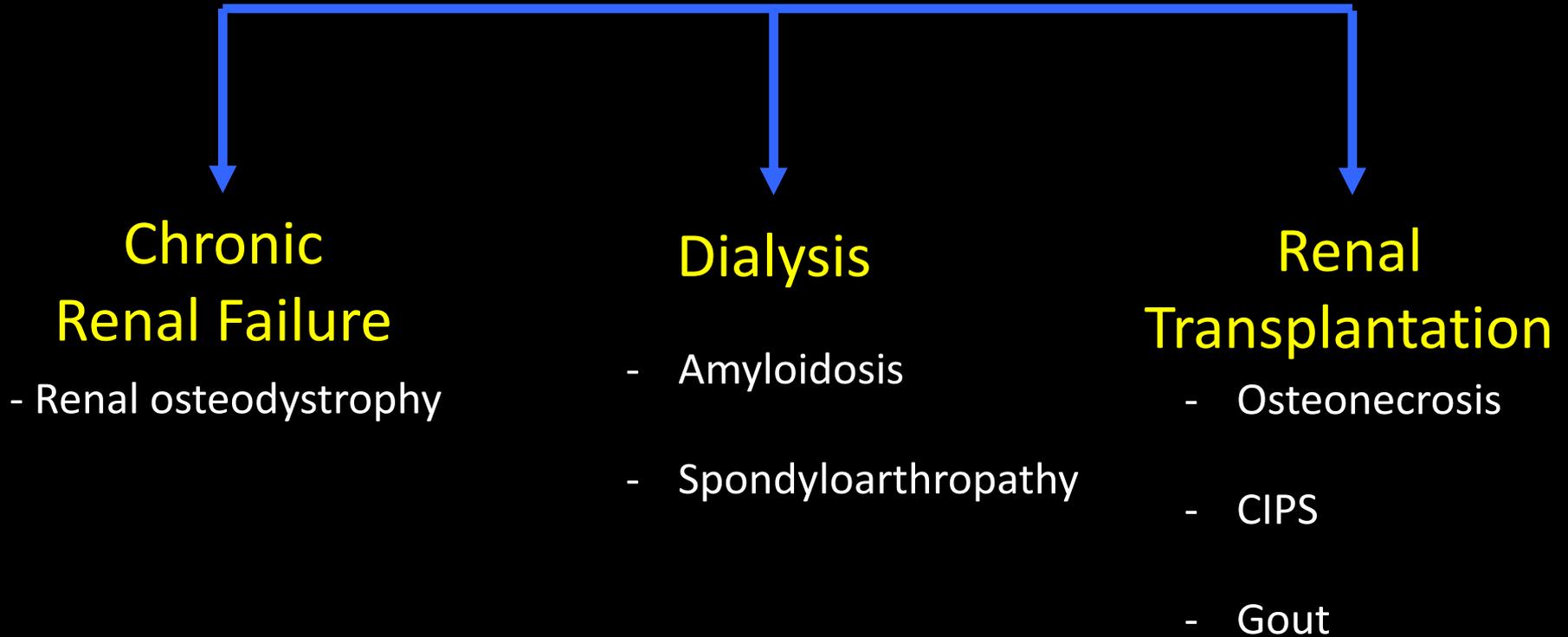


# Musculoskeletal Manifestations in the Setting of Chronic Renal Failure

Yatin Chadha

June 23, 2016

# Outline

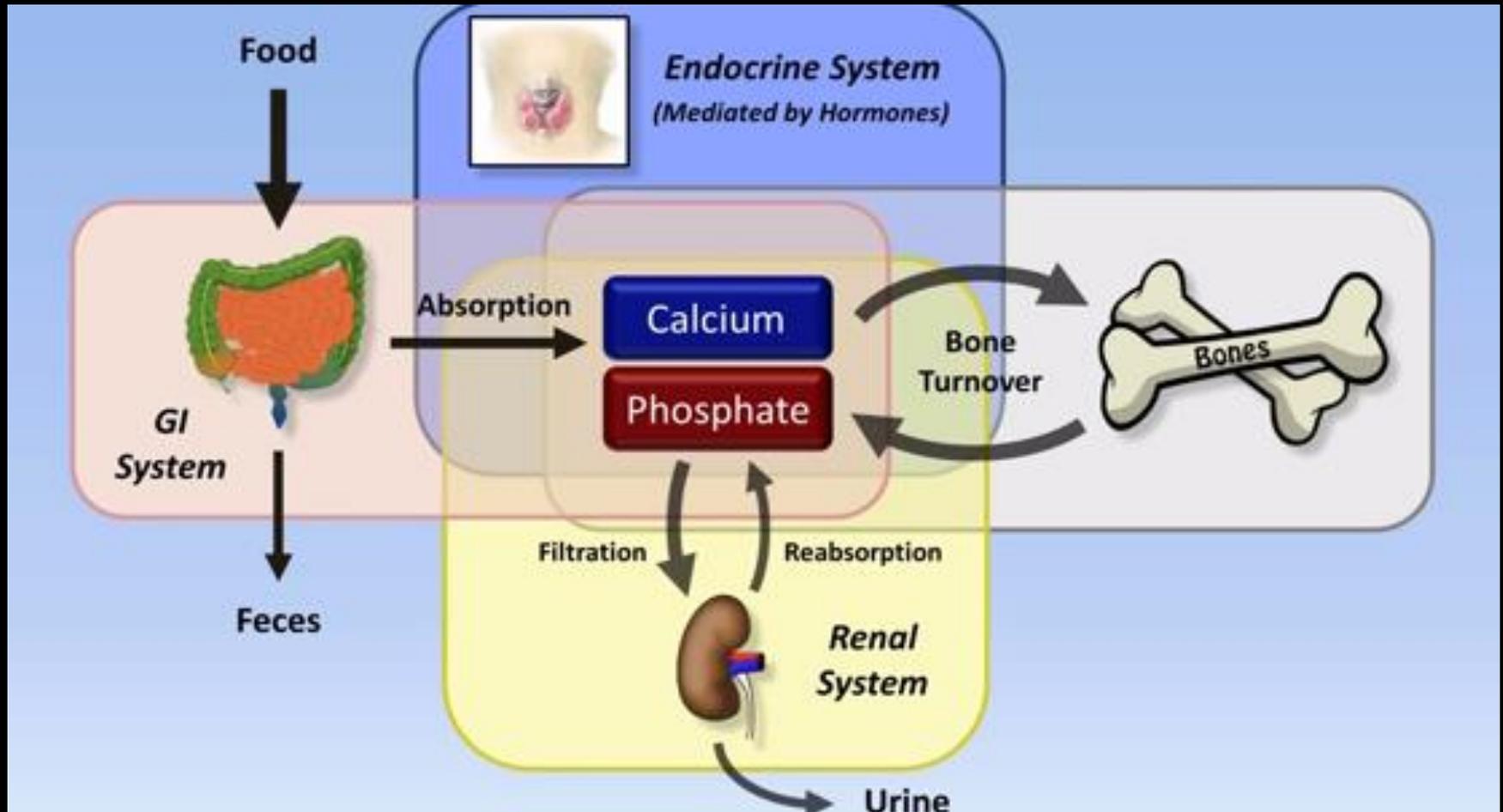




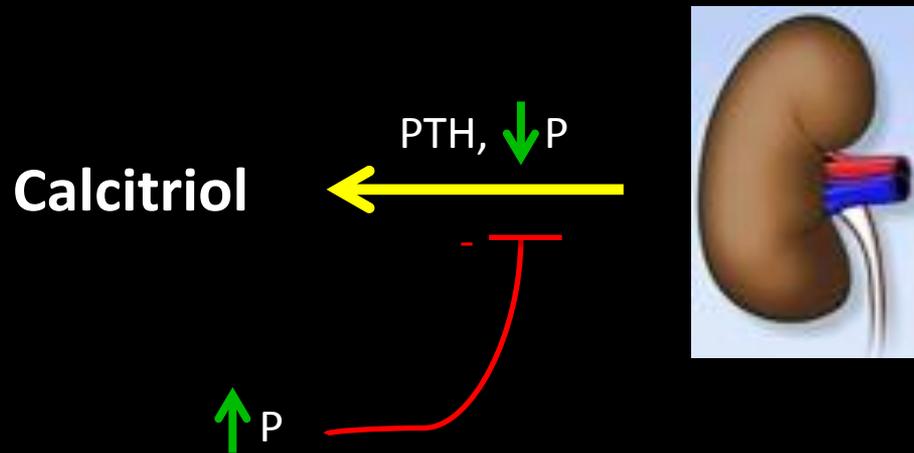
Sorry eh!



# Normal Physiology

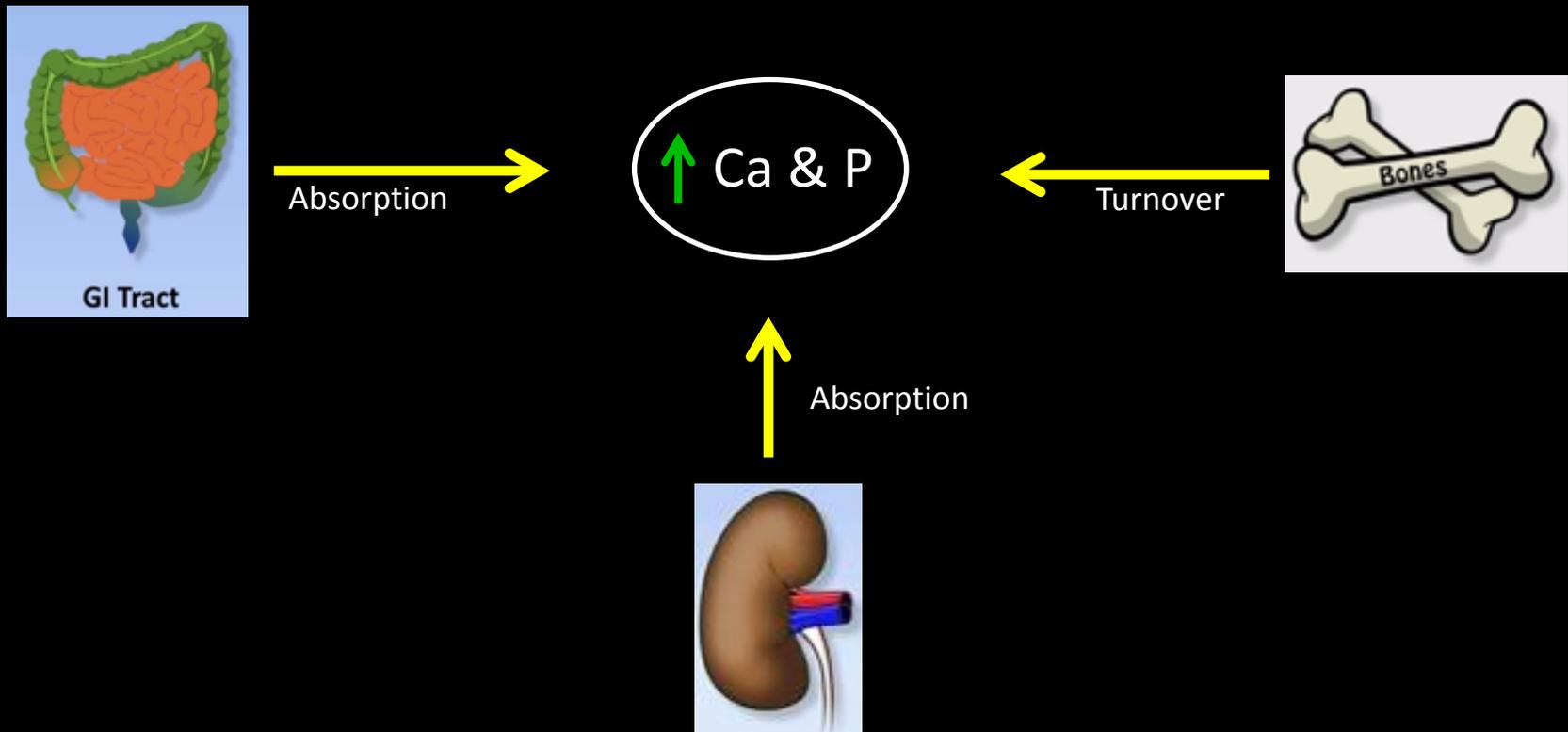


# Normal Physiology



# Normal Physiology

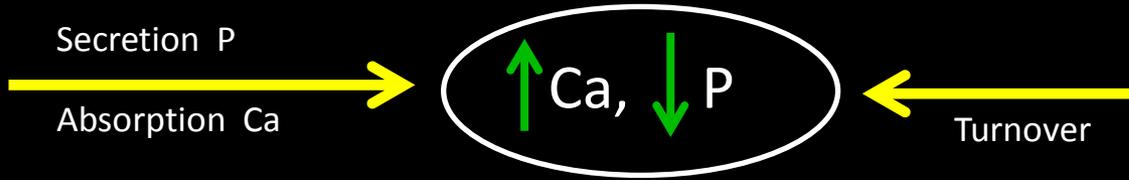
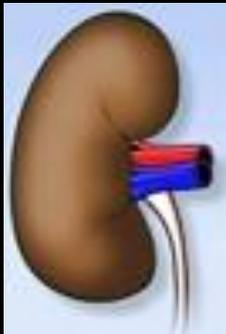
- Calcitriol
  - Net effect :  $\uparrow$  Ca & P



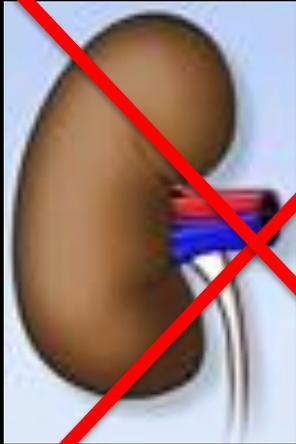
# Normal Physiology

- PTH

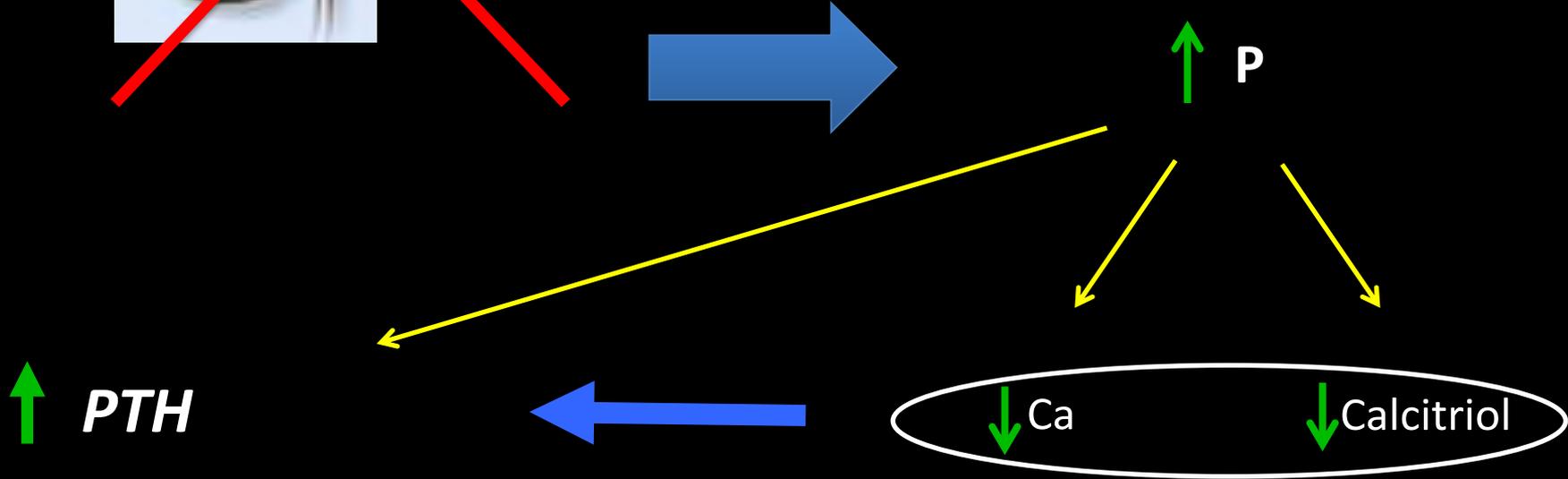
– Net effect:  $\uparrow$  Ca,  $\downarrow$  P



