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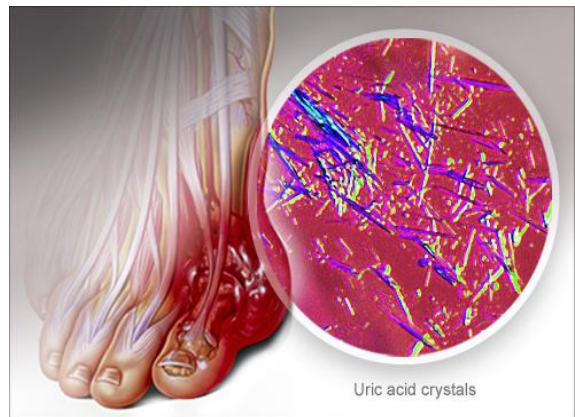
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Gout

Gout is a common and complex form of arthritis that can affect anyone. It's caused by a buildup of uric acid crystals in the joints. Uric acid is a breakdown product of purines found in many foods. It's characterized by sudden, severe attacks of pain, swelling, redness and tenderness in the joints, often the joint at the base of the big toe.

It is the most common form of inflammatory arthritis in men, and although it is more likely to affect men, women become more susceptible to it after the menopause. An attack of gout can occur suddenly, often waking you up in the middle of the night with the sensation that your big toe is on fire. The affected joint is hot, swollen and so tender that even the weight of the sheet on it may seem intolerable.



Symptoms

The signs and symptoms of gout almost always occur suddenly, and often at night. Pain can be excruciating:

- **Intense joint pain:** Gout usually affects the large joint of the big toe, but it can occur in any joint. Other commonly affected joints include the ankles, knees, elbows, wrists and fingers. The pain is likely to be most severe within the first four to 12 hours after it begins.
- **Lingering discomfort:** After the most severe pain subsides, some joint discomfort may last from a few days to a few weeks. Later attacks are likely to last longer and affect more joints.
- **Inflammation and redness:** The affected joint or joints become swollen, tender, warm and red.
- **Limited range of motion:** As gout progresses, patient may not be able to move his joints normally.

Causes

- Gout occurs when urate crystals accumulate in joints, causing the inflammation and intense pain of a gout attack. Urate crystals can form when high levels of uric acid are found in blood.
- The body produces uric acid when it breaks down purines — substances that are found naturally in the body.
- Purines are also found in certain foods, such as steak, organ meats and seafood. Other foods also promote higher levels of uric acid, such as alcoholic beverages, especially beer, and drinks sweetened with fruit sugar (fructose).
- Normally, uric acid dissolves in the blood and passes through the kidneys into urine. But sometimes either the body produces too much uric acid or the kidneys excrete too little uric acid. When this happens, uric acid can build up, forming sharp, needlelike urate crystals in a joint or surrounding tissue that cause pain, inflammation and swelling.

Risk factors

There are a number of factors that can increase the likelihood of hyperuricemia, and therefore gout:

- **Age and gender:** Men produce more uric acid than women, primarily because women tend to have lower uric acid levels. Though women's levels of uric acid approach those of men after the menopause.

- **Genetics:** A family history of gout increases the likelihood of the condition developing.
- **Lifestyle choices:** Alcohol consumption interferes with the removal of uric acid from the body. Eating a high-purine diet also increases the amount of uric acid in the body.
- **Lead exposure:** Chronic lead exposure has been linked to some cases of gout.
- **Medications:** Certain medications can increase the levels of uric acid in the body; these include some diuretics and drugs containing salicylate.
- **Weight:** Being overweight increases the risk of gout as there is more turnover of body tissue, which means more production of uric acid as a metabolic waste product. Higher levels of body fat also increase levels of systemic inflammation as fat cells produce pro-inflammatory cytokines.
- **Recent trauma or surgery:** Increases risk.
- **Other health problems:** Renal insufficiency and other kidney problems can reduce the body's ability to efficiently remove waste products, leading to elevated uric acid levels. Other conditions associated with gout include high blood pressure, diabetes, and an underactive thyroid gland.



Complications

People with gout can develop more-severe conditions, such as:

- **Recurrent gout:** Some people may never experience gout signs and symptoms again. Others may experience gout several times each year. Medications may help prevent gout attacks in people with recurrent gout. If left untreated, gout can cause erosion and destruction of a joint.
- **Advanced gout:** Untreated gout may cause deposits of urate crystals to form under the skin in nodules called tophi. Tophi can develop in several areas such as fingers, hands, feet, elbows or Achilles tendons along the backs of ankles. Tophi usually aren't painful, but they can become swollen and tender during gout attacks.
- **Kidney stones:** Urate crystals may collect in the urinary tract of people with gout, causing kidney stones. Medications can help reduce the risk of kidney stones.

