Gout

(monosodium urate crystal deposition disease)

Is an inflammatory arthritis associated with hyperuricemia.
“The Gout” by James Gilray, 1799. Gout depicted as an evil demon attacking a toe.

Gout, Latin: gutta, a drop
-Epidemiology
-prevalence of Gout approximately 0.2%
-hyperuricemia occurs in about 5%
-Men: women 10:1
-rarely before young adulthood
-Seldom premenopausal females
-Most people with hyperuricemia are asymptomatic
-Serum uric acid levels increase with
-Age – obesity – high protein diet
-High alcohol consumption
-Combined hyperlipidaemia. D.M. I.H.D - and hypertension
-Family History of Gout.
Pathogenesis

Uric acid level in the blood depend on the balance between purine synthesis and elimination of urate “by Kidney and intestine”
Uric acid synthesis

Uric acid is the last step in the breakdown pathway of purines:

hypoxanthine
→ xanthine
oxidase
→ Uric acid
Uric acid excretion

Uric acid is completely filtered by glomerulus reabsorbad in the proximal tubule 98-100% 50% is secreted by distal tubule.
90% of patients with Gout have impaired exertion of urate.
1% an inborn error of metabolism leads to purine over production.
1/3 of uric acid is eliminated in the faeces
Primary Gout – renal clearance of uric acid 90%
Over production < 10%
Secondary Gout
undersecretion

- Glomerular infiltration (renal disease)
- Diuretic therapy
- Volume depletion → tubular reabsorption → ↓ secretion
- Low dose Aspirin → ↓ urate excretion
- Adrenal insufficiency → volume depletion
- Accumulation of organic acid → inhibitor uric acid secretion
- Starvation, alcoholic ketocidosis, diabetic ketoacidosis.
- Lead intoxication, hyperparathyrodism
- Hyperthyrodism → unclear.
Secondary urate over production

- HPRT Deficiency
- PRPP overactivity
- Myeloproliferative and lymphoproliferative
  - multiple myeloma
  - secondary polycythemia
- pernicious anemia
- hemolytic anemia
- infectious mononucleosis
- Alcohol consumption
- MI
- Respiratory failure
- Statusepilepticus

→ ATP degradation to uric acid
## Hyperuricemia

<table>
<thead>
<tr>
<th>Overproduction (10%)</th>
<th>Underexcretion (90%)</th>
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<tbody>
<tr>
<td>Ethanol</td>
<td>Renal insufficiency</td>
</tr>
<tr>
<td>HGPRT or G6PD deficiency</td>
<td>Drugs and toxins</td>
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<tr>
<td>PRPP synthetase overactivity</td>
<td>Diuretics</td>
</tr>
<tr>
<td>Myeloproliferative disorders</td>
<td>Ethanol</td>
</tr>
<tr>
<td>Cytotoxic chemotherapy</td>
<td>Cyclosporine A</td>
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<tr>
<td>Sickle-cell anemia</td>
<td>Pyrazinamide</td>
</tr>
<tr>
<td></td>
<td>Lead nephropathy</td>
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<td></td>
<td>Low-dose aspirin</td>
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Ketosis
Clinical manifestations

Gouty arthritis

TOPHASEOUS GOUT
Accumulation of urate crystals in the form of tophaceous deposits
Uric acid nephrolithiasis
Gouty nephropathy
1) Asymptomatic hyperuricemia.
2) Acute gouty arthritis.
3) Intercritical (interval) gout.
4) Chronic tophaceous gout.
All patients with gout have hyperuricemia (supersaturation of serum for urate) at some point in their disease. Most hyperuricemic individuals never experience a clinical event resulting from urate crystal deposition.

