



PAGET'S DISEASE OF BONE

NHUAN VIET NGO, MD

2018

ON A FORM
OF
CHRONIC INFLAMMATION OF BONES
(OSTEITIS DEFORMANS).

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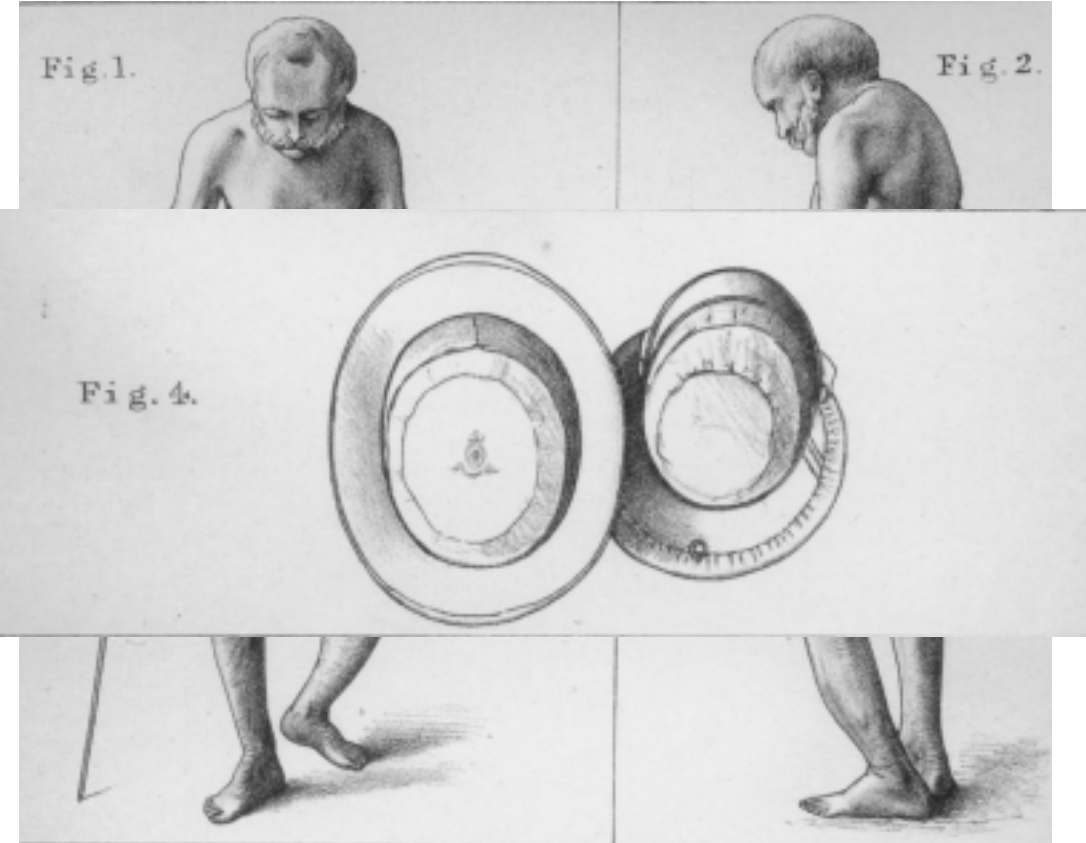


Clinical Description of Paget's original case report

At forty-six, from no assigned cause, unless it were that he lived in a rather cold and damp place in the North of England, he began to be subject to aching pains

Three years later I saw the patient with Mr. Stanley. He was in the same good general health, but the left tibia had become larger, and had a well-marked anterior curve, as if lengthened while its ends were held in place by their attachments to the unchanged fibula. The left femur also was now distinctly enlarged, and felt tuberos at the junction of its upper and middle thirds, and was

The skull became gradually larger, so that nearly every year, for many years, his hat, and the helmet that he wore as a member of a Yeomanry Corps needed to be enlarged. In 1844 he wore a shako measuring twenty-two and a half inches inside; in 1876 his hat measured twenty-seven and a quarter inches inside (Pl. I, fig 4).



Post – Mortem Examination of Paget's original case

- Gross examination

The bones examined after death show the consequences of an inflammation affecting, in the skull the whole thickness, in the long bones chiefly the compact structure, of their walls, and not only the walls of their shafts but, in a very characteristic manner, those of their articular surfaces.



- Microscopic examination

careful observation not uncommonly discovers that the sides of the widened canals, instead of being smooth and even (Plate III, fig. 10), are eaten out in a series of curves or concavities with the production of what are called Howship's lacunæ, so characteristic of inflammation.

