



Erythema Nodosum

What is Erythema Nodosum?



- A painful inflammatory disorder in which crops of tender nodules occur in response to antigenic stimuli.
- Usually it is limited to the extensor aspects of the lower legs.

ERYTHEMA NODOSUM

- DEFINITION-THIS IS A REACTIVE DERMATOSIS THAT OCCURS IN RESPONSE TO A MYRIAD OF CONDITIONS CHARACTERISED BY TENDER, ERYTHEMATOUS SUB CUTANEOUS NODULES PRIMARILY AFFECTING THE LOWER EXTREMITIES
- MOST COMMON TYPE OF PANNICULITIS
- AGE 20 TO 30 YEARS BUT ANY AGE GROUP MAY BE AFFECTED
- FEMALE:MALE 3-6 :1

Erythema NODOSUM - Mnemonic

NO cause found in 60% of cases

D rugs (antibiotics e.g., sulfonamides, amoxicillin)

O ral Contraceptives

S arcoidosis or Lofgren's syndrome

U lcerative Colitis, Crohns, Bechet's

M icro: TB

- Viral: HSV, EBV, HIV, HepB, HepC
- Bacterial: Campylobacter, Rickettsiae, Salmonella, Psittacosis, Bartonella, Syphilis
- Parasitic: Amoebiasis, Giardiasis



Common Causes of Erythema Nodosum

Drugs	Infectious	Systemic disorders
Sulfonamides	Hepatitis C virus	Sarcoidosis
Penicillins	Tuberculosis	Lymphoma
Oral contraceptives	Streptococcal	Leukemia
Phenytoin	<i>Mycoplasma</i>	Lupus
Gold	<i>Yersinia</i>	Leprosy
Bromides	Epstein-Barr	Inflammatory bowel disease
	Coccidioides	



TABLE 2

Causes of Erythema Nodosum

Common

Idiopathic (up to 55 percent)

Infections: streptococcal pharyngitis (28 to 48 percent),
Yersinia spp. (in Europe), mycoplasma, chlamydia,
histoplasmosis, coccidioidomycosis, mycobacteria

Sarcoidosis (11 to 25 percent) with bilateral hilar adenopathy

Drugs (3 to 10 percent): antibiotics (e.g., sulfonamides,
amoxicillin), oral contraceptives

Pregnancy (2 to 5 percent)

Enteropathies (1 to 4 percent): regional enteritis, ulcerative
colitis

Rare (less than 1 percent)

Infections

Viral: herpes simplex virus, Epstein-Barr virus, hepatitis B
and C viruses, human immunodeficiency virus

Bacterial: *Campylobacter* spp., rickettsiae, *Salmonella* spp.,
psittacosis, *Bartonella* spp., syphilis

Parasitic: amoebiasis, giardiasis

Miscellaneous: lymphoma, other malignancies

Erythema Nodosum: Pathogenesis and clinical findings

Authors:

Merna Adly

Reviewers:

Taylor Ewart Woo

Crystal Liu

Yan Yu*

Laurie Parsons*

* MD at time of publication

Genetic
Dysregulation

Infections (Ex.
Streptococcal
Pharyngitis)
~28-48% of cases

Medications
(Ex. Birth Control
Pills, Sulfa drugs)
~3-10% of cases

Malignancy (ex.
Lymphoma)

Autoimmune conditions
(ex. Sarcoidosis and
Inflammatory Bowel Disease)
~11-25% of cases

Pregnancy
~1-3% of cases

Antigenic Stimuli / Bacteria / Viruses / Chemical Agents all could trigger the following process:

Phase 1. Neutrophils infiltrate the fibrous septa between fat lobules in the subcutaneous fat

Phase 2. Neutrophils release reactive oxygen species, leading to oxidative tissue damage and inflammation

Phase 3. Opening of inter-endothelial junction and the migration of more inflammatory cells into the septal venules, including macrophages, histocytes, and eosinophils

Phase 4. Macrophages secrete inflammatory cytokines, which stimulates the proliferation of more helper T cells (Th1)

Phase 5. Th1 cells secrete more cytokines, leading to the further release of Th1 cytokines and mediating the immune complexes deposition in the septal venules of the subcutaneous fat (panniculitis). The Th1 immune reaction is called Type IV Delayed Hypersensitivity Reaction

