Sickle Avascular Necrosis

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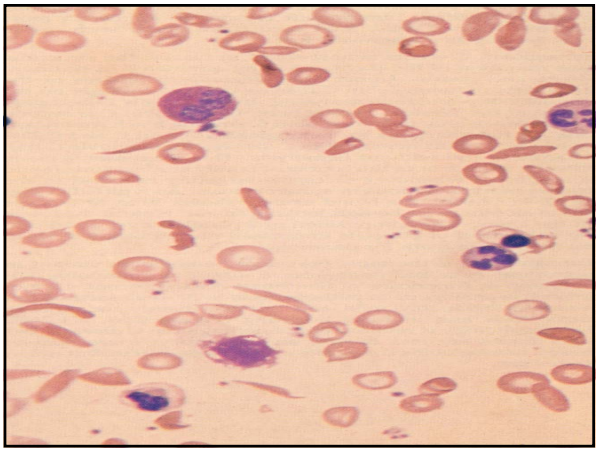
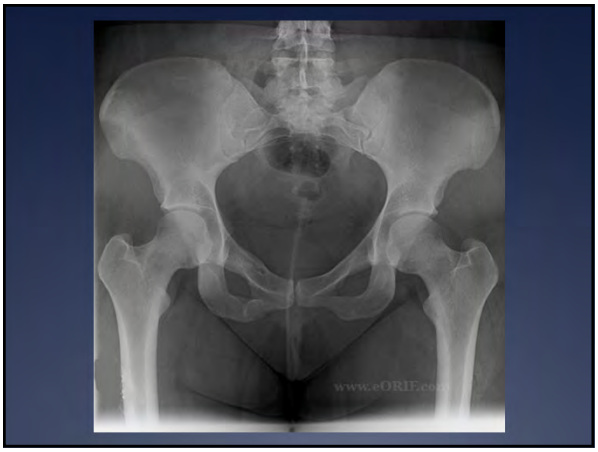
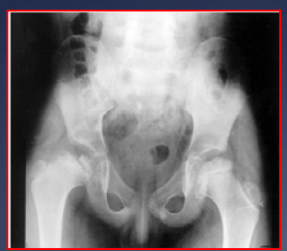
Objectives

- Definition, epidemiology
- Pathophysiology
- Clinical Presentation
  - diagnostic tools
  - classification
- Public Health burden
- Treatment options
- Research opportunities

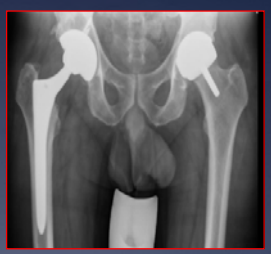




Avascular Necrosis of Femoral Heads



Bilateral Femoral Arthroplasty



What do they have in common?

Avascular Necrosis Definition

- **Osteonecrosis, Aseptic necrosis, ischemic bone necrosis,**
- Complete disruption of vascular supply to the articular surfaces and ends of long bones,
- Cellular death (necrosis) of bone due to interruption of the blood supply.
- **Osteonecrosis is bone death caused by poor blood supply to the area.**

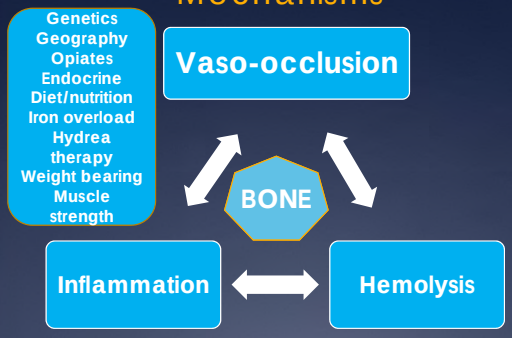
Epidemiology

- **Femoral head > shoulder > knees**
- **Can occur in any bone with blood supply**
- **Extremely common, starts early**
  - **26% by age 10y**
  - **48% by 27y**
  - **>50% prevalence by age 35y**
- **4y progression rate of 67%**
- **Bilateral in 41-90%**
- **Progression to collapse in 3-5y**