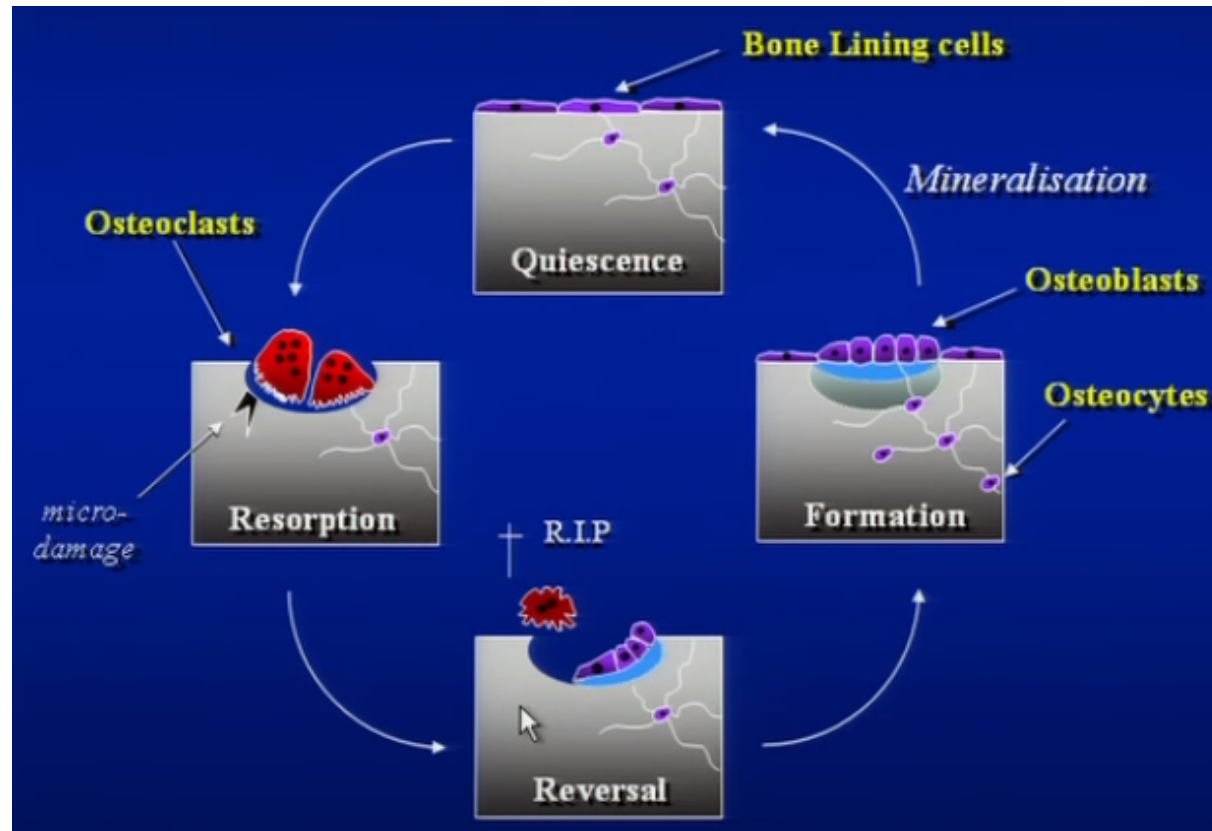


Definition

Paget's disease /paj'əts/: a metabolic disease of bone of unknown cause, usually affecting middle-aged and elderly people and characterized by excessive bone destruction and unorganized bone repair.

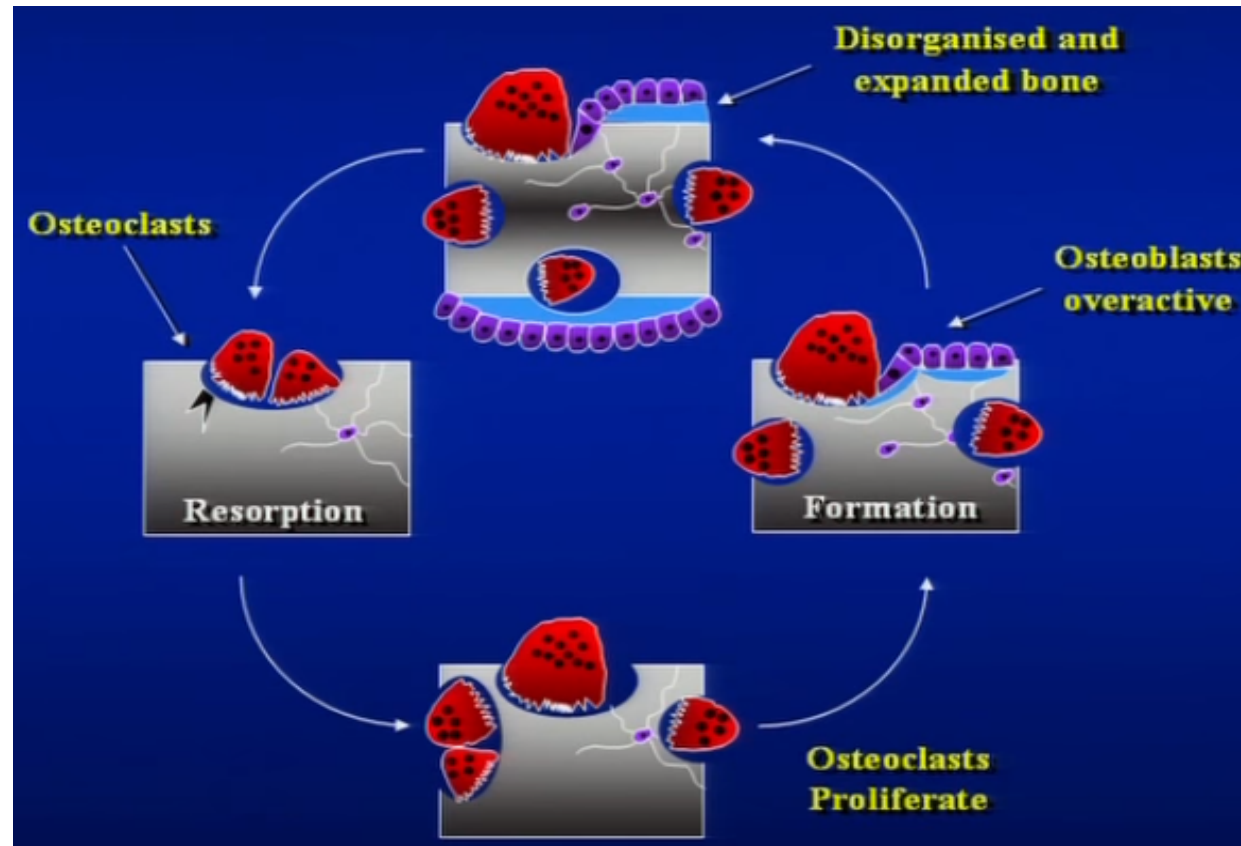


Pathophysiology



Normal Bone Remodeling Cycle

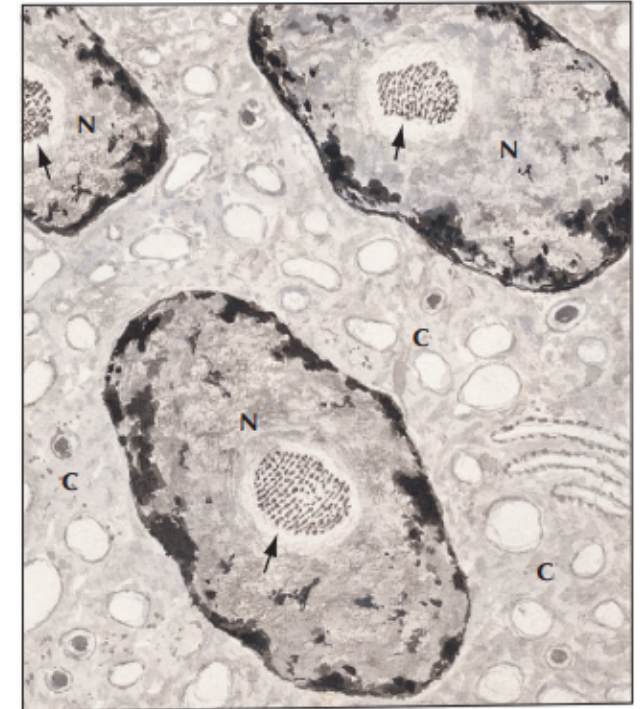
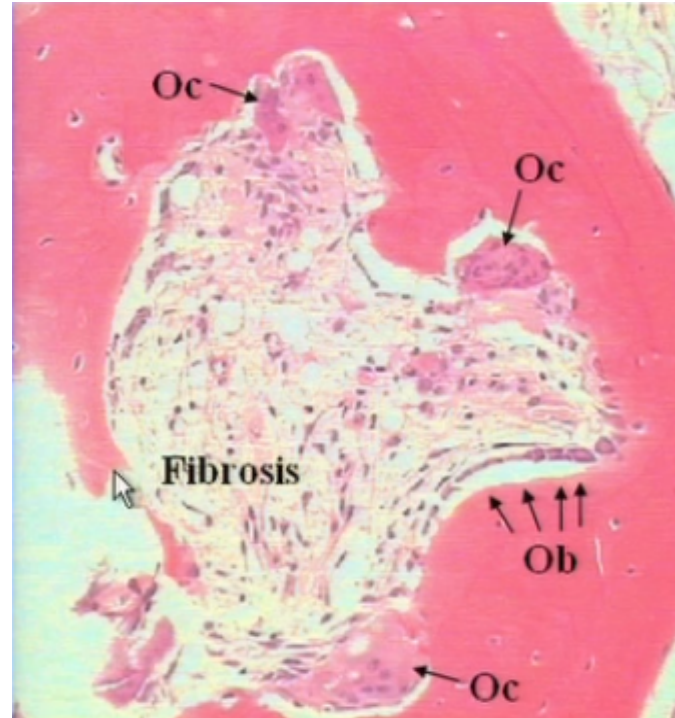
Pathophysiology



