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Dermatologic Manifestations of Rheumatic Disease: Cutaneous Manifestations of Sarcoidosis

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Cutaneous Manifestations of Sarcoidosis

Sarah Shapiro, Sindhuja Koppu, Mavra Masood

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A note:

This module uses terminology related to race and ethnicity in order to describe fictional patients and discuss medical conditions. We recognize that “race” (i.e. an individual’s socially-constructed phenotype, which is often misconstrued as biologic) and “ethnicity” (i.e. an individual’s geographic birthplace or cultural/national heritage) are imperfect terms that do not fully encapsulate the breadth of human diversity.

Additionally, we recognize that race, ethnicity, sex, and gender have traditionally been attributed as risk factors for certain health condition, when in reality, many of these risks may be more accurately explained by underlying socioeconomic and sociocultural factors, including racism and prejudice.

In efforts to emphasize patient-centered care and autonomy, this module assumes that all racial-, ethnic-, sex-, and gender-related terms utilized are those specifically preferred by the patient. We are also committed to dissecting potentially biased risk factors in order to promote more equal, just, and comprehensive healthcare for all persons, regardless of their identity, beliefs, or background.

For more information, please visit the [Institute for Healing and Justice in Medicine](#)

Outline

- Objectives
- Pre-test
- Case 1
- Case 2
- Summary
- Post-test

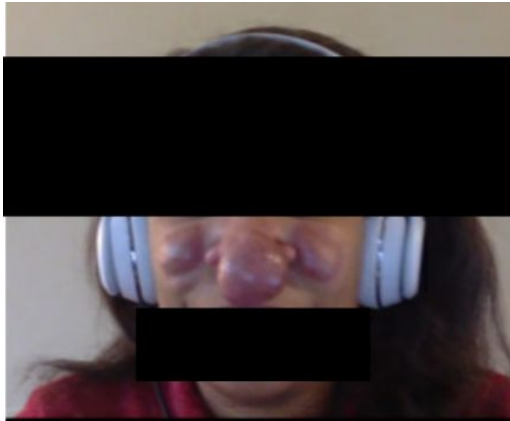
Objectives

By the end of the module, the learner should be able to:

- Define sarcoidosis
- Recall the non-cutaneous manifestations of sarcoidosis
- Recall the basic workup for sarcoidosis
- Identify dermatologic findings in cutaneous sarcoidosis, such as:
 - Lupus pernio
 - Erythema nodosum

Case #1

TL is a 50-year-old female (she/her/hers) who presents with a chief complaint of reddish-purple plaques on her nose and cheeks. She states that these plaques were barely noticeable a year and a half ago but have now gotten so large that she feels that the shape of her nose has changed. She also reports increased SOB on exertion and a nonproductive cough.



Syed 2021

Medications

Atorvastatin, 80mg

Levothyroxine 12mcg

Medical Hx

Hypothyroidism

Hyperlipidemia

Interstitial lung disease

Social Hx

Denies tobacco, alcohol, and illicit drug use

Family Hx

Mother - Sjogren syndrome

Pertinent ROS

Dyspnea, cough

Differential Diagnosis and Clinical Pearl

Lupus pernio is a form of cutaneous sarcoidosis that presents as **reddish-purple plaques and nodules over the nose, cheeks, and ears**. It does not present with pain or pruritus; rather, the chief complaint is cosmetic. While lupus pernio can be suspected based on history and physical exam, the diagnosis is confirmed by a skin biopsy showing sarcoidal non-caseating granulomas.

- Lupus pernio
 - Most likely: Plaques around nose and cheeks, respiratory symptoms, history of interstitial lung disease
- Tuberculosis
 - Red plaques, dyspnea, cough
 - **M. tuberculosis on sputum culture**
- Discoid lupus erythematosus
 - Red plaques around nose and on cheeks
 - **Anti-dsDNA antibodies, photosensitivity, arthritis**

Symptoms found in patient

Symptoms not found in patient

Lupus Pernio

- Red-violet papules and plaques found on nose, cheeks, and ears; can result in scarring
- **Specific** to sarcoidosis and represents chronic sarcoidosis; associated with more severe systemic problems
- Biopsy shows granulomatous inflammation.
- More commonly found in Black patients

[Lupus pernio on the nose and cheeks.](#) Visual Dx. Updated August 02, 2022. Accessed September 20, 2022.

[Lupus pernio on the tip of the nose.](#) VisualDx. Updated August 02, 2022. Accessed September 20, 2022.