Prevention

During symptom-free periods, these dietary guidelines may help protect against future flares or prevent gout from occurring in the first instance::

- Maintain a high fluid intake of around 2 to 4 liters a day. Limit sweetened beverages.
- Limit intake of meat, fish and poultry. A small amount may be tolerable, but close attention should be paid to what types, and how much seem to cause problems.
- Avoid alcohol.
- Maintain a healthy body weight. But avoid fasting or rapid weight loss, since doing so may temporarily raise uric acid levels.

Important!

It's important to take the uric-acid-lowering medicine regularly, even when you no longer have symptoms.

Tests & Diagnosis

- Gout can be tricky to diagnose, as its symptoms, when they do appear, are similar to those of other conditions. While hyperuricemia occurs in the majority of people that develop gout, it may not be present during a flare. On top of that, the majority of people with hyperuricemia do not develop gout.
- One diagnostic test that doctors can carry out is the **joint fluid test**, where fluid is extracted from the affected joint with a needle. The fluid is then examined to see if any urate crystals are present.
- As joint infections can also cause similar symptoms to gout, a doctor can look for bacteria when carrying out a joint fluid test in order to rule a bacterial cause.

- Doctors can also perform a blood test to measure the levels of uric acid in the blood, but, as mentioned, people with high uric acid levels do not always experience gout.
- Finally, doctors can search for urate crystals around joints or within a tophus using **ultrasound** or **CT scans**. X-rays cannot detect gout, but may be used to rule out other causes.

Treatment

Gout medications can be used to treat acute attacks and prevent future attacks. Medications can also reduce risk of complications.

Medications to treat gout attacks

Certain medications reduce the pain and inflammation of gout attacks, such as anti-inflammatory drugs (ibuprofen and naproxen as well as more powerful prescription NSAIDs such as indomethacin or celecoxib), colchicine, and corticosteroids such as prednisone. Corticosteroids are generally used only in people with gout who can't take either NSAIDs or colchicine.

Medications to prevent gout complications

Other medications decrease the level of uric acid in the blood and prevent the deposit of uric acid in joints (gouty arthritis), the kidneys (stones), and in tissue (tophi), helping to prevent further attacks and complications. These drugs include; xanthine oxidase inhibitors (XOIs), including allopurinol and febuxostat lesinurad, and the uricosurics probenecid and lesinurad. Uricosuric drugs improve the kidneys' ability to remove uric acid from the body. This may lower uric acid levels and reduce risk of gout, but the level of uric acid in urine is increased. Side effects include a rash, stomach pain and kidney stones. Lesinurad can be taken only along with an XOI.

References:

- 1) McIntosh J. *Everything you need to know about gout*. [Internet]; Nov 2017 [cited Dec 1, 2018]. Available from: <https://www.medicalnewstoday.com/articles/144827.php>
- 2) Mayo Clinic Staff. *Gout* [Internet]; Jan 2018 [cited Dec 1, 2018]. Available from: <https://www.mayoclinic.org/diseases-conditions/gout/symptoms-causes/syc-20372897>
- 3) AidsInfo. *Gout Pictures Slideshow: Causes, Symptoms, and Treatments of Gout*. [Internet]; May 2018 [cited Dec 1, 2018]. Available from: <https://www.webmd.com/arthritis/ss/slideshow-gout>
- 4) NHS. *Gout*. [Internet]; Aug 2017 [cited Dec 1, 2018]. Available from: <https://www.nhs.uk/conditions/gout/>

OTC Medicines Corner

A Bleak Picture of Aspirin for Primary Prevention in Older Adults



Three publications in the *New England Journal of Medicine* from the ASPREE trial showed that daily use of low-dose aspirin in healthy, community-dwelling older people without documented cardiovascular (CV) disease, dementia, or physical disability did not prolong disability-free survival, did not reduce the risk of CV disease (CVD), and was associated with a higher risk of all-cause mortality and major hemorrhage compared with placebo.