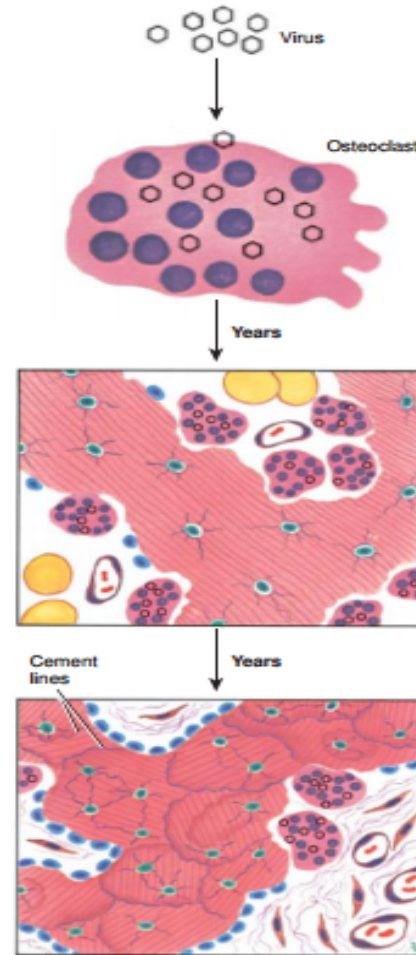
Bone Remodeling Cycle in Paget Disease

Pathogenesis

- **Osteoclast phenotype**
 - Number
 - Intranuclear inclusion bodies
- **Osteoclast physiology**
 - Hypersensitive to Vit D
 - Antiresorptive agents



Pathogenesis - Viral



Pathogenesis - Viral

Failure to Detect Paramyxovirus Sequences in Paget's Disease of Bone Using the Polymerase Chain Reaction

STUART H. RALSTON,¹ FRANCESCO S. DIGIOVINE,¹ STEPHEN J. GALLACHER,²
IAIN T. BOYLE,² and GORDON W. DUFF¹

**No evidence of MV
in Paget disease of bone**

Failure to Detect Measles Virus Ribonucleic Acid in Bone Cells from Patients with Paget's Disease

Brya G. Matthews, Muhammad A. Afzal, Philip D. Minor, Usha Bava, Karen E. Callon, Rocco P. Pitto, Tim Cundy, Jill Cornish, Ian R. Reid, and Dorit Naot

1. Ralston, S. H., Digiovine, F. S., Gallacher, S. J., Boyle, I. T., & Duff, G. W. (1991). Failure to detect paramyxovirus sequences in Paget's disease of bone using the polymerase chain reaction. *Journal of Bone and Mineral Research*, 6(11), 1243-1248.
2. Matthews, B. G., Afzal, M. A., Minor, P. D., Bava, U., Callon, K. E., Pitto, R. P., ... & Naot, D. (2008). Failure to detect measles virus ribonucleic acid in bone cells from patients with Paget's disease. *The Journal of Clinical Endocrinology & Metabolism*, 93(4), 1398-1401.