# CRD - Pathophysiology



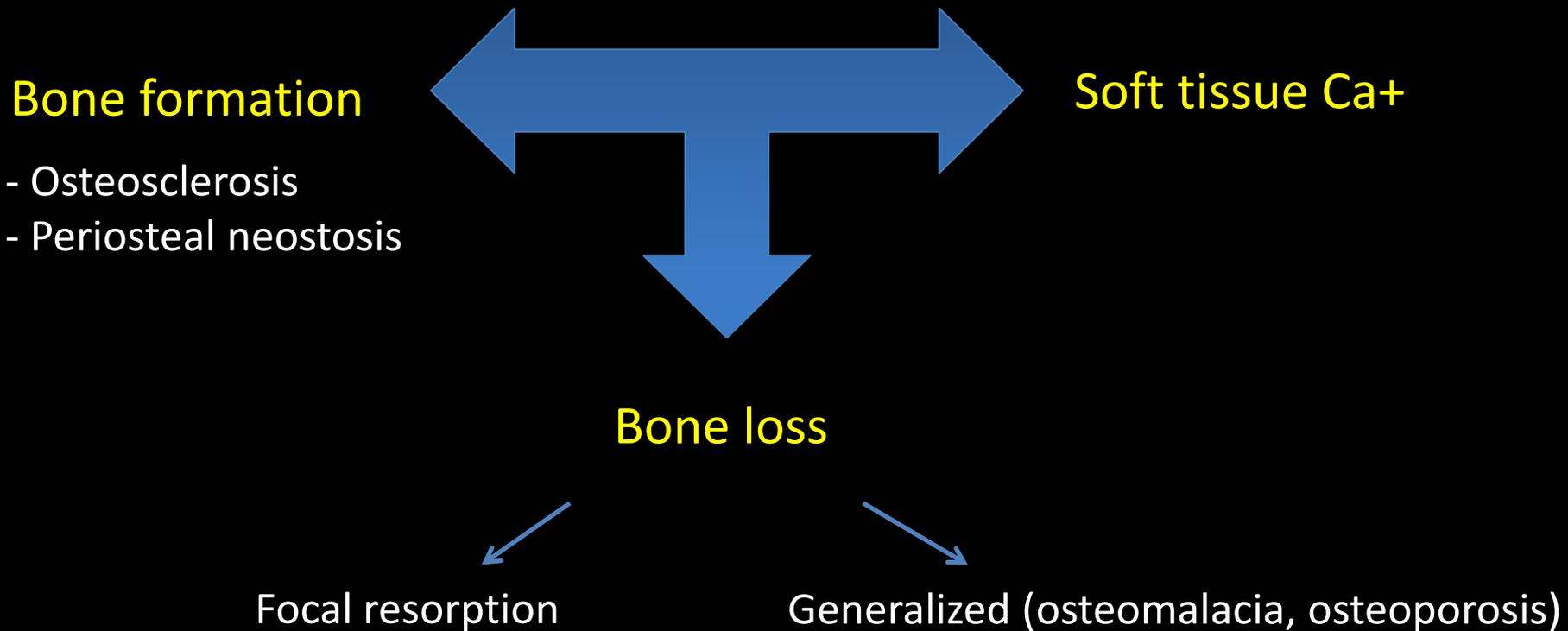
- Excretes excess P



# Renal osteodystrophy/CKD-MBD

- Also referred to as chronic kidney disease – mineral bone disorder (CKD-MBD)
- Key player:
  - 2° Hyperparathyroidism (HPT)
    - Affects osteoblasts and osteoclasts

# Renal osteodystrophy/CKD-MBD



# Bone resorption in Renal Osteodystrophy

- Subperiosteal
- Cortical
- Endosteal
- Trabecular
- Subchondral
- Subphyseal
- Subligamentous & subtendinous

