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In This Issue…

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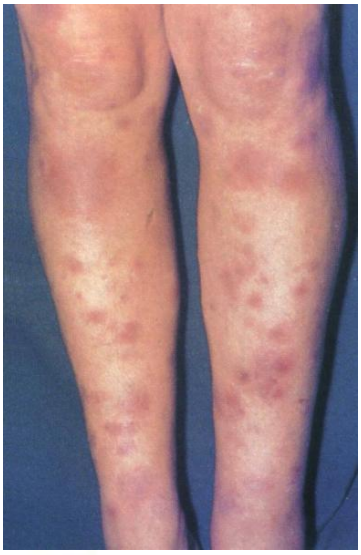
Erythema nodosum

Erythema nodosum is a dermatological condition. It is a type of panniculitis. Panniculitis is a condition where there is inflammation of the layer of fat lying underneath the skin. It causes red nodules (rounded lumps) to form just below the skin surface, usually on the shins (extensor aspects of the lower legs).

Presentation



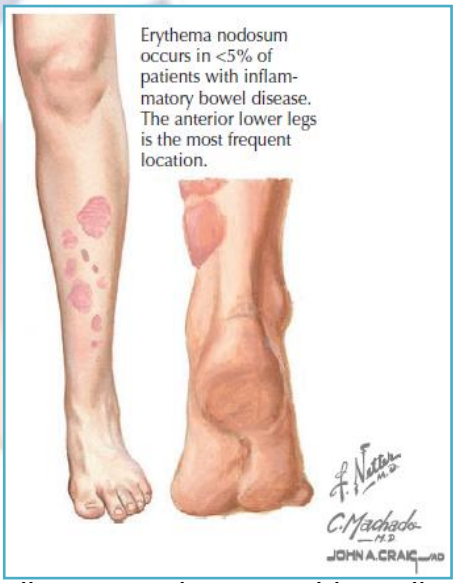
The eruptive phase begins with fever, aching and arthralgia whilst a painful rash usually appears within a couple of days.

Lesions begin as red, tender nodules. The borders are poorly defined and they are 2-6 centimeters in diameter.

In the first week the lesions become tense, hard and painful. In the second week, they may become fluctuant, rather like an abscess but they do not suppurate or ulcerate. Individual lesions last around two weeks but, occasionally, new lesions continue to appear for three to six weeks.

Aching legs and swollen ankles may persist for many weeks. In the first week they are bright red but in the second week there is a blue or purple hue, even turning yellow like a resolving bruise before disappearing in a couple of weeks.

They can occur anywhere but are usually on the anterior aspect of the lower leg.



What causes erythema nodosum?

EN primarily affects people in their 20s and 30s but can occur at any age; women are more often affected. Etiology is unknown as up to one third of cases of EN are idiopathic, but an immunologic reaction is suspected because EN is frequently accompanied by other disorders.

The most common disorders are:

- Streptococcal infection (especially in children)
- Sarcoidosis
- Inflammatory bowel disease

Other possible triggering disorders include:

- Other bacterial infections (e.g., *Yersinia, Salmonella,* mycoplasma, chlamydia, leprosy, lymphogranuloma venereum)
- Fungal infections (e.g., kerion, coccidioidomycosis, blastomycosis, histoplasmosis)
- Rickettsial infections
- Viral infections (e.g., Epstein-Barr, hepatitis B)
- Use of drugs (e.g., sulfonamides, iodides, bromides, oral contraceptives)
- Hematologic and solid cancers
- Pregnancy
- Behçet disease
- Tuberculosis (TB)

Diagnosis

Laboratory Studies

Throat culture is performed as part of the initial workup to exclude group A beta-hemolytic streptococcal infection.