Pathogenesis - Genetic

Paget's Disease (Osteitis deformans) and Heredity

M. F. ASHLEY MONTAGU

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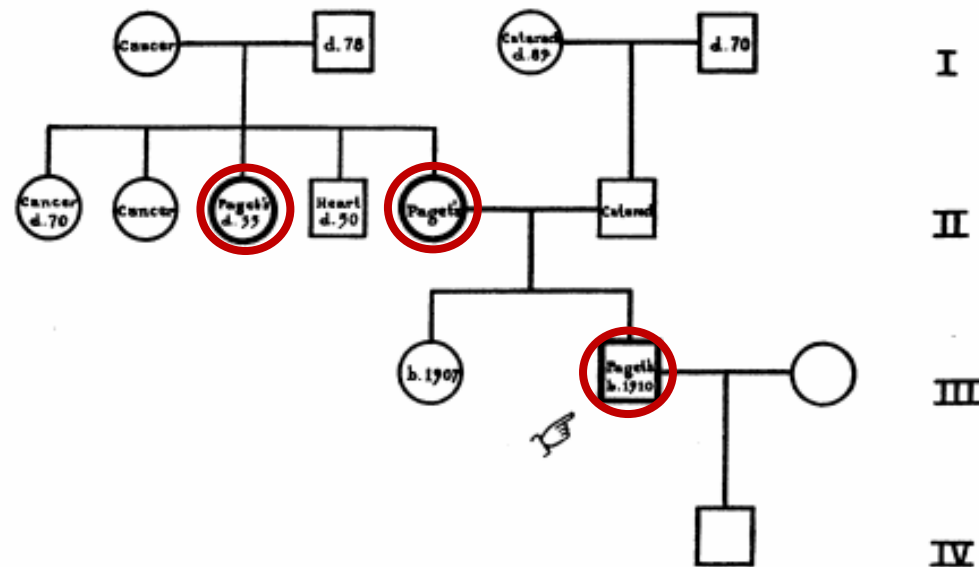
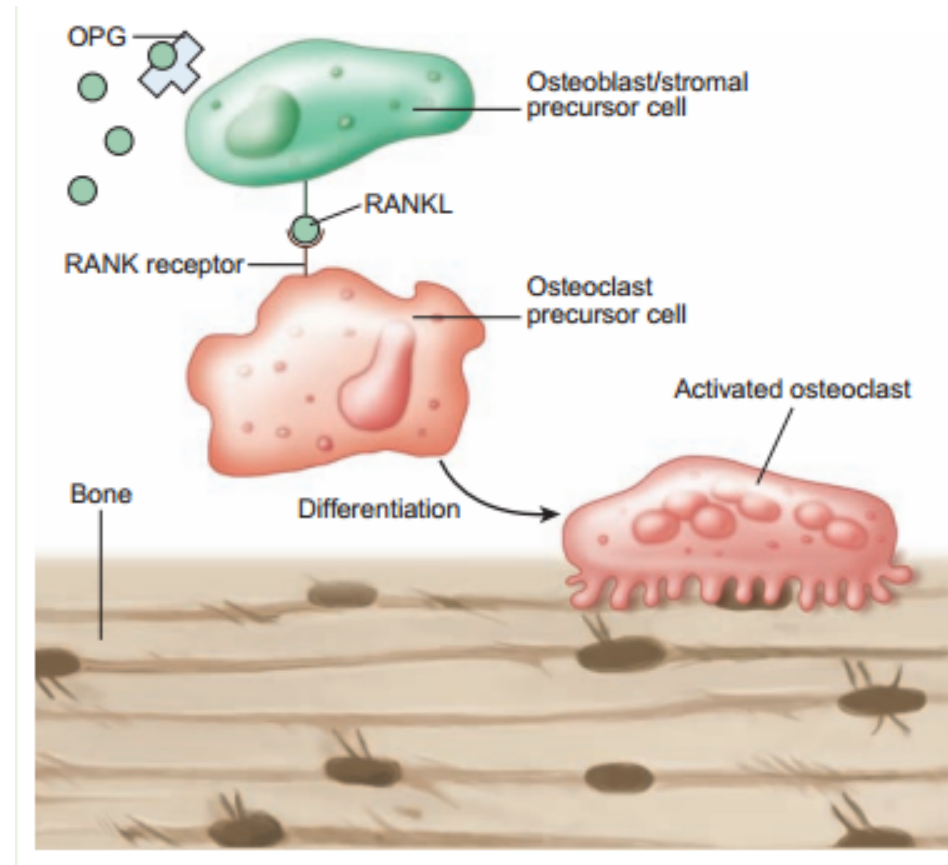


FIG. 1. Pedigree of Paget's Disease (Osteitis deformans).

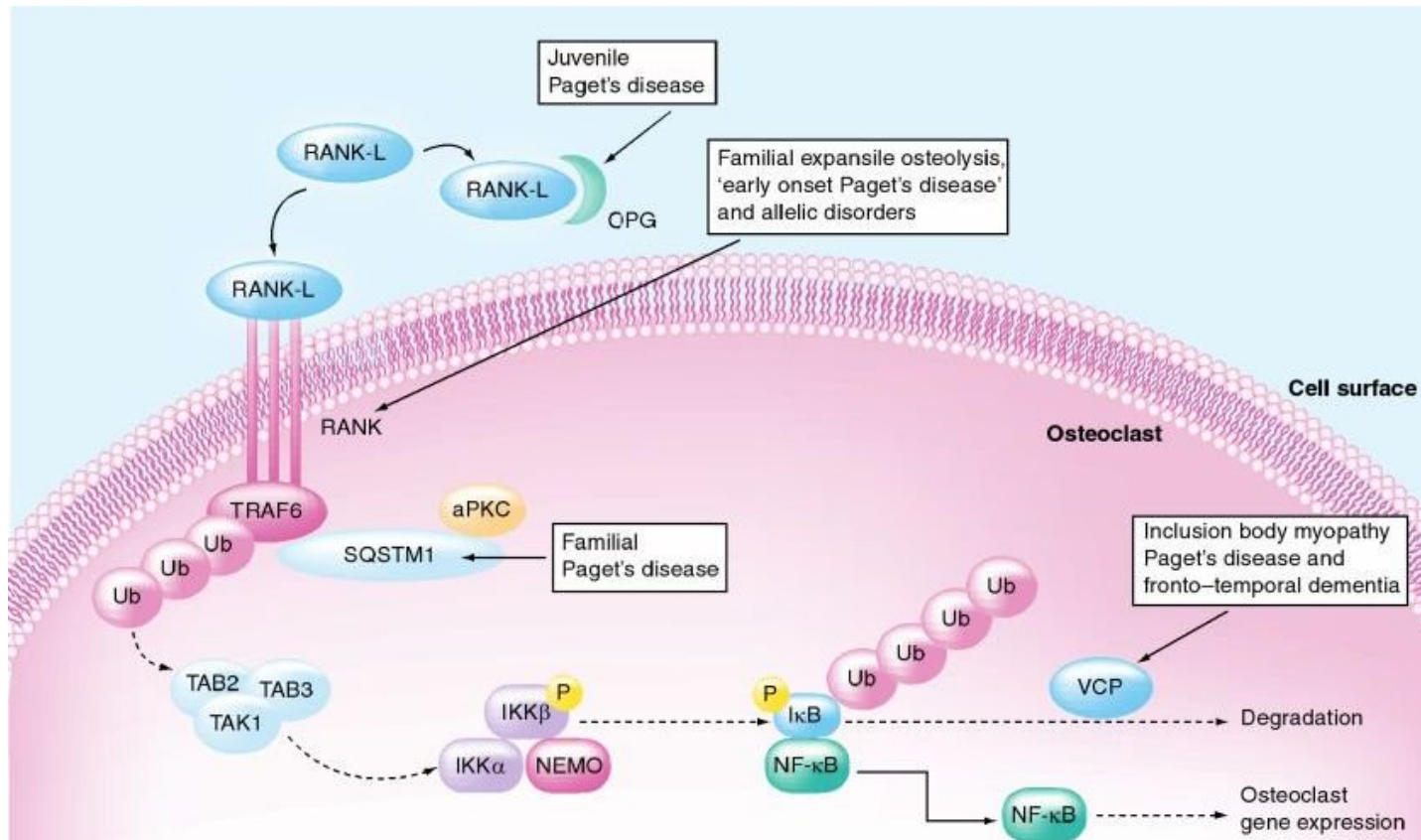
... the predisposition to Paget's disease, when inherited, is transmitted as an incompletely dominant gene carried on an X-chromosome.