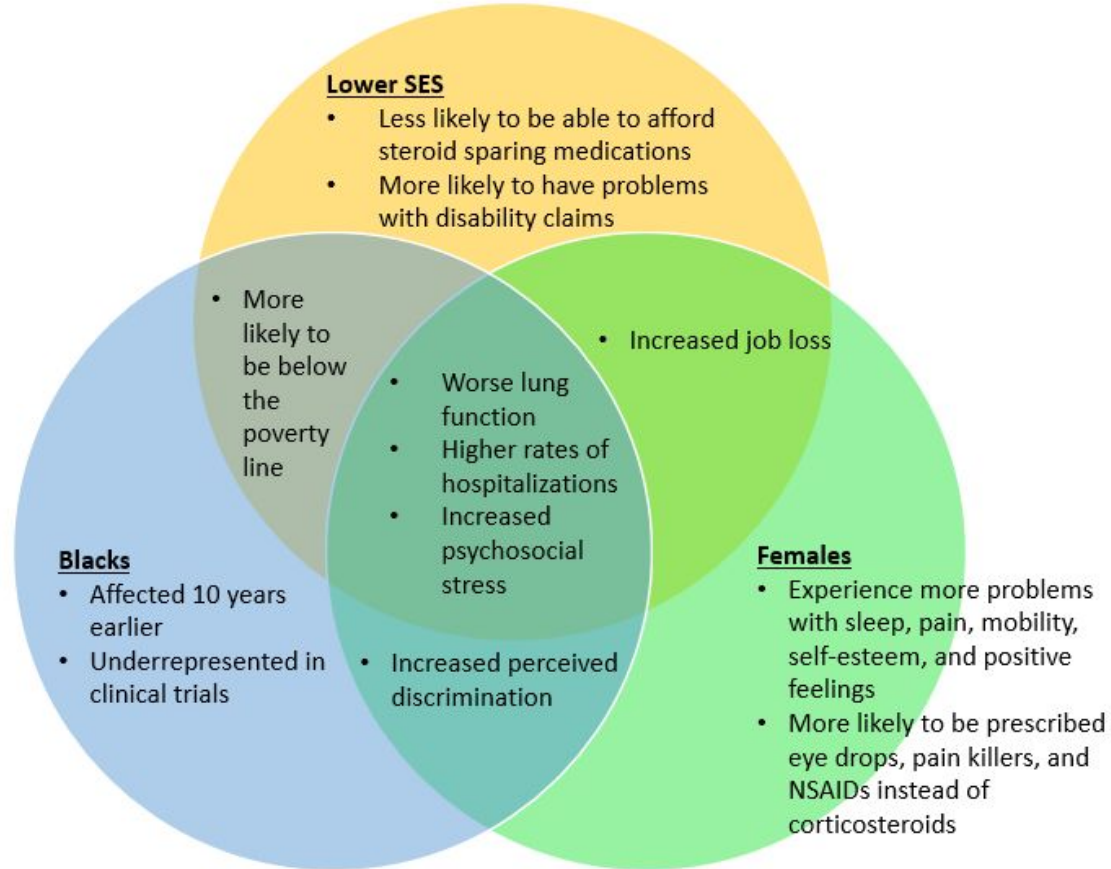
[Lupus pernio on the nose, cheeks, and eyelid.](#) VisualDx. Updated August 02, 2022. Accessed September 20, 2022.

[Verrucous lupus pernio on the nose.](#) VisualDx. Updated August 02, 2022. Accessed September 20, 2022.

Sarcoidosis

- Systemic immune-mediated disease with an unknown etiology characterized by granulomas, especially in the lung parenchyma and skin
- Common systemic symptoms: **fever, night sweats, weight loss**
- Patient characteristics:
 - Ages: 25-35 and 45-65 years
 - Sex: Females > Males
- Divided into cutaneous and non-cutaneous sarcoidosis
- Cutaneous sarcoidosis can affect skin, hair, nails, and tattoos.

