Erythema Nodosum = اﻠﻌﻘدﺔ اﻠﺤﻤاﻤﻰ
Erythema Nodosum
Clinical Presentation. An acute form and a chronic form of erythema nodosum exist, which differ in their clinical manifestations but do not have uniformly recognized differences in their histologic characteristics.

In the acute form of erythema nodosum, there is a sudden appearance of tender, bright red or dusky red-purple nodules to plaques that only last for a few days. These lesions usually resolve without scarring, although they can recur.

Erythema nodosum occurs in 10% to 20% of patients with sarcoidosis and is thought to portend a good prognosis.
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The chronic form of erythema nodosum is also known as erythema nodosum migrans or subacute nodular migratory panniculitis of Vilanova and Pinol. There are one or several red, subcutaneous nodules that are found, usually unilaterally, on the lower leg. Vilanova ... by peripheral extension into plaques, often with central clearing. The duration may be from a few months to a few years.

Histopathology. The histologic changes are present mainly in and near the septa of the subcutaneous adipose tissue. The overlying dermis often has only a minimal to moderate, superficial and deep perivascular lymphocytic infiltrate.
In the early lesions of acute erythema nodosum, there is edema of the septa with a lymphohistiocytic infiltrate, having a slight admixture of neutrophils and eosinophils. Focal fibrin deposition and extravasation of erythrocytes occur frequently and can be revealed by spectral microscopy. Often, the inflammation is most intense at the periphery of the edematous septa and extends into the periphery of the fat lobules between the individual fat cells in a lace-like fashion. Necrosis of the fat is not...
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Erythema nodosum that is secondary to medications or estrogenic oral contraceptives.

Later lesions of acute erythema nodosum show widening of the septa, often with fibrosis and
when late lesions are compared with early ones. The granulomas often are loosely formed with macrophages predominating in the cytoplasm. The oldest lesions have septal widening and fibrosis with a decrease in all of the inflammatory cells.
In chronic erythema nodosum, histologic findings are generally similar to those of the early stages of the disease, with granulomas, fibrous septa, and capillary proliferation. Several authors have considered erythema nodosum migrans as a distinct entity separate from the late lesions of acute erythema nodosum. Others believe that all these histologic patterns fall within the spectrum of chronic erythema nodosum.
**Pathogenesis**
Although the cause of erythema nodosum cannot always be determined, streptococcal infection is the most common among the known causes, especially in children, as evidenced by elevation of antistreptolysin O titers. The diseases that can be associated with erythema nodosum are numerous and have been reviewed recently. In the absence of appropriate infection control measures, streptococcal infection is one of the most common causes of erythema nodosum. The most frequent bacterial infections are streptococcal infection, tuberculosis, Yersinia enterocolitica infection, brucellosis, leptospirosis, tularemia, Chlamydia infection, and Mycoplasma pneumoniae infection. The most frequently associated fungal infections are coccidioidomycosis, histoplasmosis, dermatophytosis, and candidiasis. Protozoal infections such as toxoplasmosis, amoebiasis, and Giardia infection can cause erythema nodosum. Among the associated viral and rickettsial infections are herpes simplex, varicella-zoster, molluscum contagiosum, and rickettsia. The sarcoidal granulomas that can occur in erythema nodosum are less frequent, are septal in location, and are associated with chronic inflammatory states. Likewise, Crohn's disease can be associated with erythema nodosum, and the two diseases can be difficult to distinguish from each other histologically in the skin involvement. In some cases, Crohn's disease may resemble erythema nodosum clinically but often is different histologically in having neutrophilic and eosinophilic infiltration of granulomas.
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lymphocytic vasculitis, which is predominantly lobular in distribution. Erythema nodosum and Sweet's syndrome have been reported in the same patient. Among the many medications that can cause erythema nodosum, antithyroid drugs and clozapine, a serotonin-dopamine receptor agonist, are the most frequent. Other drugs, such as sulfa antibiotics, nonsteroidal anti-inflammatory agents, and cytotoxic agents, and several infections, including tuberculosis and Staphylococcus, have been implicated as triggers of the disease. The exact mechanisms may be capable of triggering the clinical and histopathologic changes that are classified as erythema nodosum.

Direct immunofluorescence studies have shown deposits of immunoglobulins only very rarely in the blood vessel walls.
The occurrence of erythema nodosum as a response to medications and to tuberculin skin testing in patients with sarcoidosis and erythema nodosum. In approximately 50% of cases, there is no cause identified. The predilection for the anterior shins and for...
**Differential Diagnosis**


Erythema nodosum needs to be distinguished from erythema induratum and nodular vasculitis. Vasculitis and zones of fat necrosis are absent in erythema nodosum and frequent in erythema induratum. In patients suspected to have erythema nodosum but with necrotizing vasculitis, the possibility of cutaneous polyarteritis nodosa must be considered. In the latter disease, medium-sized arteries rather than veins or small-caliber blood vessels are affected, with necrosis of the walls of affected arteries. In contrast, nodular vasculitis has mainly lymphocytic infiltration with fibrous thickening and obliteration of vascular lumens. Superficial migratory thrombophlebitis, unlike erythema nodosum, has a large vein containing thrombus in the center of the lumen. Syphilitic gummas are ulcerative irregular granulomatous lesions that produce depressed scars. Subcutaneous tuberculosis can mimic erythema nodosum in lesions that are extending from underlying organs, soft tissues, or bone. Stains for ARS and LE cells are positive in patients with these conditions. Erythema nodosum is nonspecifically associated with inflammatory bowel disease, sarcoidosis, and pyoderma gangrenosum. It may also occur with other inflammatory conditions, including necrobiosis lipoidica diabeticorum, ruptured follicular cysts, and factitial traumatic panniculitis.
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