Pathogenesis - Genetic



RANK-NF- κ B signaling pathway

Pathogenesis - Genetic



RANK-NF-κB signaling pathway

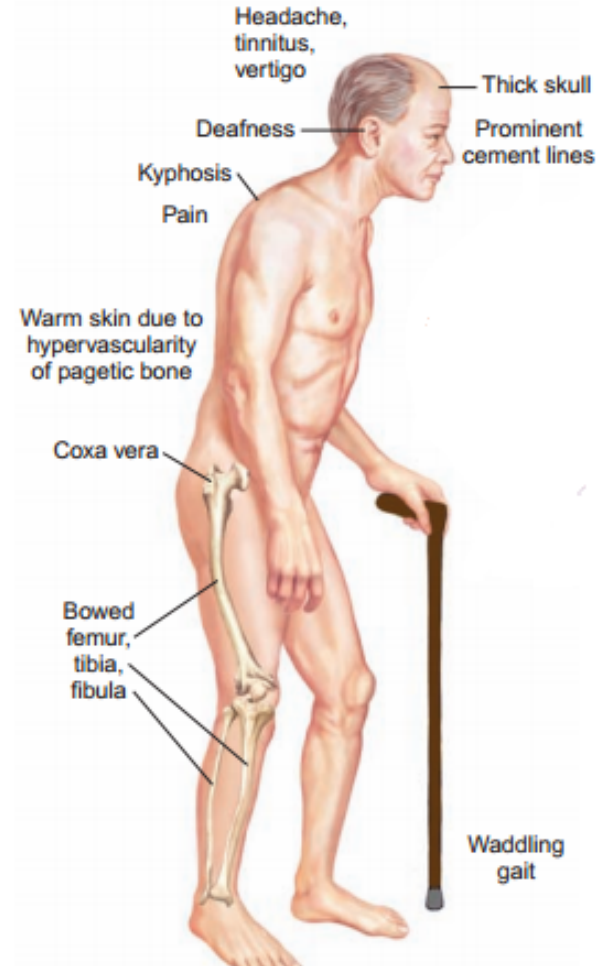
Clinical Manifestations

- Asymptomatic (+++)
 - Incidental findings
- Symptomatic
 - Pain: 50%
 - Pagetic bone
 - Altered biomechanics, nerve compression
 - Arthritis
 - Bone deformity
 - Fracture