Pathophysiology

- Obstructed perfusion
- Ischemia -> Necrosis
- Hemolysis -> NO deficit-> Oxidant stress
- Inflammation – Edema -> Increased intra-osseous pressure
- Failure of weight bearing
- Collapse of joint/bone

Mechanisms



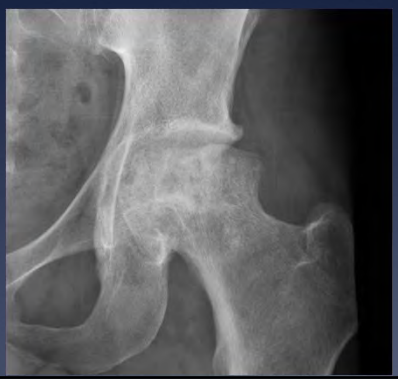
Risk Factors for AVN

- Male
- High Hgb
- Low Hgb F
- Vitamin D deficiency
- Frequent VOC
- Alpha thal trait

Case I

- 16y Hgb SC,
- Frequent VOC, psychiatric symptoms
- Chronic knee pain
- Severe Headaches
- Unable to stand up straight
- Neurology referral
- Hip AVN

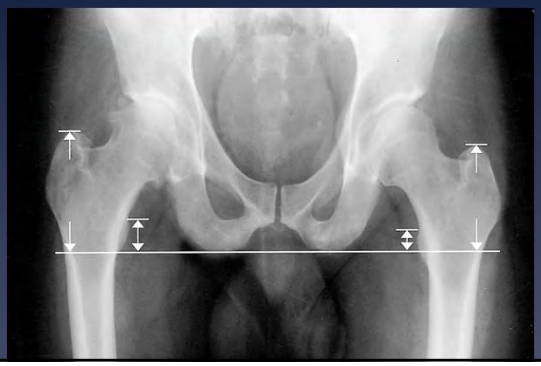
Case I



Case II

- 14y Hgb SS, Abnormal TCD, delayed puberty
- Chronic transfusion x 4 years
- Weaned to Hydrea
- Limping, no admits for pain x 4years
- Home Pain diary showed daily pain after school
- PE – unequal limb length

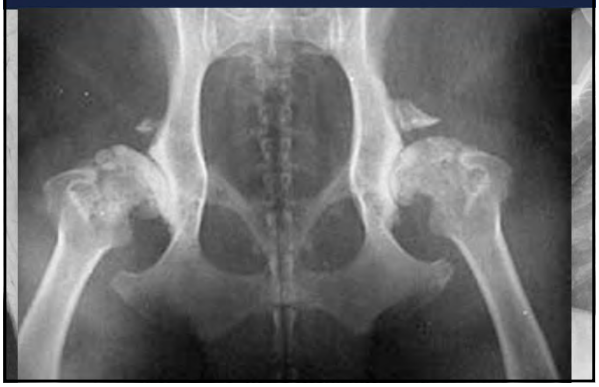
Case II



Case III

- 17y Hgb SS, recurrent ACS
- Early Retinopathy since 7y
- Frequent VOC, gall stones
- Short Stature and delayed growth
- Vitamin D deficiency
- On Hydrea with good response
- Playing on inflatable gym → hip dislocation

Case III



Clinical presentation

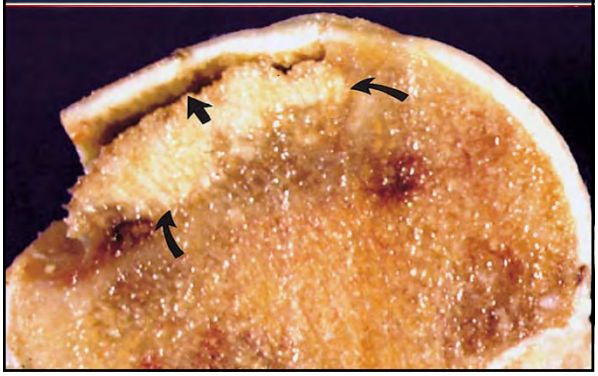
- Variable
- X-ray and symptoms don't always match up
- Pain in back, hip, knee, ankle or shoulder
- Reduced Range of Motion at joint
- Limp, "popping sound"
- Limb length discrepancy