# Subperiosteal Resorption



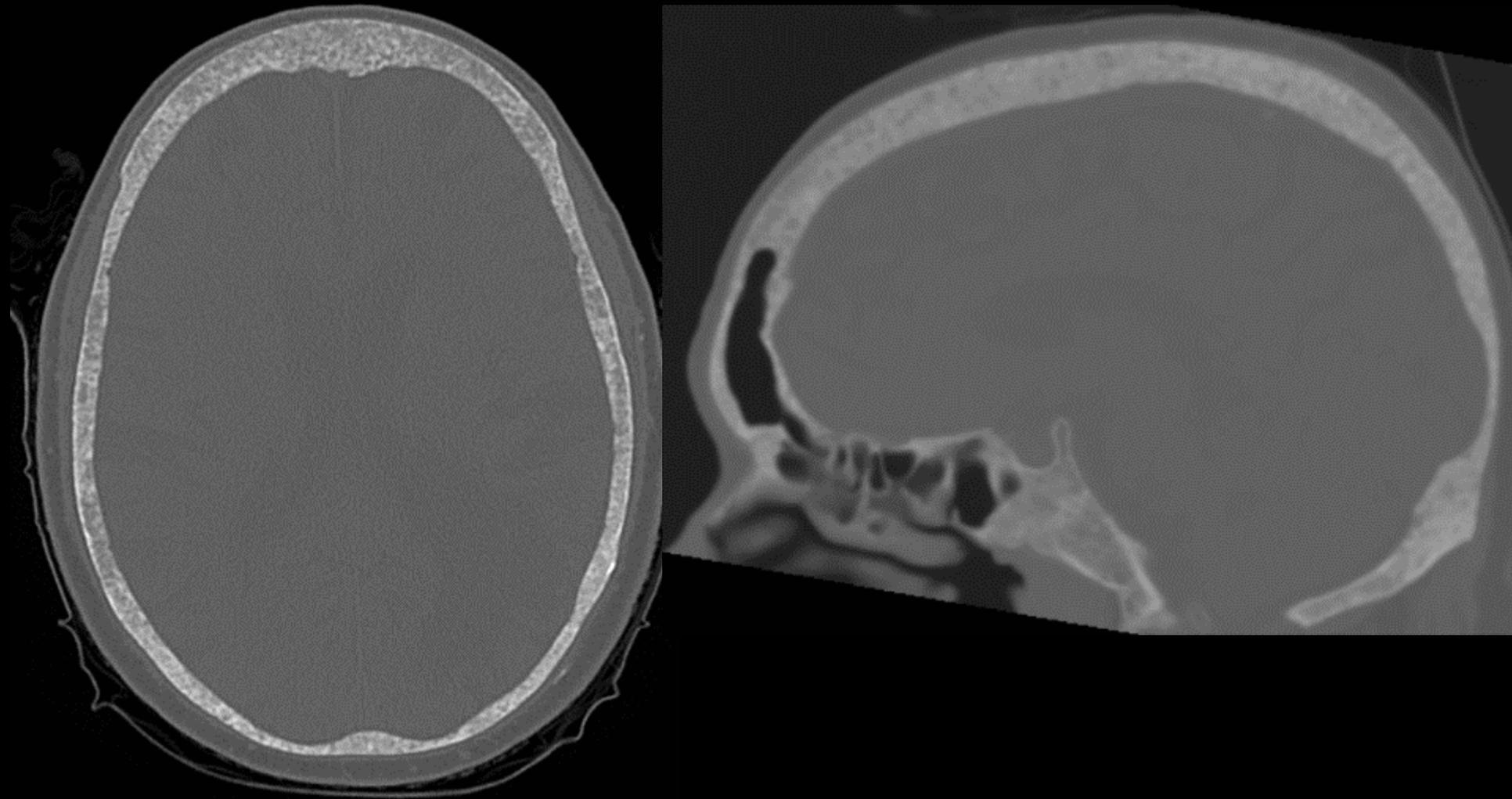
Case courtesy  
Edward Smitaman



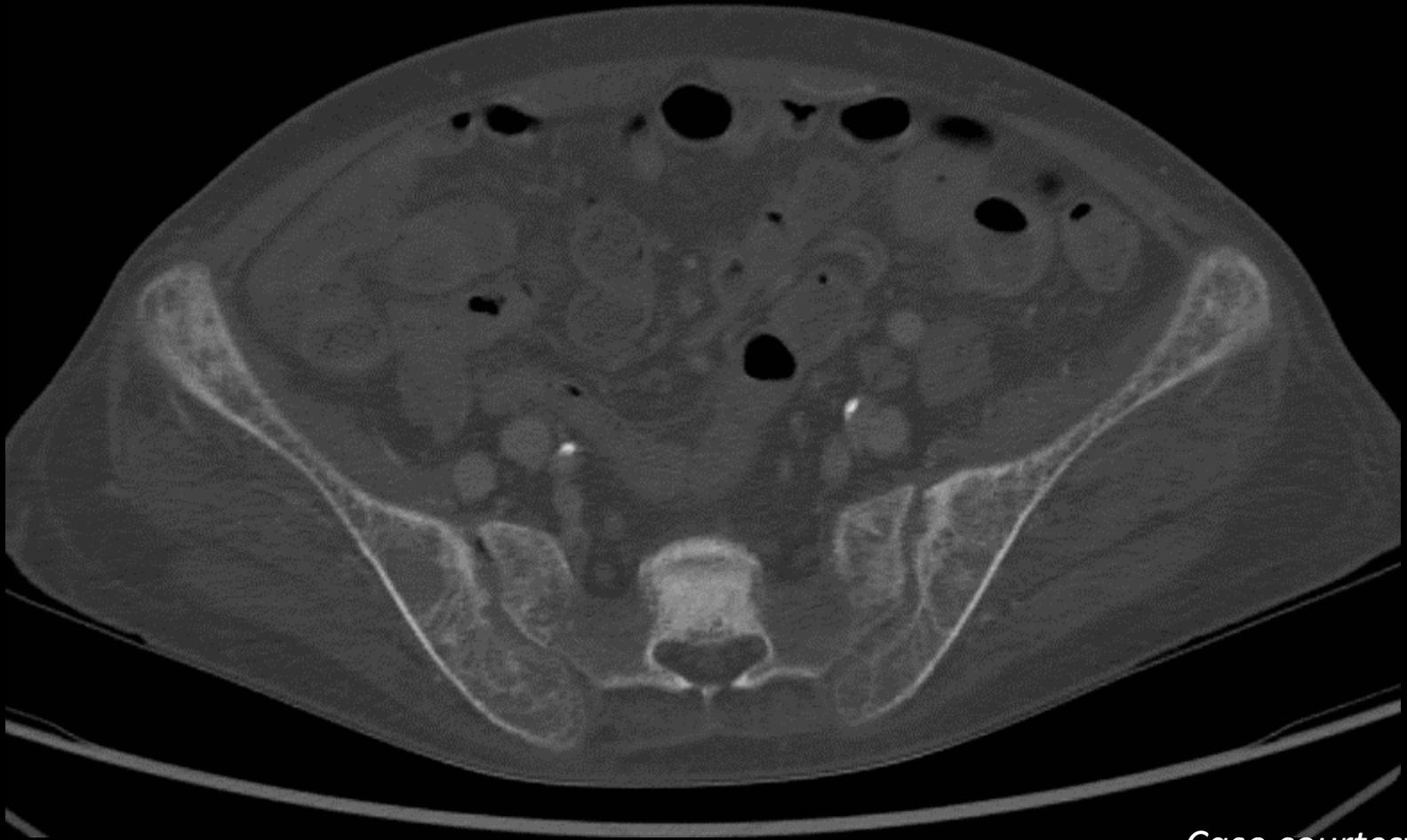
*Case courtesy  
Edward Smitaman*



# Trabecular resorption

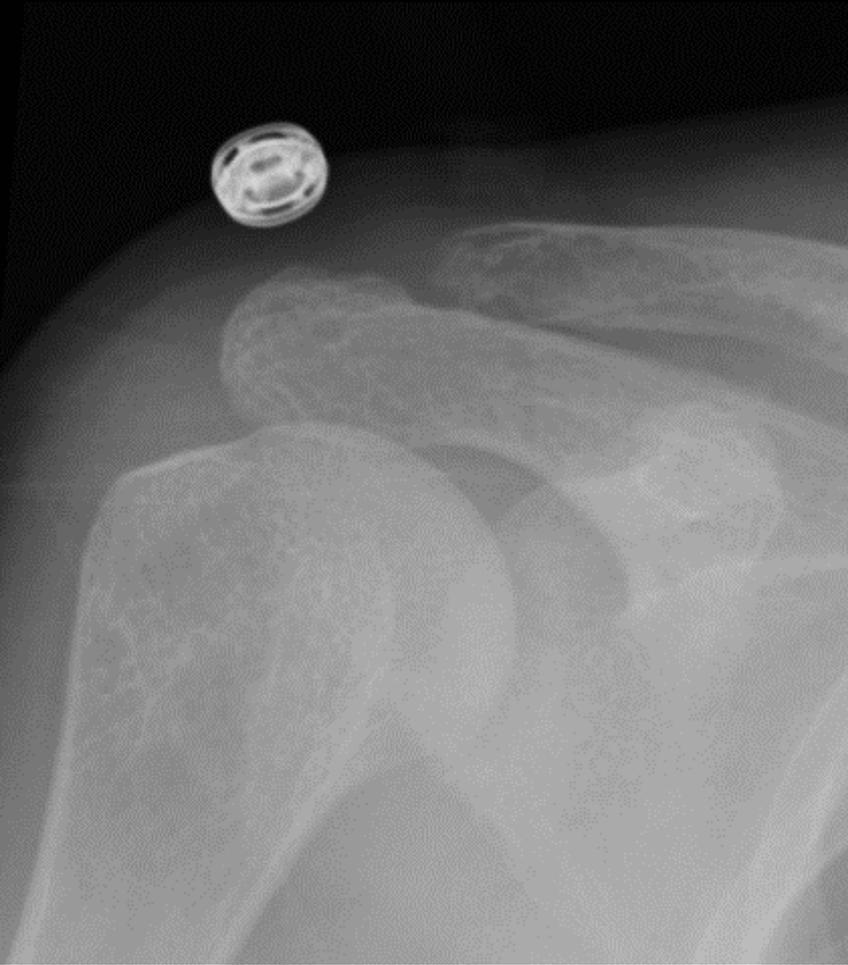


# Subchondral resorption



*Case courtesy  
Edward Smitaman*

# Subchondral resorption

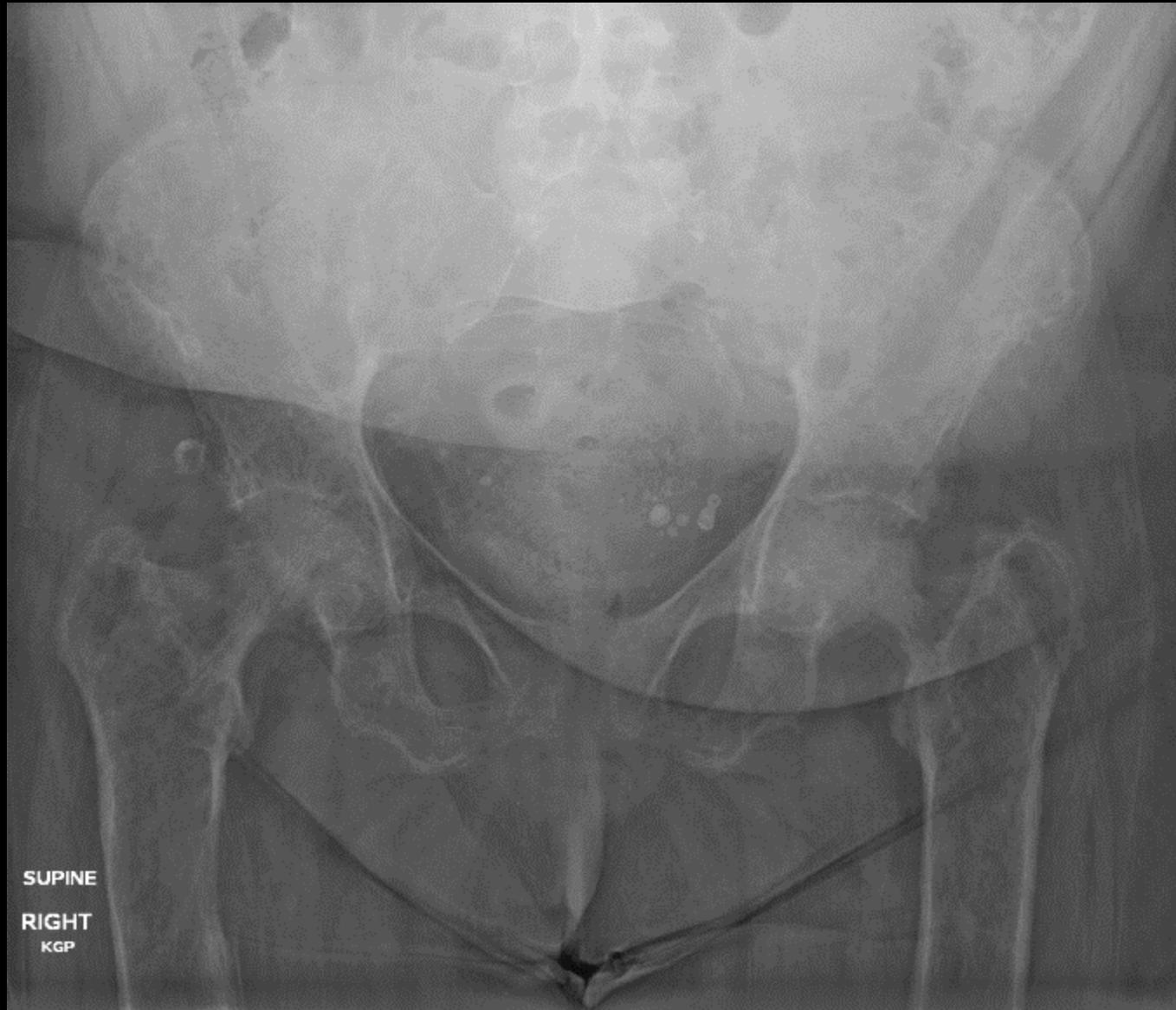


*Case courtesy Edward Smitaman*



*Case courtesy Paul Fenton, Queen's U.*

# Subchondral and Subtendinous Resorption



# Subtendinous resorption



*Murphey et al. Radiographics.  
1993(2)*

# Endosteal and Cortical Resorption



# Bone resorption – summary

- Earliest sign in 1° and 2° HPT
- Subperiosteal resorption most common (pathognomonic for HPT), responds to therapy
- Sites:
  - Subperiosteal: Radial aspects 2<sup>nd</sup>/3<sup>rd</sup> middle phalanges (pathognomonic), phalangeal tufts, femur, tibia, humerus, ribs, lamina dura
  - Trabecular: skull (salt & pepper)
  - Subchondral: SI, AC, sternoclavicular, discovertebral, pubic symphysis, patella
  - Subligamentous/tendinous: femoral trochanters, ischial tuberosities, humeral tuberosities, conoid tubercle of clavicle, elbow, inferior calcaneus

