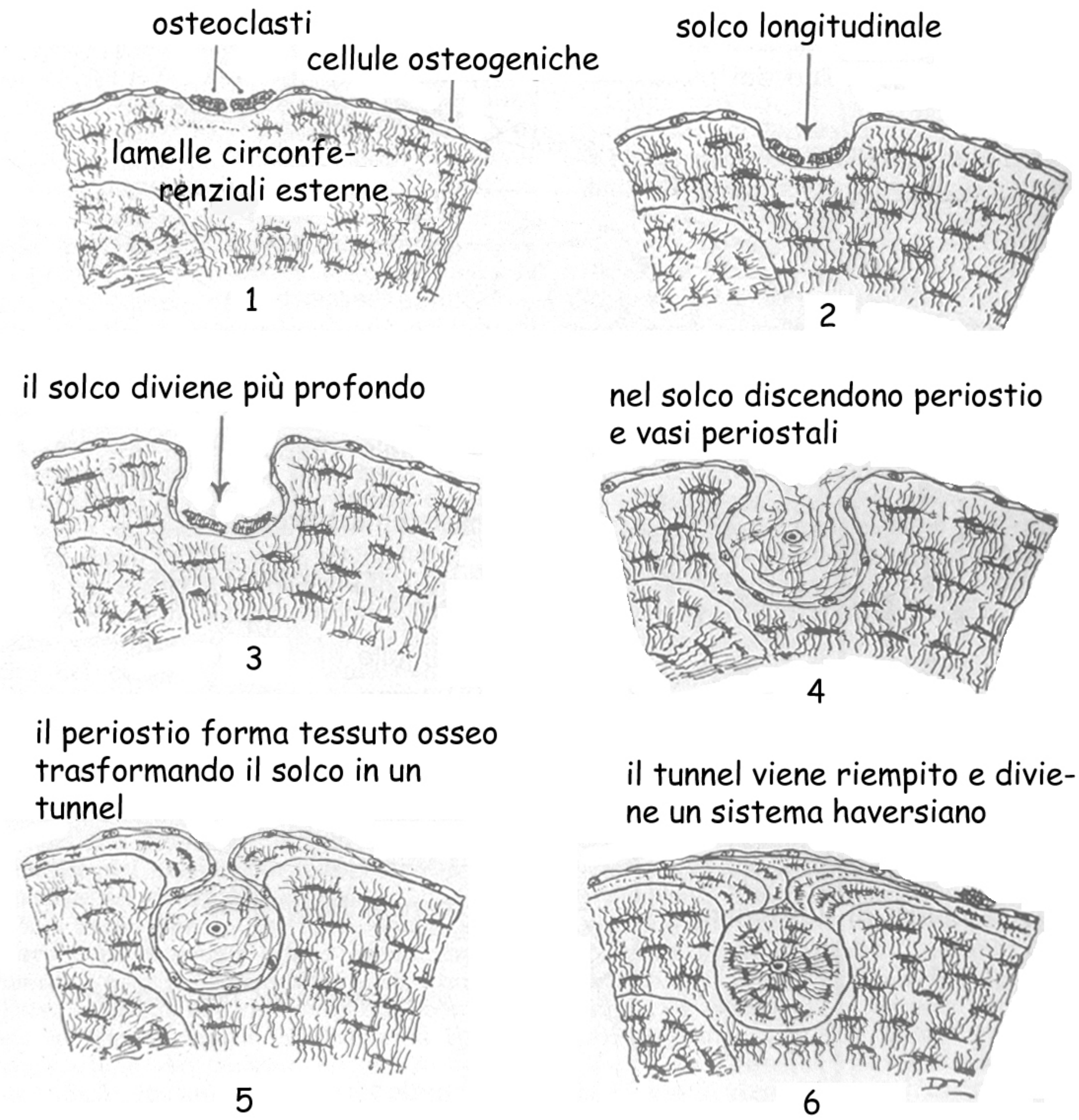


L’adesione alle fibre collagene delle vescicole mediata dalla annessina V e della fosfatasi alcalina favorisce l’internalizzazione di Ca^{2+} e Pi nelle vescicole

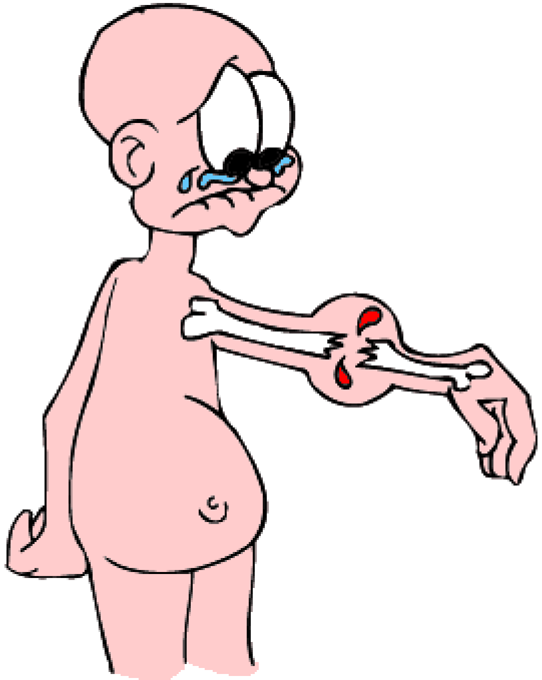
Phase I of the mineralization process takes place in 100 nm matrix vesicles released from adjacent osteoblasts. Ca^{2+} and Pi are internalized, forming non-crystalline, amorphous CaP. Amorphous CaP is then converted to octa-CaP crystals, and finally into insoluble hydroxyapatite crystals (phase I). During phase II of the mineralization process, phospholipases mediate penetration of the hydroxyapatite through the vesicle membrane. The levels of extra-vesicular Ca^{2+}, Pi, and H^{+}, as well as Ca^{2+}-binding proteins including BSP-1, osteocalcin, and osteopontin regulate the continued enucleation of crystals.

