

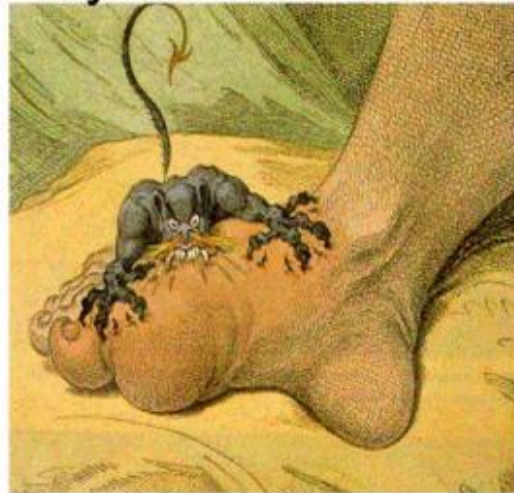
1. Gout and Other Crystal Diseases: Slide 1

## Gout and Other Crystal Diseases

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**The Gout.** James Gillray, 1799. From Philadelphia Museum of Art.  
Purchased with the SmithKline Beckman (now SmithKline Beecham) Fund for the Ars Medica Collection.

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2. Gout and Other Crystal Diseases: Slide 2

## On Gout...

**Ambrose Bierce**, 1906

Gout, n. A physician's name for the rheumatism of  
a rich patient.

**Source:** Bierce, Ambrose. *The Devil's Dictionary*. 1906  
[Reprinted in New York: Dover Publications; 1993, p. 44].

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3.

## Highlights

# Highlights

- Epidemiology
- Pathophysiology
- Gout and Metabolic Syndrome
- Stages of Gout
- Diagnosis
- Treatment
- Other crystal diseases

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4.

## Gout and Other Crystal Diseases: Slide 4

# On Gout...

**Hildegard of Bingen**, 12th century AD

Those who have soft and rich flesh on their bodies and who frequently eat incompatible and exquisite foods will easily contract gout... Bad humors . . . descend to the lower parts of the bodies and begin to rage in the legs and feet... Women do not incur gout so easily. These humors become part of the menstrual purgation and so women remain free of gout.

**Source:** Hildegard of Bingen. On natural philosophy and medicine: selections from *Cause et cure*. Berger M, translator. Cambridge (UK): D. S. Brewer; 1999, pp. 78-9.

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5. Gout and Other Crystal Diseases: Slide 5



Bunbury, Henry William, 1750-1811  
Origin of the Gout / [England] , 1815.  
Image courtesy of NLM.

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6. Prevalence of Gout Increases with Serum Uric Acid and Age

## Prevalence of Gout Increases with Serum Uric Acid and Age

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Copyright restrictions.

AP Hall et al. Epidemiology of gout  
and hyperuricemia. A long term  
population study. Am J Med 1967  
42: 27-37

WJ Currie. Prevalence and  
incidence of the diagnosis of gout  
in Great Britain. Ann Rheumatic  
Dis 1979 38: 101-106.

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7. Gout risk, weight, and EtOH intake

## Gout risk, weight, and EtOH intake

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Choi et al. Lancet 2004; 363; 1277-81

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8. Uric Acid

## Uric Acid

- “Molecular crossroads”
- An inborn error of metabolism
- A problem of solubility

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## 9. Overproducers and Underexcreters

# Overproducers and Underexcreters

- Overproduction: 10%
  - HGPRT → Lesch-Nyhan syndrome
  - PRPP → enzyme overactivity
  - Onset of gout in early 20's
  - Acute illness → increased ATP turnover
- Underexcretion: 90%
  - Renal failure
  - Lead
  - Drugs (SPEED, cyclosporin)
  - Idiopathic

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Choi HK et al. *Annals Intern Med* 2005; 143: 499-516  
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## 10. Uric Acid Transporters

# Uric Acid Transporters

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11. Gout and Other Crystal Diseases: Slide 11

## On Gout...

**Hippocrates**, [460-375 BC]

Eunuchs do not take the gout, nor become bald.

A woman does not take the gout, unless her menses be stopped.

**Source:** Hippocrates. *Aphorisms*, vol. II, sec. VI, no. 28. In Adams F (ed). *The Genuine Works of Hippocrates*. London: C & J Adlard Printers; 1849 [Reprinted in Birmingham, AL: Classics of Medicine Library; 1985, p. 756].

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12. Risk Factors for Gout

## Risk Factors for Gout

- Hyperuricemia is necessary but not sufficient
- Increased risk of gout with
  - Increased production:
    - Weight gain
    - Trauma
    - Acidosis
  - Reduced clearance:
    - Renal insufficiency, lead
    - Drugs: SPEED (salicylates, pyrazinamide, ethambutol, ethanol, diuretics)
  - Increased nucleation:
    - Trauma (RBC's)
    - Lead

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13.

