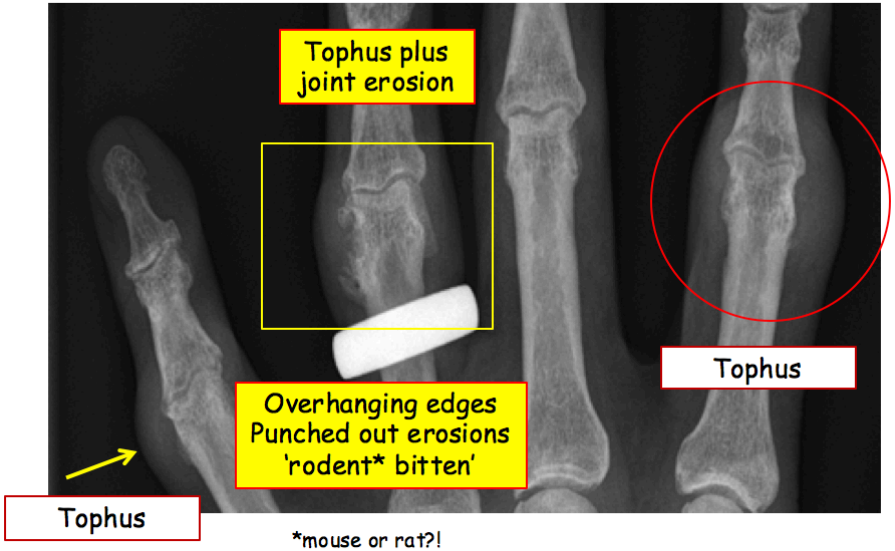
Podcast (Video Recorded Lecture Series):
Gout for the USMLE Step One Exam



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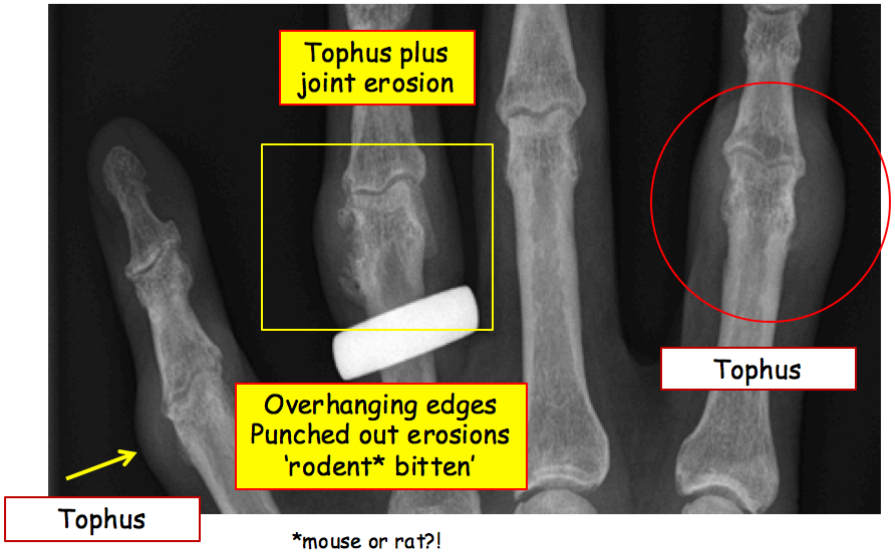

Tutorial Services

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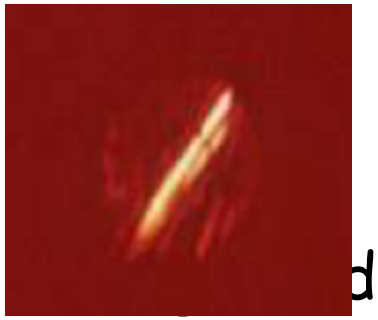
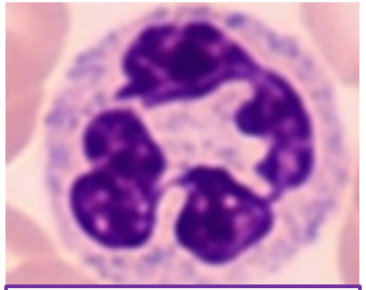


Crystal Arthropathy: Gout

- d:



LKTB4; IL-8; C5a

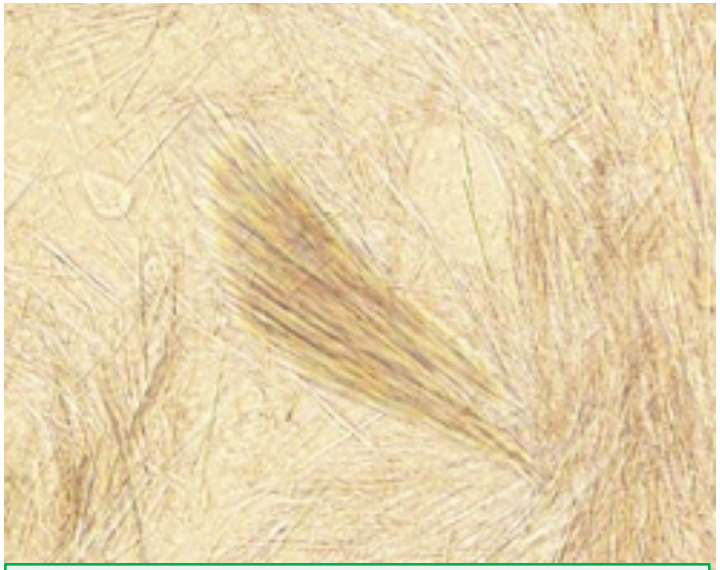
- What will these patients complain about?: Acute pain, swelling, redness
- Stick a needle in it…what will we find?: Monosodium urate crystals
- What won't we find?: Organisms
- Lots of diseases cause joint swelling and pain. How do we know it isn't:
  - Systemic Sclerosis?
  - OA?
  - Overuse Syndrome/Bursitis?

