37 Drugs Used in Gout

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Gout is characterized biochemically as a disorder of uric acid metabolism and clinically by hyperuricemia and recurrent attacks of acute arthritis. Gouty arthritis is most frequently seen as an acute inflammation primarily in the large toe, instep, ankle, or heel. Less often the initial symptoms appear in the knee or elbow; occasionally they are seen in the wrist. If the condition remains untreated over years, sodium urate crystals may form in the subcutaneous tissue, joints, renal parenchyma, and renal pelvis. Uric acid stones may form in the lumen of the urinary tract, and progressive renal failure often occurs in the later stages of untreated gout. Also, microcrystalline deposits of sodium urate frequently result in inflammatory bulges or bumps, termed *tophi,* appearing in the subcutaneous tissue of the earlobes, elbows, and hands and at the base of the large toe.

The elevated blood uric acid concentration in gout is an easily identified and readily treated abnormality. However, it is essential to identify the condition and institute therapy early to avoid the complications that result from a prolonged elevated uricemia. Complications include arthritis, tophi, urinary calculi, and gouty nephropathy.

Although all forms of gout have the common trait of hyperuricemia, their causes can be manifold. *Primary, or genetic, gout results from either increased synthesis of uric acid or decreased renal excretion of the substance.* Some gout patients have an unusual shunt mechanism that converts glycine directly to uric acid rather than to its normal metabolic products. *Secondary gout may result from either overproduction or impaired elimination of uric acid.* Overproduction is usually secondary to some other disorder, most frequently of hematological origin. For instance, in leukemia, myeloid metaplasia, lymphoma, polycythemia vera, and rapid weight loss (dieting), breakdown of cellular nucleoprotein is increased, which can lead to excess formation of uric acid.

In secondary gout, diminished elimination of uric acid can be due to lead nephropathy, glycogen storage disease, or sickle cell anemia. In addition, several drugs, including salicylates, pyrazinamide, alcohol, ethambutol, nicotinic acid, cyclosporine, fructose, cytotoxic agents, and certain diuretics (e.g., thiazides, furosemide, bumetanide) will impair the renal elimination of uric acid. These drugs competitively inhibit the active secretion of uric acid (see Chapter 4) into the urine, with resulting hyperuricemia.

CHEMISTRY OF URIC ACID

Humans excrete approximately 0.7 g uric acid daily. Most of this is derived from the metabolic breakdown of the purine bases adenine and guanine. Uric acid is less ionized and less water soluble at most acidic pH's. It exists mostly as the monovalent salt *sodium urate*. However, uric acid itself may be the predominant form found in an acid urine. Because the urine becomes more acidic as it moves through the renal tubular system, filtered urate is increasingly converted to uric acid. The relatively limited solubility of urate at a urinary pH of 5 is clinically significant in patients with gout because of the possibility of the formation of uric acid stones.

RENAL URATE HOMEOSTASIS

The binding of uric acid to plasma proteins is relatively small and probably does not have great physiological significance. However, even this limited binding may be affected by administration of drugs, such as salicylates, phenylbutazone, probenecid, and sulfinpyrazone. These drugs probably affect urate protein binding only secondarily; that is, their principal action is to interfere with renal transport of uric acid, which in turn leads to alterations in plasma urate binding.

The renal mechanisms involved in the handling of uric acid are complex and involve filtration, reabsorption, secretion, and possibly postsecretory reabsorption. The proximal tubule is the principal site of both carrier-mediated reabsorption and secretion of urate. Urate is believed to be transported from the ultrafiltrate to the intracellular space by an anion (hydroxyl, bicarbonate, chloride, or lactate) exchange mechanism in the *luminal membrane*. This active transport system can be inhibited by drugs, such as probenecid, sulfinpyrazone, and salicylate. The urate accumulated in the cell moves passively across the basolateral membrane and into the peritubular fluid down its electrochemical gradient. Conversely, active tubular secretion of urate occurs as a consequence of carrier-mediated transport across the *basolateral membrane* of the proximal tubule. The urate accumulated in the cell moves passively across the luminal membrane into the ultrafiltrate along its concentration gradient. The carrier-mediated secretion of urate can be inhibited by a variety of organic anions, including the thiazide and loop diuretics.

