

GGUT 1 [Compatibility Mode] - Microsoft PowerPoint

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Slides Outline

23

- Strategic use of NSAIDs
- NSAIDs are used to treat resulting in adverse effects
- Includes the mechanism of NSAIDs
- NSAIDs are used to treat resulting in adverse effects

24

**FEBUXOSTAT**

- It requires active renal excretion
- Approved by FDA
- Well tolerated
- No need of dose adjustment in pts of renal impairment and its adverse reactions

25

**PROBENECID** - Potent & selective inhibitor of U.S. & uric acid formation of uric acid

- No other adverse reactions in pts of uric acid metabolism are observed
- It is used in pts. with chronic uric acidemia
- It is used in pts. with chronic uric acidemia

26

**Dose & Indication:**  
80 & 120 MGS for treatment of ch. gout.

**AD. EFFECTS:** Disturbances in LFTs.  
Diarrhea, nausea, headache.

- Well tolerated in pts. of allopurinol intolerance.
- Prophylactic treatment with colchicine or NSAIDs should start at the beginning of treatment to avoid gout flares.

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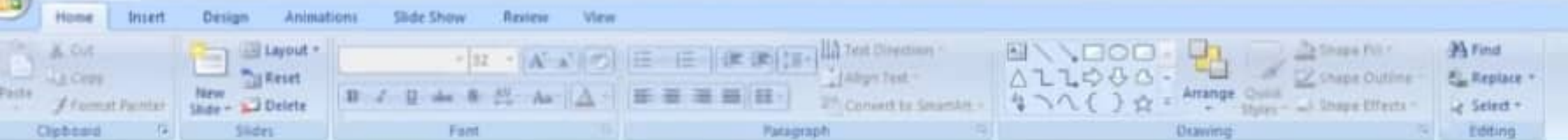
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Slides Outline

- Allopurinol mechanism:
  - Inhibits xanthine oxidase (X.O.) in 25% of pts.
  - Fewer side effects resulting in better tol.
  - Inhibits the metabolism of heterocypurine and xanthopurine, drugs that depend on X.O. for activation.
  - **ADVERSE:** induces all types of rash
  - **CONTRA:** depending on serum urate levels.
- FEBUXOSTAT**
  - xanthine oxidase inhibitor
  - Approved in 2006
  - **ADVERSE:** 60% increase in cardiovascular risk, severe skin reactions in pts. in systemic hypertension, in pts. & chronic kidney.
  - No need of dose adjustment in pts. of renal impairment & in extensive metabolism.
- PHARMACODYNAMICS:** Potent & selective inhibitor of X.O. & so dec. formation of xanthine & uric acid.
  - No other enzyme involved in purine or pyrimidine metabolism are inhibited.
  - In standard doses, more effective than allopurinol in lowering serum urate levels.
  - **1<sup>st</sup> new drug for treatment of gout over 40 yrs.**
- DOSE & INDICATION:**
  - **DOSE:** 80 & 120 mg/d for treatment of pts. with gout.
  - **ADVERSE EFFECTS:** Skin reactions in 20%, GI-related, renal, headache.
  - **CONTRA:** contraindicated in pts. of hypersensitivity to febuxostat.
  - **Prevention:** treatment with febuxostat of pts. with gout should start at the beginning of treatment to avoid a gout flare.

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Slides Outline

- Average in studies...  
• ...
- FEBUXOSTAT**
  - 1<sup>st</sup> nonpurine xanthine oxidase inhibitor
  - Approved by FDA.
  - ...
- ...
- ...
- ...

# FEBUXOSTAT

- 1<sup>st</sup> nonpurine xanthine oxidase inhibitor
- **Approved by FDA.**

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oral administration. Peak plasma conc. attained in 01 hr. Extensively metabolized in liver. Eliminated in urine.

- No need of dose adjustment in pts. of renal impairment B/O its extensive metabolism.

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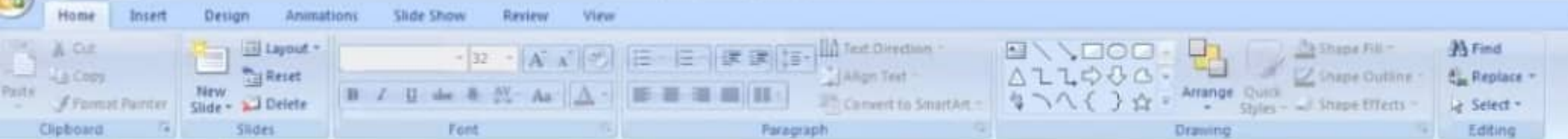
Microsoft PowerPoint interface showing a slide with medical information. The slide content includes:

- Allergic skin reaction(**PRURITIC MACULOPAPULAR RASH**) in 3% of pts.
- Rarely can bind to lens resulting in
- Inhibits the metabolism of mercaptopurine and azathioprine, drugs that depend on X.O. for elimination.
- DOSAGE:** Initially 100 mgs/d ↑ to 300mgs/d depending on serum urate levels.