  } Because we're not idiots.

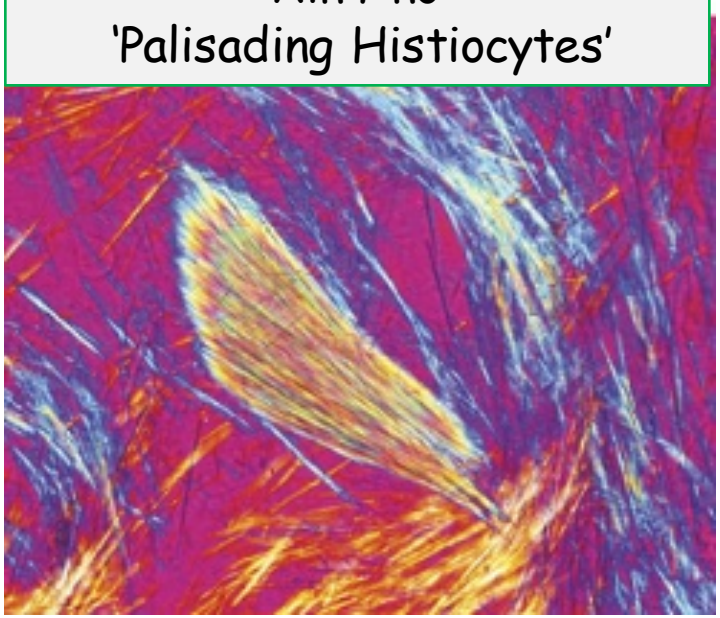
  - Pseudogout?
  - Septic Arthritis?

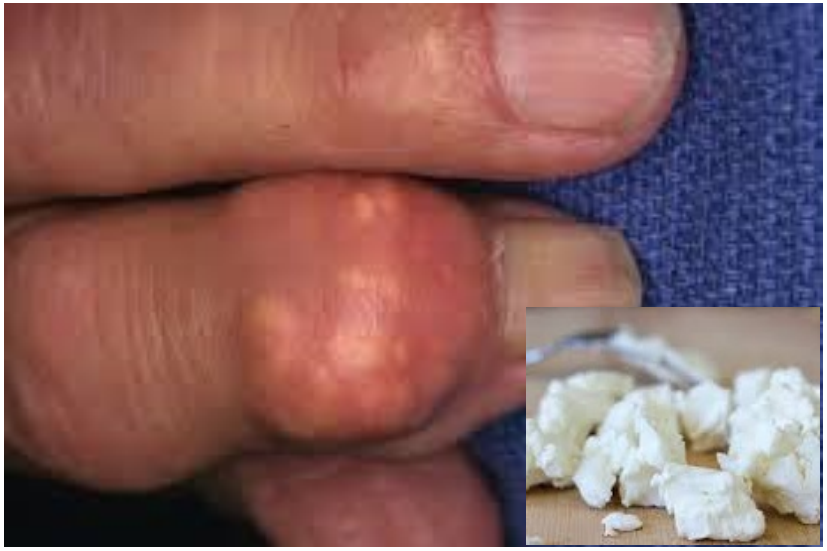
  } Synovial fluid analysis

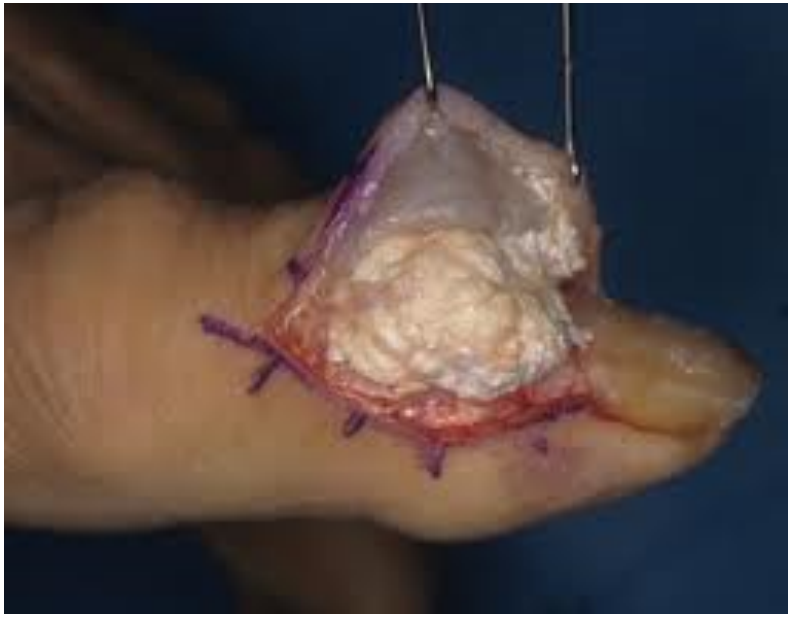
- Difference between a tophus and a rheumatoid nodule?: Next slide please…