The intracellular concentration of urate in the proximal tubule will ultimately be determined by the balance of influx and efflux. When the transport of urate from the *peritubular fluid* is high, there is a net elimination of urate across the luminal membrane. In contrast, when the transport of urate from *luminal fluid* is high, there is a net reabsorption across the basolateral membrane.

Urate excretion is subject to modification by a variety of organic anions, including uricosuric agents, phenylbutazone, diuretics, radiographic contrast agents, and certain anticancer compounds. A further complicating feature is that drug effects may be biphasic; that is, small amounts may depress urate excretion, while larger doses have uricosuric effects.

RELATIONSHIP OF URIC ACID LEVELS TO GOUT

The degree of risk of acquiring gouty arthritis is related primarily to the extent and duration of the hyperuricemia. The risk is essentially zero at serum urate concentration below 7 mg/dL, whereas at concentrations of 10 to 11 mg/dL, the likelihood of having the disorder is relatively high. Gouty arthritis due to impaired renal excretion of uric acid may be diagnosed through a quantification of the patient's uric acid excretion. If a patient on a purine-restricted diet for 1 week excretes more than 600 mg uric acid per 24 hours, the individual is probably an overproducer. If, however, less than 350 mg of uric acid is eliminated in 24 hours, suspect impaired renal function.

ROLE OF PHAGOCYTOSIS IN ACUTE GOUTY ARTHRITIS

The mere presence of urate crystals in the joint cannot be correlated with the appearance of acute gouty arthritic symptoms. Individuals who have never had any gouty arthritic problems have nonetheless been found to have uric acid deposited on their articular cartilage. Acute attacks are generally the result of granulocytic phagocytosis of the urate crystals. This engulfing of the crystals is accompanied by cellular release of chemotactic lipids, lysosomal enzymes, and acidic substances into the synovial tissues. The lipids appear to trigger further phagocytosis, whereas the acidic compounds decrease local pH to the point that increased urate crystal formation is favored.

In addition to the phagocytic activity of the leukocytes, small peptide substances, such as the kinins, which are thought to be partially responsible for the local inflammatory response in gouty arthritis, accumulate in the joint space. The inflammation is associated with local vasodilation, increased vascular permeability, and pain.

PRINCIPLES OF GOUT MANAGEMENT

Initial treatment of gout and its associated hyperuricemia must involve therapy directed toward terminating the painful inflammatory process that is a prominent feature of acute gouty arthritis. A variety of nonsteroidal antiinflammatory compounds (e.g., in-

domethacin, oxyphenbutazone, ibuprofen, naproxen, sulindac) can be administered either alone or in combination with *colchicine,* a relatively specific agent for use in acute gouty attacks. Glucocorticosteroids, such as prednisone, can be given as a tapered dose over 10 days to replace colchicine. These steroids cause fewer side effects than does colchicine. If the diagnosis is uncertain, colchicine should be used, since a response to this drug is generally taken as establishing the diagnosis of acute gouty arthritis.

Although the treatment of the hyperuricemia of gout depends upon lowering blood uric acid levels, most physicians caution against employing drugs such as *allopurinol, probenecid,* or *sulfinpyrazone* during an acute attack, since the therapy itself, at least during the initial stages, may exacerbate the condition. Once the acute symptoms are under control and the patient is asymptomatic, appropriate treatment should include not only drug therapy but also management of body weight and control of dietary purine intake. *Long-term treatment is directed toward decreasing uric acid production from nucleoprotein, increasing excretion, or both.*

Uric acid production is more easily controlled by drug therapy than by dietary restriction, because only a small portion of blood uric acid is derived from the dietary intake of purines. Excretion of uric acid may be increased by increasing the rate of urine flow or by using uricosuric agents. Since uric acid is filtered at the glomerulus and both actively secreted and reabsorbed by the proximal tubule cells, both approaches are effective.

Since overproducers are already excreting large quantities of uric acid in their urine, drugs that further increase the rate of excretion (i.e., uricosuric compounds) increase the likelihood of renal stone formation. In these patients, the use of a compound that inhibits uric acid synthesis is preferable. Although at first glance the use of a combination of drugs—a drug that reduces production along with one that is uricosuric—would seem to be a rational therapeutic approach, in practice this has not worked well. Apparently the effectiveness of a drug that inhibits uric acid synthesis can be diminished by uricosuric agents, and therefore the combination has less value than each drug used separately. Furthermore, side effects appear to occur more frequently during combination drug therapy.