A yellow box highlights the text: **Please move this window away from the shared application.**

Slide Outline (left sidebar):

- Pharmacodynamics
- INDICATIONS:
  1. Indicated for gout with elevated uric acid
  2. In acute exacerbations of gout
  3. In chronic gouty arthritis
  4. In asymptomatic hyperuricemia
  5. In uric acid nephropathy
- AD. EFFECTS:
  - Allergic reactions
  - Rarely can bind to lens resulting in
  - Inhibits the metabolism of mercaptopurine and azathioprine, drugs that depend on X.O. for elimination.
- DOSAGE:** Initially 100 mgs/d ↑ to 300mgs/d depending on serum urate levels.
- FEBURISTAT**



**Pharmacodynamics**

- Uric acid is formed only from dietary purines but also from amino acids, fructose and CO<sub>2</sub>. In fact Purines convert into uric acid and fructose and then oxidised to uric acid. Allopurinol inhibits the last step resulting in decrease of uric acid level.
- **AD effects uric acid & hyperuricaemia** are acute and more serious than hyperuricaemia. In 6% being hyperuricemic events more uric acid & hyperuricemia than uric acid. Therefore some more serious than uric acid and hyperuricemia with normal allopurinol. Also both more readily controlled in

**INDICATIONS:**

- 1. Prophylaxis of gout with allopurinol has to be continued for years if not life long.
- 2. In general patients continue following blood uric acid level of 0.15-0.20 mg/dl.
- 3. Allopurinol also used as adjunctive agent of uric acid to also the formation of uric acid from purines derived by the both of large number of metabolic cells.
- 4. As an antihistamine.
- 5. Other uses are being used to assist.

**AD Effects or hyperuricaemia:**

- 6. After starting allopurinol, Colchicine or NSAIDs should also be used until steady state serum uric acid is normalised or dec. to less than 6 mg/dl.

**AD EFFECTS:** GI intolerance (N,V,D) Peripheral neuritis, necrotising vasculitis, bone marrow depression. Rarely aplastic anemia.

- Hepatic toxicity & interstitial nephritis.

**allergic skin reaction (hives)**

- incidence about 10% in 2% of pts.
- rarely can lead to loss resulting in blindness.
- inhibits the reabsorption of hypoxanthine and xanthine, drugs that depend on it for elimination.
- **Dosage:** initially 100 mg/d 1 to 200 mg/d depending on serum uric acid level.

**FEBUKOSTAT**

- 1st non-purine xanthine oxidase inhibitor
- Approved by FDA
- **AD EFFECTS:** 80% started after oral administration. Few severe cases.

ad. effects or hypersensitivity.

- 6. When starting allopurinol, Colchicine or NSAIDs should also be used until steady state serum uric acid is normalised or dec. to less than 6 mg/dl.

**AD. EFFECTS:** GI intolerance (N,V,D)  
Peripheral neuritis, necrotising vasculitis,  
bone marrow depression. Rarely aplastic  
anemia.

- Hepatic toxicity & interstitial nephritis.

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renal failure.

## INDICATIONS:

- 1. TREATMENT of gout with allopurinol has to be continued for years if not life time.
- 2. To prevent massive uricosuria following blood dyscrasias which can lead to renal calculi.
- 3. Allopurinol is also used as an adjunct to cancer chemotherapy to slow the formation of uric acid from purines released by the death of large numbers of neoplastic cells.
- 4. As an antiprotozoal.
- 5. When uricosuric drugs cannot be used B/O ad.

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## Allopurinol(purine analog)

- X.O.inhibitor which decreases total body uric acid.

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- Allopurinol is metabolized by X.O. resulting in compound, alloxanthine. Alloxanthine is an irreversible suicide inhibitor of the enzyme & has long  $t_{1/2}$  15 hrs. So given once daily. Excreted unchanged as alloxanthine by kidneys.

**DRUG TREATMENT OF GOUT**

- 1. Drugs that suppress symptoms
- 2. anti-inflammatory drug with or without analgesic: *indomethacin, ibuprofen, naproxen, diclofenac*
- 3. corticosteroids & alcohol avoidance
- 4. Drugs that prevent urate synthesis: *allopurinol & febuxostat*
- 5. uricolytic agents: *rasburicase & pegloticase*

**DRUG TREATMENT OF AC GOUT**

- 1. **NSAIDs** highly effective in relieving acute attack. IV or IM *indomethacin* 4 or 8 doses. 20-30 mg. 100 mg IV dose 81 hours. *naproxen, diclofenac, ibuprofen, sulindac* are alternatives.
- 2. **COLCHICINE** given when pts cannot tolerate NSAIDs.
- 3. if these drugs fail, then **prednisolone** starting 40 mg bid then tapering as symptoms subside.

- No use of **colchicine** & **corticosteroids** in acute gout unless they are used in recurrent & progressive gout.
- Only if renal dysfunction they get to slowly tapering course. This will result in reabsorption of all uric acid resulting uric acid in pt.

**COLCHICINE**

- Plant alkaloid isolated from *Colchicum autumnale*
- Rapidly absorbed after oral administration. Peak levels within 02 hrs. Some is metabolised in liver & some is excreted unchanged in bile & then reabsorbed from gut. It increases its gut toxicity.
- MOA:** Drammatically relieves pain & inflammation of gouty arthritis in 12-24 hrs without altering metabolism or excretion of

**PROBENECID** anti-inflammatory action is produced by blocking in distal tubule tubular secretion of uric acid. This drug also has function such as inhibition of gastric mucosa as leading to inhibition of **HCL** secretion & absorption.