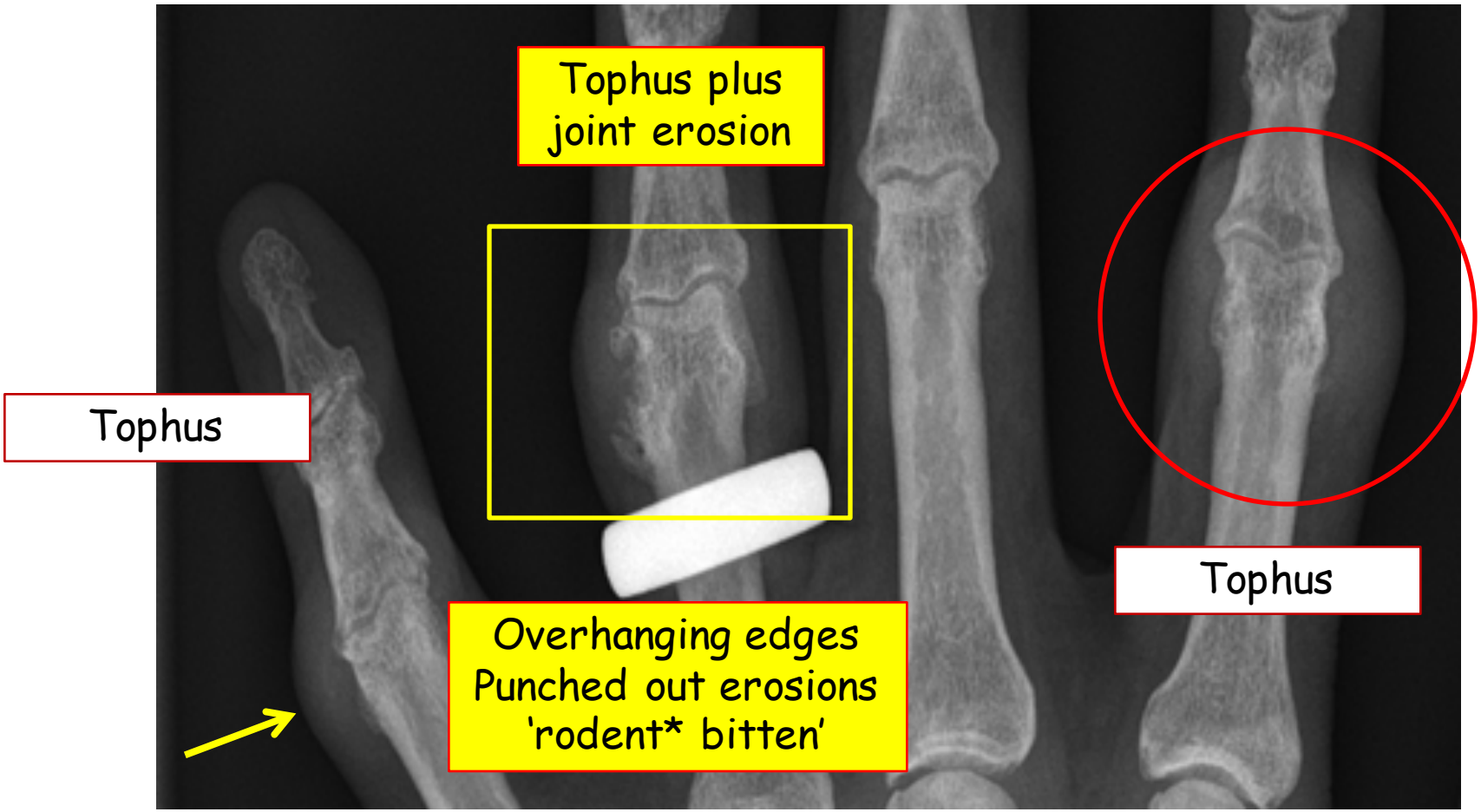


Ain't no
'Palisading Histiocytes'

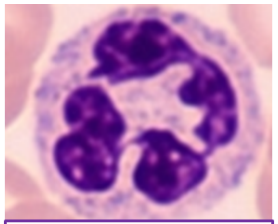






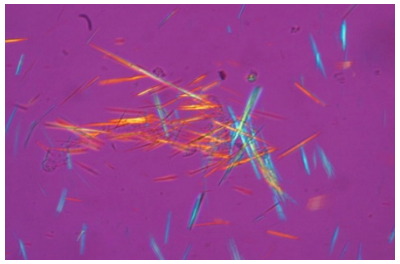

Tophus plus joint erosion
Tophus
Tophus
Overhanging edges
Punched out erosions
'rodent* bitten'

*mouse or rat?!