Health Disparities in Sarcoidosis



For more information, please visit [Sharp et al. 2020](#)

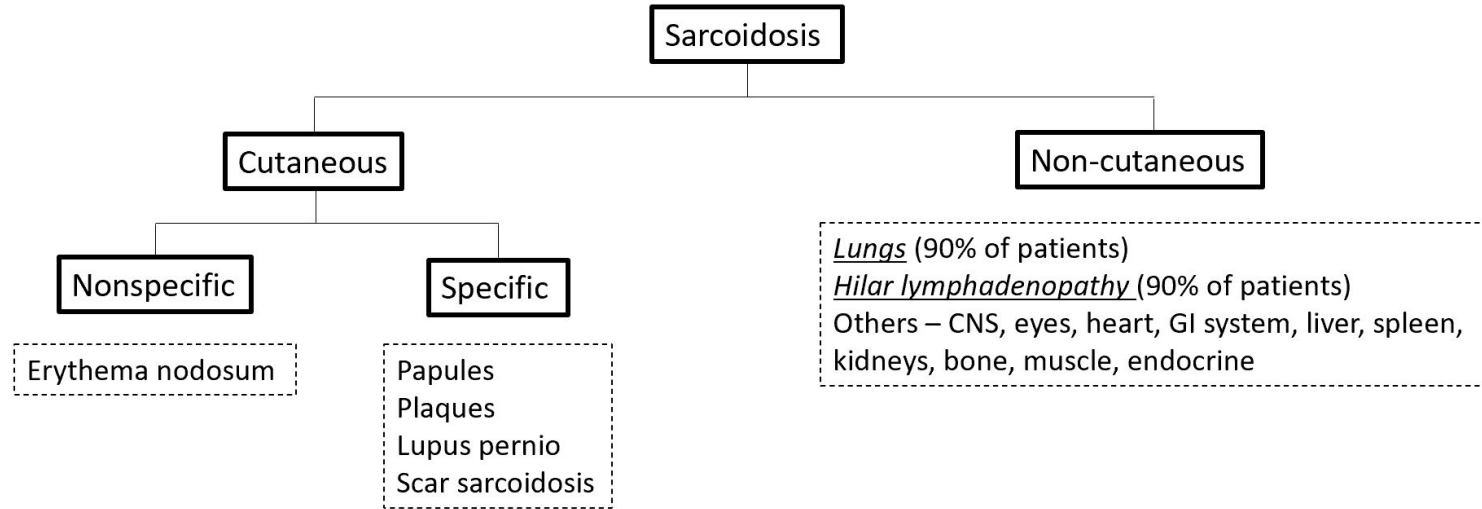
Factors affecting Patient Outcomes in Sarcoidosis

- Socioeconomic status
 - Associated with a **more severe phenotype** even when controlled for race, sex, education
 - **Income is a risk factor** for **increased symptoms** and development of new sarcoidosis-associated and steroid associated **comorbidities of disability** at diagnosis
 - Low income individuals are more likely to receive glucocorticosteroid-only regimens (steroid sparing regimens are typically more expensive) and have a higher burden of glucocorticosteroid-related comorbidities
- Race
 - **Black patients develop more severe comorbidities** on avg. **10 years earlier** than non-Hispanic whites and present with more advanced disease (could be due to delayed diagnosis from **lack of access** and other factors)
- Gender
 - **Females** reported to have **higher rates** of **hospitalization** and **depressive symptoms**, and have a **lower quality of life** in regards to physical and psychological health
 - Females more likely to be prescribed eye drops, NSAIDs, and painkillers, while males more likely to receive corticosteroids

Racial Differences in Sarcoidosis in the U.S.

	White patients	Black patients
Disease Incidence	5/100,000	39/100,000
Lifelong Risk of Developing Sarcoidosis	1% for women; 0.7% for men	2.7% for women; 2.1% for men
Age of Onset		Peak incidence is 10 years earlier
Pulmonary Complications		Higher risk of pulmonary hypertension
Extrapulmonary Complications		More common; can present with eye, skin, and bone marrow involvement
Mortality	Crude rate of 4/1,000,000	Crude rate of 37/1,000,000
States with Highest Mortality	Vermont, Rhode Island, Maine, Utah, Washington	District of Columbia, Pennsylvania, North Carolina, South Carolina, New Jersey
States with Lowest Mortality	Arizona, Oklahoma, Nevada	Florida, Texas, Arizona

Sarcoidosis Algorithm



- Cutaneous sarcoidosis can occur in approximately $\frac{1}{3}$ of patients with non-cutaneous sarcoidosis and can occur without non-cutaneous sarcoidosis.
- Nonspecific means that granulomas are not found on biopsy. Specific means that granulomas are found on biopsy.
- Examples of conditions that are categorized under specific cutaneous sarcoidosis are NOT all specific for sarcoidosis. For example, plaques and papules occur in many other conditions.