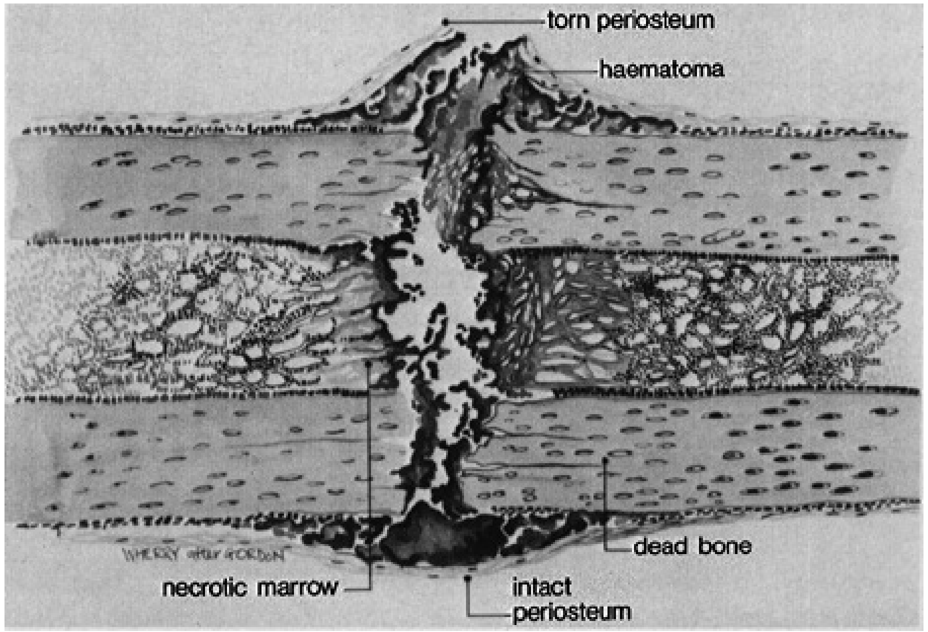
il rimodellamento delle ossa continua per tutta la vita

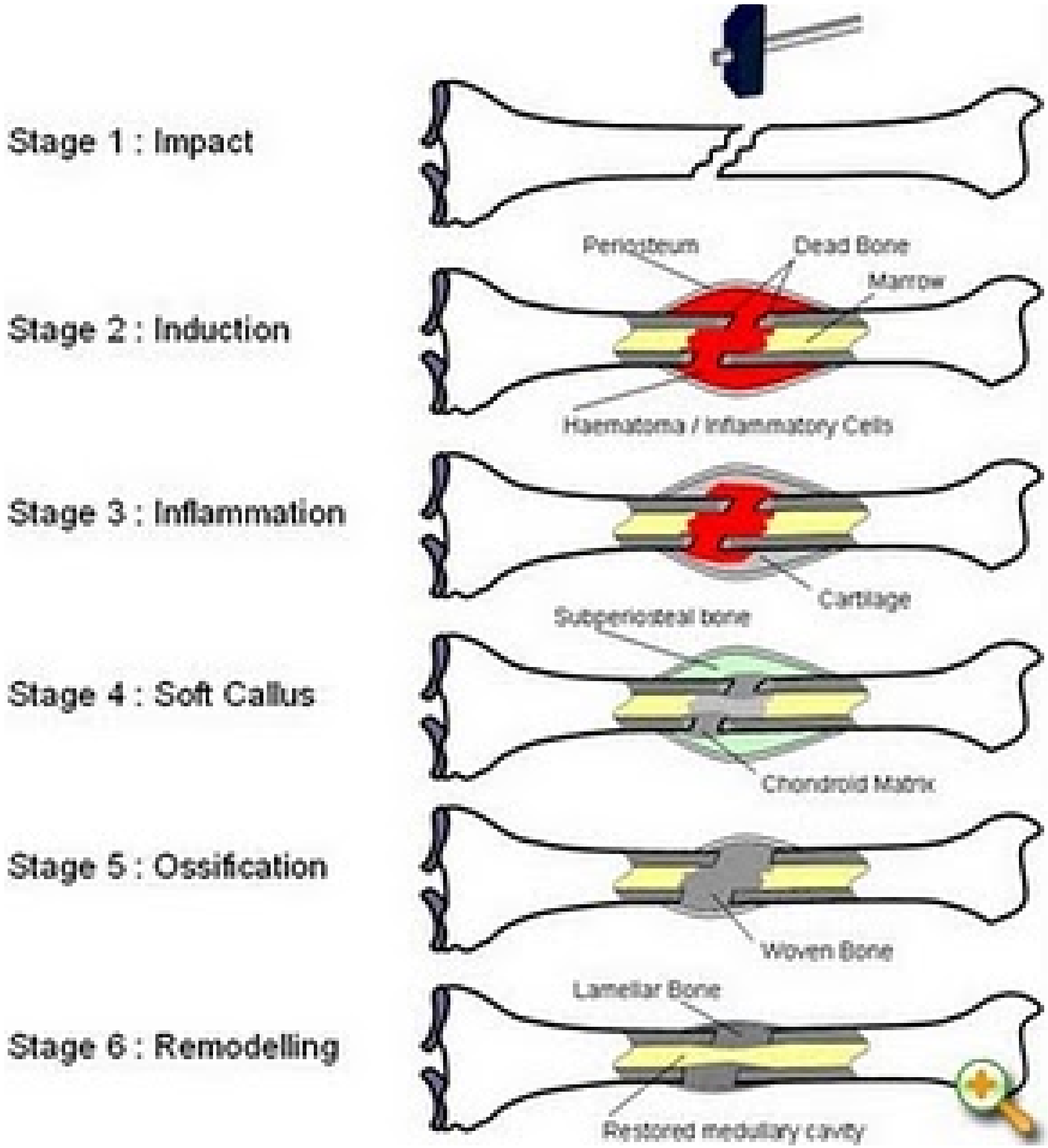



osteoclasti
cellule osteogeniche
lamelle circonfe-
renziali esterne
1
solco longitudinale
2
il solco diviene più profondo
3
nel solco discendono periostio
e vasi periostali
4
il periostio forma tessuto osseo
trasformando il solco in un
tunnel
5
il tunnel viene riempito e divie-
ne un sistema haversiano
6

Fratture ossee: come si riparano?