- Erythrocyte sedimentation rates (ESR) are often performed as part of the initial workup. The rate often is very high.
- Antistreptolysin titer is elevated in some patients with streptococcal disease, but normal values do not exclude streptococcal infection. Evaluate titer levels during the initial workup, since streptococcal disease is a common cause of erythema nodosum.
- Stool examination is ordered, since along with the appropriate history of gastrointestinal complaints, a stool examination can exclude infection by *Yersinia, Salmonella,* and *Campylobacter* organisms.
- Blood cultures may be ordered according to preliminary indications and findings.

Imaging Studies

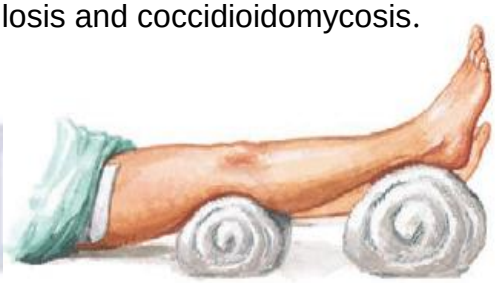
Chest radiographs may be done as part of the initial workup to exclude sarcoidosis and tuberculosis and to document hilar adenopathy.

Other Tests

Intradermal skin tests can be used to exclude tuberculosis and coccidioidomycosis.

Management

In most patients, erythema nodosum is a self-limited disease and requires only symptomatic relief. However if they are tender or painful treatments may include:



One of the mainstays of therapy is leg elevation.

- Most cases are self-limiting and require only symptomatic relief.
- If an infective aetiology has been discovered then appropriate therapy is in order but it should not be given blind.
- A degree of relief can be obtained with cool compresses and bed rest with elevation of the foot of the bed. Bed rest has been advocated for many years and is anecdotally useful but the evidence base is lacking.
- Non-steroidal anti-inflammatory drugs (NSAIDs) are useful and no other drugs are usually needed. Steroids are beneficial but should be used with caution and may be contra-indicated if infection has not been excluded.
- In difficult cases, oral potassium iodide may be valuable, as may tetracycline and, in erythema nodosum of leprosy, thalidomide has seen a resurgence but further research is required.

Refrences:

1) Anderson B. *The Netter Collection of Medical Illustrations: Integumentary System*. 2nd ed. Philadelphia: Elsevier; 2012.
2) www.msdmanuals.com/professional/dermatologic-disorders/hypersensitivity-and-inflammatory-disorders/erythema-nodosum
3) patient.info/doctor/erythema-nodosum-pro
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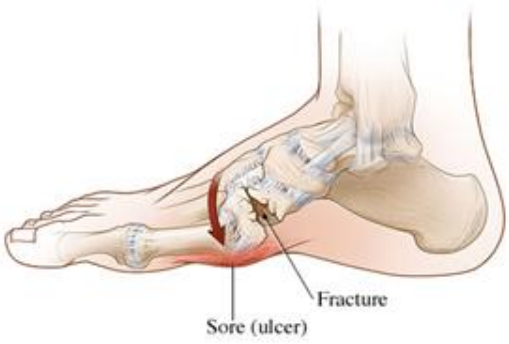
Terminology
Charcot's Foot



Charcot foot is a deformity that results from nerve damage (neuropathy) in the foot or ankle. The nerve damage causes a loss of sensation that increases the risk of injury to the feet. When the foot is repeatedly injured, the weight-bearing joints start breaking down. Early signs of Charcot foot include redness, swelling, and increased temperature of the foot.

Source: www.webmd.com/a-to-z-guides/charcot-foot

Complementary Medicine
Artichoke

Species
Cynara scolymus L. (Asteraceae/Compositae)

Synonyms
Globe Artichoke. Globe artichoke should not be confused with Jerusalem artichoke, which is the tuber of Helianthus tuberosus L.

Part Used: Leaf

Constituents
Acids Phenolic, up to 2%. Caffeic acid, mono- and dicaffeoyl-quinic acid derivatives, e.g. cynarin (1,5-di-O-caffeoylquinic acids) and chlorogenic acid (mono derivative).

Flavonoids 0.1–1%. Flavone glycosides, e.g. luteolin-7b-rutinoside (scolymoside), luteolin-7b-D-glucoside and luteolin-4b-D-glucoside.