Source: MacLaughlin E. *A bleak picture of aspirin for primary prevention in older adults*. [Internet]; Nov 2018 [cited Dec 1, 2018]. Available from: <http://www.aphanet.org/cardiology/bleak-picture-aspirin-primary-prevention-older-adults>

Case Report from Alexandria Pharmacovigilance center: Risk of developing aggravated Cough, increased Sputum excretion and Neonatal tachypnea

The regional center in Alexandria has received an Individual Case Safety Report (ICSR) concerning an 8 days old neonate who suffered from rhinitis. He was administered Dimetindene drops (4 drops three times daily), desalted sea water spray and dried Ivy leaf extract syrup for treatment. After administration of Dimetindene drops, the baby developed aggravated cough, increased sputum excretion and neonatal tachypnea. One day later, the patient was diagnosed with neonatal pneumonia and was placed under incubator therapy. The patient stopped Dimetindene drops and other concomitant drugs after developing those events; the adverse events resolved after about 13 days.

Dimetindene is a Histamine H blocker 1 receptors. Has antiallergic and antipruritic effect. Reduces the increased permeability of capillaries, associated with allergic reactions. **Neonatal tachypnea** means rapid breathing (faster than most normal newborns, who breathe 40 to 60 times per minute).

Labeled information:

According to Dimetindene drops Summary of product Characteristics (SmPC) it was stated under *Contraindications* that: "dimethindene is contraindicated in newborns under 1 month, especially premature babies".

Recommendations for Healthcare Professionals:

- For infants from 1 month to 1 year old, dimethindene drops should only be used in accordance with medical advice and strict medical indications for antihistamines. The recommended dosage should not be exceeded.
- Caution should be exercised when administering the drops to children under the age of 1 year: the sedative effect may be accompanied by apnea episodes during sleep.
- The recommended daily dose is: 0.1 mg / kg body weight / day (equivalent to 2 drops per kg of body weight per day, divided into 3 receipts)
- The usual daily doses for children 1 month - 12 years or according to kg body weight is:

Patients age/ weight	Single dose (drop *)	Daily dose (drop *)
Children 1 Months before 1 year	3-10	10-30
Children 1 Year to 3 years/ 15-22.5 kg	10-15	30-45
Children 3 to 12 years/ 22.5-30 kg	15-20	45-60

*20 drops = 1 ml = 1 mg dimetindmaleate.

- Even though it may be rare, some people may have very bad and sometimes deadly side effects when taking a drug like signs of an allergic reaction, like rash; hives; itching; red, swollen, blistered, or peeling skin with or without fever; wheezing; tightness in the chest or throat; trouble breathing, swallowing, or talking; unusual hoarseness; or swelling of the mouth, face, lips, tongue, or throat.

Source: The Egyptian Pharmaceutical Vigilance Center Newsletter. 9 (9); Sept 2018.

Test Your Knowledge

- 1) When should antibiotics be administered intravenously in patients with cellulitis? In patients with:
(A) Dermal necrosis
(B) Septicemia.
(C) Suspected fascial involvement
(D) A or B
(E) A, B, or C
- 2) Which of the following products could be responsible for causing constipation?
(A) Naprosyn
(B) Adalat
(C) Vegaskin
(D) Amoxil
(E) Abilaxine
- 3) The Summaries of Product Characteristics (SPCs):
(A) are issued by a medicines regulatory agency
(B) have to be updated every year
(C) are intended for patients' use
(D) are the same for generic formulations as for the originator products
(E) reflect information in the marketing authorisations of medicinal products

Complementary Medicine

Devil's Claw

Harpagophytum procumbens (root)

Common uses

Osteoarthritis and non-specific lower back pain

Evidence: A systematic review of five trials investigating use in osteoarthritis, four in low back pain and three in mixed pain found moderate evidence for use in osteoarthritis of the spine, hip and knee and in the treatment of acute exacerbations of chronic non-specific low back pain. A systematic review of use in low backpain found strong evidence that doses standardised to 50 mg or 100 mg harpagoside daily were better than placebo for short-term improvements in pain and need for rescue medication. The trials were of moderate or high quality, but they were limited to short-term use (up to six weeks). The Cochrane review noted potential conflicts of interest in half of the reviewed studies.



Musculoskeletal pain

Evidence: A randomised double-blind, placebocontrolled trial in 65 patients taking the equivalent of 24 mg of harpagoside daily found an improvement in visual analogue scale (VAS) scores for muscle pain after four weeks' treatment for mild to moderate musculoskeletal pain.

Other reported uses: Gout, myalgia, fibrositis, lumbago and pleurodynia.

Notes

- Increased stomach acidity may cause diarrhoea and gastrointestinal discomfort in sensitive patients. Avoid in patients with acid reflux or duodenal ulcer.

- May lower blood sugar levels.
- Alteration in calcium influx regulation in smooth muscle may affect heart rhythm and rate. Use with caution in patients on anti-arrhythmic therapy.