# COLCHICINE

- Plant alkaloid isolated from **COLCHICUM AUTUMANLE**.
- Rapidly absorbed after oral administration. Peak levels within 02 hrs. Some is metabolised in liver & some is excreted unchanged in bile & then reabsorbed from gut. It increases its gut toxicity.

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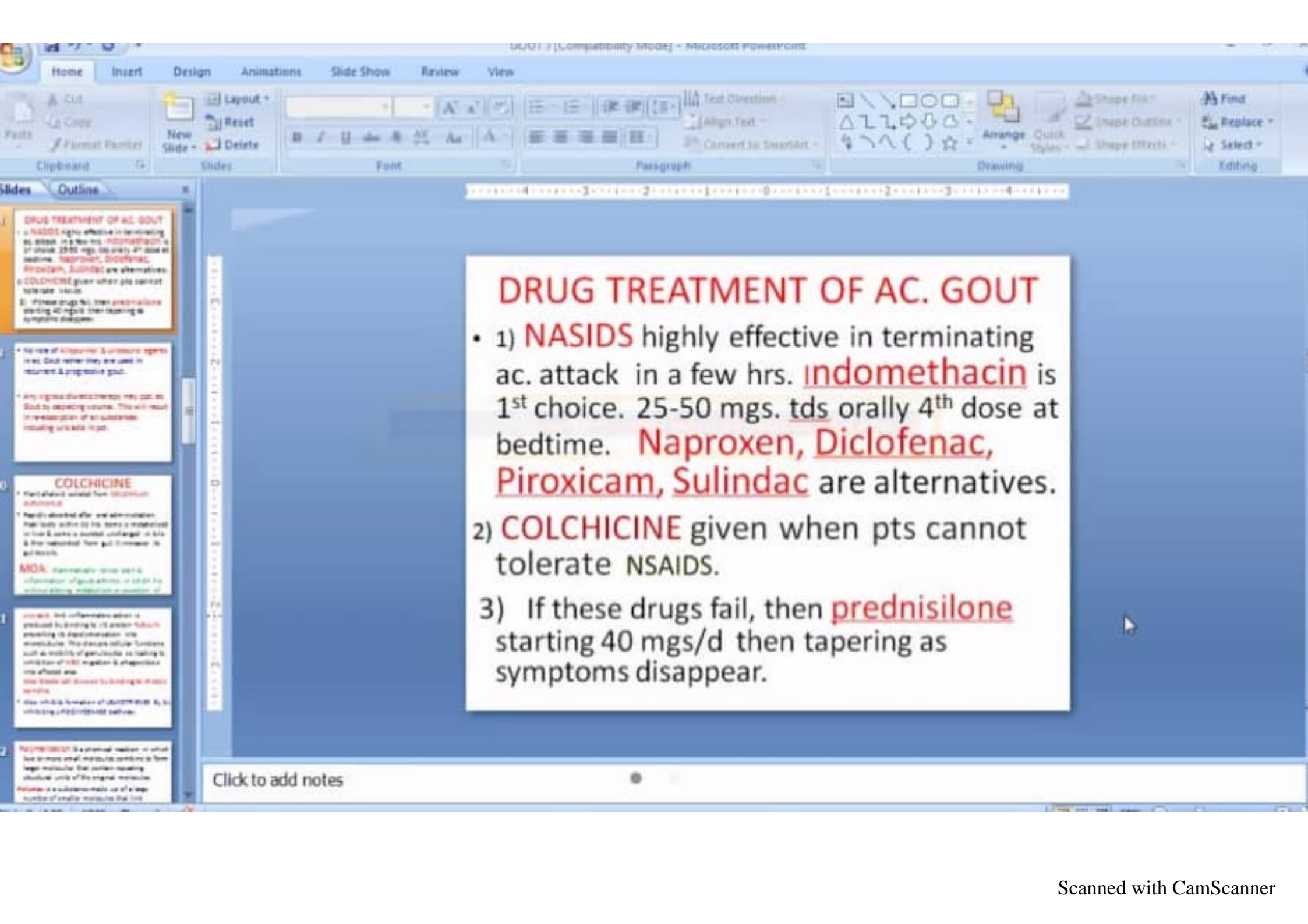
Microsoft PowerPoint interface showing a slide titled "DRUG TREATMENT OF AC GOUT". The slide content includes:

- No role of **Allopurinol & uricosuric agents** in ac. Gout rather they are used in recurrent & progressive gout.
- Any **vigorous diuretic therapy** may ppt. ac. Gout by depleting volume. This will result in re-absorption of all substances including uric acid in pct.

The slide also features a yellow-bordered box with the text: "Please move this window away from the shared application".