Volatile oils Sesquiterpenes b-selinene and caryophyllene (major); also eugenol, phenylacetaldehyde, decanal, oct-1-en-3-one, hex-1-en-3-one, and non-trans-2-enal.

Other constituents Phytosterols (taraxasterol and b-taraxasterol), tannins, glycolic and glyceric acids, sugars, inulin, enzymes including peroxidases, cynaropicrin and other sesquiterpene lactones, e.g. grosheimin, cynarotriol.

The root and fully developed fruits and flowers are devoid of cynaropicrin; highest content reported in young leaves.

Herbal Use
Artichoke is stated to possess diuretic, choleretic, hypocholesterolaemic, hypolipidaemic, and hepatostimulating properties.
Modern use of artichoke is focused on its use in the treatment of hyperlipidaemia, hyperlipoproteinaemia, non-ulcer dyspepsia and conditions requiring an increase in choleresis. There is also interest in the potential hepatoprotective properties of globe artichoke, although this has not yet been tested in controlled clinical trials.

Dosage
The German Commission E recommended an average daily dose of 6 g drug, or an equivalent dose of extract (based on the herb-to-extract ratio) or other preparations, for dyspeptic problems.
A recommended dosage regimen for liquid extract (1 : 2) is 3–8mL daily.
Dosages used in clinical trials of globe artichoke leaf extract have assessed the effects of dosages of up to 1.92 g daily in divided doses for up to six months.

Warnings
Globe artichoke yields cynaropicrin, a potentially allergenic sesquiterpene lactone. Individuals with an existing hypersensitivity to any member of the Compositae family may develop an allergic reaction to globe artichoke.

Drug interactions None documented. However, the potential for preparations of artichoke to interact with other medicines administered concurrently, particularly those with similar or opposing effects, should be considered.

Source: Barnes J, Anderson A, Phillipson D. *Herbal Medicines,* 3rd ed. London: Pharmaceutical Press;2007.

1- Which of the following drugs is NOT liable to cause dry mouth?

A- trihexyphenidyl
B- cinnarizine
C- imipramine
D- sumatriptan
E- orphenadrine

2- Calculate the dose of a drug to be administered to a patient if the dosing regimen is listed as 5 mg/kg per day in divided doses every 8 hours. The patient weighs 67 kg:

A- 67 mg t.d.s.
B- 42 mg t.d.s.
C- 335 mg t.d.s.
D- 14 mg t.d.s.
E- 112 mg t.d.s.

3- When comparing amlodipine and nifedipine, amlodipine:

A- has a longer duration of action
B- can be used in hypertension
C- is available as a spray formulation
D- causes ankle swelling as a side-effect
E- cannot be used in angina

4- Which of the following drugs is associated with precipitation of a migraine attack?

A- aspirin
B- combined oral contraceptives
C- metoclopramide
D- propranolol
E- diazepam

FDA News

FDA Approves Repatha to Treat Certain Patients with High Cholesterol

Repatha (evolocumab) is a monoclonal antibody targeting PCSK9 (proprotein convertase subtilisin/kexin type 9) for the treatment of patients with heterozygous familial hypercholesterolemia, homozygous familial hypercholesterolemia, or patients with atherosclerotic heart disease who require additional lowering of LDL-cholesterol.

The FDA approved Amgen's **Repatha** (evolocumab) for U.S. marketing on August 27, 2015.

Repatha injection is indicated for use in addition to diet and maximally-tolerated statin therapy in adult patients with heterozygous familial hypercholesterolemia (HeFH), homozygous familial hypercholesterolemia (HoFH), or clinical atherosclerotic cardiovascular disease (ASCVD), such as heart attacks or strokes, who require additional lowering of LDL cholesterol.

Common side effects with **Repatha** use include nasopharyngitis (common cold), upper respiratory tract infections, influenza, back pain, and injection site reactions like redness, pain or bruising. Allergic reactions, such as rash and hives, have been reported. Patients should stop using **Repatha** and seek emergency medical care if they experience symptoms of a serious allergic reaction, such as swelling of the lips, tongue or throat.