<table>
<thead>
<tr>
<th>Serum uric acid level (mg/dl)</th>
<th>Incidence of gout</th>
</tr>
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<tbody>
<tr>
<td>&gt;9.0</td>
<td>7.0-8.9</td>
</tr>
<tr>
<td>7.0-8.9</td>
<td>0.5±0.37</td>
</tr>
<tr>
<td>&lt;7.0</td>
<td>0.1%</td>
</tr>
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Predisposing factors

- Trauma
- surgery
- Starvation
- alcohol ingestion
- dietary overindulgence
- ingestion of certain drugs
  - Low dose ASA
  - Thiazides and loop diuretics
  - Cyclosporine
  - Pyrazinamide
  - Nicotinic acid
  - Theophylline
  - levodopa
Acute gouty arthritis

Abrupt onset of severe joint inflammation, often with onset in the night

75% of initial attacks in first MTP joint

Usually monarticular, may be polyarticular

Attack subsides in 3-10 days

Urate crystals present in synovial fluid

Hyperuricemia may or may not be present
ACUTE GOUTY ARTHRITIS

typically occurs after years of asymptomatic hyperuricemia

Acute gout is intensely inflammatory, and is characterized by severe pain, redness, swelling, and disability

Maximal severity of the attack is usually reached over several hours

Complete resolution of the earliest attacks occurs within a few days to several weeks, even in untreated individuals
80% of initial attacks involve a single joint, typically in the lower extremity most often at the base of the great toe. The signs of inflammation often extend beyond the confines of the joint that is primarily involved and, in the foot or ankles, may give the impression of arthritis in several contiguous joints, tenosynovitis, or even cellulitis. Gouty attacks of lesser severity may be mimicked by a stress fracture or traumatic process in the bone or joint.
Resolution of the acute gouty attack is sometimes accompanied by desquamation of the skin overlying the affected joint

- The response of neutrophils to proteins coating the surface of urate crystals
- The recruitment of additional neutrophils to sites of crystal deposition
- The activation of neutrophils by proinflammatory cytokines
<table>
<thead>
<tr>
<th>Joint</th>
<th>Cumulative frequency (%)</th>
</tr>
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<tbody>
<tr>
<td>Big toe</td>
<td>76</td>
</tr>
<tr>
<td>Ankle or foot</td>
<td>50</td>
</tr>
<tr>
<td>Knee</td>
<td>32</td>
</tr>
<tr>
<td>Finger</td>
<td>25</td>
</tr>
<tr>
<td>Elbow</td>
<td>10</td>
</tr>
<tr>
<td>Wrist</td>
<td>10</td>
</tr>
<tr>
<td>Other joint</td>
<td>4</td>
</tr>
<tr>
<td>Bursitis</td>
<td>3</td>
</tr>
<tr>
<td>More than one site simultaneously</td>
<td>11</td>
</tr>
</tbody>
</table>

Half the patients had experienced gout for more than 10 years.
Gout: podagra
Gout: olecranon bursitis
<table>
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<tr>
<th>Duration between initial attack and second attack</th>
<th>% Patients</th>
</tr>
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<tbody>
<tr>
<td>1 year</td>
<td>62%</td>
</tr>
<tr>
<td>1-2 years</td>
<td>16%</td>
</tr>
<tr>
<td>2-5 years</td>
<td>11%</td>
</tr>
<tr>
<td>5-10 years</td>
<td>6%</td>
</tr>
<tr>
<td>no recurrence in 10 years</td>
<td>7%</td>
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</table>
polyarticular initial presentation of gouty arthritis may be more frequent in patients in whom hyperuricemia and gout arise secondary to a myeloproliferative or lymphoproliferative disorder, or in organ transplant recipients who are receiving cyclosporine A
Chronic tophaceous gout

-the time from the initial attack to beginning of chronic gout (tophaceous)
Averge (medium) 11.6 years.
-deposits of urate crystals appears in cartilage, synovial membranes, tendons, soft tissue
-fingers, hands, knees or feet
Gout of distal interphalangeal joints simulating osteoarthritis
Gout: hands
Gout: tophi, hands
Gout: tophus, finger (clinical and polarized light microscopy)
Gout: tophi, ear
Gout: tophi of the pinna, ear
Monoarticular gouty arthritis can give a clinical picture indistinguishable from acute septic arthritis, including fever, leukocytosis, and elevated erythrocyte sedimentation rate. On rare occasions, acute gout and septic arthritis may even coexist. Aspiration of synovial fluid from the affected joint and analysis of the fluid by:

- Cell count >50,000 predominantly neutrophils
- Gram stain, culture
- Polarized light microscopic examination
- Acute gout
- Pseudogout (calcium pyrophosphate crystal deposition disease)
Polarizing microscope (diagram)

Analyzer

Compensator

Polarizer
Crystals found in synovial fluid

Monosodium urate monohydrate
   Acute and tophaceous gout
   May be seen in asymptomatic hyperuricemia or intercritical gout