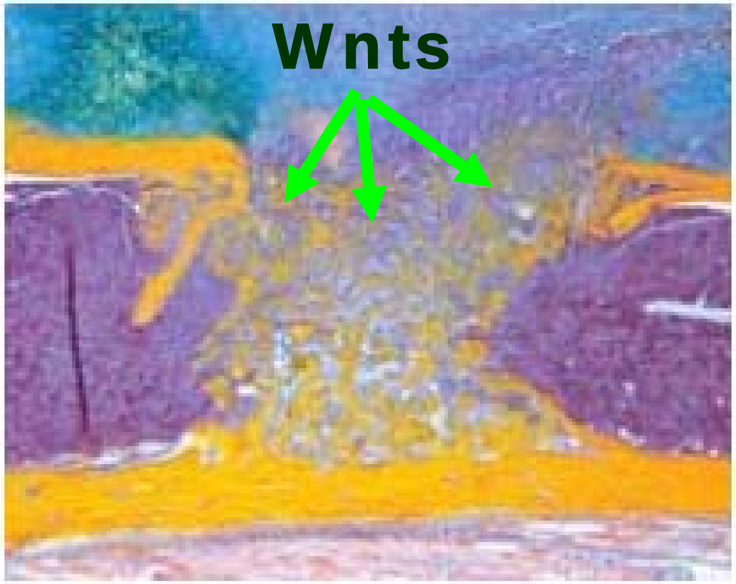



Stage 1 : Impact
Stage 2 : Induction
Periosteum
Dead Bone
Marrow
Haematoma / Inflammatory Cells
Stage 3 : Inflammation
Cartilage
Subperiosteal bone
Stage 4 : Soft Callus
Chondroid Matrix
Stage 5 : Ossification
Woven Bone
Lamellar Bone
Stage 6 : Remodelling
Restored medullary cavity

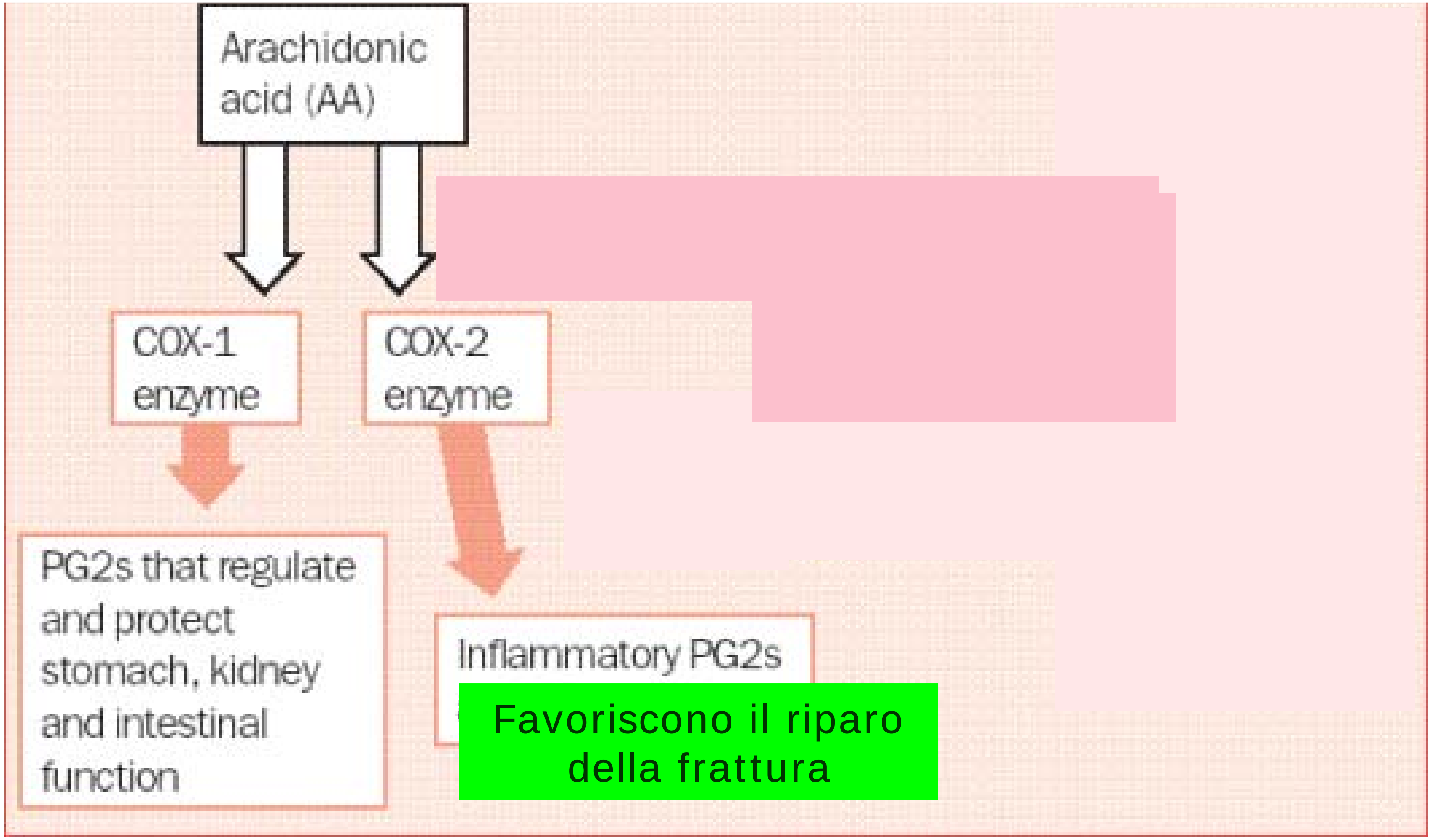
Researchers Speed Healing of Broken Bones