Repatha is the second PCSK9 inhibitor drug to be approved this summer. Sanofi-Aventis and Regeneron's Praluent (alirocumab) was given the agency go-ahead on July 24, 2015 for treatment of adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease who require additional lowering of low-density lipoprotein (LDL) cholesterol.

The recommended dose of **Repatha** for adults is 140 mg every two weeks or 420 mg once a month. **Repatha** is available as a single-use 140 mg prefilled autoinjector or prefilled syringe that patients can self-administer. For adults with HoFH, the recommended dose is 420 mg once a month.

Source: www.drugs.com/history/repatha.html

Real Enquiries

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

Enquiry received from: Dr. M. M. - Al-Azhar University.

Enquiry: How safe are Sovaldi & Ribavirin in an adult patient with an increased serum creatinine value?

***Summary of* Answer:**

Normal levels of creatinine in the blood are approximately 0.6–1.2 mg/dL or 71–106 mol/L for males, 0.4–1.0 mg/dL or 36–90 mol/L for females.
Creatinine blood levels that reach 10.0 or more in adults may indicate severe kidney impairment.

A- Sovaldi (Sofosbuvir) in renal impairment:

No dose adjustment of Sovaldi is required for patients with mild or moderate renal impairment. The safety, efficacy and appropriate dose of ***Sovaldi*** have not been established in patients with severe renal impairment (estimated glomerular filtration rate [eGFR] <30 mL/min/1.73 m2) or end stage renal disease (ESRD) requiring haemodialysis. No dosage recommendation can be given for patients with severe renal impairment or ESRD.

B- Ribavirin in renal impairment:

The recommended dose regimens (adjusted by the body weight cutoff of 75 kg) of ribavirin give rise to substantial increases in plasma concentrations of ribavirin in patients with renal impairment. The total daily dose of ***Ribavirin*** should be reduced for patients with creatinine clearance less than or equal to 50 ml/min as shown in this table:

Dosage Modification for Renal Impairment	
Creatinine Clearance	**Ribavirin Dose (daily)**
30 to 50 ml/min	Alternating doses, 200 mg and 400 mg every other day
Less than 30 ml/min	200 mg daily
Hemodialysis	200 mg daily

Therapy should be initiated (or continued if renal impairment develops while on therapy) with extreme caution and intensive monitoring of haemoglobin concentrations, with corrective action as may be necessary, should be employed throughout the treatment period.

If severe adverse reactions or laboratory abnormalities develop, ***Ribavirin*** should be discontinued, if appropriate, until the adverse reactions abate or decrease in severity. If intolerance persists after restarting ***Ribavirin***, therapy should be discontinued.

References: 1) American Society of Health System Pharmacists. *AHFS Drug Information Essentials*. Bethesda: American Society of Health System Pharmacists; 2011.
2) Joint Formulary Committee. *British National Formulary (BNF)*. London: Pharmaceutical Press; 2014.
3) SPC of Sovaldi at: www.medicines.org.uk/emc/medicine/28539#
4) SPC of Ribavirin at: www.medicines.org.uk/emc/medicine/11755#
5) Sovaldi Prescribing Information at: www.gilead.com/~/media/Files/pdfs/medicines/liver-disease/sovaldi/sovaldi_pi.pdf
6) www.drugs.com/monograph/sofosbuvir.html

Ask the Expert

Why Does Cancer Therapy Make Food Taste Terrible?

People who go through chemotherapy say one of the most frustrating side effects is that even their favorite foods taste awful. Pasta tastes like cardboard, meat tastes metallic. Patients have no desire to eat and end up getting fewer calories and less nutrition when they need it most—to battle the cancer as well as the ravages of the therapy.

Chemotherapy is supposed to work by killing cancer cells. How might that affect taste?