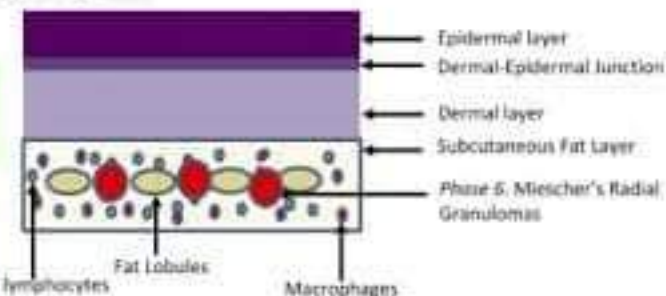
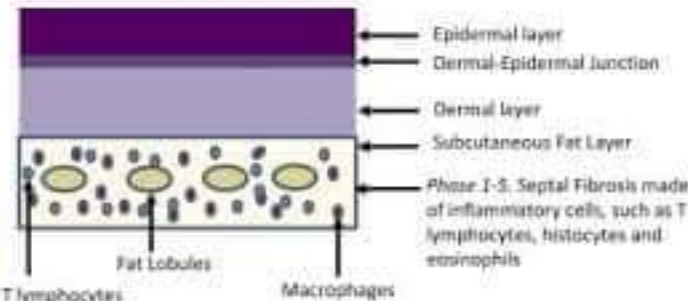
Phase 6. Activated macrophages produce hydrolytic enzymes and transform into multi-nucleated giant cells, called Miescher's Radial Granulomas. These consist of small, well defined aggregations of small histocytes arranged radially around a small cleft of variable shapes in the septal venules of the subcutaneous fat

Phase 1-4. Lesions are red tender nodules, poorly defined, vary in size from 2-6 cm, and usually on shins (1st week)

Note: we've done extensive research and can't figure out why erythema nodosum happens mostly on the shins. If you have an answer, please email us!

Phase 5. Lesions become tense, hard, and painful; and they change in color into bluish or livid (2nd week)

Phase 6. Lesions become fluctuant as in abscess, but do not ulcerate. Lesions fade to a yellowish color



CLINICAL FEATURES

- Erythema nodosum usually starts with flu-like symptoms of fever and bodyaches
 - Arthralgia may precede the eruptive phase
 - Red tender nodules usually on the anterior surface of legs-shins
 - Other areas- arms, trunk and face
-
- Lesions borders are poorly defined and vary from 2 cm to 10 cm
 - 1 st week - tense, hard, red and painful



- 2nd week - fluctuate and attain a yellowish hue, resembling a bruise
- Do not suppurate or *ulcerate*
- Individual lesions usually last for 2 weeks but occasionally new lesions appear up to 3–6 weeks
- Lesions disappear as the overlying skin desquamates
- Joint tenderness and morning stiffness may occur.
- *No destructive changes occur.* Synovial fluid is acellular and rheumatoid factor (RF) negative



LABORATORY DIAGNOSIS

- Careful history, physical examination and drug history
- Prior diarrheal illness, URTI and any endemic infections
- Throat culture—rules out streptococcal infection
- CBC and ESR
- Antistreptolysin O (ASO)/DNase titer at 2 weeks and 4 weeks interval
- Stool examination.
- Chest X-ray (CXR)— purified protein derivative (PPD) to rule out Koch's, unilateral hilar lymph nodes—Infections and malignancy
- CXR to rule out sarcoid—bilateral hilar lymph nodes
- Biopsy the lesion to rule out vasculitis—Collagen vascular disease.

Table 3. Treatments for Erythema Nodosum	
First Line Agents	NSAIDs (3)
Second Line Agents	Colchicine (2)
	Potassium iodide (2) (may not be available)
Topical Agents	Heparinoid ointment under occlusion (3)
Severe Disease	Prednisone (3)
Recalcitrant Nodules	Intra-lesional corticosteroid (3)
Chronic/ Recurrent Disease	Dapsone (3)
	Hydroxychloroquine (3)
Other agents	Anti- TNF monoclonal antibodies (3)
	Thalidomide (3)
	Methotrexate (3)
Level of evidence: 1. double-blind studies; 2. case series; 3. case reports.	

Erythema nodosum

→ A **delayed-type hypersensitivity** reaction that most often presents as **erythematous, tender nodules** on the **shins**



Etiology

- Infectious (Strep., *Mycoplasma*, Tb, HCV, *Yersinia*)
- Drugs (Sulfonamides, Penicillins, Phenytoin, OCPs)
- Systemic (Sarcoidosis, Lymphoma, Lupus, IBD)

Epidemiology

- More common in women
- Most common in women in their second to fourth decade

Clinical

- Tender erythematous nodules on bilateral shins
- Possible infectious prodrome
- Nodules typically resolve without scarring after 8 weeks

Management

- Self-limiting
- NSAIDs
- Potassium iodide
- Corticosteroids (second line)