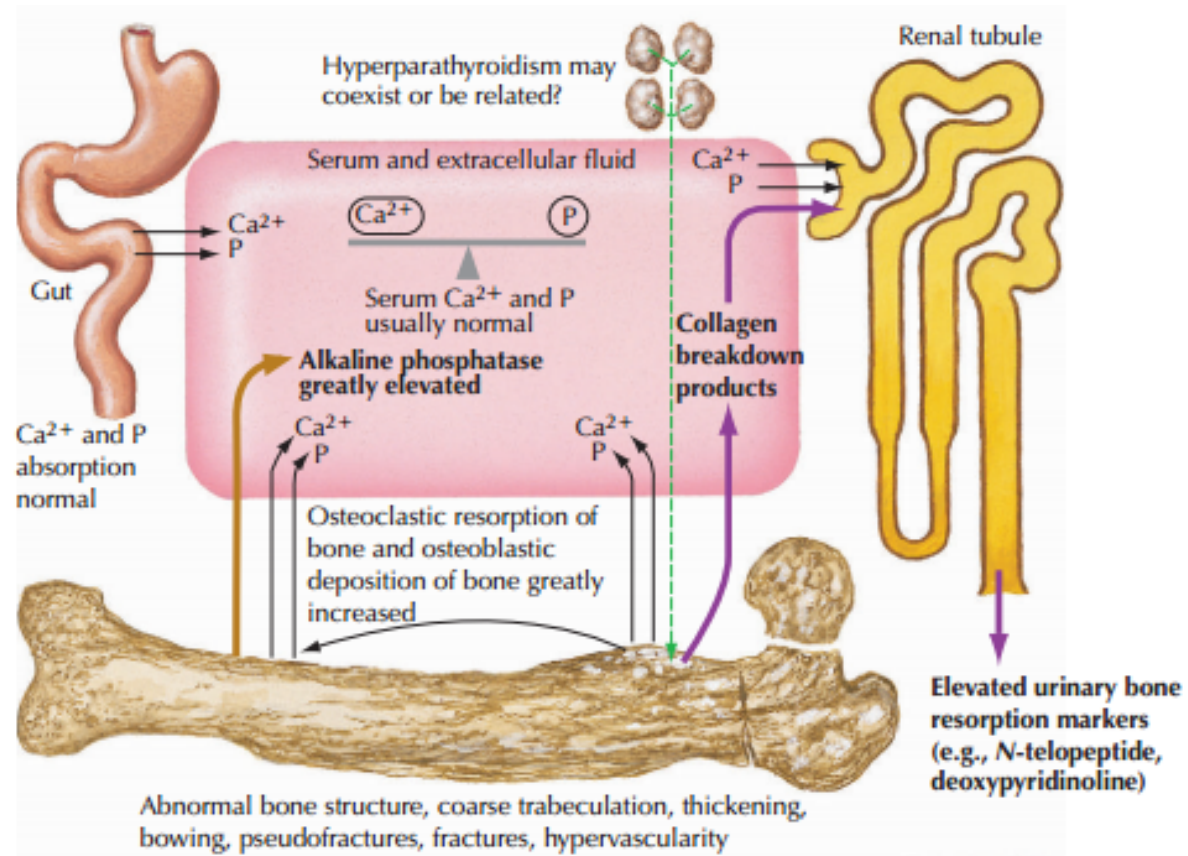


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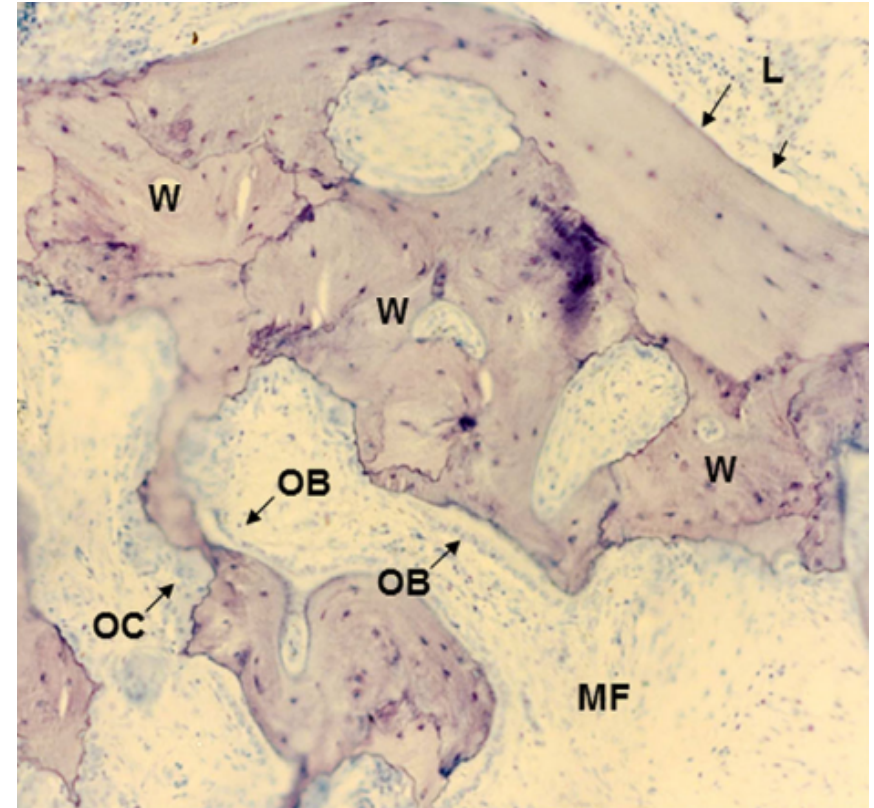


Laboratory Findings



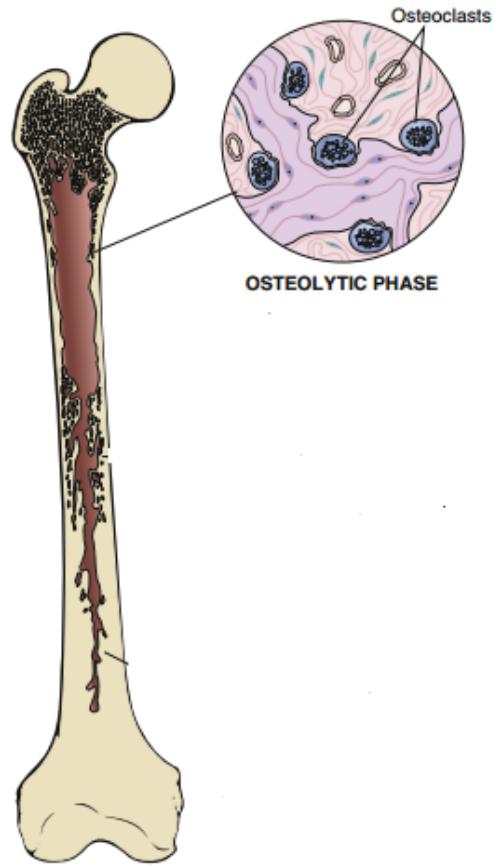
Pathology

- OC: multinucleated, excessive in number
- Disorganized
 - Lamellar bone -> interspersed with woven bone -> variably thickened trabeculae -> mosaic pattern
 - Woven bone -> increase bone volume
- Bone marrow: replaced by stromal tissue



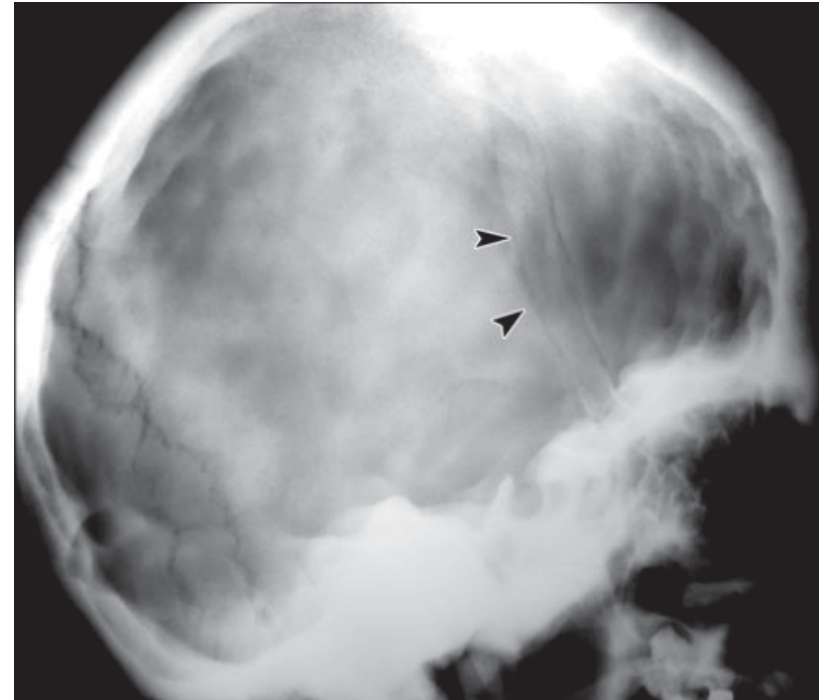
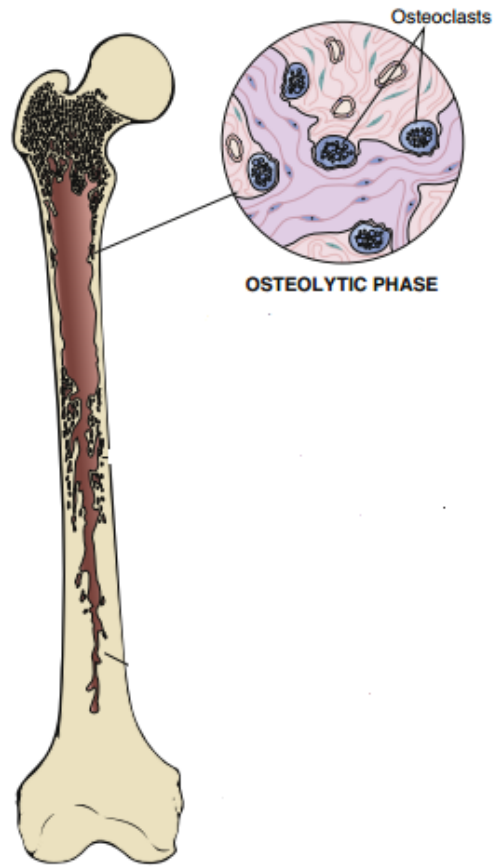
Photomicrograph of Pagetic bone