# Brown Tumors (aka osteitis fibrosa cystica)

Osteoclasts

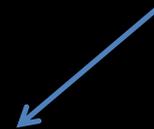


Resorption/osteopenia

Osteoblasts

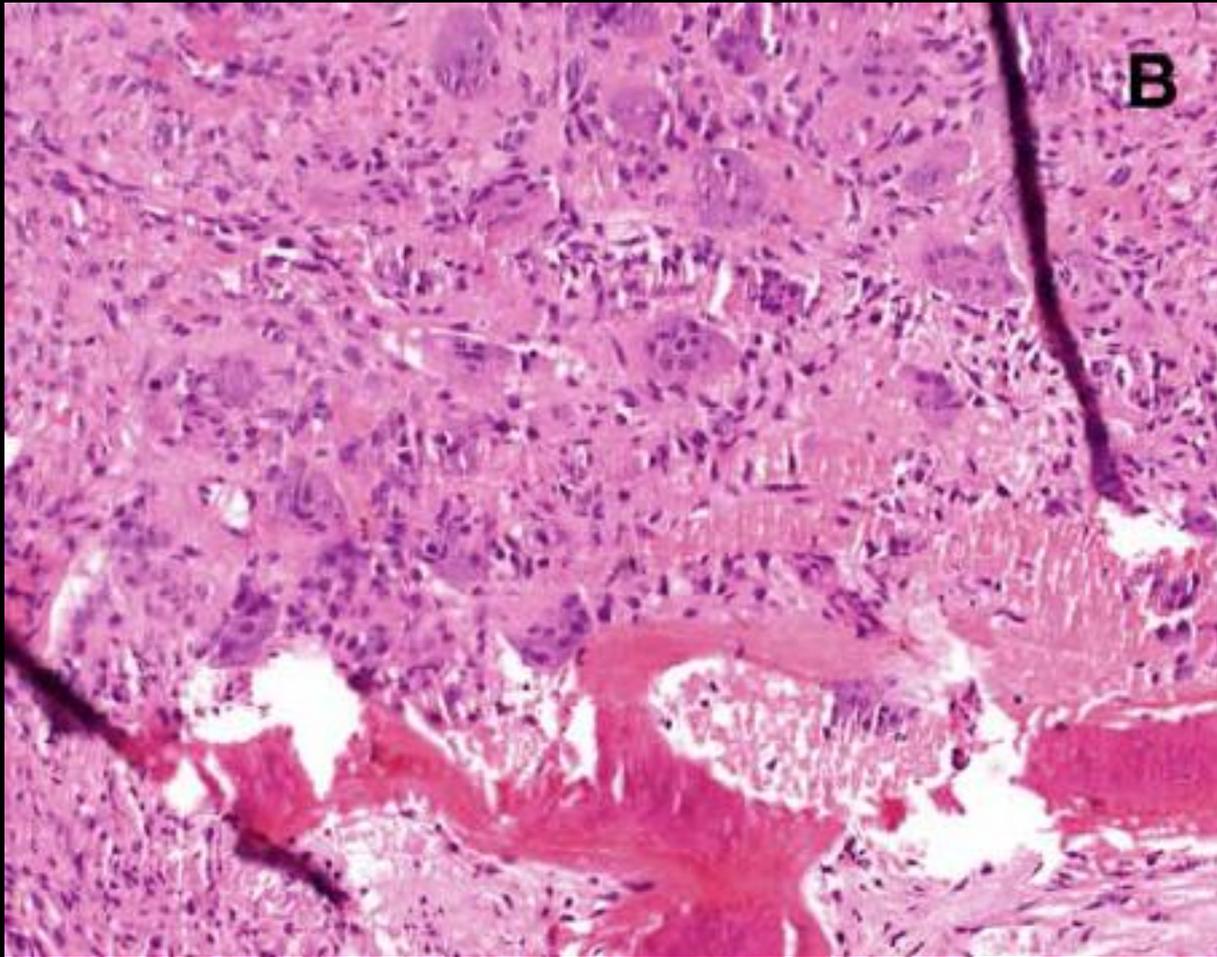


Fibrovascular tissue ingrowth



Microfractures, hemorrhage,  
multinuclear macrophages

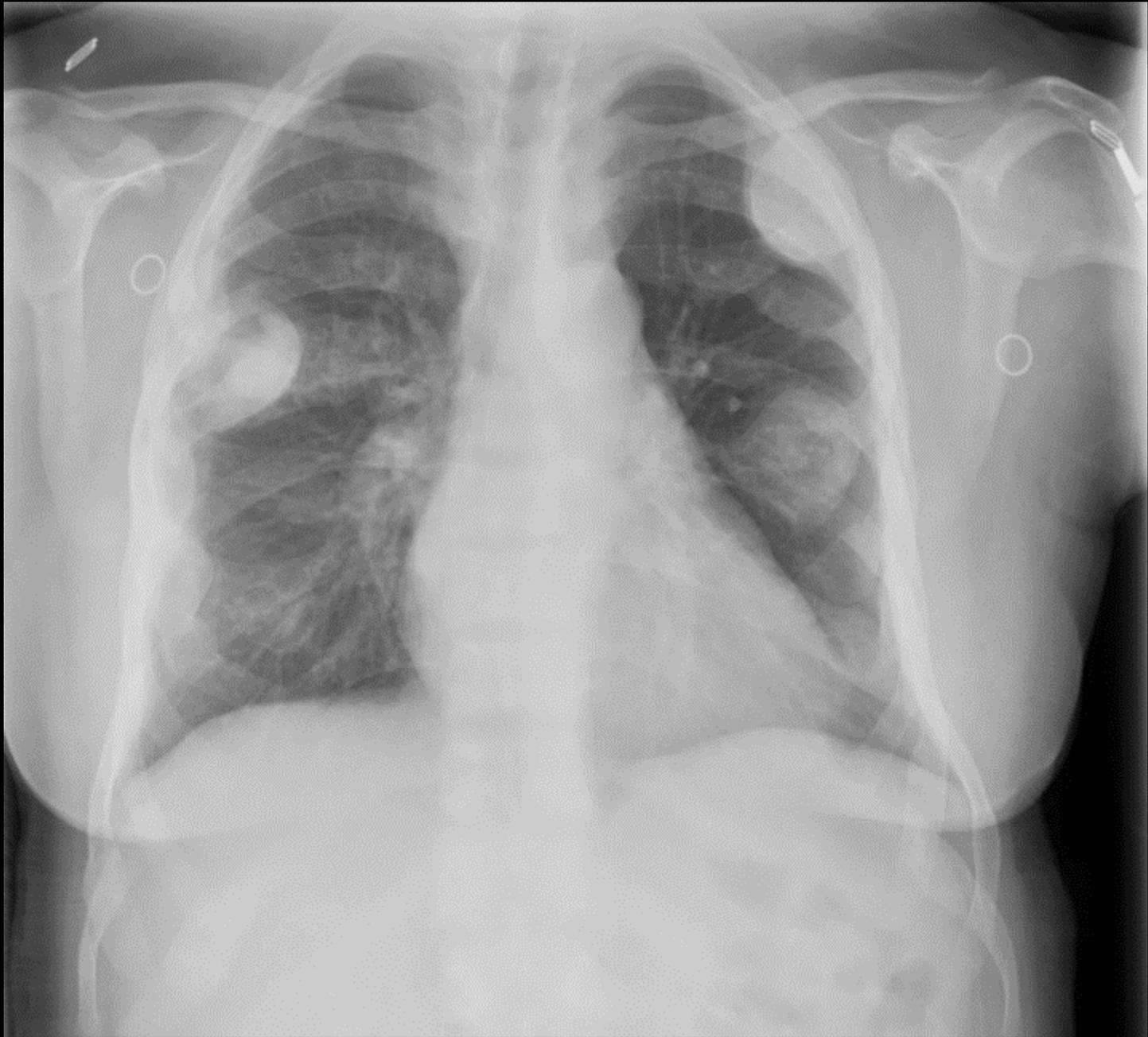
# Brown tumors - histopathology

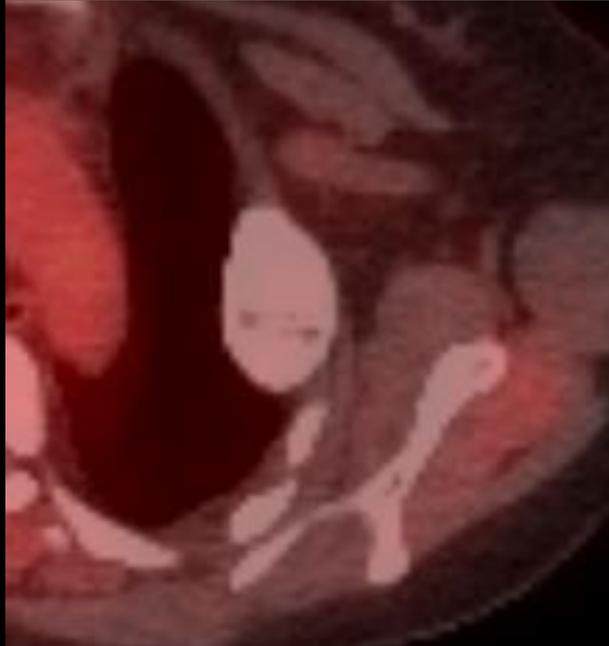
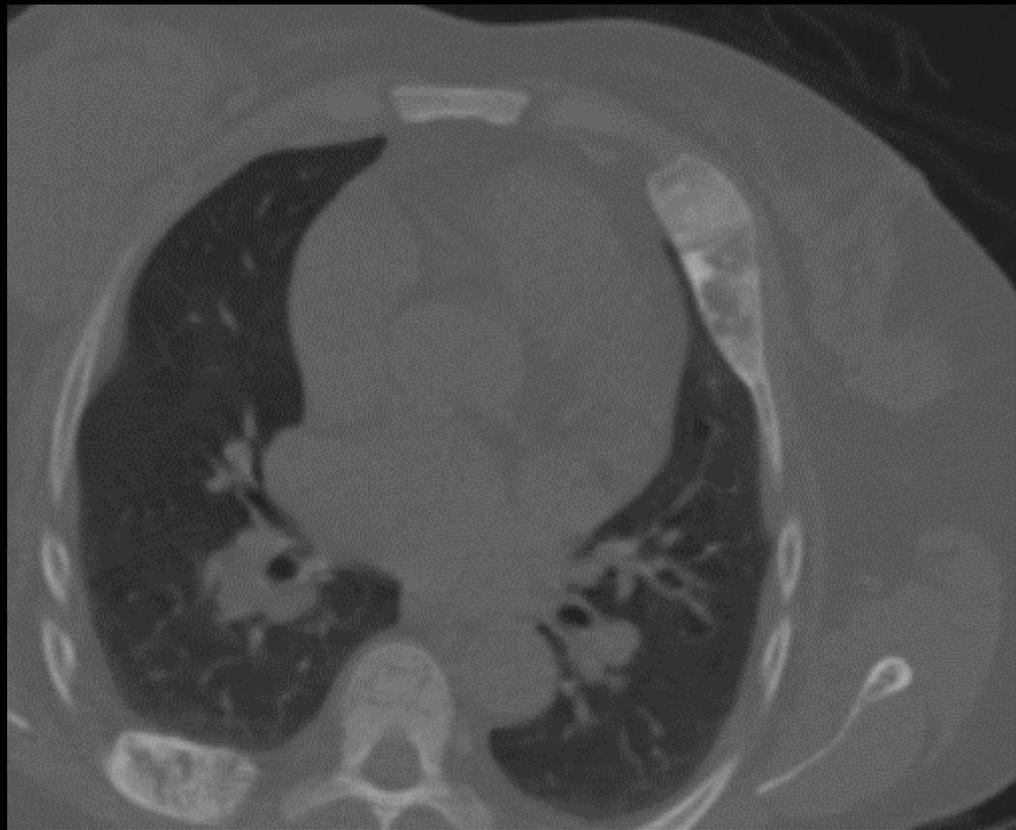
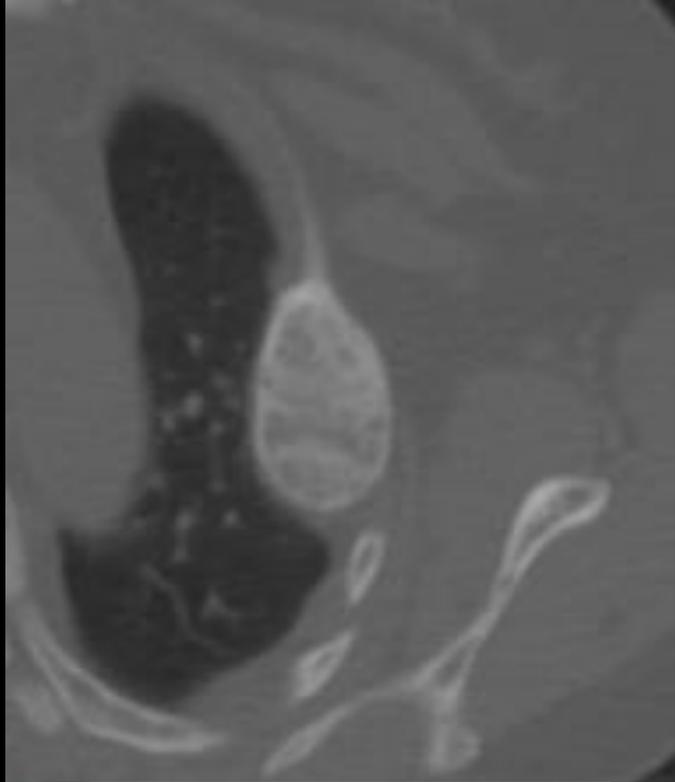


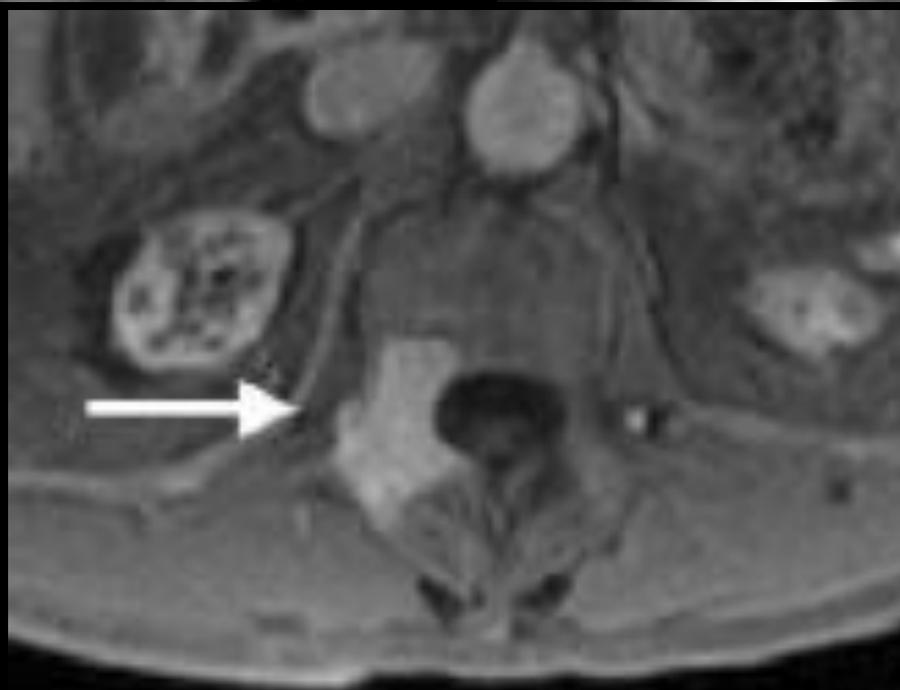
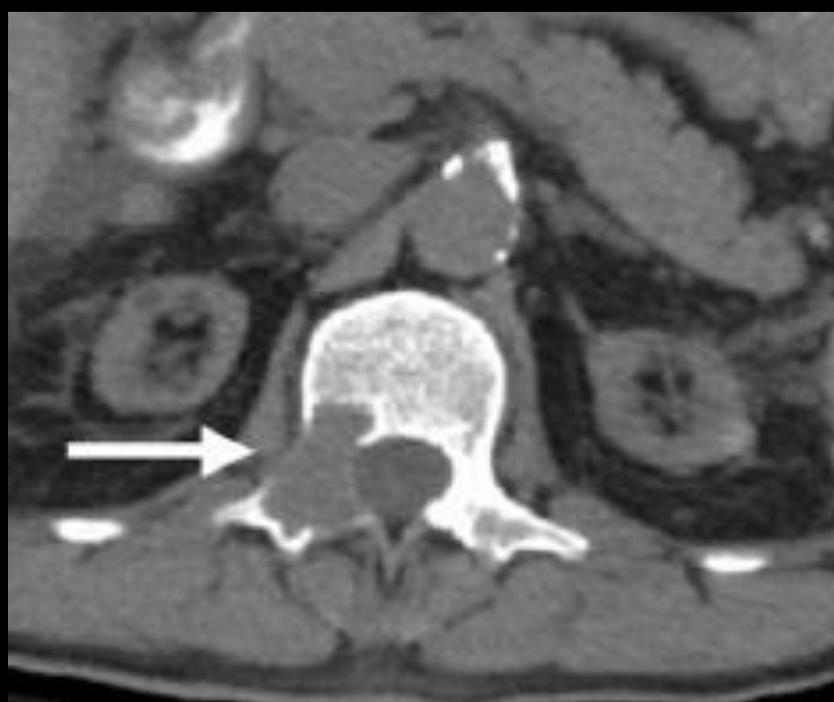
- Fibrous stroma
- Multinucleated giant cells
- Hemorrhage/hemosiderin

# Brown Tumors

- Occurs in 1° and 2° HPT, very uncommon
- Osseous resorption should co-exist
- Sites: Pelvic girdle, hands, extremities, ribs, clavicle, facial (can be multiple)
- Focal bone pain
- Imaging:
  - Well-defined, expansile
  - MRI: low T2 signal, hemosiderin, enhancement
- Responds to therapy (sclerosis)







# Generalized osteopenia

- Osteomalacia (reduced osteoid mineralization)
  - Imaging:
    - Osteopenia
    - Poor trabecular/cortical distinction
    - **Looser's zones** (femoral neck, pubic rami, ilium, ribs, scapulae, acromion)
    - Rickets
- Osteoporosis
  - Aluminum may also have a role
  - **BMD screening not routinely recommended in 2°HPT**
  - Fractures → vertebrae, distal forearm, femur

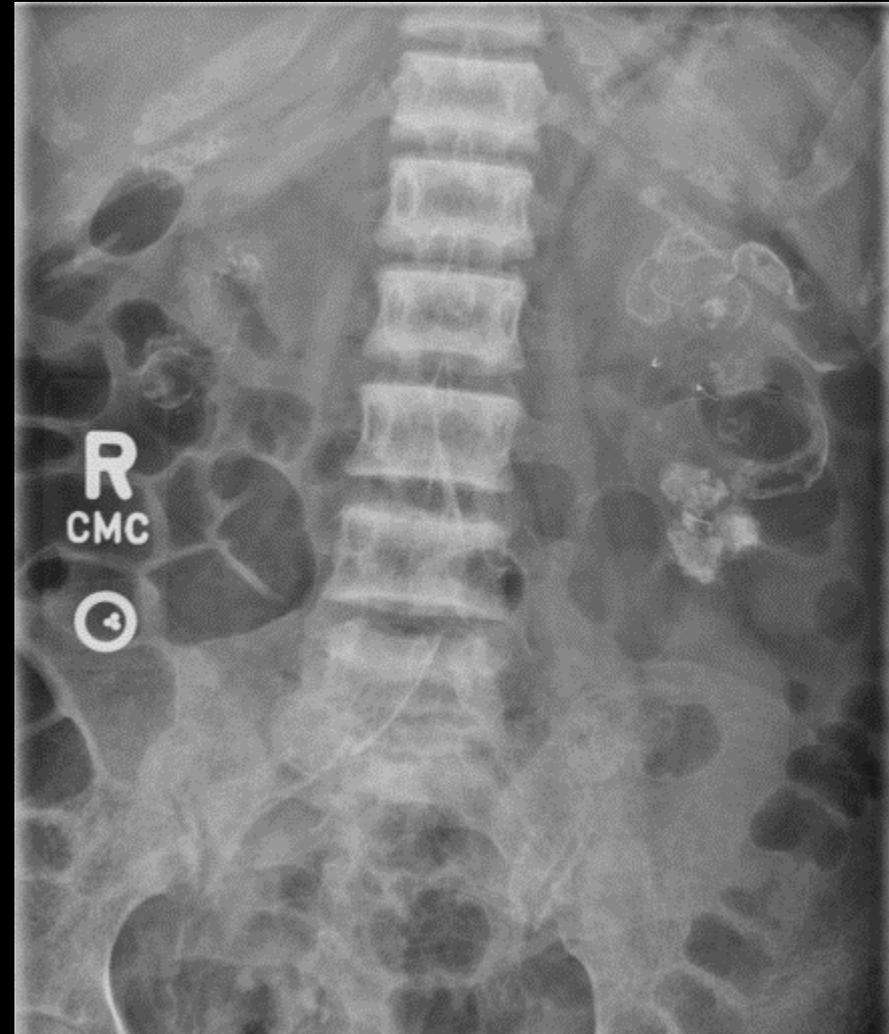
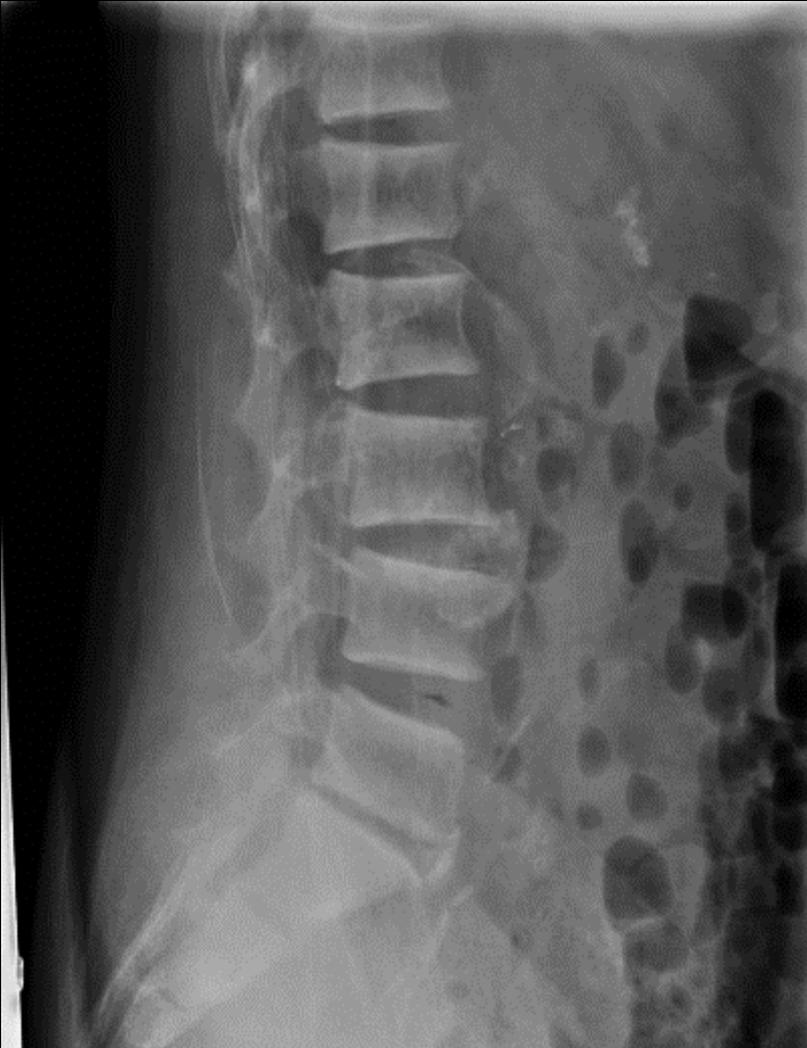
# Osteomalacia