by Sarah Reed on 28 April 2010

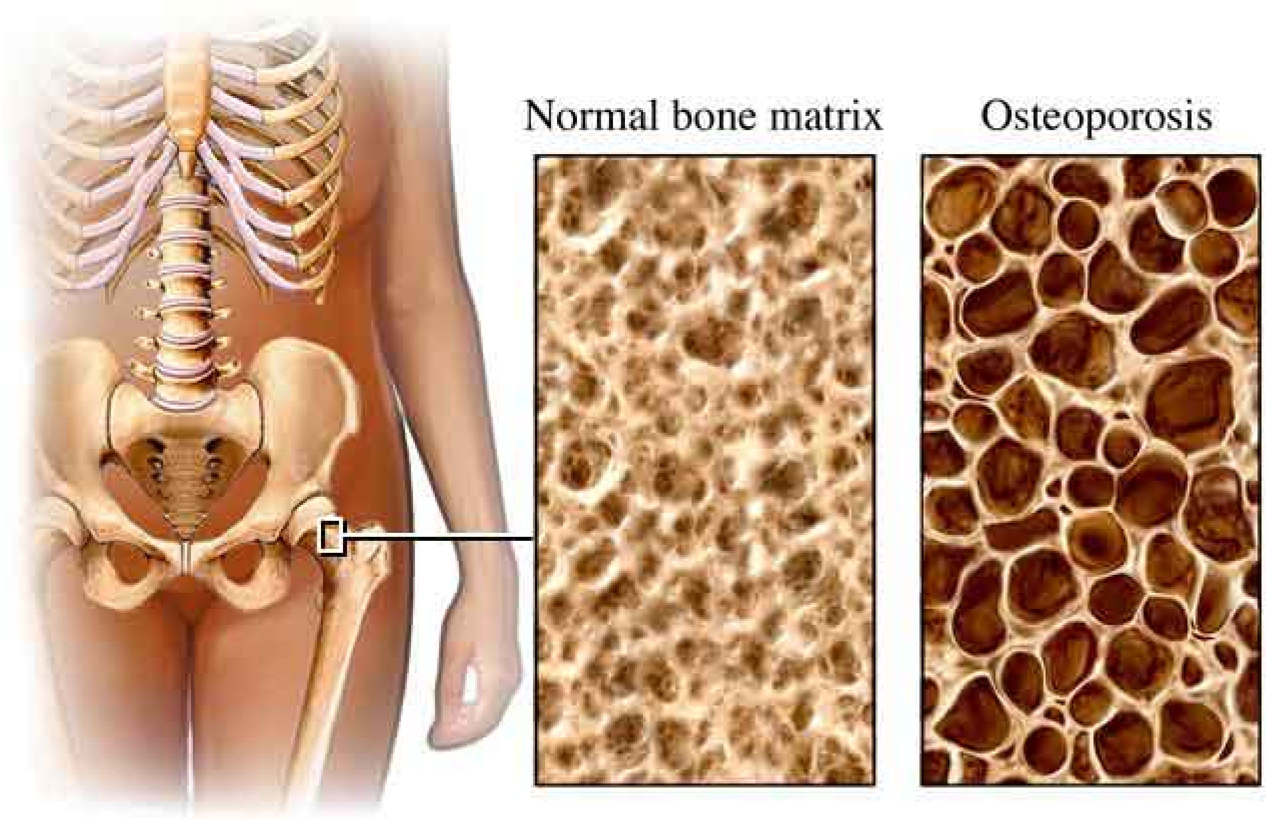
- In the new study, Helms and colleagues tested the packaged Wnts in mice. First, they drilled a 1-millimeter hole into the tibia (in humans, the bone between the knee and the ankle) of anesthetized mice to simulate a bone break. They then injected liposomes loaded with the Wnt protein Wnt3a into the injured area and compared the time that those fractures took to heal with the repair time for identical injuries in mice that received saline instead. The Wnt-treated mice had three-and-a-half times more bone in the injury site after 72 hours than the mice that received only saline, the team reports today in *Science Translational Medicine*. And after 28 days, the damaged bone in the Wnt-treated mice had completely mended, whereas mice treated with saline took another 2 weeks to heal.

