Hashemite University
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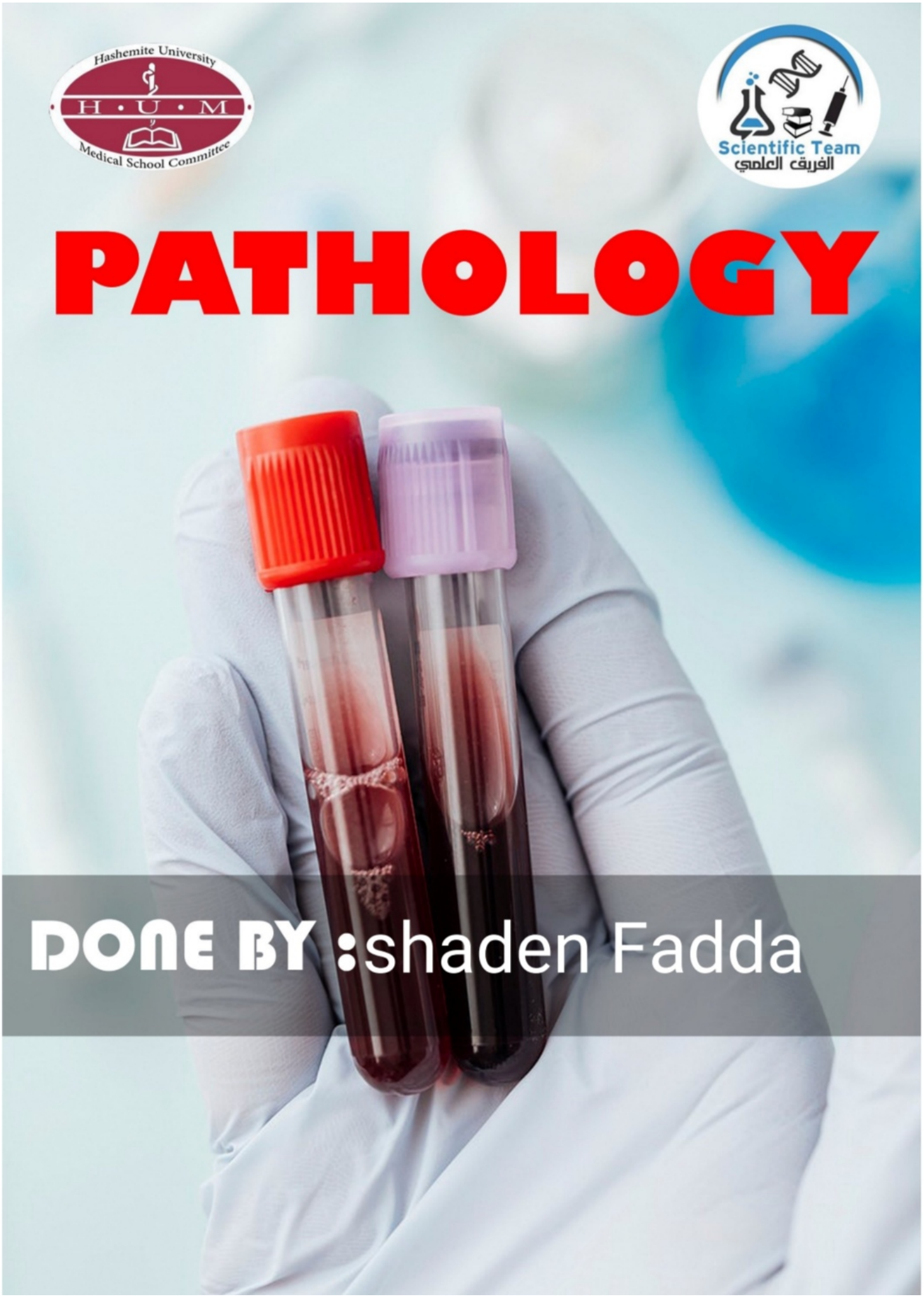
Medical School Committee

Scientific Team
الفريق العلمي

PATHOLOGY



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Paget Disease (Osteitis Deformans) تشوه العظام
A DISORDER WITH A LOT OF BONE REMODELING

*It is a skeletal disease characterized by:

1) Osteolytic stage and bone resorption >> **regional osteoclastic stage**
2) Exuberant (lively) bone formation >> **mixed osteoclastic-osteoblastic stage**
3) Exhaustion of cellular activity >> **osteosclerotic stage**

>>>>>>>>>>>>> The net effect : - Gain in bone mass
- Thick but weak newly formed bone

*It affects : 1) elderly people
2) whites in the (US, Europe, Australia, New Zealand)
3) 10% of the adults

*Morphology :

- Monostotic (solitary lesion) >> 15% of cases >> (skull, vertebra, ilium, femur, tibia, & humerus)
- Polystotic (affect multiple sites in the skeleton) >> 85% of cases >> (skull+ spine+ pelvis)

1) **lytic phase** : numerous amount of abnormally large osteoclasts (Howship lacunae) (الاوستيوكلاستس هون زي المجانين وقاعدين بياكلوا الأخضر واليابس)

   NOTE >> (Howship lacunae) : irregular grooves in bone that are being resorbed by osteoclasts
2) **mixed phase :** osteoclasts persist & the bone surfaces become lined by prominent osteoblasts
3) **sclerotic phase** : the marrow is replaced by **loose connective tissue** containing **osteoprogenitor cells**, as well as **numerous BVs** inorder to meet the ↑ metabolic demands of the tissue
4) The newly formed bone may be woven or lamellar, but eventually all of it is remodeled into a heightened caricature of **lamellar bone**.

*Histologic feature : **mosaic pattern of lamellar bone** (like a jigsaw puzzle)
>> and this is due to :- prominent cement lines that haphazardly unite lamellar bone units
>> the resulting cortex is thick ,however it is softened & prone to deformation & fracture under stress.

*Pathogenesis :

1) First Sir James Paget said that : From its name (osteitis deformans) : the skeletal changes of Paget ds. are attributed to **inflammatory process**
2) Current evidence suggests that : **Paramyxovirus infection** ultimately underlies Paget disease.
   Paramyxovirus antigens can be demonstrated in osteoclasts >> the results are :
   1- induce the cytokine IL-1 secretion from osteoclasts & & M-CSF secretion from pagetic bone
   2- activate osteoclasts and induce the osteolytic stage and bone resorption

   HOWEVER, up till now, NO infectious virus has been isolated from affected tissue!

*Clinical Course :

1. Monostotic (solitary lesion) >> 15% of cases >> (skull, vertebra, ilium, femur, tibia, & humerus)
   Polystotic (affect multiple sites in the skeleton) >> 85% of cases >> (skull+ spine+ pelvis)
   >>>The **axial skeleton or proximal femur** is involved in up to 80% of cases ; while Involvement of other bones is unusual.

2) **cardiovascular complications (aortic incompetence),** most cases are mild & discovered only as incidental radiographic finding
3) **↑ serum alkaline phosphatase**
4) **↑ urinary excretion of hydroxyproline**, and that reflect excessive bone turnover

*Effects & complications of Paget disease : ***IMPORTANT***

1. In pts. with extensive polyostotic disease & marrow hypervascularity, this will result in high-output congestive HF

2. Deformities of the bones of the skull (bcs of overgrowth of bone// LEONTIASIS)
   & impingement on cranial nerves causing symptoms of **nerve impingement** ضغط على الاعصاب
   INCLUDING : * headache
   * visual & auditory disturbances

   Pts. with vertebral lesions will have back pain associated with disabling fractures & nerve root compression.

3. The inability of pagetoid long bones to appropriately remodel is due to the stress of weight-bearing , and this will result in **deformed affected long bones in the legs** . Brittle long bones in particular are subject to **chalkstick fractures**.
   >> the long bones : زي الطباشير fractures بتكون هشة ومعرضة لل

4. A rare complication of Paget disease is (occurring in only an estimated 1% of patients) : **Sarcoma development with osteoblastic lesions**.
   The sarcomas are : - usually osteogenic (60% of cases)
   - chondrogenic (30%)
   - fibrogenic (10%)

   This distribution happens generally in all Paget lesions **EXCEPT** legions of vertebral bodies, which rarely harbor malignancy.

*Prognosis :

- most patients have mild symptoms that are readily controlled by calcitonin or bisphosphonates , the prognosis of these patients usually follows a relatively **benign course .**

- the prognosis of patients who develop secondary sarcomas is **exceedingly poor**.

*Important PICs : slide 13+15