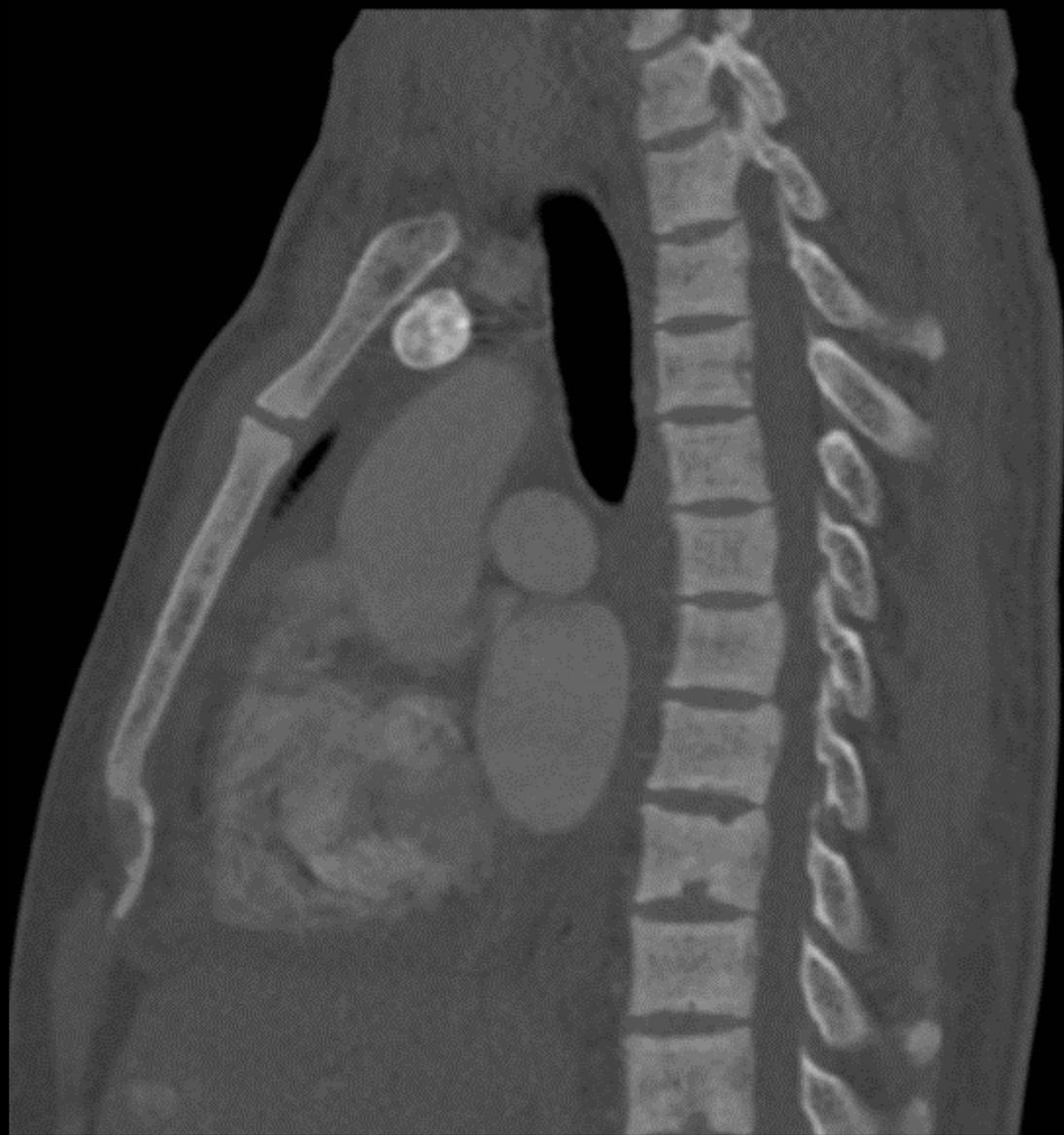
# Increased bone density - osteosclerosis

- **Axial skeleton > appendicular skeleton**
  - Spine (rugger jersey)
  - Pelvis, calvarium, clavicles
  - Metaphysis of long bones
- PTH action on osteoblasts
- Does not improve after dialysis

# Osteosclerosis



*Case courtesy Edward Smitaman*





*Case courtesy Paul Fenton, Queen's U.*

# Bone formation – periosteal neostosis

- Late sign
- Mature periosteal bone formation with cleft
- Hand & feet, long bones, pelvis

R

IK

e



# Soft tissue calcifications

- Periarticular
- Cartilaginous
- Arterial (pipestem, dorsalis pedis & radial)
- Visceral
- Ocular

# Periarticular calcifications

- Resemble tumoral calcinosis
- Metabolic panel (GFR, Ca, P)
- Often large joints (hip, shoulder, elbow, wrist foot)
- Often symmetric
- Imaging:
  - Cloud-like
  - May be cystic with  $\text{Ca}^{+}$  sedimentation (more active)
  - No bony erosion
- Can improve following dialysis



*Case courtesy Paul Fenton, Queen's U*

# Chondrocalcinosis

- Sites:
  - Knee
  - Wrist
  - Hip
  - Pubic symphysis
  - Shoulder
- More common in 1° than 2° HPT

# Arthropathy of Hyperparathyroidism

- Mixed features:
  - Erosions
  - Relative preservation joint space
  - Periosteal whiskering
  - **Subperiosteal resorption coexists**



*Resnick. Radiology. 1974;110: 263-269*

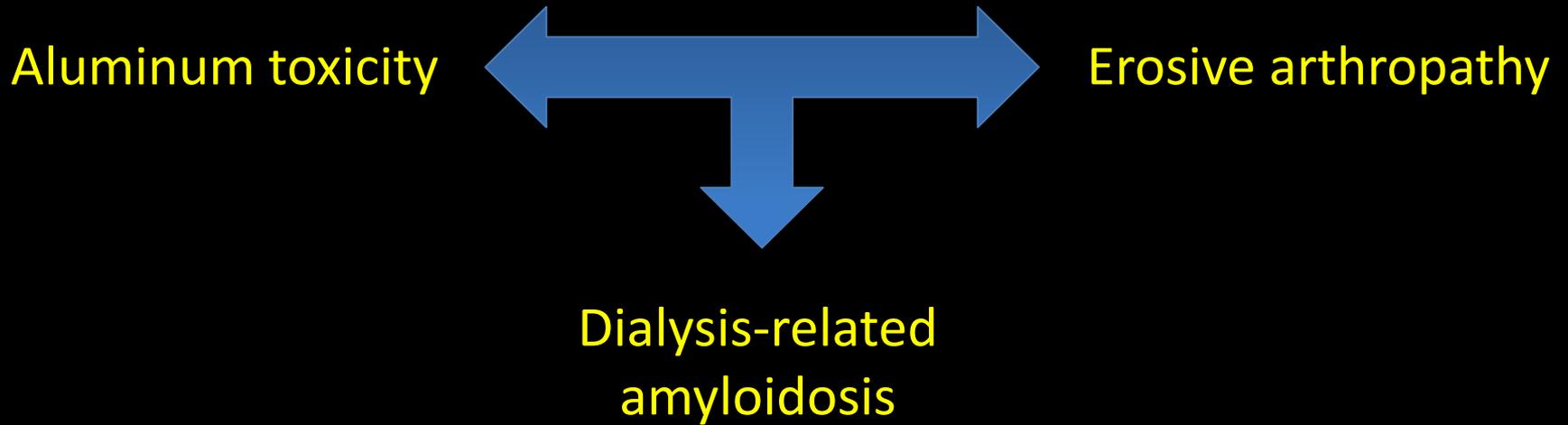
## Primary versus Secondary Hyperparathyroidism

<b>Findings</b>	<b>Primary Hyperparathyroidism</b>	<b>Secondary Hyperparathyroidism*</b>
Brown tumors	Common	Less common
Osteosclerosis	Rare	Common
Chondrocalcinosis	Not infrequent	Rare
Periostitis	Rare	Not infrequent





# Dialysis-related Bone Disease



# Aluminum toxicity

- Main source is aluminum salts (bind phosphate)
- Aluminum in dialysate is now less of an issue

# Aluminum toxicity

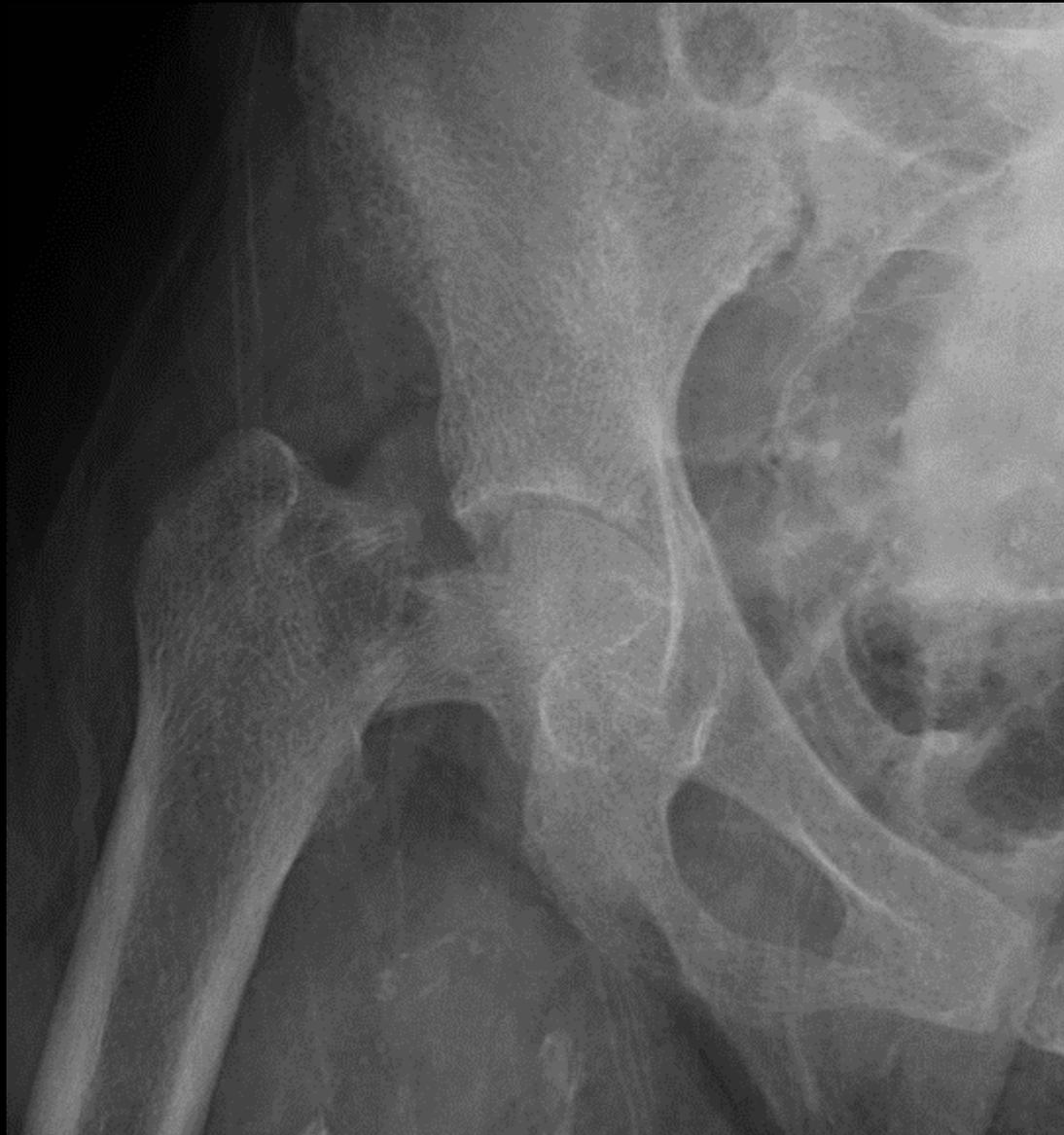
- Osseous
  - Osteomalacia
  - **Fractures** (ribs, vertebrae, pelvis, hips, sternum, clavicles)
  - Possible role in spondyloarthropathy, osteonecrosis
- Encephalopathy

# Amyloidosis 2° hemodialysis

- B2-microglobulin (B2-M)
- Three main forms:
  - Peripheral (arthopathy)
  - Destructive spondyloarthropathy
  - Carpal tunnel syndrome