Navigation pane on the left shows slide thumbnails:

- DRUG TREATMENT OF GOUT
  - Drugs that suppress symptoms
  - anti-inflammatory drugs with or without analgesics
  - Colchicine & other steroids
  - Drugs that prevent acute symptoms
  - Uricosuric agents
- DRUG TREATMENT OF AC GOUT
  - NSAIDs highly effective in relieving ac. attack
  - COLCHICINE** given when pts cannot tolerate NSAIDs
- No role of **allopurinol & uricosuric agents** in ac. Gout rather they are used in recurrent & progressive gout.
- Any **vigorous diuretic therapy** may ppt. ac. Gout by depleting volume. This will result in re-absorption of all substances including uric acid in pct.
- COLCHICINE**
  - Mechanism of action
  - Pharmacokinetics
- MOA**: Chemically binds to & inhibits the enzyme xanthine oxidase



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**DRUG TREATMENT OF AC. GOUT**

- **NASIDS** highly effective in terminating ac. attack in a few hrs. **indomethacin** is 1<sup>st</sup> choice. 25-50 mgs. tds orally 4<sup>th</sup> dose at bedtime. **Naproxen, Diclofenac, Piroxicam, Sulindac** are alternatives.
- **COLCHICINE** given when pts cannot tolerate NSAIDS.
- If these drugs fail, then **prednisilone** starting 40 mgs/d then tapering as symptoms disappear.

- No use of **aspirin** & **uricosuric agents** in ac. Gout rather they are used in recurrent & prophylactic gout.
- Any vigorous diuretic therapy may put ac. Gout by increasing volume. This will result in reabsorption of uric acid resulting in acute gout.

**COLCHICINE**

- Mechanism of action: Inhibits **xanthine oxidase**.
- Rapidly absorbed after oral administration. Peak levels within 2-3 hrs. Some is metabolized in liver & excreted in urine. Half-life is 3-6 hrs. Therapeutic level is 0.5-1.0 mg/dl.

**MOA:** Mechanism of action is inhibition of **xanthine oxidase** which is involved in the metabolism of purines.

- **NSAIDs** and **colchicine** action is produced by binding to **COX** and **xanthine oxidase** respectively. This blocks cellular functions such as synthesis of prostaglandins leading to inhibition of **NSAID** receptor & subsequent analgesic effect.
- **NSAIDs** are reversible inhibitors of **COX** and **colchicine** is a reversible inhibitor of **xanthine oxidase**.

**NSAIDs** are a group of drugs which have analgesic, anti-inflammatory and antipyretic effects. They are reversible inhibitors of **COX** and **colchicine** is a reversible inhibitor of **xanthine oxidase**.

## DRUG TREATMENT OF AC. GOUT

- 1) **NASIDS** highly effective in terminating ac. attack in a few hrs. **indomethacin** is 1<sup>st</sup> choice. 25-50 mgs. tds orally 4<sup>th</sup> dose at bedtime. **Naproxen, Diclofenac, Piroxicam, Sulindac** are alternatives.
- 2) **COLCHICINE** given when pts cannot tolerate NSAIDS.
- 3) If these drugs fail, then **prednisilone** starting 40 mgs/d then tapering as symptoms disappear.

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Slides Outline


**ACTINOPHAGOCYTES:** uric acid crystals are initially phagocytosed by macrophages which then release PGE<sub>2</sub>, lysosomal enzymes & iL-1, attracted by these chemotactic mediators.

**polymorphonuclear leukocytes** migrate into joint space & amplify the ongoing inflammatory process. **white star**

**phase of attack:** T<sub>H</sub>1 macrophages secrete iL-1 into the joint spaces & release more inflammatory mediators.

In addition, there is T<sub>H</sub>1 cells cell production in synovial fluid which causes a cytokine storm which causes degradation of uric acid crystals.

**Acute gouty attacks** result from a number of conditions, including excessive alcohol consumption, a diet rich in purines or fatty acids.



**DRUG TREATMENT OF GOUT**

- Drugs that address symptoms
- Anti-inflammatory drugs with or without analgesia: Indomethacin, Diclofenac, Naproxen, Piroxicam.
- Colchicine & adrenal steroids.
- Drugs that prevent urate synthesis: Allopurinol & Febuxostat.
- Uricosuric agents: Sulphinpyrazone & Probenecid.

# DRUG TREATMENT OF GOUT

- 1) Drugs that suppress symptoms.
  - Anti-inflammatory drugs with or without analgesia: Indomethacin, Diclofenac, Naproxen, Piroxicam.
  - Colchicine & adrenal steroids.
- 2) Drugs that prevent urate synthesis:
 

Allopurinol & Febuxostat.
- 3) Uricosuric agents:
 

Sulphinpyrazone & Probenecid.

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**PATHOPHYSIOLOGY:** uric acid crystals are initially phagocytosed by synoviocytes which then release PGE<sub>2</sub>, lysosomal enzymes & IL-1. Attracted by these chemotactic mediators, polymorphonuclear leukocytes migrate into joint space & amplify the ongoing inflammatory process. In the acute phase of attack, ↑ no. of macrophages appear along the urate crystals & release more inflammatory mediators.

In addition, there is ↑ in uric acid production in synovial fluid which causes a ↓ in local pH which fosters deposition of urate crystals.

Acute gouty attacks can result from a number of conditions, including excessive alcohol consumption, a diet rich in purines or fatty foods.