Cancer cells proliferate rapidly, and most chemotherapies target rapidly growing cells. Taste cells turn over rapidly, too; stem cells in the base of a taste bud regularly replenish the taste cells. So the chemicals attack the taste cells as well. They either attach to a cell or enter it, then destroy it. As many cells die, taste disappears.

What about bad tastes, such as metallic or bitter sensations, instead of a lack of taste?

Like most medications the chemicals enter the bloodstream and they get into saliva that way. The saliva brings them to the taste cells and the cells send messages of “metallic” or “bitter” to neurons that lead to the brain. It’s strange to think of it this way but we can “taste” things in the bloodstream. For example, researchers in Japan injected saccharin into people’s bloodstreams and the people quickly tasted it.

Patients often complain of nausea. That also makes food less appetizing.

The body is programmed to tie nausea to something you ate. If you eat a specific food and get sick, you will find it hard to eat that food again. Cancer patients who feel nauseous become conditioned to avoid all kinds of foods they may be eating.

What about radiation?
If radiation is being used near the mouth area, such as for oral cancer, it can have an effect. Radiation elsewhere in the body does not. In these cases, even though the radiation is highly targeted, it's still impossible to avoid hitting salivary glands. The glands get knocked out, and the patient gets chronic dry mouth. To taste something, it has to go into solution so it can enter a taste bud's taste pore; saliva is there to dissolve food into solution. Without saliva, it is hard to taste anything.

Does chemotherapy also affect smell, which is central to taste?
The smell system's receptors also interact with chemicals in the bloodstream, but the cells turn over more slowly than taste cells, so the chemicals might not attack them as much. They regenerate from stem cells, too, but that takes longer and it's more complicated, because smell cells are actually the ends of neurons, signaling the brain directly. When they regrow they have to mature and they also have to connect to the brain. Overall, smell cells get involved but they seem to be less affected than taste cells.

What are common, good tactics patients can use to help make food more appealing?
Because nausea associates sickness with specific foods, patients shouldn't eat the things they regularly eat before a chemotherapy treatment. They should eat so-called scapegoat foods—unusual or unusually flavored foods they wouldn't be likely to eat otherwise. They may end up hating them, but it won't matter for their other meals.

If the problem is diminished taste, liquid nutrients should be relied on to create solution that penetrates the taste pores—especially in case of a dry mouth.

In general, patients are advised to eat slowly and chew a lot, to give food more of a chance to enter the few healthy taste buds that are there. Sour flavors tend to come through more readily, so things like lemon can be used to enhance flavor. To enhance smell, jack up the volatile compounds—herbal ingredients and liquid spices.

Does taste return to patients after treatment is done?
With chemotherapy, once the drugs clear from the body the taste system usually returns over time. Recovery from radiation can take longer, even a few months, but there can also be some permanent damage to the salivary glands. Patients sometimes use artificial salivas to help themselves.

Source: www.scientificamerican.com/article/why-does-cancer-therapy-make-food-taste-terrible1/

Answers to " Test Your Knowledge":

1. **(D)**
Sumatriptan is a serotonin (5HT1) agonist, which does not cause dry mouth. Trihexyphenidyl, cinnarizine, imipramine and orphenadrine all tend to cause antimuscarinic side-effects, including dry mouth, constipation, blurred vision and urinary retention.
2. **(E)**
The daily dose for a patient weighing 67 kg is 335 mg (67 x 5), meaning that the drug must be administered 112 mg three times daily (every 8 hours).
3. **(A)**
Amlodipine and nifedipine are dihydropyridine calcium-channel blockers. Amlodipine differs from nifedipine in that it has a longer duration of action and can therefore be given once daily, unlike nifedipine. Both are indicated in hypertension and angina and tend to cause ankle oedema that does not respond to diuretic therapy. Neither amlodipine nor nifedipine are available as spray formulations.
4. **(B)**
Combined oral contraceptives may cause migraine and are contraindicated in such patients. Progesterone-only contraceptives are more suitable in this case.