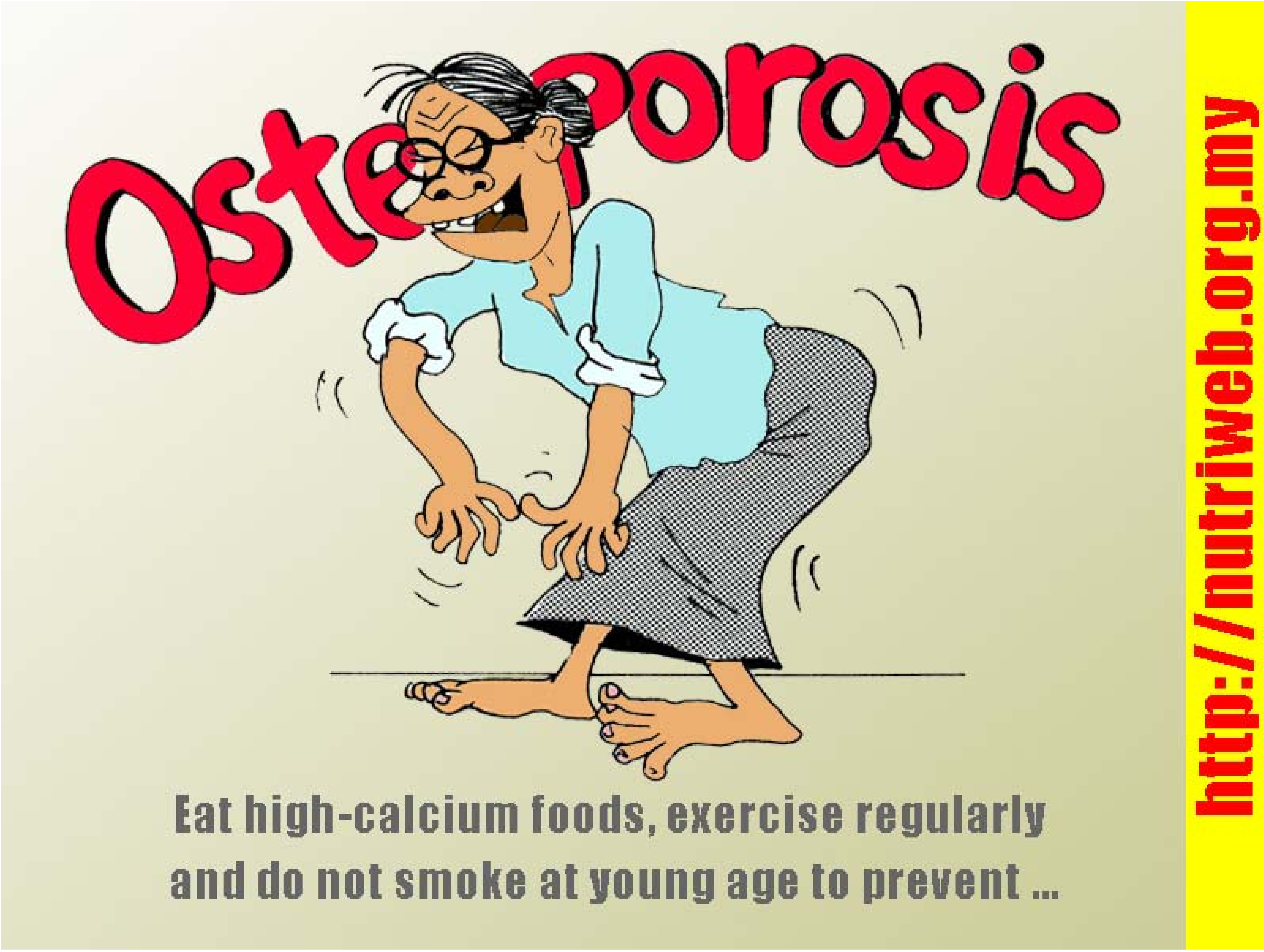


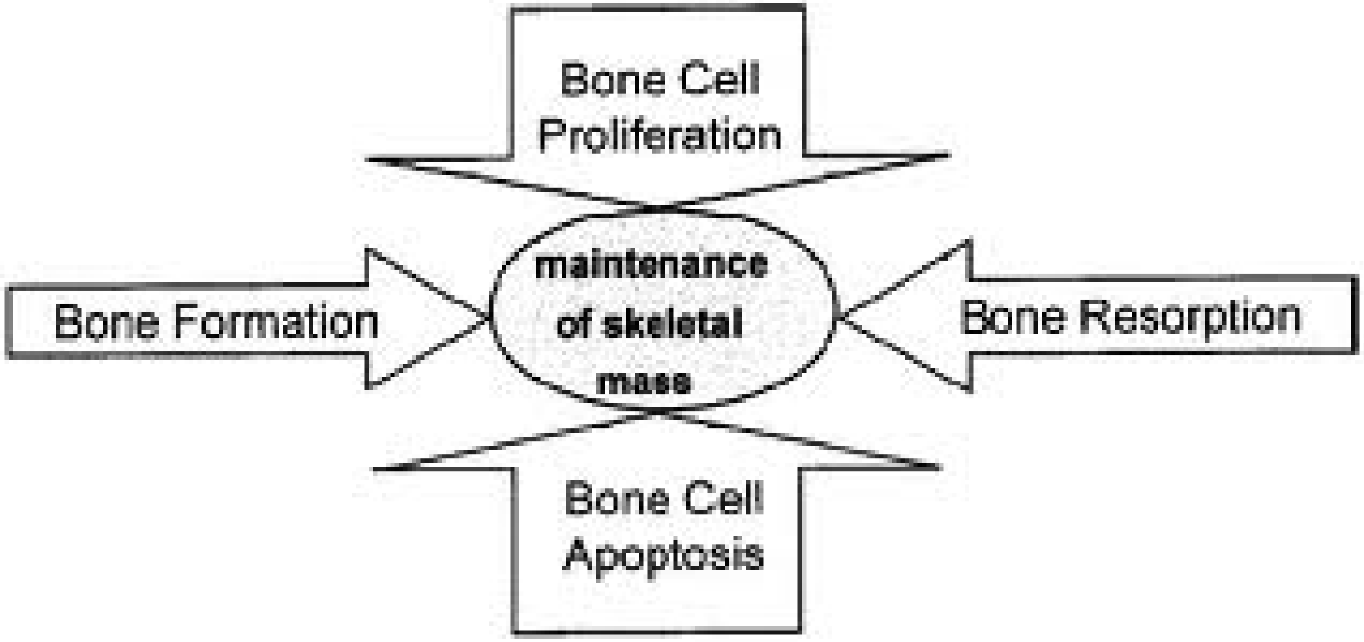
Regeneration. Yellow staining shows new bone tissue being generated at a mouse's fracture site following treatment with Wnt proteins.

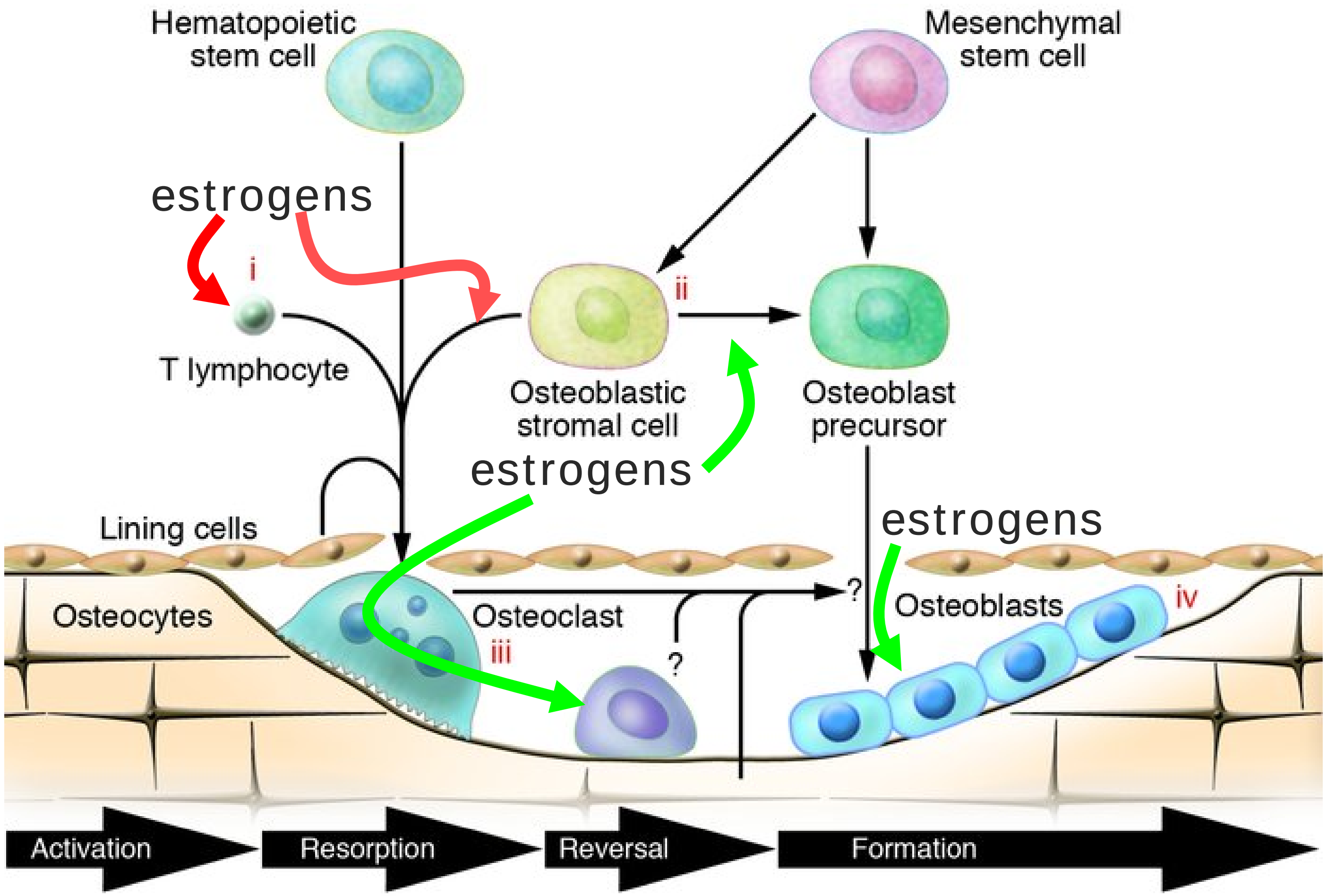

Arachidonic acid (AA)
COX-1 enzyme
COX-2 enzyme
PG2s that regulate and protect stomach, kidney and intestinal function
Inflammatory PG2s
Favoriscono il riparo della frattura