LKTB4; IL-8; C5a

Pathology, Gout

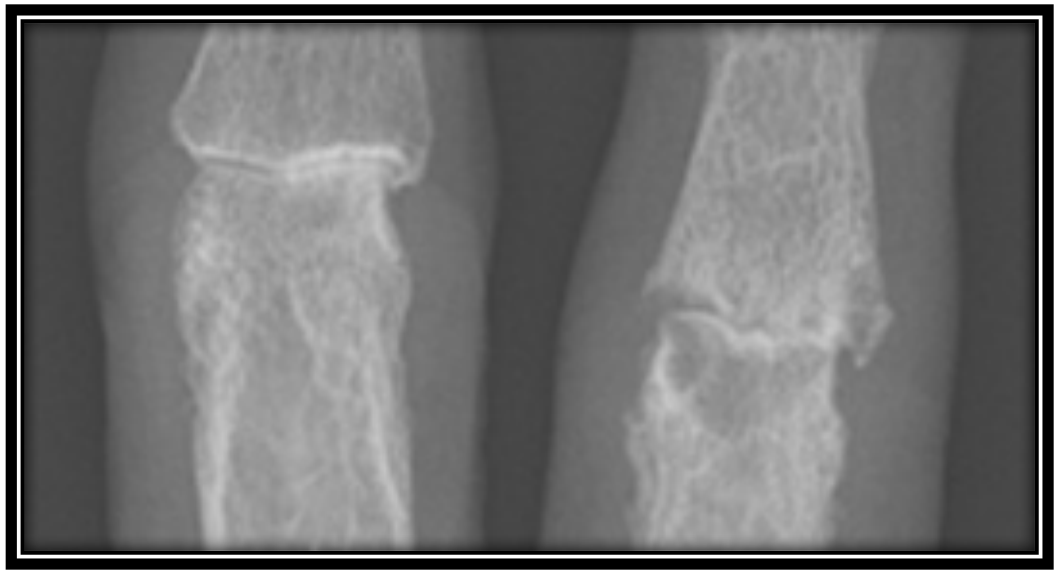


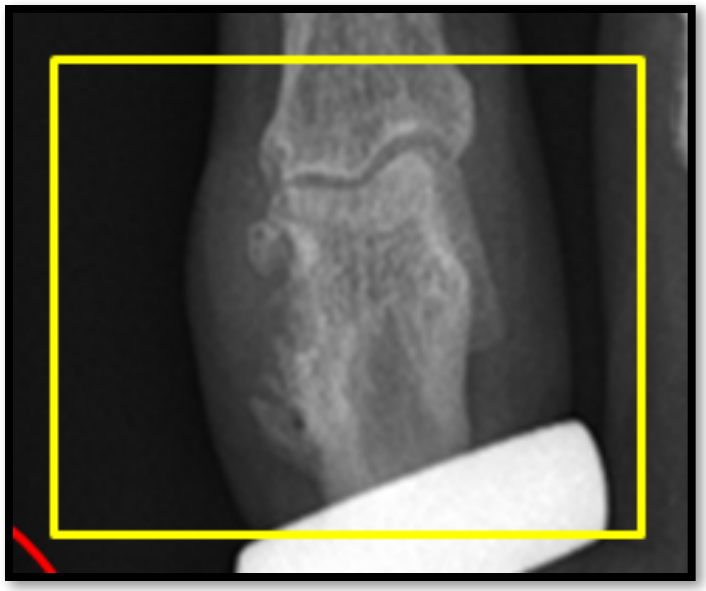
- Background:
  - Acute mono- or polyarticular arthritis; recurrent episodes
  - Foot most common; chronic disease a/w tophi

Test	Result
CRYSTALS SYNOVIAL FLUID	Monosodium Urate
Both intracellular and extracellular crystals present.	

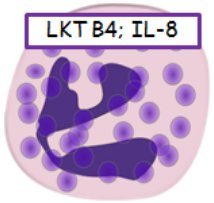
- Pathology/Pathogenesis:
  - Monosodium urate accumulates in the synovial fluid and forms crystals that deposit in synovium and cartilage
  - Uptake of monosodium urate crytals activate synovial cells releasing C5a, which is chemotactic for PMN
  - The crystals are phagocytized by PMNs leading to free radical release & cytokine production.

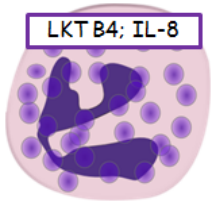
Gout: an inflammatory, erosive arthropathy

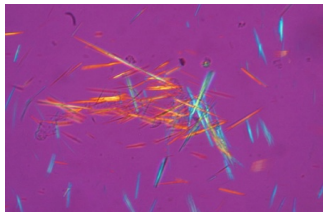




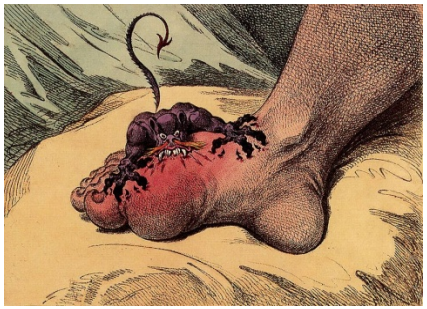
'Punched-out' erosions with sclerotic margins in a juxta-articular distribution with overhanging edges.