FICAT STAGING

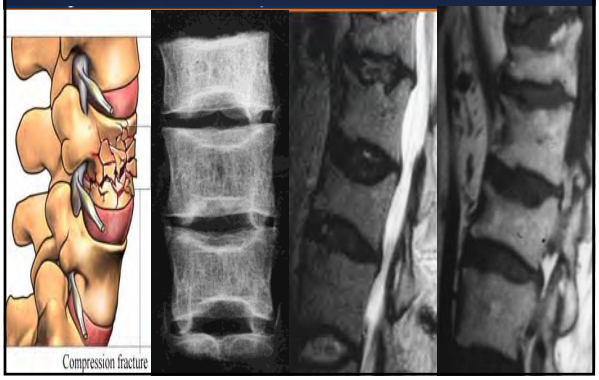
	Pain	X-ray image	Magnetic resonance image
Stage I	+	Normal	+
Stage II	+	Changes on bone trabeculate with sclerosis or osteolysis areas	+
Stage III	+	Osteochondral fracture with sequestrum and flattening of the head	+
Stage IV	+	Advanced lesions	+

Table 1 – Classification by Ficat et Arlet[10] and Steingberg[11]

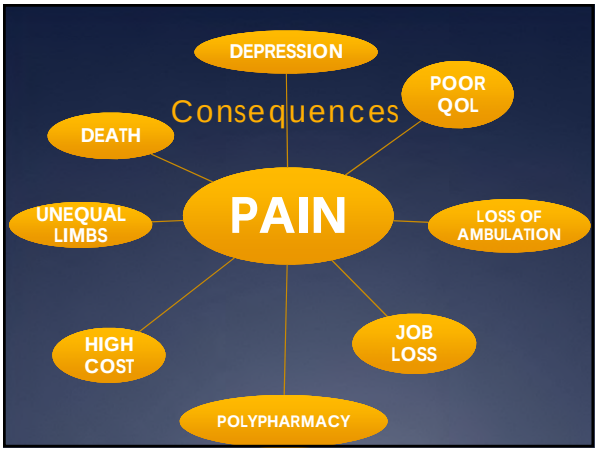
Avascular Necrosis



Compression fractures- fish mouthing



Consequences



Treatment

- Physical Therapy
  - Strengthen limb girdle, joint
  - Flexibility
  - Re-perfusion and healing
- Non weight bearing
  - If advanced/collapse
- Core decompression +/- osteotomy
  - Inject stem cells
- Hip replacement
  - Longevity limited 10-15y, failure
  - Location (poor in shoulder)
  - Muscle imbalance, joint instability, length discrepancy,

What do they have in common?

Differences

- Older (>50y)
- Caucasian
- Female
- No hemoglobinopathy
- Insurance
- Drinks milk
- Prevention possible
- Young (<20y)
- African descent
- Male
- Sickle Cell Disease
- Self pay
- Lactose Intolerance
- No data on effective prevention – YET!

What do they have in common?

Similarities

- Osteoporosis
- Hip replacement
- Chronic back/limb pain
- Wheelchair confined
- Poly pharmacy pain meds
- High risk of fall, death
- Osteoporosis
- Hip replacement
- Chronic back/limb pain
- Wheelchair confined
- Poly pharmacy pain meds
- High risk of fall, death

Take Home

- **AVN is VERY common in SCD**
- **Occurs as early as age 7y**
- **May be asymptomatic in early stages**
- **X-ray may miss early stage**
- **All SCD genotype are at risk**
- **No proven prevention**

Research directions

- Epidemiology in era of Hydroxyurea
- GWAS to identify gene polymorphisms e.g. BMP
- Mouse models of bone disease
- Perfusion imaging of target bone
- Platelet pore plasma injected into core
- others

Resources

- **www.scinfo.org**
- **www.cdc.gov/ncbddd/sicklecell/**
- **www.choa.org/sicklecell**