Uric Acid is Phlogistic

## Uric Acid is Phlogistic

- Patients with gout make antibodies to uric acid
  - Uric acid exposure induces
    - MΦ TNF
    - Complement
    - PMN oxidative burst
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Choi HK et al. *Annals Intern Med* 2005; 143: 499-516  
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Gout and Other Crystal Diseases: Slide 14

## Nobody Dies of Gout, BUT...

- Gout is closely linked to
  - Hypertriglyceridemia
  - Low HDL-cholesterol
  - Insulin resistance
  - Obesity (esp. central)
  - Hypertension
- These conditions kill millions, but they don't hurt
- Coming to medical attention for gout is a chance to screen for these conditions!

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15.

## Four Stages of Gout

### Four Stages of Gout

- Asymptomatic hyperuricemia
- Acute gout
- Intercritical gout
- Chronic tophaceous gout

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## Asymptomatic Hyperuricemia

### Asymptomatic Hyperuricemia

- Not a disease, but a risk factor
- Risk of gout directly related to SUA concentration
- Do not treat

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17.

## Gout and Other Crystal Diseases: Slide 17



Gillray, James, 1757-1815. Punch cures the gout, -the Colic, -and the 'Tisick. London: H. Humphrey, July 13, 1799. Image courtesy of the NLM.

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18.

## Acute Gout

### Acute Gout

- (Sydenham description)
- Joint predilection =  $f$  (joint temperature)
  - Podagra – 90% (presentation in 50%)
  - Instep, ankle, knee, wrist, hand, elbow
- Also tendonitis, cellulitis
- Differential diagnosis of podagra
  - Acute gout
  - Septic joint
  - Hallux rigidis
  - Traumatic arthritis

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19. Gout and Other Crystal Diseases: Slide 19

The victim goes to bed and sleeps in good health. About 2 o'clock in the morning, he is awakened by a severe pain in the great toe; more rarely in the heel, ankle or instep. **This pain is like that of a dislocation,** and yet the parts feel as if cold water were poured over them. **Then follows chills and shiver and a little fever.** The pain which at first moderate becomes more intense. With its intensity the chills and shivers increase. After a time this comes to a full height, accommodating itself to the bones and ligaments of the tarsus and metatarsus. **Now it is a violent stretching and tearing of the ligaments-** now it is a gnawing pain and now a pressure and tightening. So exquisite and lively meanwhile is the feeling of the part affected, that **it cannot bear the weight of bedclothes nor the jar of a person walking in the room.** — Sydenham, Thomas. *Tractatus de Podagra et Hydrope*. London: G. Kettilby; 1683

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20. Intercritical Gout

## Intercritical Gout

- Time from first attack to second:
  - < 1 yr 2/3
  - > 1 yr 1/3
- Most treat after second attack

Duration between initial attack and second attack	% Patients
1 year	62%
1-2 years	16%
2-5 years	11%
5-10 years	6%
no recurrence in 10 years	7%

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21.

## Chronic Tophaceous Gout

# Chronic Tophaceous Gout

- Completely preventable!
- 25% of patients disabled at 20 years
- Progressive joint destruction
- Chronic, continuous arthritis with fewer acute attacks

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22.

## Diagnosis of Gout

# Diagnosis of Gout

- Any *undiagnosed* acute arthritis is a **medical emergency**
- Arthrocentesis indicated:
  - First time
  - Question of septic joint
- Serum uric acid is supportive but not definitive either for or against diagnosis!
- Definitive diagnosis = negatively birefringent intracellular crystals under polarized light microscopy

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23. Gout and Other Crystal Diseases: Slide 23

## On Gout...

**Anton van Leeuwenhoek**, 1679

There was... a hole in his arm on his elbow from which the chalk had come during quite six months on end.... I asked him to let me have some of the chalk.... [Under the lens] I observed the solid matter which to our eyes resembles chalk and saw to my... astonishment that... it consisted of nothing but long, transparent little particles, many pointed at both ends and about 4 "axes" of the globules in length.

**Source:** von Leeuwenhoek, Anton. Letter to Lambert Velthuysen, July 11, 1679. In *The Collected Letters of Antoni van Leeuwenhoek*. Amsterdam, Netherlands: Swets & Zeitlinger; 1939.

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24. Gout and Other Crystal Diseases: Slide 24

## On Gout...

**Alfred Baring Garrod**, 1859

That colchicum in its various forms has a most powerful influence upon the progress of gouty inflammation is undeniable, and this action is not simply limited to the removal of gout when it attacks the joints, but it proves efficacious even in its masked and irregular forms.... I would even go to the length of asserting that we may sometimes diagnose gouty inflammation from any form by noting the influence of colchicum upon its progress.

**Source:** Garrod, Alfred Baring. *A Treatise on Gout and Rheumatic Gout (Rheumatic Arthritis)*, 3rd ed. London: Longman's, Green; 1876 [As cited in Talbott JH, *A Biographical History of Medicine*, p. 1085 (q.v.)].

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25.

## Treatment of Acute Gout

### Treatment of Acute Gout

- Intramuscular triamcinolone, 60 mg, or ACTH, 40 U (if available)
- Oral
  - NSAID's: indomethacin 200-100-50-25
  - Colchicine: 0.6 mg q1-2 hr → effect or diarrhea
  - Steroids: 60 mg prednisone taper over 1 week
- IV
  - Colchicine 1 mg iv x 1 (may repeat x 1 in 2 d)
  - No more colchicine for 2 weeks!