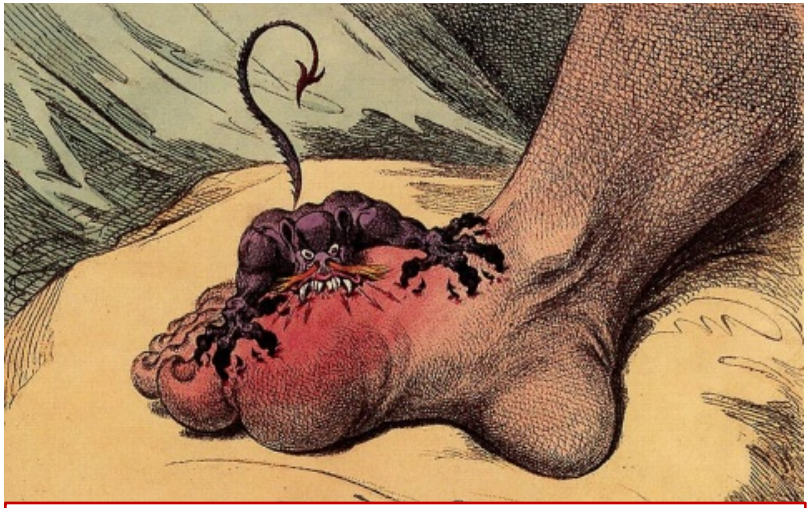




Crystal Arthropathy: Gout

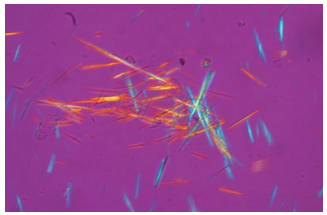


- Presentation:
  - Podagra (classic), foot/ankle, acute & severe true arthritis

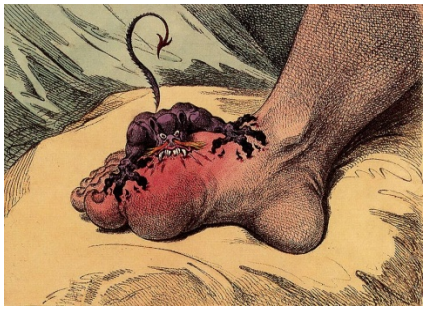


Foot Seizure

1250–1300; ME < L < Gk podágra lit., foot-trap =pod-pod - +ágra a catching, seizure

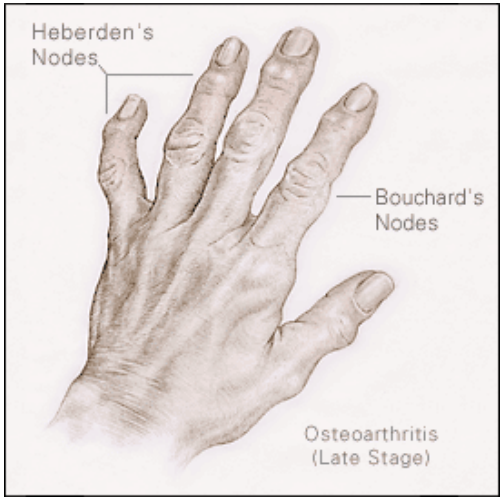


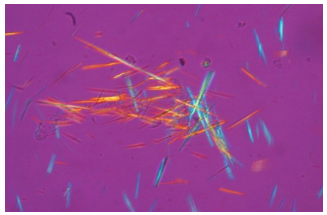
Pathology, Gout



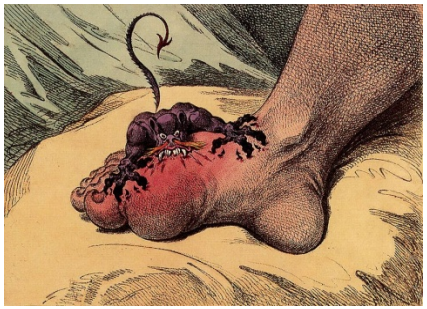
- Presentation:
  - Podagra (classic), foot/ankle, acute & severe true arthritis

Do you see that little gremlin in OA?