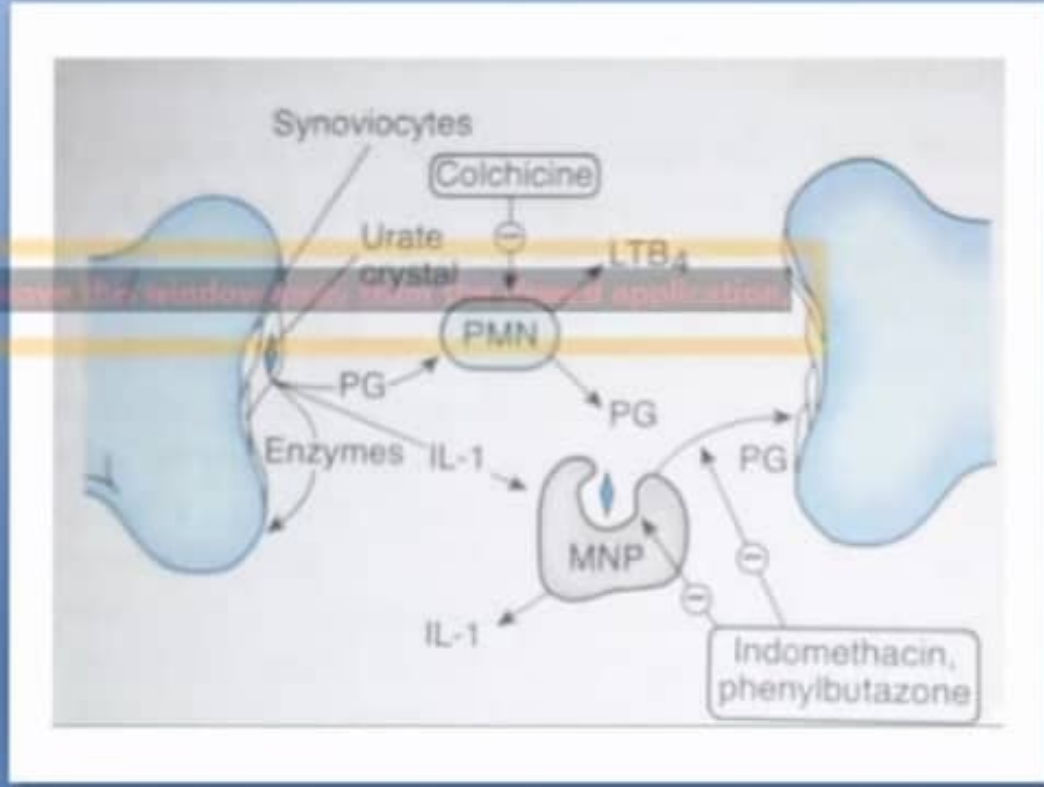


**DRUG TREATMENT OF GOUT**

- Drugs that suppress symptoms
- Anti-inflammatory drugs with or without analgesic: indomethacin, ibuprofen, naproxen, piroxicam
- Colchicine & steroid steroids
- Drugs that prevent urate synthesis: allopurinol & febuxostat
- Uricosuric agents: sulfinpyrazone & probenecid

**DRUG TREATMENT OF ACUTE GOUT**

- NSAIDs highly effective in terminating an attack in a few hrs. indomethacin is 1<sup>st</sup> choice. 25-50 mg tid early in dose at bedtime. Naproxen, Diclofenac, Ibuprofen, Sulindac are alternatives.



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Slides Outline

**GOUT**  
BY DR. JAVAID NAZIR

**Gout:** a local metabolic disorder characterized by recurrent attacks of arthritis due to deposition of monosodium urate in joints & soft tissue. Formation of urate and deposit in tissues may also occur that is often associated with high serum uric acid level, especially in individuals who are regarded as product of acute metabolism.

**CAUSATION:** hyperuricemia does not always lead to gout but gout is often preceded by hyperuricemia.



**HISTOPATHOLOGIC:** uric acid crystals are initially precipitated by monocytes which then release PGs, tumour necrosis & IL-1. Attracted by these chemotactic mediators, polymorphonuclear leukocytes migrate into joint space & embark on ongoing inflammatory process. Some are phagocytosed, 75% of macrophages adhere to urate crystals & release more inflammatory mediators.

In addition there is ↑ in lactic acid production in synovial fluid which causes a ↓ in local PH which fosters deposition of urate crystals.

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In addition, there is ↑ in lactic acid production in synovial fluid which causes a ↓ in local PH which fosters deposition of urate crystals.

Acute gouty attacks can result from a number of conditions, including excessive alcohol consumption, a diet rich in purines or kidney disease.

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Slides Outline

**PATHOPHYSIOLOGY:** uric acid crystals are initially phagocytosed by synoviocytes which then release PGs, lysosomal enzymes & IL-1. Attracted by these chemotactic mediators, polymorphonuclear leukocytes migrate into joint space & amplify the ongoing inflammatory process. In the later phase of attack, ↑ no. of macrophages appear, ingest the urate crystals & release more inflammatory mediators.

In addition, there is ↑ uric acid production in synovial fluid which causes a ↑ in local pH which favors deposition of urate crystals.

Acute gouty attacks can result from a number of conditions, including excessive alcohol consumption, a diet rich in purines or uric acid.