COLCHICINE

Gouty inflammation of the tissues or joints is associated with local accumulation of urate microcrystals by the phagocytic neutrophils. After sufficient amounts of these crystals have been taken up into the phagolysosomes of the neutrophil, these organelles disrupt and release their degradative enzymes, accumulated microcrystals (which may be rephagocytized), and chemotac-

tic factors. It is these released substances that are responsible for much of the local inflammation and pain associated with acute attacks of gout.

Colchicine, an alkaloid obtained from the autumn crocus, has long been used and is relatively selective for the treatment of acute gouty arthritis. Unlike many of the newer agents for use in gout, *colchicine has minimal effects on uric acid synthesis and excretion;* it decreases inflammation associated with this disorder. *It is thought that colchicine somehow prevents the release of the chemotactic factors and/or inflammatory cytokines from the neutrophils, and this in turn decreases the attraction of more neutrophils into the affected area* (Fig. 37.1). The ability of colchicine to bind to leukocyte microtubules in a reversible covalent complex and cause their depolymerization also may be a factor in decreasing the attraction of the motile leukocytes into the inflamed area.

Colchicine is rapidly absorbed after oral administration and tends to concentrate in the spleen, kidney, liver, and gastrointestinal tract. Leukocytes also avidly accumulate and store colchicine even after a single intravenous injection. Since colchicine can accumulate in cells against a concentration gradient, it is postulated that an active transport process may be involved in its cellular uptake. The drug is metabolized, primarily in the liver, by deacetylation. Fecal excretion plays a major role in colchicine elimination, since it and its metabolites are readily secreted into the bile. Only about 15 to 30% of the drug is eliminated in the urine except in patients with liver disease; urinary excretion is more important in these individuals.

The major use of colchicine is as an antiinflammatory agent in the treatment of acute gouty arthritis; it is not effective in reducing inflammation in other disorders. It also can be used to prevent attacks. Since colchicine is so rapidly effective in relieving the acute symptoms of gout (substantial improvement is achieved within hours), it has been used as a diagnostic aid in this disorder.

Therapy with colchicine is usually begun at the first sign of an attack and is continued until symptoms subside, adverse gastrointestinal reactions appear, or a maximum dose of 6 to 7 mg has been reached. The drug can be given intravenously as well as orally, but care must be exercised, since extravasated drug may result in local sloughing of skin and subcutaneous tissues. Relief of pain and inflammation usually occurs within 48 hours. Small doses of colchicine can be used during asymptomatic periods to minimize the reappearance or severity of acute attacks. It should be used with caution in patients with preexisting compromised heart, kidney, gastrointestinal tract, and liver disease.