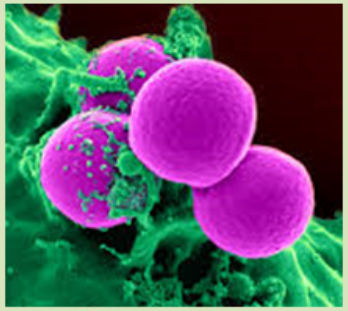
Pathology, Gout

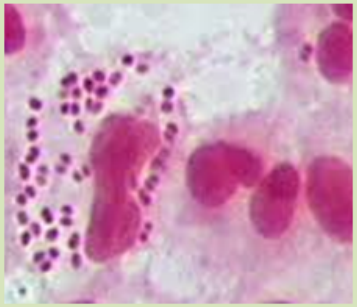


- Presentation:
  - Podagra (classic), foot/ankle, acute & severe true arthritis

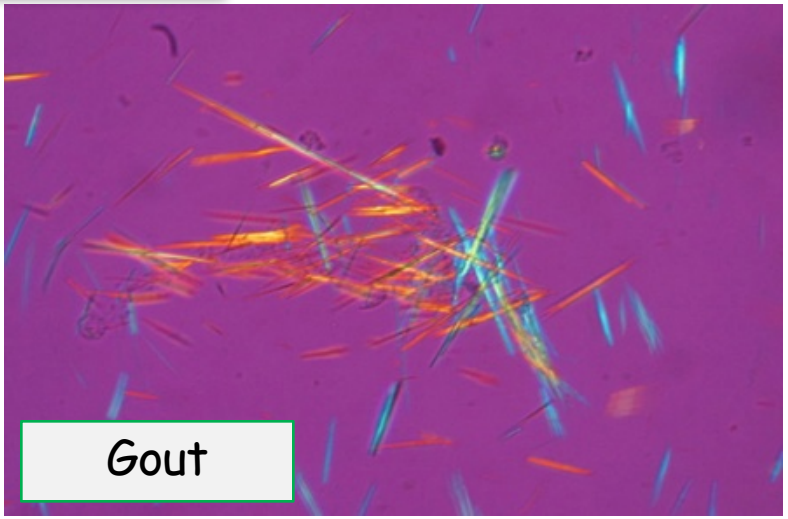
- Diagnosis:
  - Synovial fluid analysis
    - Inflammatory, no BUGS, MSU crystals (+); (not uric acid)
    - Crystal is YELLOW (negative birefringence w/ polarizing lens)
  - Hyperuricemia is NOT a diagnostic criteria; it is generally elevated and used to monitor hypouricemic therapy.
  - Diff Dx: Pseudogout, Septic arthritis

Septic

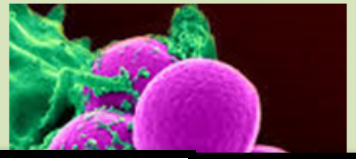




ψ-gout

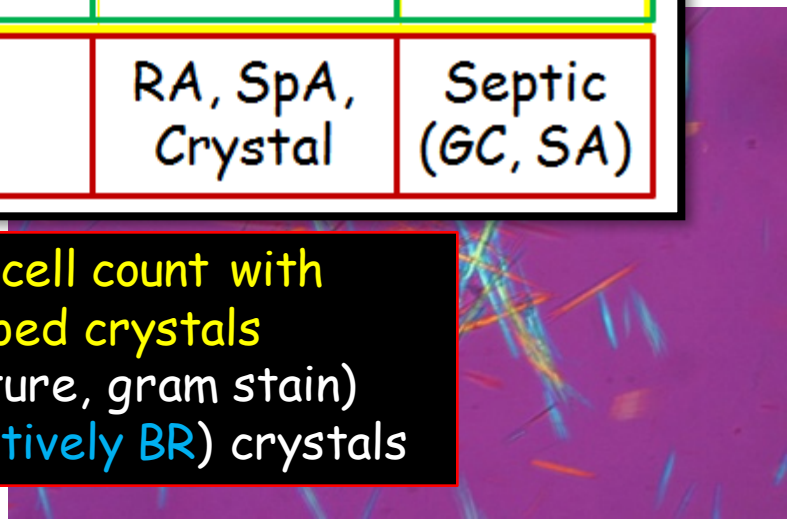


Gout



Osteoarthritis	Straw/ Yellow	<3000
Inflammatory Crystals, SSp, RA, Lyme	**Yellow**	>3000
Staph, GC	Mixed	>50,000

		Non-inflammatory	Inflammatory	Septic
		Clear to yellow	Yellow	Variable
		Transparent	Translucent	Opaque
WBC/mm^3	<200	200-2000	2000-75000	>100,000
PMNs	< 25%	<25%	>50%	>75%
		OA	RA, SpA, Crystal	Septic (GC, SA)



Inflammatory cell count with
Needle shaped crystals
No bugs (on culture, gram stain)
No rhomboid (positively BR) crystals

Pathology, Gout

- Etiology:
  - Primary assoc w/ Lesch-Nyhan (X-linked rec; deficiency of HGPRT; salvage pathway of purines): MR, hyperuricemia, self mutilation)
  - Secondary: ↓ excretion of U.A. (90%; assoc w/ lead, alcohol) or overproduction (minority; tumor lysis syndrome)

Kidney is primary means of eliminating uric acid

Hypoxanthine-guanine phosphoribosyltransferase

Pathology, Gout

- Etiology (related to drugs):
  - Primary assoc w/ Lesch-Nyhan (X-linked rec; deficiency of HGPRT; salvage pathway of purines): MR, hyperuricemia, self mutilation)
  - Secondary: ↓ excretion of U.A. (90%; assoc w/ lead, alcohol) or overproduction (minority; tumor lysis syndrome)

Mechanisms:

Thiazides: compete with U.A. for organic anion transporter (OAT).

Did you know that thiazides get pumped into tubular lumen?