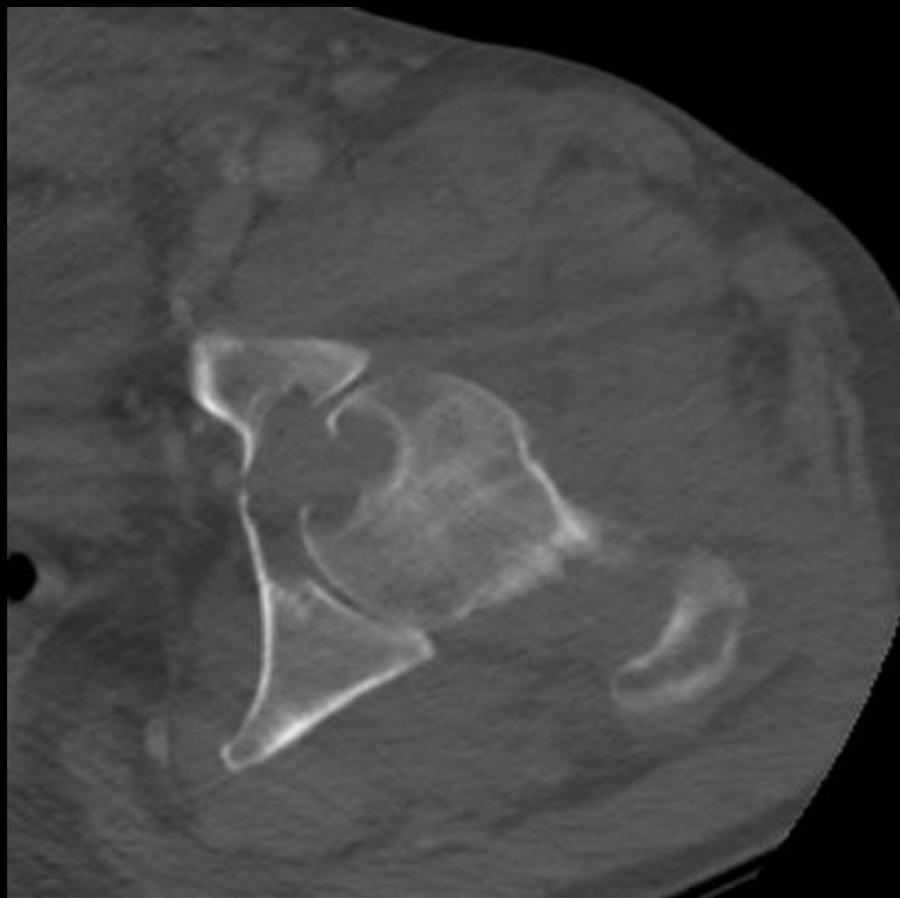
*Case courtesy Edward Smitaman*



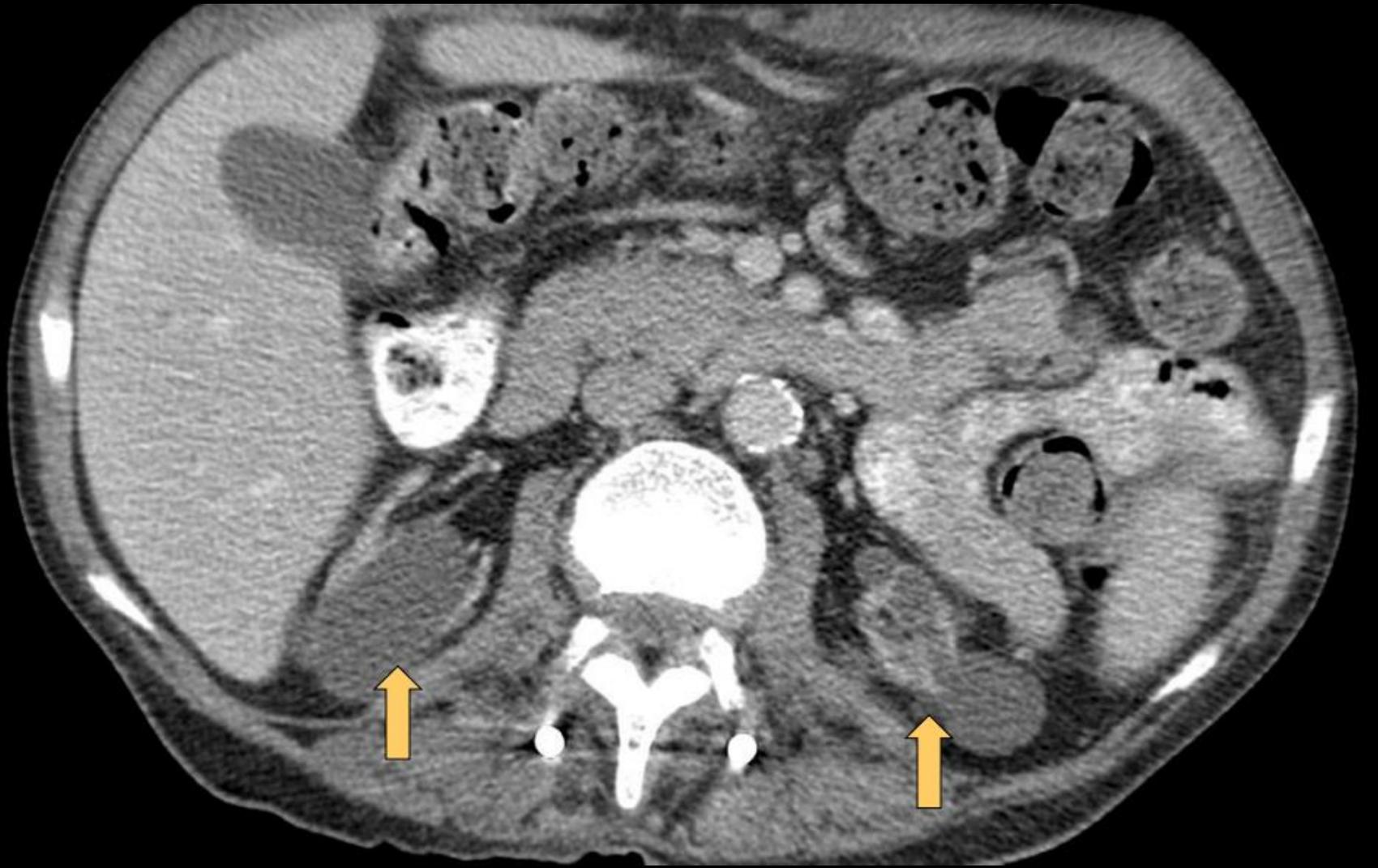
*Case courtesy Edward Smitaman*



*Case courtesy Brad Entwistle, UWO*



*Case courtesy Brad Entwistle, UWO*



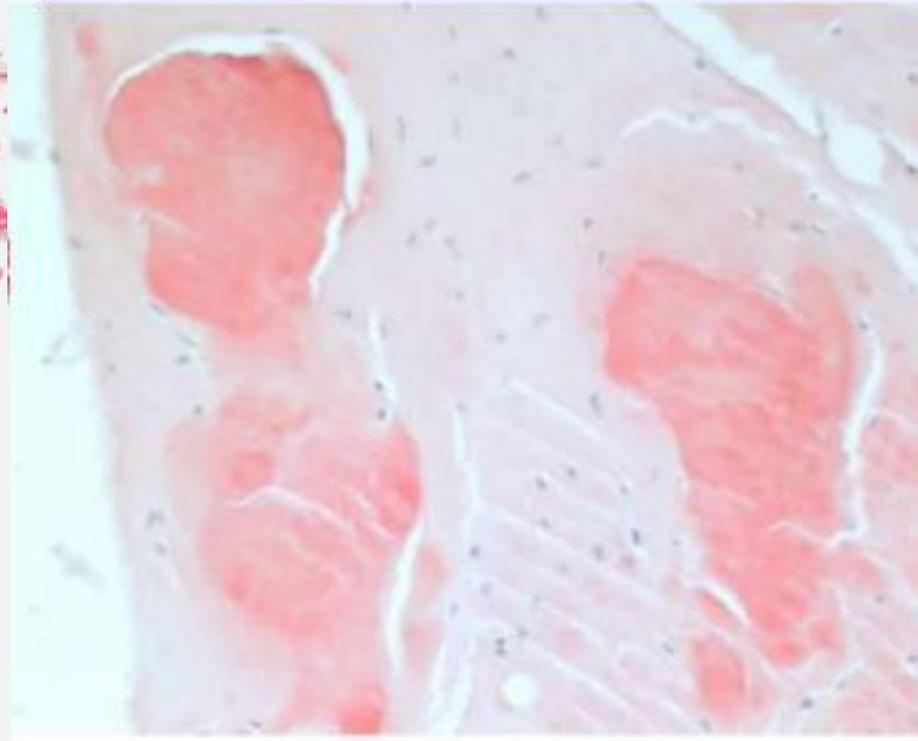
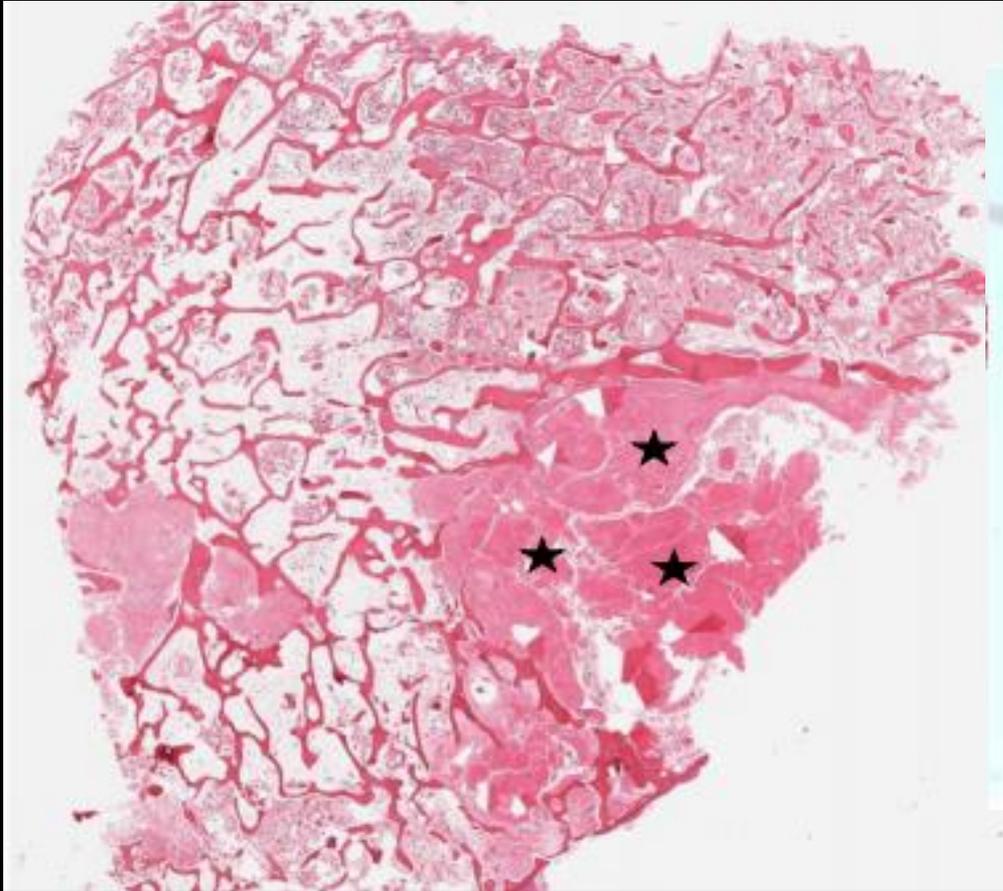
*Case courtesy Brad Entwistle, UWO*



*Case courtesy Brad Entwistle, UWO*



*Case courtesy Brad Entwistle, UWO*



*Case courtesy Brad Entwistle, UWO*

# Amyloidosis – peripheral arthropathy

- Chronic hemodialysis (> 5 years)
- Sites: hip, wrist, shoulder (periarticular location)
- Osseous and soft tissue involvement (includes bursa)
- May result in pathologic fracture
- Imaging:
  - Joint space narrowing late feature
  - May show low T2 signal

# Destructive spondyloarthropathy

- Chronic hemodialysis (> 4 years)
- B2-M deposition in disc and posterior elements
- Other predisposing factors?
  - Parathyroid mediated subchondral bone resorption
  - Aluminum

# Destructive spondyloarthropathy

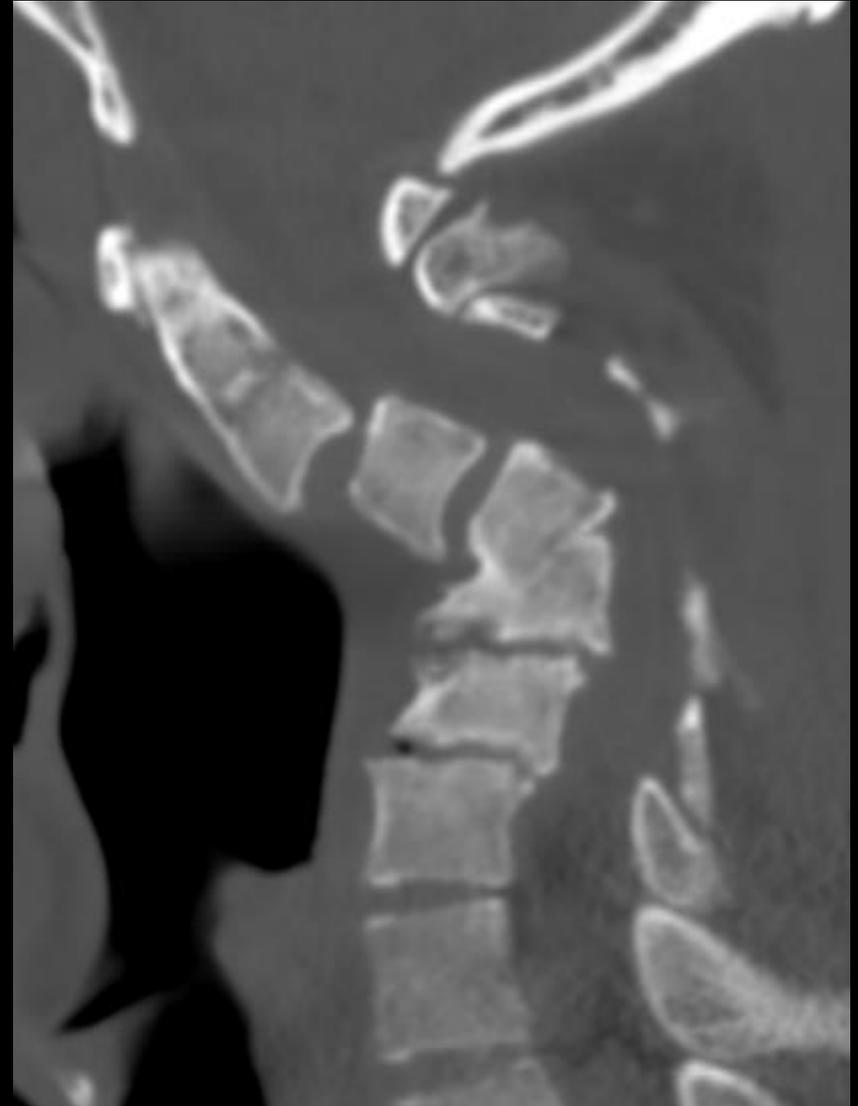
- Key findings:
  - Disc space narrowing
  - End plate erosions
  - Lack of osteophytes
  - Low T2 signal
  - No fluid collections



*Case courtesy Eman Alqahtani, UCSD*

# Destructive spondyloarthropathy

- Key findings:
  - Disc space narrowing
  - End plate erosions
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*Case courtesy Eman Alqahtani, UCSD*

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*Case courtesy Eman Alqahtani, UCSD*