**DRUG TREATMENT OF GOUT**

- 1) Drugs that suppress symptoms
- 2) anti-inflammatory drugs with or without analgesic: NSAIDs, Colchicine, Naproxen, Paracetamol
- 3) Corticosteroids & steroid analogs
- 4) Drugs that prevent uric acid crystals: Allopurinol & Febuxostat
- 5) uric acid agents: Sulfinpyrazone & Probenecid

**DRUG TREATMENT OF AC GOUT**

- 1) NSAIDs highly effective in terminating ac attack. In a few hrs, indomethacin is 1<sup>st</sup> choice (25-50 mg, 3-4 times a day or bedtime). Naproxen, Diclofenac, Etoricoxib, Sulindac are alternatives.

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**GOUT**  
BY DR.JAVAID NAZIR

**Gout:** a hereditary disease characterized by recurrent attacks of arthritis due to deposition of monosodium urate in joints & soft tissue. Hereditary of urate acid defect in kidney makes acute.

Gout is also associated with high serum uric acid level, which results in uric acid crystals, which is important product of purine metabolism.

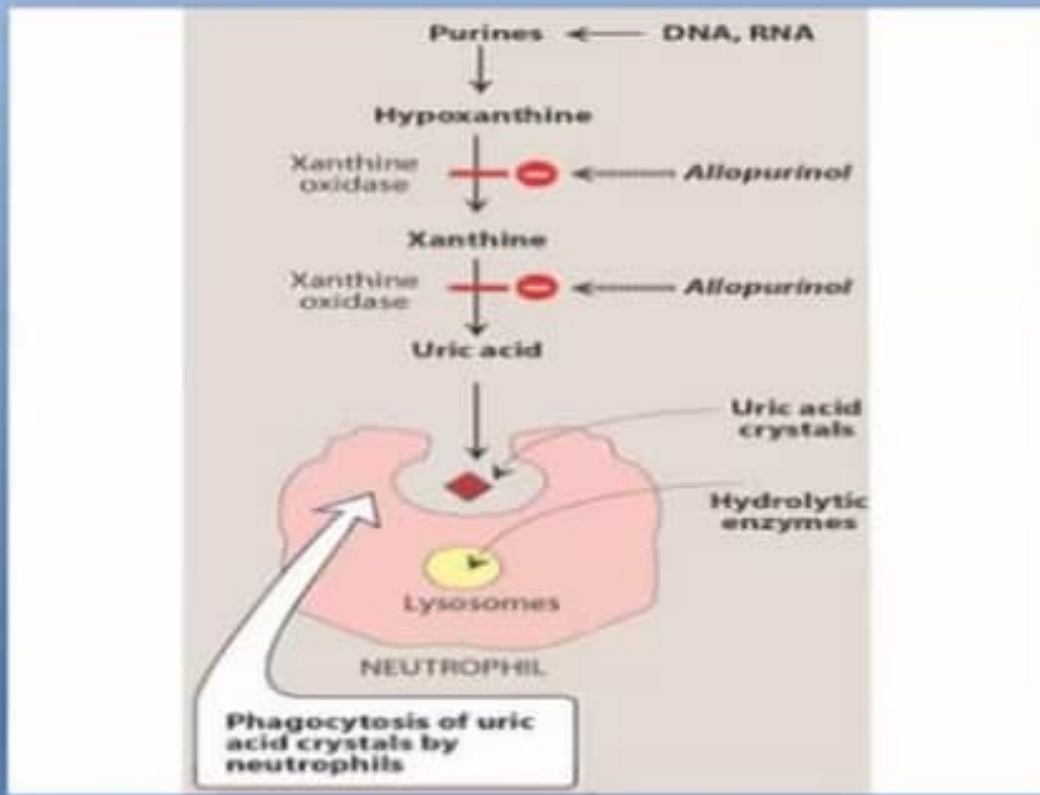
**Causes:** hyperuricemia does not always lead to gout. Gout is often caused by hyperuricemia.

**PATHOPHYSIOLOGY:** Uric acid crystals are initially phagocytosed by granulocytes which then release P22, lysosomal enzymes & IL-1. Activated by these chemotactic mediators, polymorphonuclear leukocytes migrate into joint space & empty the ongoing inflammatory process. In the later phase of attack, T cell of macrophages secrete lipid like uric acid crystals & release more inflammatory mediators.

In addition, there is Tri-ortho acid production in synovial fluid which causes a further rise in uric acid levels & deposition of uric acid crystals.

After body is returned to normal, a

uric acid from



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Slides Outline

- PROBENACID 250mg/500mg/1g**
  - Use to the only look and risk of gout
  - Approved in only who would have attacks of gout and to use treatment of uric acid
  - Probenacil is used to prevent attacks of gout
  - Probenacil is used to prevent attacks of gout
  - Probenacil is used to prevent attacks of gout
- INDICATIONS**
  - Probenacil is used to prevent attacks of gout
  - Probenacil is used to prevent attacks of gout
  - Probenacil is used to prevent attacks of gout
- DOSAGE**
  - Probenacil 250 mg orally in divided doses increased up to 1 g after one week
  - Spz 200 mg orally daily increased up to 400 to 800 mg per day in divided doses with food
- Adverse/contraindications**
  - Probenacil is used to prevent attacks of gout

# DOSAGE

- Probenacil 0.5 g/d orally in

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g I

- Spz 200 mgs orally daily increased up to 400 to 800 mgs per day in divided doses with food.