If they ARE getting pumped into the lumen,
uric acid is NOT → hyperuricemia

Pathology, Gout

- Etiology (as related to Rx):
  - Primary ass… rec; deficiency of HGPRT; salv… , hyperuricemia, self mutilation)
  
  - Secondary: … oc w/ lead, alcohol) or <u>overproduction</u> (minority; tumor lysis syndrome)

Probenecid:

1. Uricosuric drug, inhibit urate-anion exchange in PCT
2. Rarely used. Main issue for USMLE:
   - Ineffective in CKD and tumor lysis syndrome
   - Contraindicated if uric acid stones (increases urinary urate).
   - Indicated (?): Young hypoexcretor without contraindication

Gout Rx: Acute
(that means not preventive)

- Acute:
  - NSAIDs/COX2
  - Colchicine
  - Prednisone

The questions are clear about preferred agents (ie. PUD/hives on NSAID, sulfa allergy, etc)

Gout Rx: Acute (that means not preventive)

- Acute (abortive rx):
  - NSAIDs/COX2 (celecoxib)
  - Colchicine
  - Prednisone

NSAID names to be familiar with:
Ibuprofen, naproxen, indomethacin
Diclofenac
Ketoralac

Colchicine:

(inhibits leukocyte motility and cytoskeletal microtubules)

- Colchicine is not an analgesic or a uricosuric agent.
- Antiinflammatory effect is due to decreased leukocyte motility and phagocytosis (Note: used for other inflammatory disorders).
  - PMN chemotaxis decreases within 12 to 24 hours
- Cytoskeletal functions are disrupted through inhibition of microtubule polymerization → prevents the activation, degranulation, and migration of neutrophils.

Language Bro

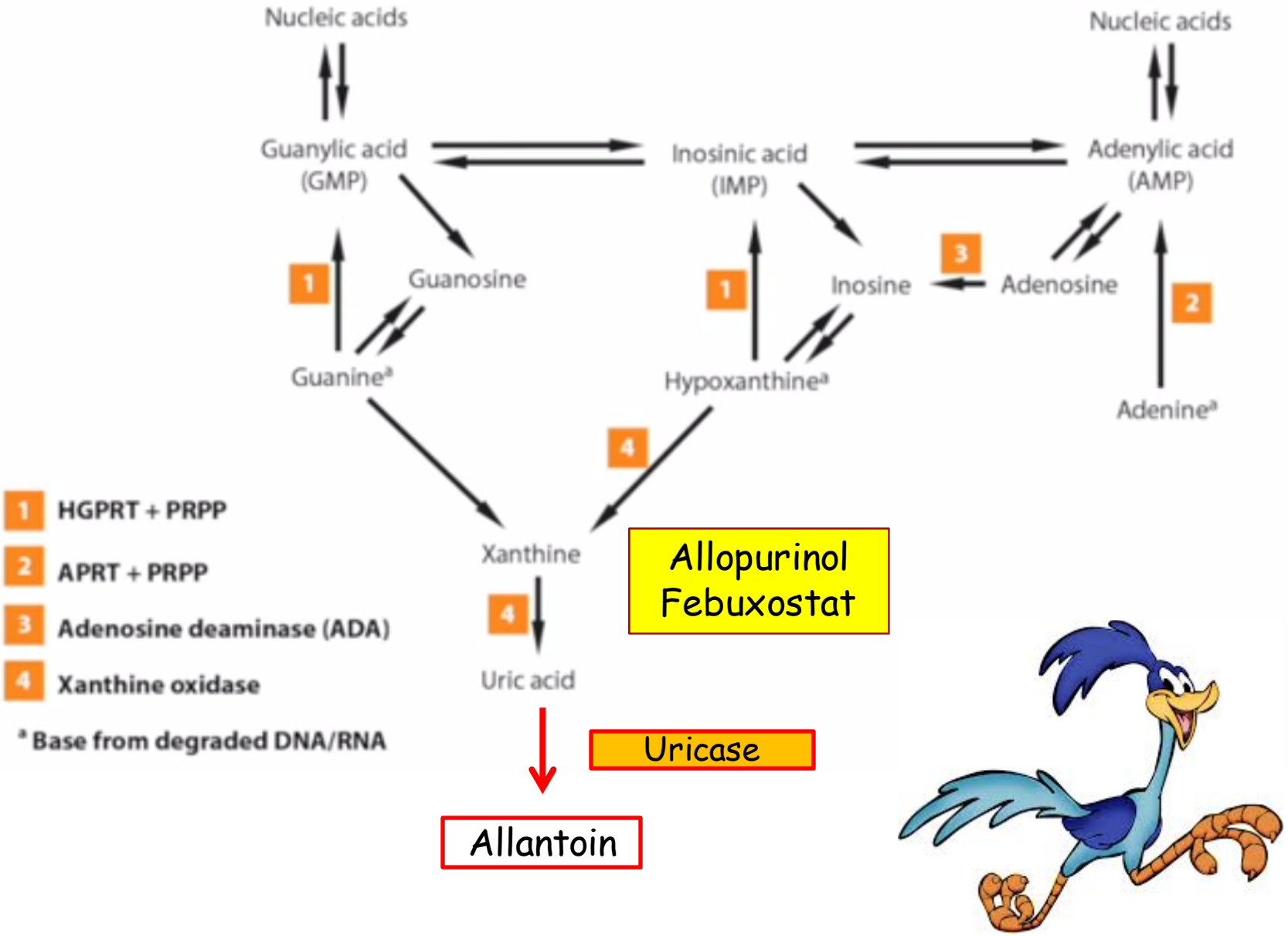
AE: diarrhea, nausea, abdominal pain

(e.g. patient w/ painful toe. Given med that caused diarrhea. The MOA of that agent includes…?