Imaging



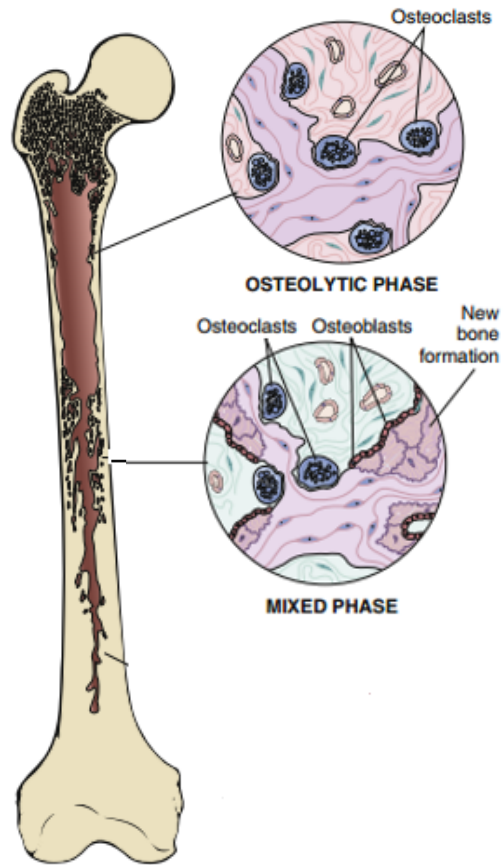
Blade of glass

Imaging



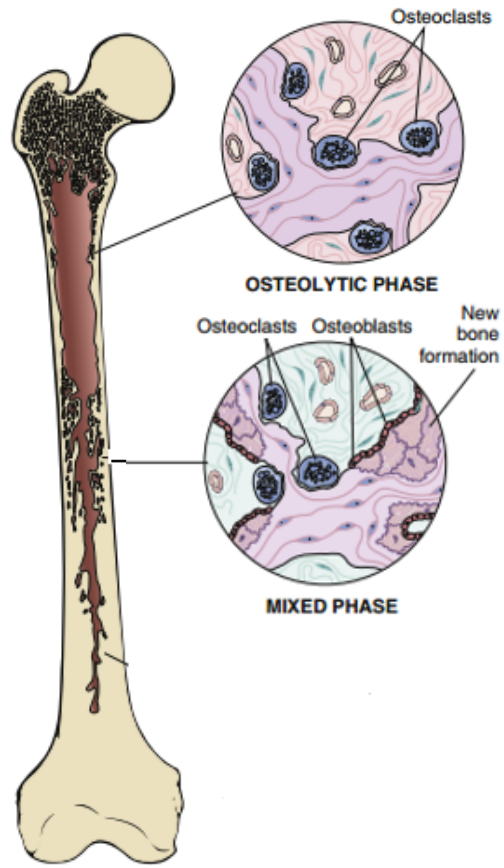
Osteoporosis circumscripta

Imaging



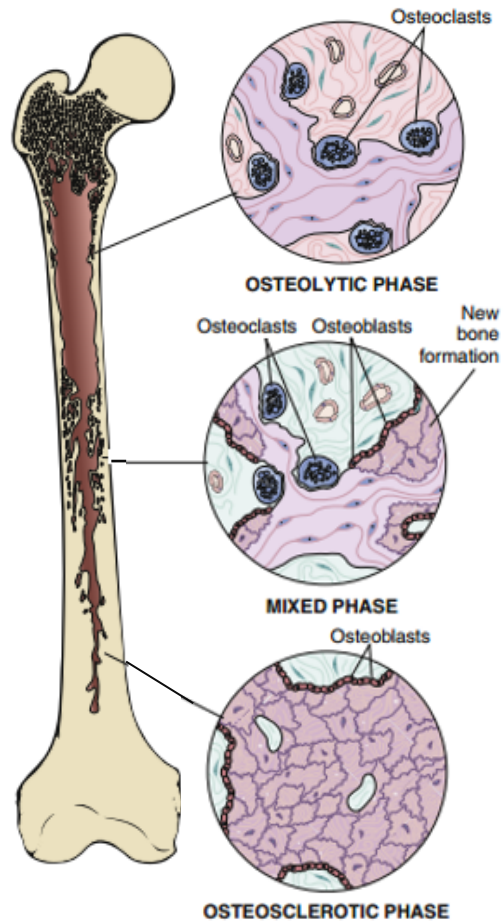
**Cross-hatched pattern
Cotton wool spots**

Imaging

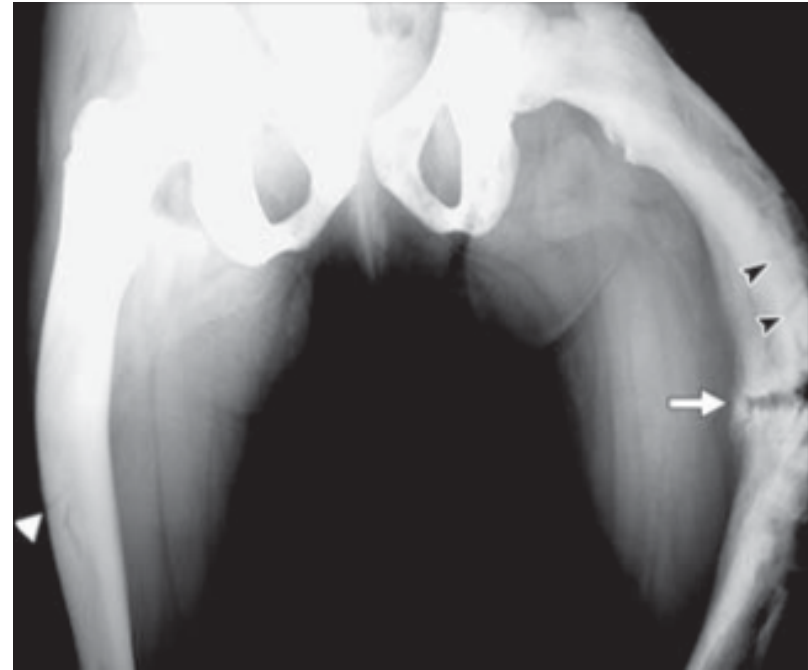
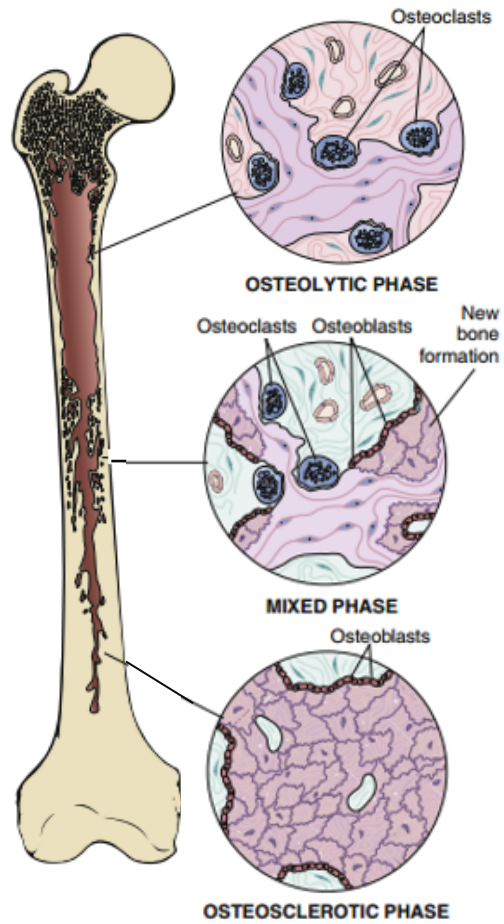