Slides Outline

**URICOSURIC AGENTS**

- **Probenecid** & **Sulfinpyrazone**
- Used to decrease both rate and rate of gout
- Avoided in pts who excrete large amounts of uric acid - to risk formation of uric acid stones
- **Sulfinpyrazone** - not as often tolerated as other uricolytics. **SPC** increased to uric acid stones. Indications of an analog of uricolytics
- **Probenecid** completely indicated to oral uricolytics and excreted metabolites - **1 to 20%**

- Specific uricolytics used over the 10 duration of its action - **benzbromarone**
- **MSA** - uric acid levels found at generally uricolytic drug - leads to reduction at the middle segment of foot. Duration of its action ends also decreased by therapy
- Specific of uric acid used as an analog of uricolytics - leads to uric acid stones. Indications of uric acid stones - **1 to 20%**
- **Probenecid** - completely indicated to uricolytics and excreted metabolites - **1 to 20%**

**Indications**

- Therapy initiated after several attacks of gouty arthritis - another indicator of both agents or when serum uric acid levels are so high that tissue damage is inevitable
- Therapy should not be started until two to three weeks after an acute attack
- **Indications** - Both are GI irritants. **Sulfinpyrazone** is more active. **Allopurinol** - both may cause aplastic anaemia rarely
- **Probenecid** may cause nephrotic syn.

**DOSAGE**

- **Probenecid** 0.2 giv every in divided doses increased upto 1g after one week
- **Sulfinpyrazone** 200 mg orally daily increased upto 400 to 500 mg per day in divided doses 4 or 5 times

**Allopurinol (purine analog)**

- 1 to 2 mg/kg to which increase 100 mg daily until

## Indications

- Therapy initiated after several attacks of gouty arthritis or when evidence of tophi appears or when serum uric acid levels are so high that tissue damage is inevitable.
- Therapy should not be started until two to three weeks after an acute attack.

**Toxicity:** Both are GI irritants but spz is more active. Allergic dermatitis both may cause aplastic anaemia rarely.

**Probenecid may cause nephrotic syn.**

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- Spz rapidly excreted by kidneys, even then its duration of its action is as long as probenacid.

**MOA:** uric acid freely filtered at glomerulus.

Uricosuric drugs block its reabsorption at the

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middle segment of the proximal tubule. Secretion of other weak acids also decreased by these agents.

- Aspirin should not be used as an analgesic in gouty patients because in low doses aspirin causes net retention of uric acid by inhibiting the secretory transporters.
- Probenacid was originally developed to prolong penicilin (weak acid) blood levels because its secretion is also decreased.



Slides Outline

16 URICOSURIC AGENTS

- **PROBENACID & SULPHINPYRAZONE:**
- Used to dec.urate body pool in pts of gout.
- Avoided in pts. who excrete large amounts of uric acid to ppt. formation of uric acid calculi.
- **ORGANIC ACIDS.** Act at anion transport sites of renal tubule. **SPZ** is related to phenylbutazone. Metabolite of an analog of phenylbutazone.
- **Probenacid** completely reabsorbed by renal tubules and slowly metabolized.  $t_{1/2}$  5-8h.

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INDICATIONS

• Probenacid after several attacks of gouty arthritis or other evidence of gouty disease in which serum uric acid levels are so high that dosage therapy is desirable.

• Probenacid not indicated until level of blood uric acid is relatively stable.

**Contraindications:** Both are contraindicated in renal insufficiency, hepatic insufficiency, and in patients with severe renal insufficiency.

**Probenacid may cause nephritis also.**

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DOSAGE

- **Probenacid** 0.5 g tid every 6 divided doses increased with 1 g after one week.
- **SPZ** 200 mg tid every 6 hrs increased up to 400 to 800 mg per day in divided doses with food.

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Allopurinol (urate analog)

• 100 mg tid every 6 hours with food.

**Allopurinol:** 200 mg divided after one week.  $t_{1/2}$  2-4 hours.

## URICOSURIC AGENTS

- **PROBENACID & SULPHINPYRAZONE:**
- Used to dec.urate body pool in pts of gout.
- Avoided in pts. who excrete large amounts of uric acid to ppt. formation of uric acid calculi.
- **ORGANIC ACIDS.** Act at anion transport sites of renal tubule. **SPZ** is related to phenylbutazone. Metabolite of an analog of phenylbutazone.
- **Probenacid** completely reabsorbed by renal tubules and slowly metabolized.  $t_{1/2}$  5-8h.

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AD EFFECTS

- Diarrhea, may be N,V. ABDOMENAL PAIN.
- Hepatic necrosis, renal failure, DIC & seizures
- Rarely hair loss, bone marrow depression, peripheral neuritis & myopathy.
- More severe ad. effects associated. with i/v admn.
- Overdosage toxicity: Symptoms are burning throat pain, bloody diarrhea, shock, hematuria & oliguria.
- DOSE: Initial dose 0.6-1.2 mgs followed by 0.6 mgs. every 02 hrs until pain is relieved. Total dose can be given IV if required.
- CAUTION: As little as 08 mgs in 24 hrs may be fatal. Prophylactic dose 0.6mg tds.