Diarrhea, nausea, vomiting, and abdominal pain are the major limiting side effects that ultimately determine the tolerated dosage. These symptoms occur in approximately 80% of patients who take colchicine, especially
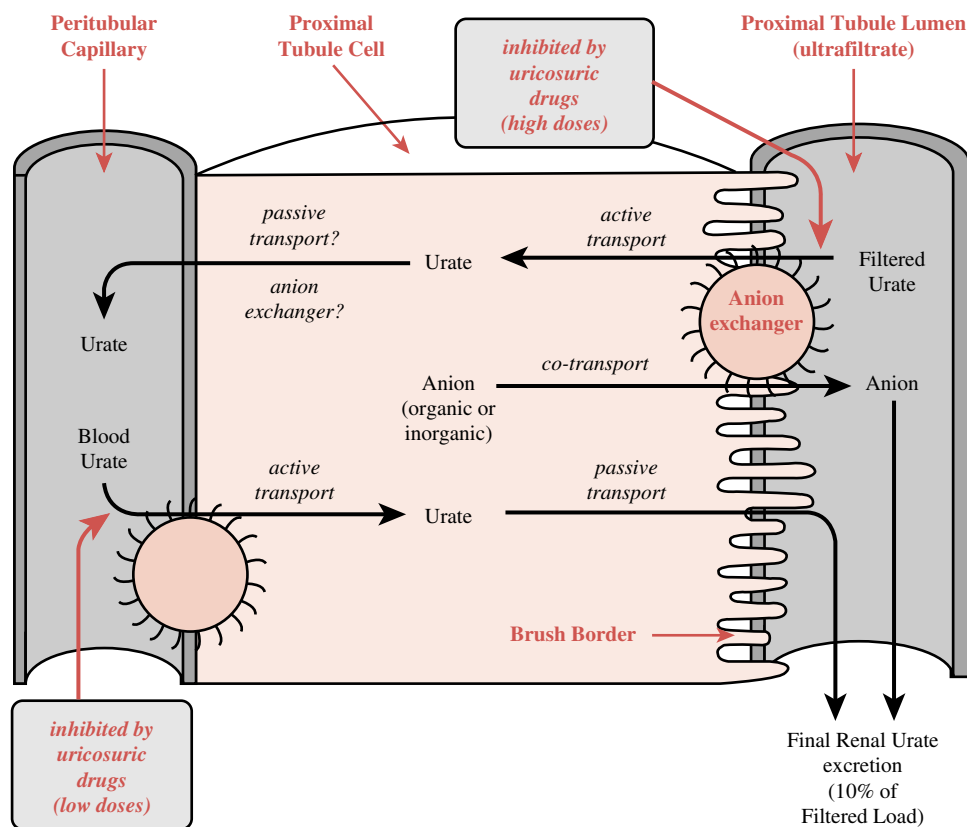
FIGURE 37.1

Renal handling of uric acid. Uric acid may be actively reabsorbed from the ultrafiltrate following its glomerular filtration or it may be secreted from the blood across the basolateral membrane into the proximal tubular cell. Both passive and active transport mechanisms are involved in the handling of urate. Uricosuric drugs at appropriate doses interfere with these processes.

in those taking high dosages. The hepatobiliary recycling of colchicine and its antimitotic effect on cells that are rapidly turning over, such as those of the intestinal epithelium, account for its gastrointestinal toxicity. Gastrointestinal symptoms generally intervene before the appearance of more serious toxicity and thereby provide a margin of safety in drug administration. Ingestion of large doses of colchicine may be followed by a burning sensation in the throat, bloody diarrhea, shock, hematuria, oliguria, and central nervous system (CNS) depression.

URICOSURIC AGENTS

The uricosuric drugs (or urate diuretics) are anions that are somewhat similar to urate in structure; therefore, they can compete with uric acid for transport sites. Small doses of uricosuric agents will actually decrease the total excretion of urate by inhibiting its tubular secretion. *The quantitative importance of the secretory mechanism is relatively minor, however, and at high dosages these same drugs increase uric acid elimination by inhibiting its proximal tubular reabsorption.* Thus, uricosuric drugs have a seemingly paradoxical effect on both serum and urinary uric acid levels: at low doses, they increase serum levels while decreasing the urinary levels; they have the opposite effect on these two levels at high dosages.

The two most clinically important uricosuric drugs, probenecid and sulfinpyrazone, are organic acids. *The initial phase of therapy with uricosuric drugs is the most dangerous period.* Until uricosuric drug levels build up sufficiently to fully inhibit uric acid reabsorption as well as secretion, there may be a temporary increase in uric acid blood levels that significantly increases the risk of an acute gouty attack. Therefore, *it is wise to begin therapy with the administration of small amounts of colchicine before adding a uricosuric drug to the therapeutic regimen.* In addition, the initial rise in urinary uric acid concentrations during uricosuric drug therapy may result in renal stone formation.

Probenecid

When probenecid (*ColBENEMID*) is given in sufficient amounts, *it will block the active reabsorption of uric acid in the proximal tubules following its glomerular filtration,* thereby increasing the amount of urate eliminated. In contrast, low dosages of probenecid appear to compete preferentially with plasma uric acid for the proximal tubule anionic transport system and thereby block its access to this active secretory system. The uricosuric action of probenecid, however, is accounted for by the drug's ability to inhibit the active reabsorption of *filtered* urate.