Cotton wool spots

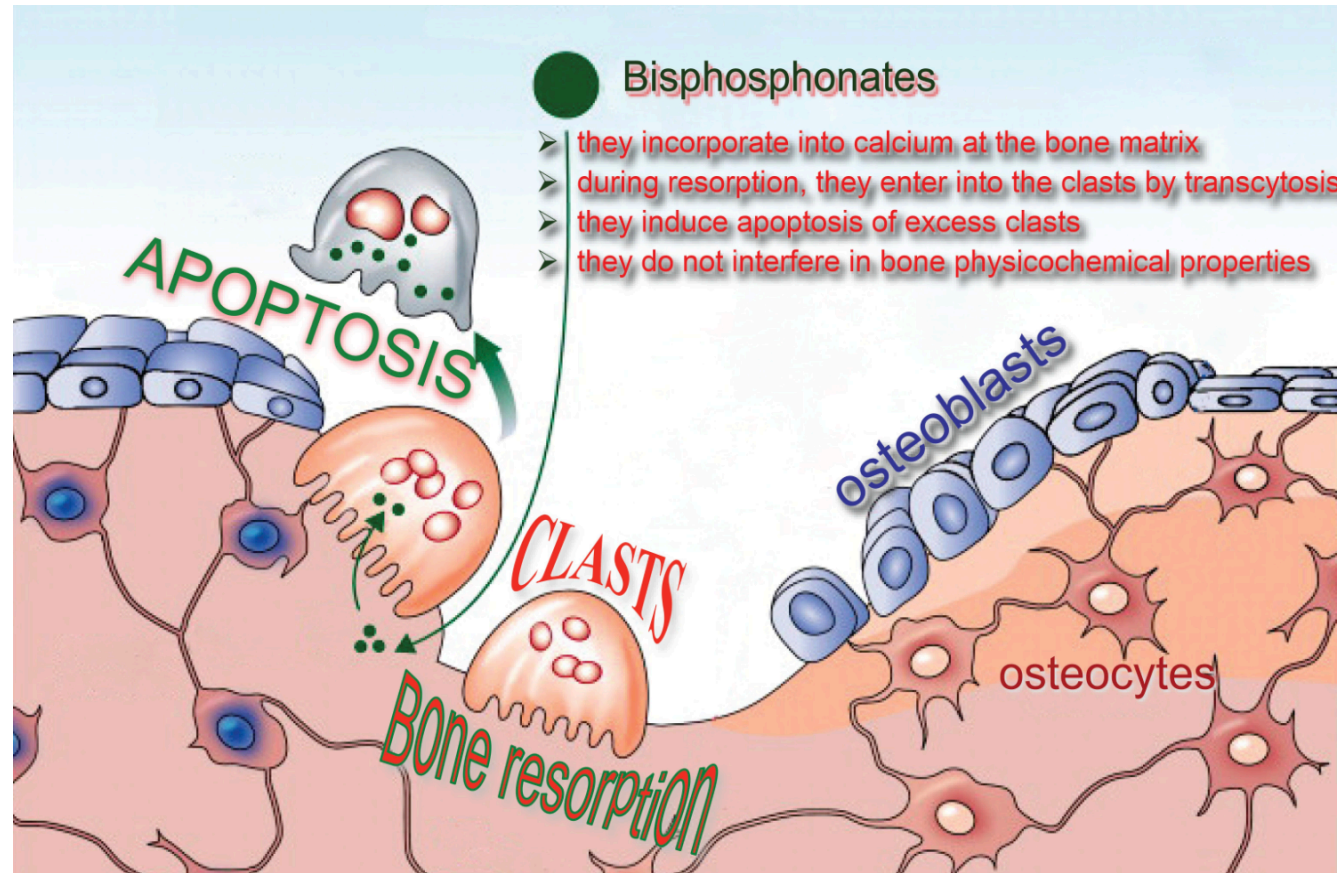
Imaging



Imaging



Treatment – Antiresorption agents

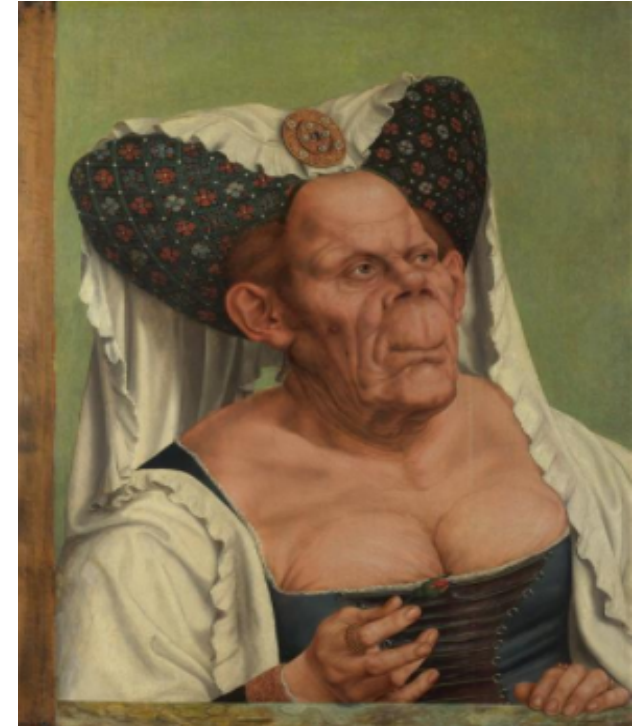


Treatment – Indications

- Symptomatic Paget disease.
- Asymptomatic Paget disease.
 - sAP (+) – complication (+/-)
 - sAP more than 2-4 times
 - sAP (-) – bone scan (+)
 - Preoperative therapy
 - Hypercalcemia/immobilization

Take home messages

- PDB is characterized by abnormalities of the Osteoclast
- PDB is often asymptomatic. Symptoms are due to overgrowth of the affected bone
- Diagnosis of PDB is confirmed by the characteristic radiographic changes
- Bisphosphonate is the first line therapy for PDB



The Ugly Duchess