# Destructive Spondyloarthropathy

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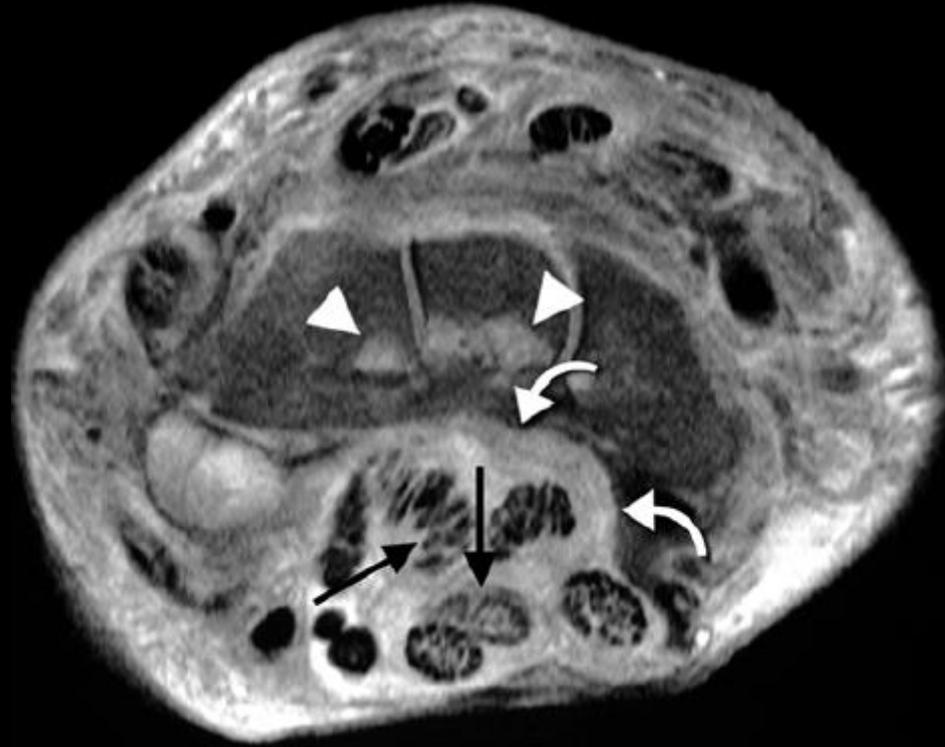
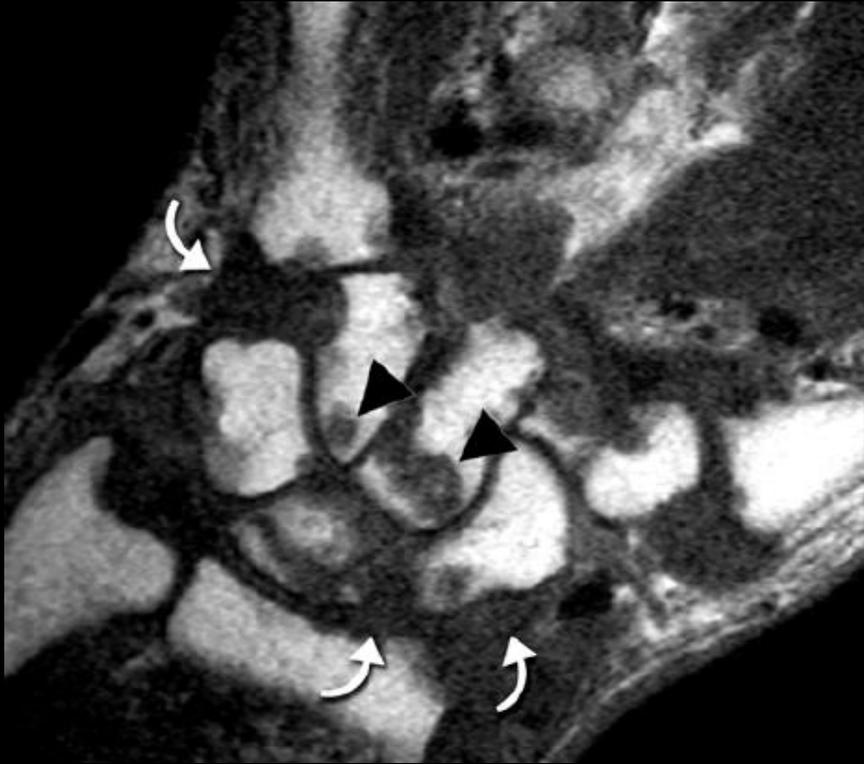


# Destructive Spondyloarthropathy – summary

- Sites: lower C-spine, craniocervical
- May be multilevel
- Often shows low T2 signal
- Rapidly progressive (months)
- Ddx
  - Early: ankylosing spondylitis
  - Advanced: infection, crystal

# Amyloid – carpal tunnel

- > 50% of patients with 10+ years dialysis
- Most common surgical indication in chronic dialysis
- **Median** > ulnar nerve
- Imaging:
  - Cysts (lunate, scaphoid), joint space preserved
  - Volar involvement > dorsal



# Dialysis-related Amyloidosis - Summary

- B2 microglobulin
- Three manifestations:
  - Peripheral arthropathy
  - Destructive spondyloarthropathy
  - Carpal tunnel syndrome
- **Chronic dialysis** (5+ years)

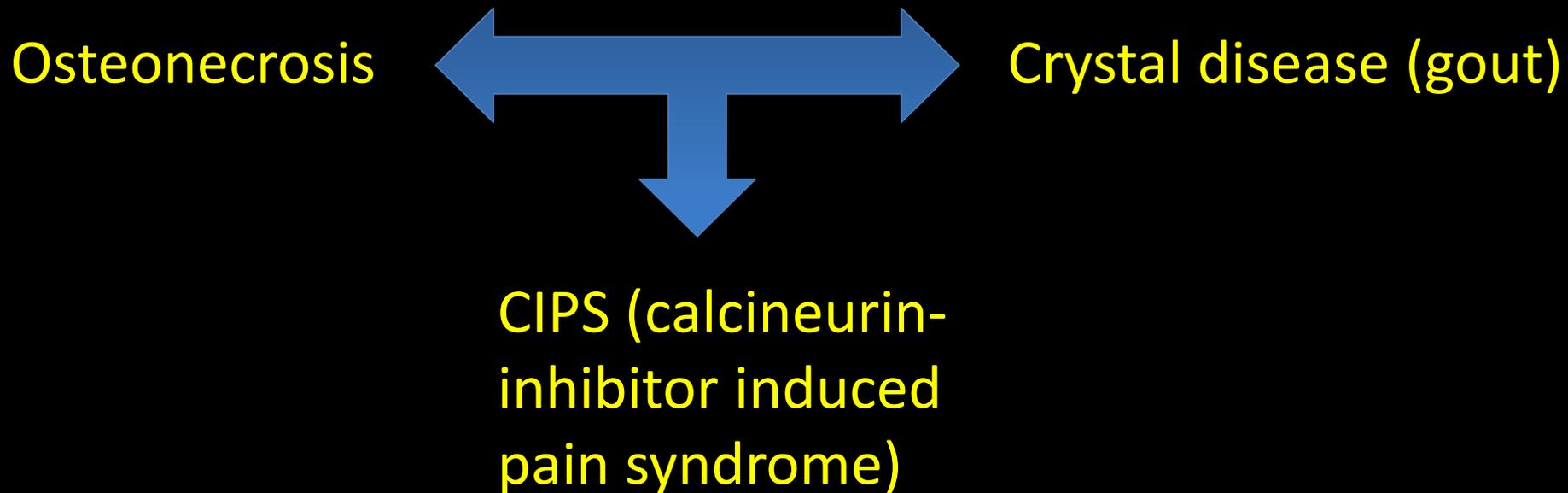
# Erosive Arthropathy of Dialysis

- Avg 5 years of dialysis
- Probably multifactorial
  - HPT, amyloid, CPPD, aluminum
- Hands/wrists
  - Radiocarpal, MCPs, **DIPs**
- Erosions with narrowing of joint space





# Bone Disease Post Renal Transplantation



# Osteonecrosis following renal transplantation

- Frequency of ON following transplantation has dramatically decreased with cyclosporine and tacrolimus
- 2 studies:
  - 232 patients → 11 with ON (4.7%)
  - 326 patients → 15 with ON (4.6%)

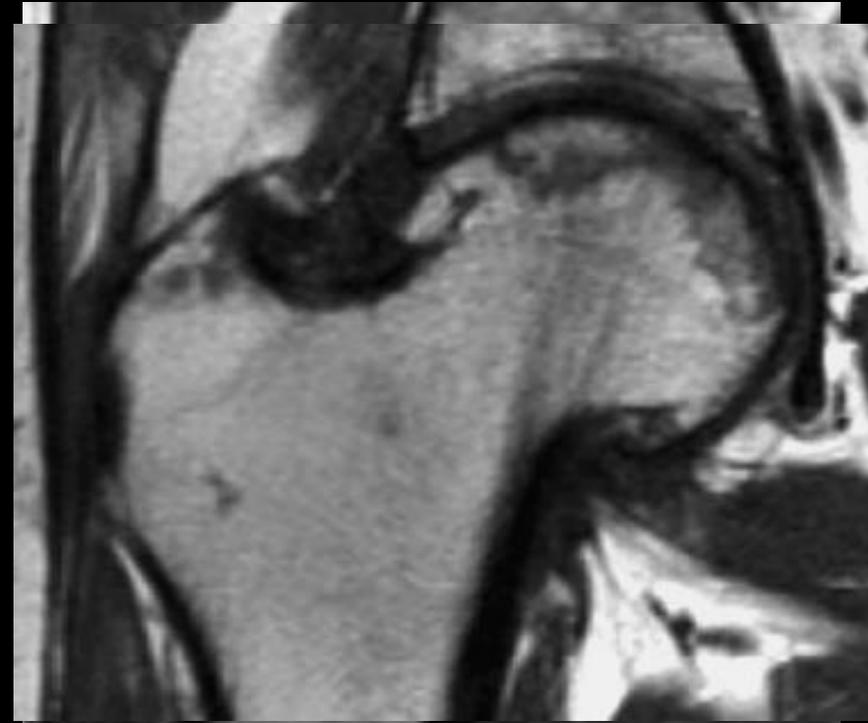
*Takao et al. Rheumatol Int. 2011;31:165-170*

*Hedri et al. Transplant Proc. 2007 May; 39(4): 1036-8*

# ON following renal transplantation

- Main risk factors
  - Cumulative steroid dose
  - Acute rejection
- Hip > knee
- Timing
  - 6 months onward (avg 3.5 years post transplant)

# Osteonecrosis



*Van De Berg et al. Eur J Radiol. 2006;58*

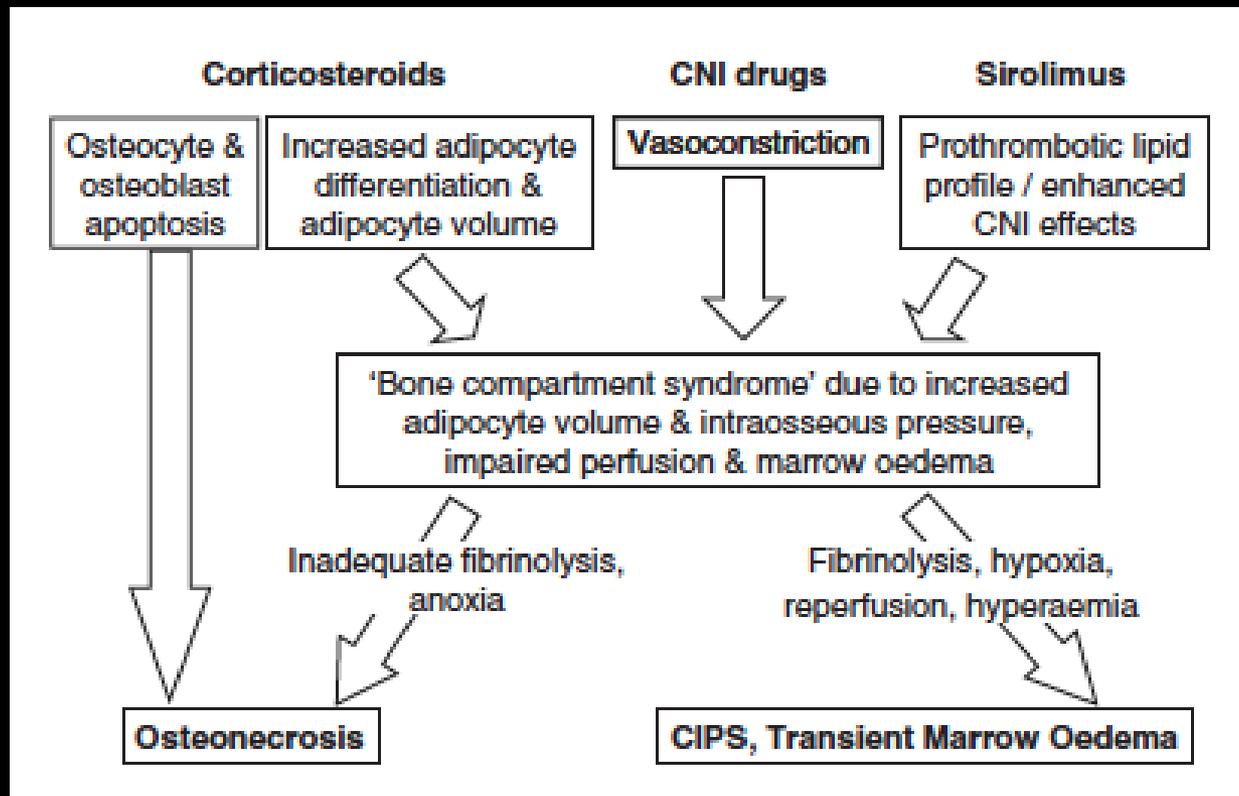
- In patients treated with steroids, osteonecrosis more common when femoral neck and intertrochanteric region contain more fat

# Calcineurin-inhibitor induced pain syndrome (CIPS)

- Reversible symmetric lower extremity pain following transplantation
- 1989 → cyclosporine
- 2001 → tacrolimus
- Solid organ and bone marrow transplant
- Frequency: 1.5-14%
- Timing: several weeks to > 1 yr post transplant

# CIPS

- Mechanism(s):
  - Altered vascular tone & permeability → marrow congestion
  - Altered bone metabolism → elevated alkaline phosphatase (ALP)



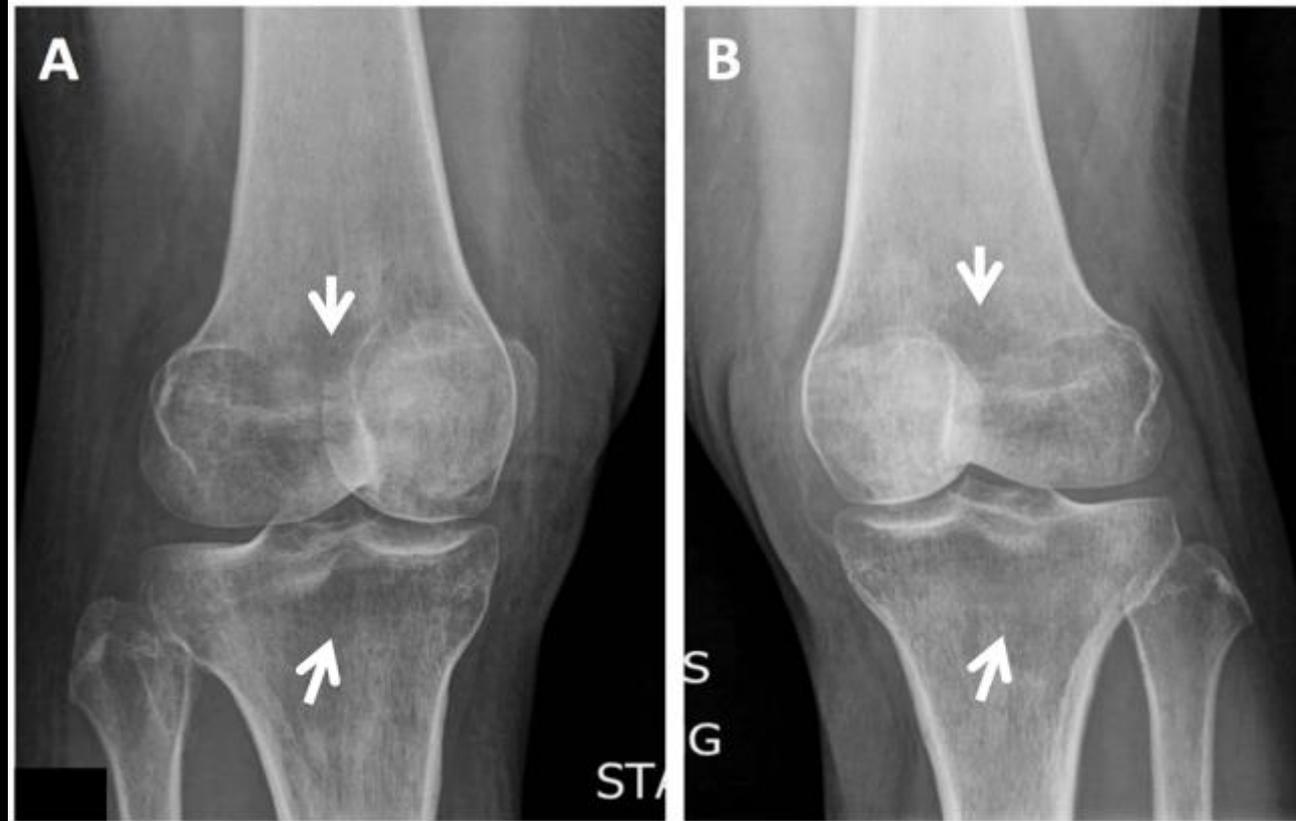
# CIPS

- Workup
  - Calcineurin-inhibitor serum level
    - Normal in first 3 months (5-15 ng/dL)
    - Trough levels not always elevated
  - Alkaline phosphatase (ALP)