Probenecid is rapidly absorbed after oral administration, with peak plasma levels usually reached in 2 to 4 hours. Its half-life is somewhat variable (6–12 hours) because of both its extensive plasma protein binding and its active proximal tubular secretion. Since tubular back-diffusion is decreased at alkaline urinary pH ranges, probenecid excretion increases with increasing urinary pH. Probenecid is rapidly metabolized, with less than 5% of an administered dose being eliminated in 24 hours. The major metabolite is an acyl monoglucuronide.

Probenecid is an effective and relatively safe agent for controlling hyperuricemia and preventing tophi deposition in tissues. Chronic administration will decrease the incidence of acute gouty attacks as well as diminish the complications usually associated with hyperuricemia, such as renal damage and tophi deposition. Probenecid is still used by some physicians to maintain high blood levels of penicillin, cephalosporin, acyclovir, and cyclosporine. It is not useful in treating acute attacks of gouty arthritis. If the total amount of uric acid excreted is greater than 800 mg/day, the urine should be alkalinized to prevent kidney stone formation and promote uric acid.

Probenecid can impair the renal active secretion of a variety of acidic compounds, including sulfinpyrazone, sulfonylureas, indomethacin, penicillin, sulfonamides, and 17-ketosteroids. If these agents are to be given concomitantly with probenecid, their dosage should be modified appropriately. *Salicylates interfere with the clinical effects of both sulfinpyrazone and probenecid and should be avoided in patients treated with uricosuric agents.* Uricosuric agents also can influence the volume of distribution and hepatic metabolism of a number of drugs.

Adverse reactions associated with probenecid therapy include occasional rashes, allergic dermatitis, upper gastrointestinal tract irritation, and drowsiness. The drug is contraindicated in patients with a history of renal calculi.

Sulfinpyrazone

Sulfinpyrazone (*Anturane*), another uricosuric agent, is chemically related to the antiinflammatory and uricosuric compound phenylbutazone. However, it lacks the antiinflammatory, analgesic, and sodium-retaining properties of phenylbutazone and possesses a number of undesirable side effects that limit its therapeutic usefulness. The mechanism of sulfinpyrazone's uricosuric activity is similar to that of probenecid.

Sulfinpyrazone is readily absorbed after oral administration, with peak blood levels reached 1 to 2 hours after ingestion. It is more highly bound to plasma protein (98–99%) than is probenecid (84–94%) and is a more potent uricosuric agent. Most of the drug (90%) is eliminated through active proximal tubular secretion of the intact parent compound. Sulfinpyrazone also undergoes *p*-hydroxylation to form a uricosuric metabolite, the formation of which undoubtedly contributes to the drug's prolonged activity (about 10 hours) and potency relative to probenecid. In contrast to probenecid, the rate of excretion of sulfinpyrazone is not enhanced by alkalinization of the urine, since the drug is largely ionized at all urinary pH ranges and therefore not a candidate for passive back-diffusion.

Sulfinpyrazone, although less effective than allopurinol in reducing serum uric acid levels, remains useful for the prevention or reduction of the joint changes and tophus deposition that would otherwise occur in chronic gout; it has no antiinflammatory properties. During the initial period of sulfinpyrazone use, acute attacks of gout may increase in frequency and severity. It is recommended, therefore, that either colchicine or a nonsteroidal antiinflammatory agent be coadministered during early sulfinpyrazone therapy.

Abdominal pain, nausea, and possible reactivation of peptic ulcer have been reported. The drug should be used with caution in patients with compromised renal function, and adequate fluid intake should always accompany sulfinpyrazone administration to minimize the possibility of renal calculus formation.

Allopurinol

Allopurinol (Zyloprim) *is the drug of choice in the treatment of chronic tophaceous gout* and is especially useful in patients whose treatment is complicated by renal insufficiency.

Mechanism of Action

Allopurinol, in contrast to the uricosuric drugs, *reduces serum urate levels through a competitive inhibition of uric acid synthesis* rather than by impairing renal urate reabsorption. This action is accomplished by inhibiting *xanthine oxidase,* the enzyme involved in the metabolism of hypoxanthine and xanthine to uric acid. After enzyme inhibition, the urinary and blood concentrations of uric acid are greatly reduced and there is a simultaneous increase in the excretion of the more soluble uric acid precursors, xanthine and hypoxanthine.