Calcium pyrophosphate dihydrate
   Pseudogout
   Asymptomatic chondrocalcinosis
   Chronic arthropathy
Gout: urate crystals (polarized and ordinary light microscopy)
Gout: urate crystal (polarized light microscopy)
Gout: monosodium urate crystals (photomicrograph)
Gout: hand (radiograph)
Gout: hand (radiograph)
Gout: foot (radiograph)
Gout: advanced disease, foot (radiograph)
Gout: toe (radiograph)
Gout: foot (radiograph)
- uric acid
- ESR
- lipid profile
- blood sugar
- KFT

-Blood pressure-
Indications for Antihyperuricemic Therapy in Gout

- Frequent and disabling attacks of acute gouty arthritis
- Clinical or radiographic signs of chronic gouty joint disease
- The presence of tophaceous deposits in soft tissues or subchondral bone
- Gout with renal insufficiency
- Recurrent nephrolithiasis
- Serum urate levels persistently in excess of 13 mg/dL in men or 10 mg/dL in women
- Urinary uric acid excretion exceeding 1100 mg/day
- Impending cytotoxic chemotherapy or radiotherapy for lymphoma or leukemia
Treatment

- Acute attack
  - Colchicine (0.5 – 0.6 hourly) ?
  - NSAID’S – Indomethacin (Indocid)
    - Naproxen (Proxen)
    - Etirocoxib (Arcoxia)
  - Steroid
Prophylaxis

After acute attack resolved
- All patients encouraged to limit their purine intake
- Alcohol reduction
- Medication promote hyperuricemia
- ↓ Body weight
- Colchicines Img for 3-6 month’s
- Xanthine oxidase inhibitor (Allopurinol).
- Started at 100 mg daily and gradually titrated up to achieve a serum urate < 6
- Febuxostat is a non purine analoage of uricacid that inhibits urate synthes
- Uricosuic agent (sulfinpyrazone. probenecid)
- Losartan.
Calcium pyrophosphate disease
“chondrocalcinosis”

calcified joint cartilage – tendons, ligaments, articular capsules and synovium.

6% of elderly population have articular CPPD

The incidence of symptomatic disease is about half of gouty arthritis

M : F (1.4 – 1)
Crystal deposition disease (CPPD): associations

Hyperparathyroidism
Hemachromatosis
Osteoarthritis
Hypomagnesemia
Familial chondrocalcinosis
Hypophosphatasia
Clinical Features

Acute pseudogout

- Inflammation in 1 or more joints lasting for several days or longer
- These episodes are generally less painful
- 50% Knee
- 7 – 10 days.

Provocation of acute attacks by

- Surgery
- C.V.A
- M.I
Pseudo R.A 5%

- Multiple joint
- Symmetrical (weeks or months)
- Morning stiffness
- Mild systemic manifestation
ESR ↑  CRP ↑  RF + 10%
Pseudo-osteoarthritis

-Chronic degenerative arthritis
-Involvement uncommon site of primary O.A
-Wrist – MCP – elbow- shoulder
Recurrent acute hemarthrosis
Asymptomatic
Calcium pyrophosphate dihydrate deposition disease (CPPD): Presentations

Acute synovitis (pseudogout)

Chronic arthropathy
  Atypical osteoarthritis
  Atypical spondyloarthropathy
  Pseudo-rheumatoid arthritis
  Pseudo-neuropathic arthropathy

Radiographic (chondrocalcinosis)
Diagnosis

-Synovial fluid analysis
-Positive birefringent CPPD crystal
-Rhomboid in shape
Chondrocalcinosis: calcium pyrophosphate crystals (ordinary, polarized, and compensated polarized light microscopy)
- Ca, PO4, Alkphosphatase, ferritin, iron, TIBC, magnesium and TSH.
- AP knee
- AP pelvis
- PA hands
Calcium pyrophosphate dihydrate deposition disease (CPPD): wrist (radiograph)
Chondrocalcinosis: hand (radiograph)
Chondrocalcinosis: shoulder (radiograph)
Chondrocalcinosis: knee (radiograph)
Treatment

- NSAIDS
- Intra-articular steroid
- Colchicine (pseudo gout)