Osteoporosi



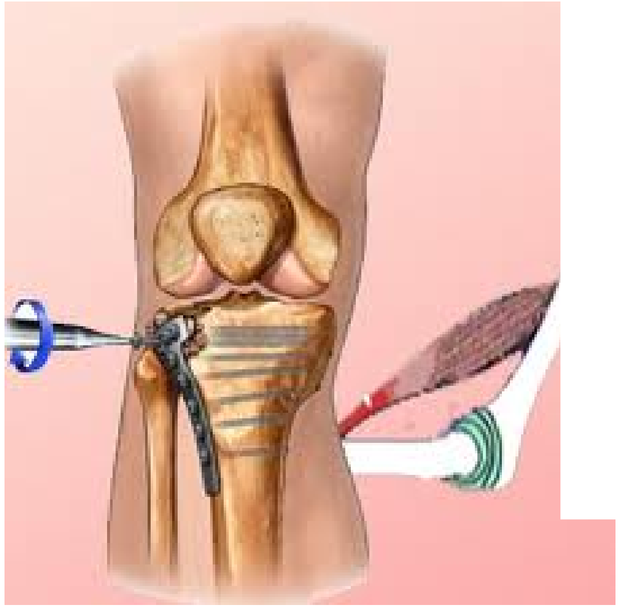

Oste porosis
Eat high-calcium foods, exercise regularly
and do not smoke at young age to prevent ...
http://nutriweb.org.my

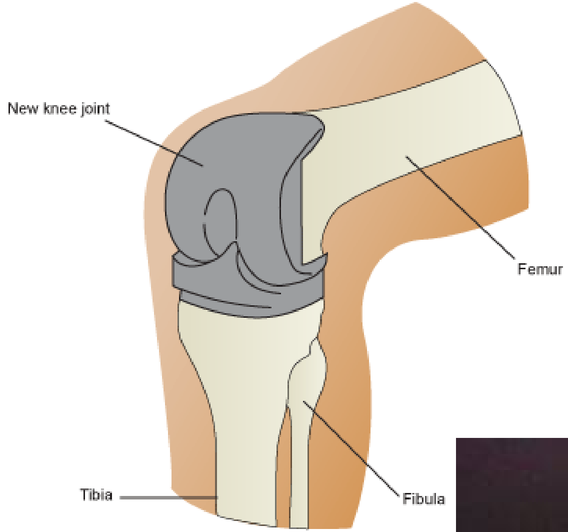

Bone Cell
Proliferation
Bone Formation
maintenance
of skeletal
mass
Bone Resorption
Bone Cell
Apoptosis

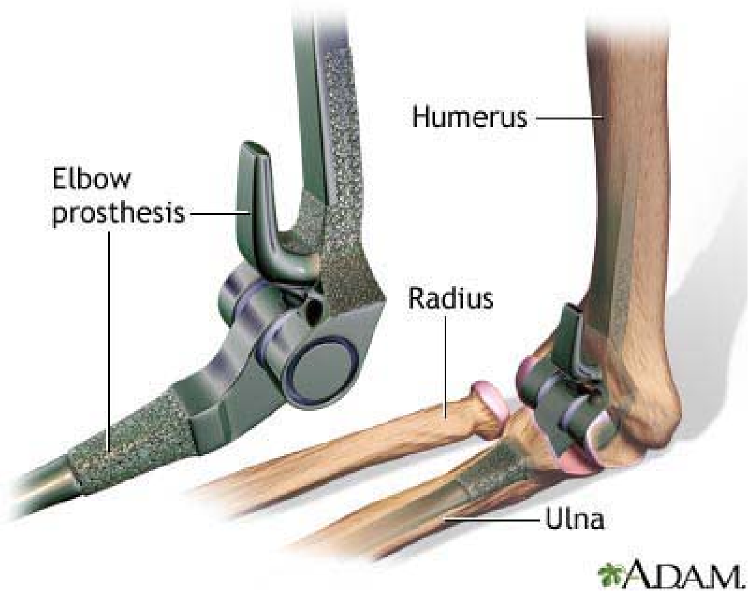


Bone remodeling on the surface of trabecular bone is illustrated here. Osteoclast activation is ordinarily initiated by an interaction of hematopoietic precursors with cells of the osteoblast lineage but may also be initiated by inflammatory cells, particularly T cells. Once osteoclasts are formed, there is a resorption phase. The formation phase is then initiated, possibly by factors produced by the osteoclast or released from the bone matrix. The formation phase, involves the production of matrix by progressive waves of osteoblasts. These then become flat lining cells, are embedded in the bone as osteocytes, or undergo apoptosis. Potential sites of action of estrogen include effects on T cell cytokine production (i); effects on stromal or osteoblastic cells to alter their production of RANKL or OPG (ii); direct inhibition of differentiated osteoclasts (iii); and effects on bone formation mediated by osteoblasts or osteocytes to enhance the response to mechanical forces initiated by these cells (iv).