# CIPS - Imaging

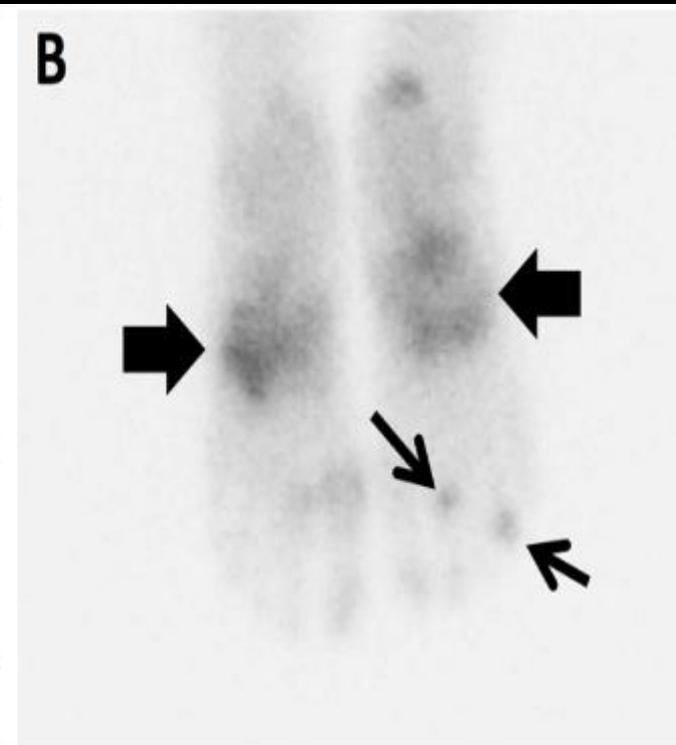
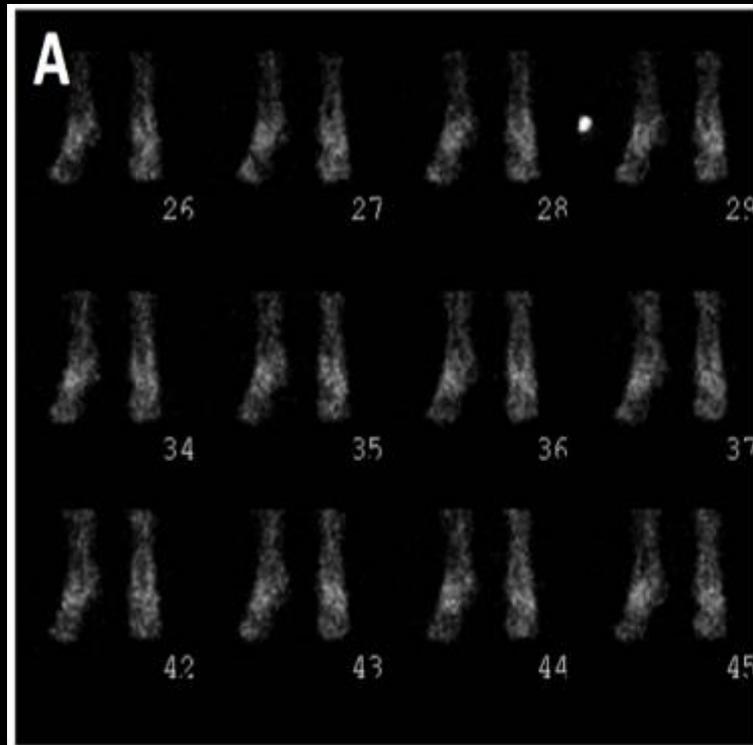
- Xrays:

- May be normal
- Epiphyseal osteoporosis
- Metaphyseal periosteal reaction
- Effusions
- Findings may persist following resolution of symptoms



# CIPS - Imaging

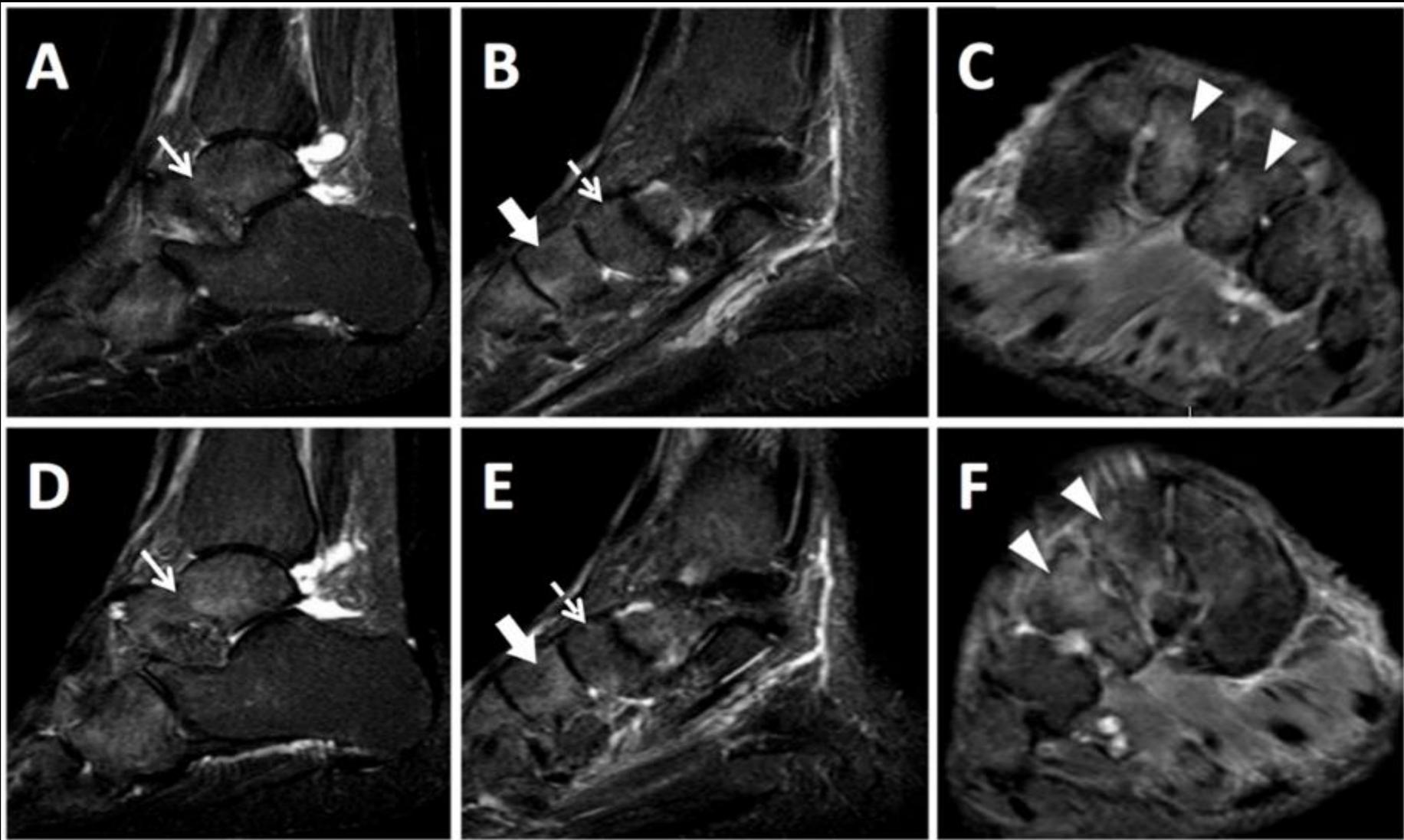
- Scintigraphy:
  - Uptake in flow and delayed phases



# CIPS - Imaging

- MRI
  - Edema around knees, ankles, feet (dependent)
  - Symmetric
  - Associated fractures
  - Findings may outlast symptoms

# CIPS – MR Imaging



# CIPS - Treatment

- Calcium channel blocker (amlodipine)
- Alteration in immunosuppressive regimen

# CIPS

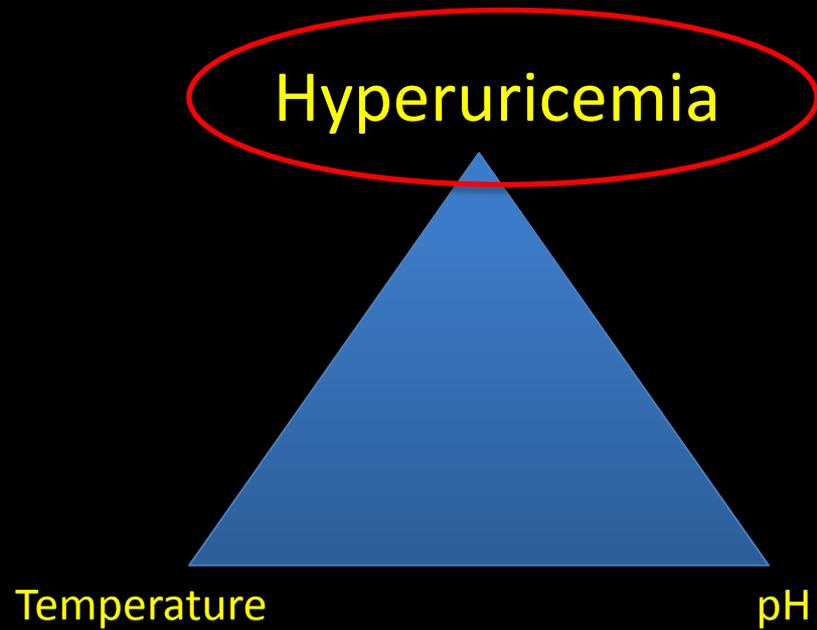
- DDX
  - Osteonecrosis
  - Complex regional pain syndrome/RDS
  - Transient osteoporosis
  - Infection

# Gout Following Renal Transplantation

- 7.6% - frequency of newly diagnosed gout within 3 years of renal transplantation (United States Renal Data System)
- Risk Factors
  - Males, age
  - BMI
  - Cyclosporine vs. tacrolimus
  - GFR (<44)

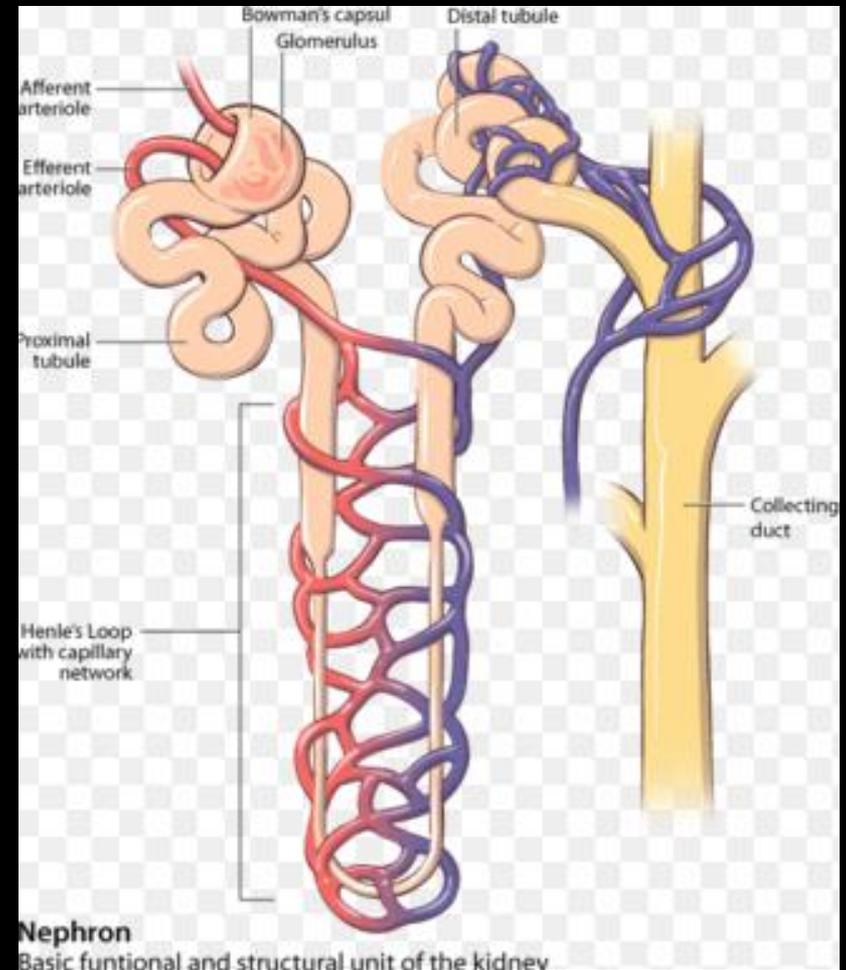


# Gout - Physiology



# Hyperuricemia in Renal Transplantation

- Cyclosporine > tacrolimus
  - Increased uric acid reabsorption
  - Decreased uric acid secretion
- Other factors
  - Diuretics
  - Poor graft function



# Gout - Distribution

- Classic sites:
  - 1<sup>st</sup> MTP, TMT, CMC, popliteal groove
- Post renal transplantation:
  - May see more proximal distribution
  - Increased burden of tophi







# Post Renal Transplant Bone Disease - Summary

- **Osteonecrosis** – incidence has dramatically decreased (~5%)
- **CIPS** – symmetric dependent lower extremity pain, marrow edema on MRI +/- fractures
- **Gout** – calcineurin-inhibitors predispose to hyperuricemia and more proximal distribution may be seen

Thank you!



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