INDICATIONS

AD EFFECTS

USCIBURIC AGENTS

Department's screen

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INDICATIONS

- 1. **Ac. Gouty arthritis:** Although more specific in gout than NSAIDS but not used frequently **B/O troublesome diarrhea** associated with it. So preferred in prophylaxis of recurrent episodes of gouty arthritis.
- 2. In preventing attacks of **Ac. Mediterrean fever.**
- 3. **May be beneficial in SARCOID ARTHRITIS & IN HEPATIC CIRRHOSIS.**

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00013 [Compatibility Mode] - Microsoft PowerPoint

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Slides Outline

1. Polymerization is a chemical reaction in which two or more small molecules combine to form larger molecules that contain repeating structural units of the original molecule.

2. Polymer is a substance made up of a large number of smaller molecules that link together to form larger molecules.

INDICATORS

- 1. No. of molecules: Although more species are present, the number of molecules is reduced.
- 2. In presence of catalyst, the reaction is accelerated.
- 3. In presence of inhibitor, the reaction is retarded.

AD EFFECTS

- 1. Heat: Most reactions are exothermic.
- 2. Pressure: Most reactions are exothermic.
- 3. Concentration: Higher concentration leads to faster reaction.
- 4. Catalyst: Catalysts speed up the reaction without being consumed.
- 5. Solvent: Solvent can affect the reaction rate.

UNUSUAL ADVERTISE

- 1. Polymerization is a chemical reaction.
- 2. Polymer is a substance made up of a large number of smaller molecules.

Click to add notes

Polymerization is a chemical reaction in which two or more small molecules combine to form larger molecules that contain repeating structural units of the original molecules.

Polymer is a substance made up of a large number of smaller molecules that link together to form larger molecules.

Microsoft PowerPoint interface showing a slide with text about uric acid and its effects. The slide content is as follows:

**uric acid.** Anti-inflammatory action is produced by binding to I/C protein **TUBULIN** preventing its depolymerization into microtubules. This disrupts cellular functions such as mobility of granulocytes so leading to inhibition of **WBC** migration & phagocytosis into affected area.

**Also blocks cell division by binding to mitotic spindles.**

- Also inhibits formation of LEUKOTRIENES B<sub>4</sub> by inhibiting LIPOXYGENASE pathway.

The slide is part of a presentation with a left-hand navigation pane containing sections like 'INDICATIONS', 'AD EFFECTS', and 'URICOTIC AGENTS'. The top ribbon includes 'Home', 'Insert', 'Design', 'Animations', 'Slide Show', 'Review', and 'View'.

Slides Outline

**GOUT**  
BY DR.JAVAID  
NAZIR

**Gout:** a familial metabolic disorder characterized by recurrent episodes of acute arthritis due to deposition of monosodium urate in joints & cartilage. Formation of uric acid calculi in kidneys may also occur.

Gout is always associated with a high serum uric acid level, poorly soluble substance which is major end product of purine metabolism.

**IMPORTANT:** hyperuricemia does not always lead to gout but gout is always preceded by hyperuricemia.



**MECHANISM:** uric acid crystals are usually precipitated by leukocytes which then release PGE<sub>2</sub>, systemic enzymes & IL-1, activated by these inflammatory mediators, polymorphonuclear leukocytes migrate into joint space & amplify the ongoing inflammatory process.

In the case of acute gout, there is increased production of uric acid in synovial fluid which results in deposition of uric acid crystals.

Windows cannot open

**Gout:** A familial metabolic disorder characterized by recurrent episodes of acute arthritis due to deposition of monosodium urate in joints & cartilage. Formation of uric acid calculi in kidneys may also occur.

Gout is always associated with a high serum uric acid level, poorly soluble substance which is major end product of purine metabolism.

**IMPORTANT:** hyperuricemia does not always lead to gout but gout is always preceded by hyperuricemia.



Microscopic image of uric acid crystals

# GOUT BY DR.JAVAID NAZIR

**GOUT:** a local metabolic disorder characterized by recurrent episodes of self-limited acute inflammation of joints & soft tissue formation of uric acid crystals in tissues may also occur. It is a disease associated with high serum uric acid levels, usually without symptoms, which is a major end product of purine metabolism. **NOTES:** Hyperuricemia does not always lead to gout but gout is always preceded by hyperuricemia.



**PATHOPHYSIOLOGY:** uric acid crystals are usually precipitated by monocytes which then release PGE<sub>2</sub>, cytokines, enzymes & IL-1. Attracted by these chemotactic mediators, polymorphonuclear leukocytes migrate into joint space & amplify the ongoing inflammatory process. In the area of the joint, T<sub>H</sub>17 macrophages appear, ingest the uric acid crystals & release more inflammatory mediators.

In addition, there is T<sub>H</sub>17 cells also production of cytokines like IL-17 which causes a lot of pain when taking medication of uric acid.

# GOUT BY DR.JAVAID NAZIR

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