Allopurinol itself is metabolized by xanthine oxidase to form the active metabolite oxypurinol, which tends to accumulate after chronic administration of the parent drug. This phenomenon contributes to the therapeutic effectiveness of allopurinol in long-term use. *Oxypurinol is probably responsible for the antigout effects of allopurinol.* Oxypurinol itself is not administered because it is not well absorbed orally.

Absorption, Metabolism, and Excretion

Allopurinol is largely absorbed after oral ingestion, reaching peak blood levels in about 1 hour. In contrast to the uricosuric drugs, allopurinol is not appreciably bound to plasma proteins and is only a minor substrate for renal secretory mechanisms. The formation of oxypurinol and the finding that this metabolite is in part actively reabsorbed in the proximal tubule account for the long half-life of the metabolite (18–20 hours) and permits once-a-day drug administration.

Clinical Uses

Allopurinol is especially indicated in the treatment of chronic tophaceous gout, since patients receiving it show a pronounced decrease in their serum *and* urinary uric acid levels. Because it does not depend on renal mechanisms for its efficacy, allopurinol is particularly beneficial for patients who already have developed renal uric acid stones, patients with excessively high urate excretion (e.g., above 1,200 mg in 24 hours), patients with a variety of blood disorders (e.g., leukemia, polycythemia vera), patients with excessive tophus deposition, and patients who fail to respond well to the uricosuric drugs.

Allopurinol also inhibits reperfusion injury. This injury occurs when organs that either have been transplanted or have had their usual blood perfusion blocked are reperfused with blood or an appropriate buffer solution. The cause of this injury is local formation of free radicals, such as the superoxide anion, the hydroxyl free radical, or peroxynitrite. These substances are strong oxidants and are quite damaging to tissues.

Adverse Effects

Common toxicities associated with allopurinol administration include a variety of skin rashes, gastrointestinal upset, hepatotoxicity, and fever. These reactions are often sufficiently severe to dictate termination of drug therapy. It is advised that therapy not be initiated during an acute attack of gouty arthritis. As with the uricosuric drugs, *therapy with allopurinol should be accompanied both by a sufficient increase in fluid intake to ensure water diuresis and by alkalinization of the urine.* Prophylactic use of colchicine also helps to prevent acute attacks of gout that may be brought on during the initial period of allopurinol ingestion.

Drug Interactions

Since allopurinol is metabolized by the hepatic microsomal drug-metabolizing enzymes, coadministration of drugs also metabolized by this system should be done with caution. Because allopurinol inhibits the oxidation of mercaptopurine and azathioprine, their individual administered doses must be decreased by as much as 75% when they are given together with allopurinol. Allopurinol may also increase the toxicity of other cytotoxic drugs (e.g., vidarabine). The actions of allopurinol are not antagonized by the coadministration of salicylates.

OTHER DRUGS

A number of drugs other than those discussed in detail in this chapter have been used to control the symptoms of acute gouty arthritis. Since the principal aspects of their pharmacology have been described elsewhere, they are mentioned only briefly here.

Indomethacin (*Indocin*) (see Chapter 36) exerts antiinflammatory, antipyretic, and analgesic properties. These qualities make it useful for the short-term management of the symptoms of acute gouty arthritis, although it has little effect on serum uric acid levels. Its antiinflammatory activity and ability to inhibit leukocytic phagocytosis make it particularly valuable in treating the early stages of gout, because a decrease in the leukocytic phagocytosis of urate crystals results in a decrease in the amount of peptides, prostaglandins, and other substances released from leukocyte lysosome organelles.

Phenylbutazone (*Butazolidin, Tandearil*) (see Chapter 36) also displays antipyretic, analgesic, and antiinflammatory activity. In addition, it possesses some uricosuric potency and therefore is widely used for the treatment of acute attacks of gouty arthritis, in which it is about equal to colchicine in effectiveness. Although the drug does promote the renal excretion of uric acid, its usefulness is generally attributed to its antiinflammatory actions.

Oxyphenbutazone (*Oxalid, Tandearil*) is the principal uricosuric metabolite of phenylbutazone. It has the same indications and toxicities as phenylbutazone.