Pregnancy and breastfeeding

Insufficient reliable data, although several sources refer to a report of ototoxicity and others note it may stimulate uterine contractions. So, avoid use.

Interactions

Anticoagulants (e.g. warfarin), antiplatelet drugs (e.g. aspirin, clopidogrel) and NSAIDs (e.g. ibuprofen): There is a theoretical increase in risk of bleeding. Monitor for signs of bleeding. An increase in INR may require adjustment of warfarin dose.

Cytochrome P450 substrates: Devil's claw constituents may inhibit CYP2C9 and CYP3A4 isoenzymes, increasing levels of related substrates.

H2 antagonists and proton pump inhibitors: May have reduced effectiveness.

Common dosage ranges

Tablets/capsules: Clinical trials for the treatment of osteoarthritis frequently use the equivalent of 57 mg of the harpagoside constituent and 87 mg of total iridoid glycosides, although a range of 30–100 mg harpagoside has also been used. 50–100 mg harpagoside daily has been used for low back pain. Dried root: 1.5–3 g as a decoction three times daily (or equivalent aqueous or hydroalcoholic extract) has been suggested for painful arthritis.

Source: Sansom, LN ed. *Australian Pharmaceutical Formulary and Handbook*. 21st edn. Canberra: Pharmaceutical Society of Australia; 2009.

Real Enquiries

At the "Drug Information Center", we respond to enquiries from the professional healthteam as well as from others. Here's one of the enquiries received at the center:

Enquiry received from: S.Y.- *Pharmacist, Assiut*

Enquiry: How long should I wait before planning pregnancy after using isotretinoin capsules? How does it adversely affect my skin and hair?

Summary of the answer:

Isotretinoin and other oral retinoids are teratogenic and therefore contra-indicated in pregnant patients. It is advisable for female patients to commence using contraceptive measures one month before starting isotretinoin treatment. Pregnancy should be excluded before starting therapy and avoided during treatment and for 1 month after treatment has been withdrawn. Isotretinoin is also contra-indicated in breast-feeding mothers.

Dry skin and lips are very common side effects. Other effects have included hair thinning (occasionally irreversible). For safety, don't have any waxing, dermabrasion, or laser skin treatment while you're taking this medicine and for at least 6 months after isotretinoin treatment because of the risk of scarring and dermatitis

References: 1) Sweetman S. *Martindale: The Complete Drug Reference*. 36th ed. London: Pharmaceutical Press; 2009.

2) NHS. *Isotretinoin capsules (Roaccutane)*. [Internet]; 2018 [cited Dec 1, 2018]. Available at:

<https://beta.nhs.uk/medicines/isotretinoin-capsules/>

3) Lexicomp. Isotretinoin. [Online Database]; regularly updated [cited Sept 30, 2018]. Accessed at: online.lexi.com

Hot Flashes Tea

Uses: Hot Flashes, Menopause.

A hot flash is a sensation of heat that begins in the head and neck regions. Hot flashes are a common symptom experienced by women prior to, and during the early stages of the menopausal transition. However, not all women approaching the menopause will develop hot flashes.

Ingredients:

1 tsp. Dong Quai root, dried
1 tsp. Black Cohosh root, dried
1 tsp. Fenugreek seeds
½ tsp. organic Rose petals
3 cups water

Bring the water to a boil, then pour it over the herbs in a pot. Cover the pot and let the mixture steep for 20 minutes. Strain off the herbs. Drink 3- 4 cups per day.

References:

- 1) The Herbal Pharmacy, By Hale Software, Inc. ©1997. V1.20.0
- 2) www.medicinenet.com/hot_flashes/article.htm

Answers:

1. (E) “Antibiotics should be administered intravenously in patients with suspected fascial involvement, septicemia, or dermal necrosis, or in those with an immunological comorbidity,” according to an article published online in *Cutis*.
2. (C) Vegaskin is a combination of paracetamol (non-opioid analgesic), aspirin (nonsteroidal anti-inflammatory drug) and codeine (opioid analgesic). One of the side-effects of opioids is constipation. Naprosyn is a proprietary (trade name) preparation of the non-steroidal anti-inflammatory drug naproxen; Adalat is a proprietary preparation of the calcium-channel blocker nifedipine; Amoxil is a proprietary preparation of the beta-lactam amoxicillin; and Abilaxine is the brand name of the stimulant laxative bisacodyl.
3. (E) The Summary of Product Characteristics (SPC) for a medicinal product reflects the information in the marketing authorisation of the product. It is prepared by the manufacturer and is intended for health professionals. Updates are necessary to reflect any approved changes by the regulatory body in the marketing authorization.