Protesi ossee





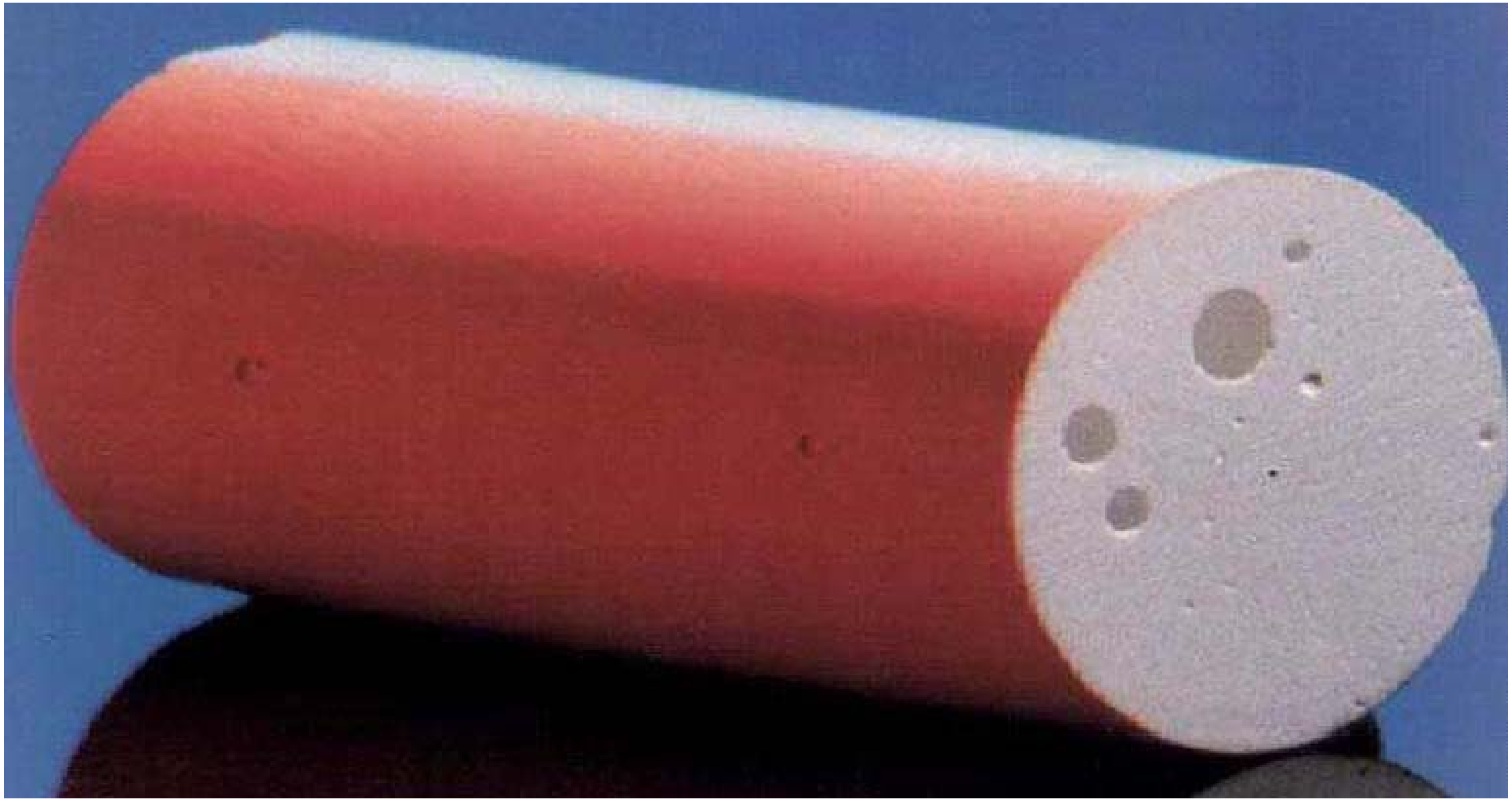


Ossa artificiali

There has been much research towards creating artificial bone. Research at the Lawrence Berkeley National Laboratory has resulted in a metal-ceramic composite that has, like bone, a fine microstructure, and which may help create artificial bone. A team of British scientists have developed "injectable bone", a soft substance which hardens in the body. They won the Medical Futures Innovation Award for their discovery, and it is planned to test this material in clinical trials.

Researchers at Columbia University have grown an anatomically correct human jawbone from stem cells, though it was solid bone without the normal accessory tissues such as bone marrow, cartilage, or a connectable blood supply. Other researchers, at the Istec bioceramics laboratory in Italy, have produced a nearly-identical substitute for human bone out of rattan wood. The substitute bone has a porous structure permitting blood vessels and other accessory tissues to penetrate it, allowing seamless integration into the host bone. The process has been tested on sheep, who showed no signs of rejection after several months

Pictured here is a hydroxyapatite-polyphosphazene composite which has been invesitgated as a possible artificial bone replacement material.



- 2008. Researchers at the Fraunhofer Institute for Manufacturing Engineering and Applied Materials
- Research developed a simulation program that calculates the internal structure and density distribution of the bone material.
- Engineers can produce complex components with the aid of rapid prototyping technology. This involves coating a surface with wafer-thin layers of special metal powder made of biomaterials such as titanium and steel alloys. A laser beam heats – or sinters – the powdered metal in the exact places that need to be firm.

Una mandibola artificiale fatta di titanio e polvere di metalli ottenute con raggi laser

Jaw bone created from stem cells

- **20090. Scientists have created part of the jaw joint in the lab using human adult stem cells.**
- The latest study used human stem cells taken from bone marrow.
- These were seeded into a tissue scaffold, formed into the precise shape of the human jaw bone by using digital images from a patient. The cells were then cultured using a specially-designed bioreactor which was able to infuse the growing tissue with exactly the level of nutrients found during natural bone development.

Turning wood into bones

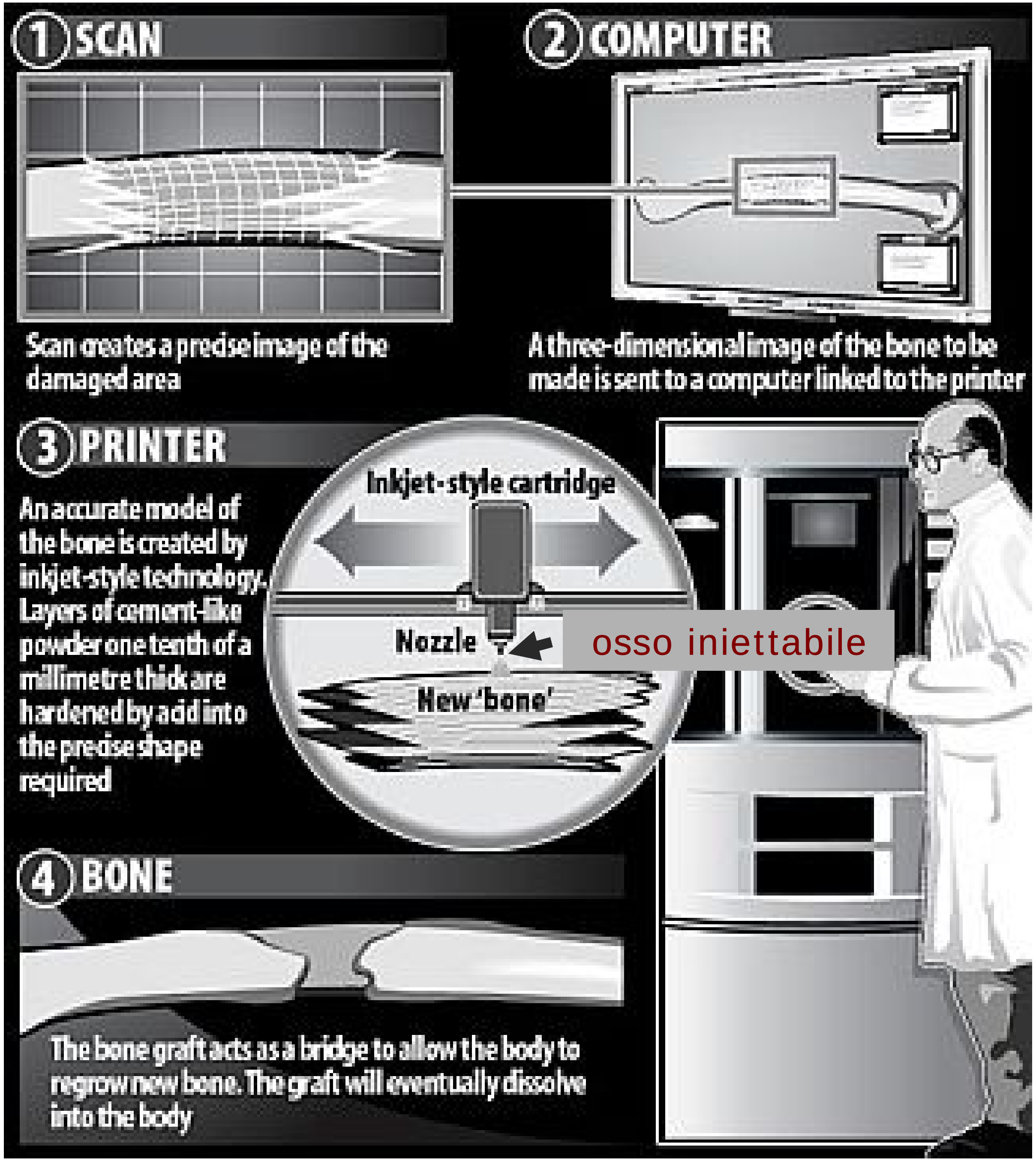
- **A novel - and natural - way of creating new bones for humans could be just a fewyears away.**
- Scientists in Italy have developed a way of turning rattan wood intobone that is almost identical to the human tissue.At the Istec laboratory of bioceramics in Faenza nearBologna, a herd of sheep have already been implanted with the bones.
- The process starts by cutting the long tubular rattan wood up into manageable pieces. It is then snipped into even smaller chunks, ready for the complex chemical process to begin.The pieces are put in a furnace and heated. In simple terms, carbon and calcium are added.The wood is then further heated under intense pressure in another oven-like machine and a phosphate solution is introduced.