Corticosteroids

The use of corticosteroids is often suggested for elderly patients with chronic tophaceous gout, since gout in the older individual often displays symptoms similar to those of rheumatoid arthritis. Patients can be given short-term administration of corticosteroids, especially for acute flare-ups. The concomitant use of alcohol, nonsteroidal antiinflammatory drugs, and most diuretics should be avoided.

Study Questions

1. The most widely used agent for the treatment of acute gouty arthritis is
   (A) Probenecid
   (B) Allopurinol
   (C) Colchicine
   (D) Indomethacin
   (E) Phenylbutazone
2. The mechanism by which probenecid lowers plasma levels of uric acid is
   (A) By inhibiting proximal tubular reabsorption of uric acid
   (B) By inhibiting production of uric acid in the liver
   (C) By promoting tubular secretion of uric acid
   (D) By inhibiting breakdown of purines to uric acid
3. Allopurinol reduces serum urate levels by
   (A) Promoting the active secretion of uric acid in kidneys
   (B) Inhibiting uric acid synthesis
   (C) Impairing renal urate reabsorption
   (D) Decreasing metabolism of uric acid
4. The primary location in the kidney where both carrier-mediated reabsorption and secretion of urate occurs is the
   (A) Ascending loop of Henle
   (B) Distal tubules
   (C) Collecting duct
   (D) Proximal tubule
   (E) Descending loop of Henle
5. Drug therapy is more effective in controlling uric acid production than is dietary restriction because
   (A) Dietary restriction does not affect production of uric acid
   (B) Drug therapy is more specific to the site of action
   (C) Only a small portion of blood uric acid is derived from the diet
   (D) The source of uric acid cannot be established

ANSWERS

1. **C.** Colchicine is relatively selective for the treatment of acute gouty arthritis because it appears to prevent the release of inflammatory cytokines and chemotactic factors. Probenecid (A) blocks renal uric acid reabsorption but is generally not used alone during the acute phase of gout. Allopurinol (B) is the drug of choice in chronic tophaceous gout. Indomethacin (D) and phenylbutazone (E) have antiinflammatory activity and are useful in treating acute gouty arthritis but are not used nearly as widely as colchicine for initial treatment.
2. **A.** Probenecid blocks active reabsorption of uric acid in the proximal tubules following glomerular filtration. It does not inhibit uric acid synthesis (B), stimulate tubular secretion (C), or inhibit the metabolism of purines (D).
3. **B.** Allopurinol inhibits xanthine oxidase, the enzyme involved in the conversion of hypoxanthine and xanthine to uric acid. It has no known ability to increase uric acid synthesis markedly (A), inhibit reabsorption (C), or impair uric acid breakdown (D).
4. **D.** While the other parts of the renal tubular system do contain active transport systems, these systems do not have an affinity of urate transport.
5. **C.** The dietary intake of purines is not a major contributing factor to uric acid blood levels. Therefore, pharmacological reduction of uric acid synthesis or increased excretion is required. Dietary restriction (A) can affect uric acid production if precursor molecules are lowered sufficiently, but this usually is not feasible. The question of drug specificity (B) is not germane to the question. Pathways of uric acid synthesis in the body (D) are well known.

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C A S E **S t u d y**   **Injudicious Food Intake Can Lead to Pain**

T. D. arrives in your office complaining of pain in his toe. He woke up in the middle of the night with the feeling that his large toe had been set on fire. He has inflammation over the ankle and toes of his right foot and complains of severe pain when you put slight pressure on the ankle. The patient is about 60 lb overweight. He consumes red meat at least 6 times a week, always with three or more glasses of red wine. You suspect that T. D. may be having an attack of acute gout. What do you do?

ANSWER: You first take a blood sample for determination of serum urate levels to substantiate your preliminary diagnosis. Pending the results of the serum urate determination, you prescribe an NSAID. Upon finding a serum urate level of 12 mg/dL and continuing pain, you prescribe colchicine. You tell your patient that he must strongly consider dietary restriction, particularly of meat and meat products. Furthermore, he should decrease his alcohol intake. Inform him that if his attacks return in spite of changes in lifestyle, you are likely going to institute other drug measures. Point out the long-term consequences of gout.