Gout Rx: Chronic Prevention (that means it doesn't abort acute attacks)

- Acute:
  - NSAIDs/COX2
  - Prednisone
  - Colchicine

- Prophylactic
  - Xanthine Oxidase Inhibitors (allopurinol, febuxostat)
  - Probenecid (requires normal GFR; contraindicated w/ uric acid stones)
  - Uricase (pegloticase, rasburicase)
    - For those who have failed (or have contraindication to) other therapies.
    - Treatment alternative in tumor lysis syndrome


Nucleic acids
Nucleic acids
Guanylic acid (GMP)
Inosinic acid (IMP)
Adenylic acid (AMP)
1
Guanosine
1
Inosine
3
Adenosine
2
Guanine[a]
Hypoxanthine[a]
Adenine[a]
4
1 HGPRT + PRPP
2 APRT + PRPP
3 Adenosine deaminase (ADA)
4 Xanthine oxidase
[a] Base from degraded DNA/RNA
Xanthine
4
Uric acid
Allopurinol
Febuxostat
Uricase
Allantoin

The patient presents with swelling of her wrist. PMH: recurrent UTI. Allergy: sulfa (hives).
Fluid is aspirated showing negatively birefringent crystals.
Which of the following is the most appropriate drug for the immediate treatment of the joint swelling in this patient?

1. Acetaminophen
2. Allopurinol
3. ASA
4. Codeine
5. Colchicine
6. Celecoxib

Patient with recurrent episodes of a disease that has radiographic features including juxta-articular erosions and overhanging edges. PMH: PUD, radiolucent nephrolithiasis. Allergies: hives on agent that inhibits conversion of hypoxanthine $\rightarrow$ xanthine; hives on agent that blocks bacterial conversion of PABA to folic acid. Data: GFR 21. Choose the appropriate therapy to decrease recurrent episodes:

A. MTX
B. Prednisone
C. Gold
D. Pegloticase
E. Probenecid
F. Indomethacin
G. Celecoxib
H. Fuboxistat

The patient presents with swelling of her wrist. PMH: recurrent UTI. Allergy: sulfa (hives).
Fluid is aspirated showing negatively birefringent crystals.
Which of the following is the most appropriate drug for the immediate treatment of the joint swelling in this patient?

1. Acetaminophen
2. Allopurinol: prevention
3. ASA (hi dose) → hyperuricemia
4. Codeine
5. Colchicine
6. Celecoxib: sulfa = hives

NSAID (indomethacin, naproxen, piroxicam, ketorolac) and prednisone are also appropriate first line.

Patient with recurrent episodes of a disease that has radiographic features including juxta-articular erosions and overhanging edges. PMH: PUD, radiolucent nephrolithiasis. Allergies: hives on agent that inhibits conversion of hypoxanthine → xanthine; hives on agent that blocks bacterial conversion of PABA to folic acid. Data: GFR 21. Choose the appropriate therapy to <u>decrease recurrent episodes</u>:

~~A. MTX~~
B. Prednisone
~~C. Gold~~
D. Pegloticase
E. Probenecid
F. Indomethacin
G. Celecoxib
H. Fuboxistat

Prophylactic

- Xanthine Oxidase Inhibitors (allopurinol, febuxostat)
- Probenecid
- Uricase (pegloticase, rasburicase)
  - For those who have failed (or have contraindication to) other therapies.
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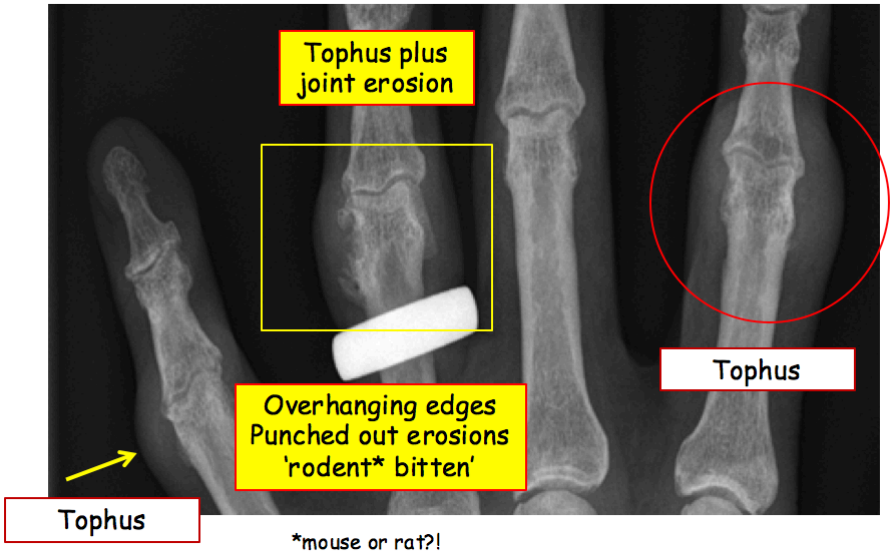

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