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26.

## Treatment of Intercritical Gout

### Treatment of Intercritical Gout

- Acute gout prophylaxis
  - Colchicine 0.6 mg bid, qd, qod
- Uric acid treatment
  - Uricosurics – underexcretors only!
    - Need GFR > 60 ml/min
    - Probenecid 500 mg 1-2 tabs bid
    - Sulfinpyrazone 50 mg 1-2 tabs bid
  - Allopurinol

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27. Gout and Other Crystal Diseases: Slide 27

### Dietary Treatment of Gout is Unsatisfactory

- Never eat:
    - Sweetbreads, kidneys, livers, brains, sardines, anchovies
    - meat extracts, consommés, and gravies
  - Use sparingly:
    - Asparagus, beans, lentils, peas, mushrooms, cauliflower, spinach, rhubarb
  - Avoid
    - dehydration
    - alcohol
  - May be of benefit:
    - cherries ?
- Meat RR 1.21/serving  
Seafood RR 1.07/serving  
Dairy RR 0.82/serving
- Choi et al. *NEJM* 2004; 350:1093-1103

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28. Vitamin C lowers SUA

## Vitamin C lowers SUA

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Huang et al. *A&R* 2005; 52: 1843

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29. Gout and Other Crystal Diseases: Slide 29

Jones, Thomas  
Howell, fl. 1824-  
1831, Artist  
John Bull & his  
new Doctor.  
London: S.W.  
Fores, April  
1829 Image  
courtesy of  
NLM.



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30. Gout and Other Crystal Diseases: Slide 30

## Probenecid

- Uricosuric
- Creatinine clearance >60 cc/min
- 24 hour urinary uric acid <800 mg/dl
- Increases risk of renal stones
- Patients under the age of 60.
- Starting dose 500 mg to 1000 mg daily
  - increase to 1500 mg to 2000 mg as needed

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31.

## Allopurinol

# Allopurinol

- Xanthine oxidase inhibitor
- Indications
  - Tophaceous gout
  - GFR < 60
  - Overproducers
  - Renal stones
  - Chemotherapy

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32.

Gout and Other Crystal Diseases: Slide 32

## **Allopurinol, Continued**

- Can be used in renal failure
- Causes bone marrow suppression, hepatotoxicity, and hypersensitivity reactions – 80 deaths reported!
- Drug interactions: raise the levels of
  - warfarin
  - theophylline
  - azathioprine
  - 6-mercaptopurine
  - cyclophosphamide
- Can prolong an acute attack of gout if started during the attack, or trigger a gout attack due to shifts in uric acid levels.
  - use prophylactic colchicine x 1 year

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33. Gout and Other Crystal Diseases: Slide 33

## Dosing Allopurinol by Renal Function

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Adapted from: Am J Med 76:55, 1984

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34. Other Interventions that Affect Uric Acid

## Other Interventions that Affect Uric Acid

- **Oxypurinol** – compassionate use in the US; ½ of patients allergic to allopurinol can tolerate it
- **Desensitization** for allopurinol – 50% success rate
- **Uricase** – approved for tumor lysis syndrome; immunogenic, G6PD hemolysis
- **Losartan** (ARB) – uricosuric, 7-15% decr. UA
- **Fenofibrate** – modest effect, ? Renal insuff.
- **Beer** > spirits > wine (contains guanosine)

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35.

## Renal Gout

### Renal Gout

- **Urate nephropathy**
  - Sodium urate salt in renal interstitium
  - Probably not a cause of renal disease, but rather a consequence of HTN & DM
- **Uric acid nephropathy**
  - Uric acid deposition in renal tubules
  - Acute UA overload – chemotherapy, status epilepticus
- **Renal stones**

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36.

## Uric Acid Stones

### Uric Acid Stones

- Radiolucent
- 10% of renal stones
- 20% of gout presentations
- Uric acid solubility =  $f$  urine pH

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37. Gout and Other Crystal Diseases: Slide 37



Rowlandson, Thomas, 1756-1827, Artist, *The Consultation Or Last Hope* (England), R. Ackermann, 1808, 1808. Image courtesy of NLM.

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38. Calcium Pyrophosphate Deposition Disease (CPPD)

## Calcium Pyrophosphate Deposition Disease (CPPD)

- Generally women > 70 y
- Wrist, hand, knee, elbow
- Diagnosis same as gout
- Treatment – colchicine, NSAID's

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39.

## Diseases Predisposing to CPPD

# Diseases Predisposing to CPPD

- Definite

Hyperparathyroidism  
Hemochromatosis  
Ochronosis  
Hypophosphatasia  
Hypomagnesaemia  
Wilson's disease  
Hypothyroidism

- Probable

Gout

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40.

## Causes of Hypouricemia

# Causes of Hypouricemia

- **Reduced production**
  - Liver disease, xanthinuria
- **Increased excretion**
  - Fanconi syndrome
  - Hodgkin's disease
  - SIDAH
  - TPN
  - DM?
  - Drugs
  - Familial URAT1 mutations

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