2009: Injectable artificial bone developed

SYDNEY: Artificial 'injectable bone' that flows like toothpaste, and hardens in the body, has been invented by British scientists.
This new regenerative medicine technology provides a scaffold for the formation of blood vessels and bone tissue, and can also deliver stem cells directly to the site of bone repair.
"Injectable bone is the first delivery system for stem cells and growth factors that forms a material with the strength of a bone," said Robin Quirk, a pharmacist and co-founder of RegenTec – the University of Nottingham, In England, spin-off company commercialising the technology.

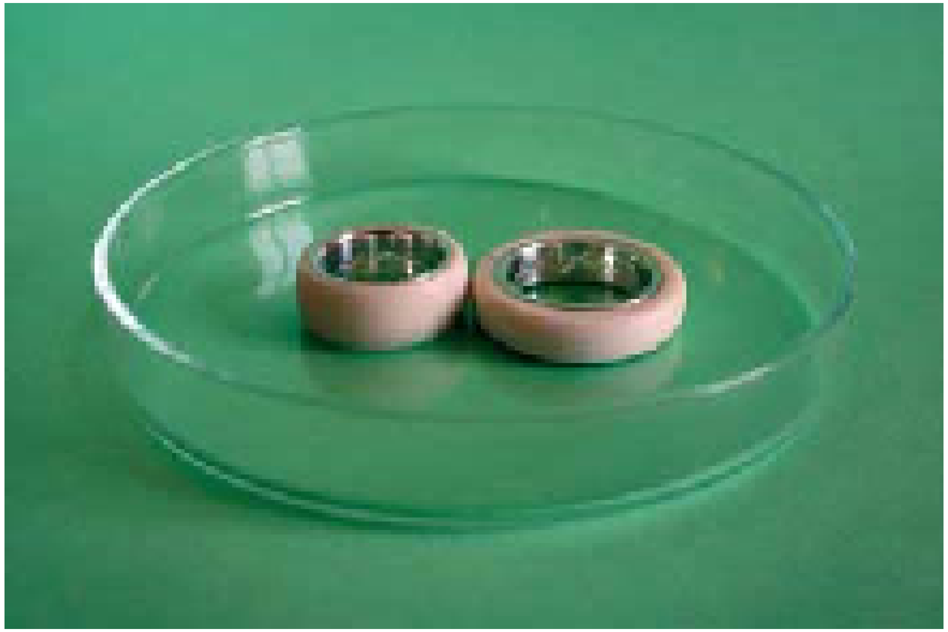
No more surgery

Quirk said he hopes that injectable bone might one day reduce or eliminate the need for bone-grafts to repair skeletal defects and fractures – which often require painful invasive surgery.
Not only does the technique reduce the need for dangerous surgery, it also avoids damaging neighbouring areas, said Kevin Shakesheff, a tissue engineer and drug delivery pharmacist at Nottingham who masterminded the breakthrough.
The technology's superiority over existing alternatives is the novel hardening process and strength of the bond, said Quirk. Older products heat-up as they harden, killing surrounding cells, whereas 'injectable bone' hardens at body temperature – without generating heat – making a very porous, biodegradable structure.
"Because the material does not heat-up, surrounding bone cells can survive and grow," added Shakesheff.


1 SCAN
Scan creates a precise image of the damaged area
2 COMPUTER
A three-dimensional image of the bone to be made is sent to a computer linked to the printer
3 PRINTER
An accurate model of the bone is created by inkjet-style technology. Layers of cement-like powder one tenth of a millimetre thick are hardened by acid into the precise shape required
Inkjet-style cartridge
Nozzle
osso iniettabile
New 'bone'
4 BONE
The bone graft acts as a bridge to allow the body to regrow new bone. The graft will eventually dissolve into the body

WHAT IF...Human tissue could be used to make objects?

Tobie Kerridge/Nikki Stott/Ian Thompson



Bone tissue cultivated outside a patient's body will soon be used in reconstructive surgery. As the bioscience behind this application develops, the promise of the technology provokes curiosity and speculation about alternative uses. Biojewellery explores such an alternative, providing couples with a symbol of their love.

Biomedical engineers, designers and clinicians set out to create unique biojewellery rings for couples. Bone tissue was cultured in a hospital laboratory, using cells from chips of bone donated by the couples during wisdom tooth extractions. The bone was combined with silver to create the rings.

Biojewellery hopes to raise questions about the relationship between individual ambitions and scientific research. The exhibit at Science Gallery comprises an archive relating to this project, funded by the Engineering and Physical Sciences Council (UK).

Twitter Hashtag #jewelSG

http://www.biojewellery.com