Diagnostic Criteria and Basic Workup for Sarcoidosis

Goals

- 1) Identify clinical and radiographic findings supporting sarcoidosis.
- 2) Find noncaseating granulomas on biopsy.
- 3) Exclude alternative diseases.

Chest radiograph
and high resolution
CT scan

Pulmonary
function tests

Electrocardiogram

Labs

Eye exam

Step #1: Detailed history (including
environmental and occupational exposures)

Step #2: Full physical exam

Step #3: Tests

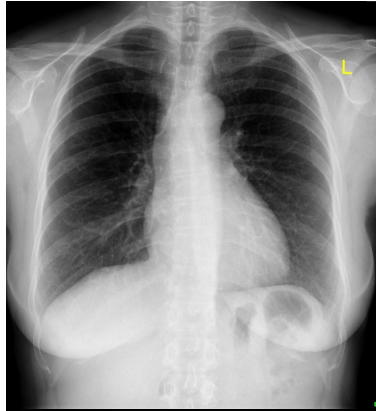
Skin biopsy

To evaluate
non-cutaneous
signs and
symptoms:

To evaluate
cutaneous
lesions:

*If the patient presents with signs/symptoms of other organ involvement, further focused tests can be conducted.

Workup of Sarcoidosis: Chest X-ray and CT scan



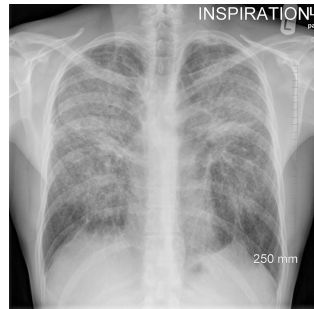
Normal

Case courtesy of Dr. Henry Knipe. Radiopaedia.org. From the case [Normal Chest X-Ray](#). [Modified CC BY-NC-SA license](#).



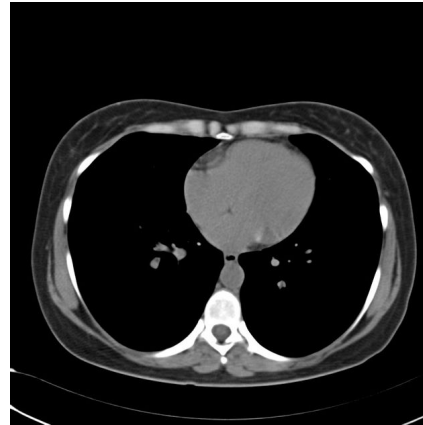
Hilar lymphadenopathy

Case courtesy of Assoc Prof Craig Hacking. From the case [Bilateral Hilar Lymphadenopathy from Sarcoidosis](#). [Modified CC BY-NC-SA license](#).



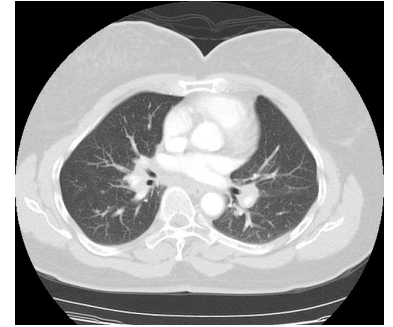
Interstitial opacification

Case courtesy of Dr. Aneta Kecler-Pietrzyk. Radiopaedia.org From the case [Pulmonary Sarcoidosis](#). [Modified CC BY-NC-SA license](#).



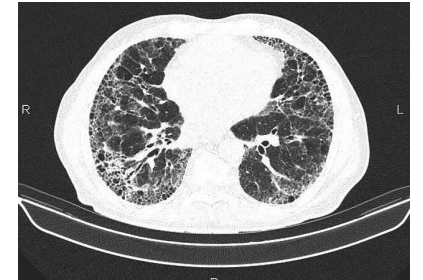
Normal

Case courtesy of Dr. Bruno Di Muzio. Radiopaedia.org. From the case [Normal Chest CT](#). [Modified CC BY-NC-SA license](#).



Hilar lymphadenopathy

Case courtesy of Dr. Robert Neidermeyer. Radiopaedia.org From the case [Sarcoidosis](#). [Modified CC BY-NC-SA license](#).



Fibrosis

Case courtesy of Dr. MT Niknejad. Radiopaedia.org From the case [Pulmonary Fibrosis](#). [Modified CC BY-NC-SA license](#).

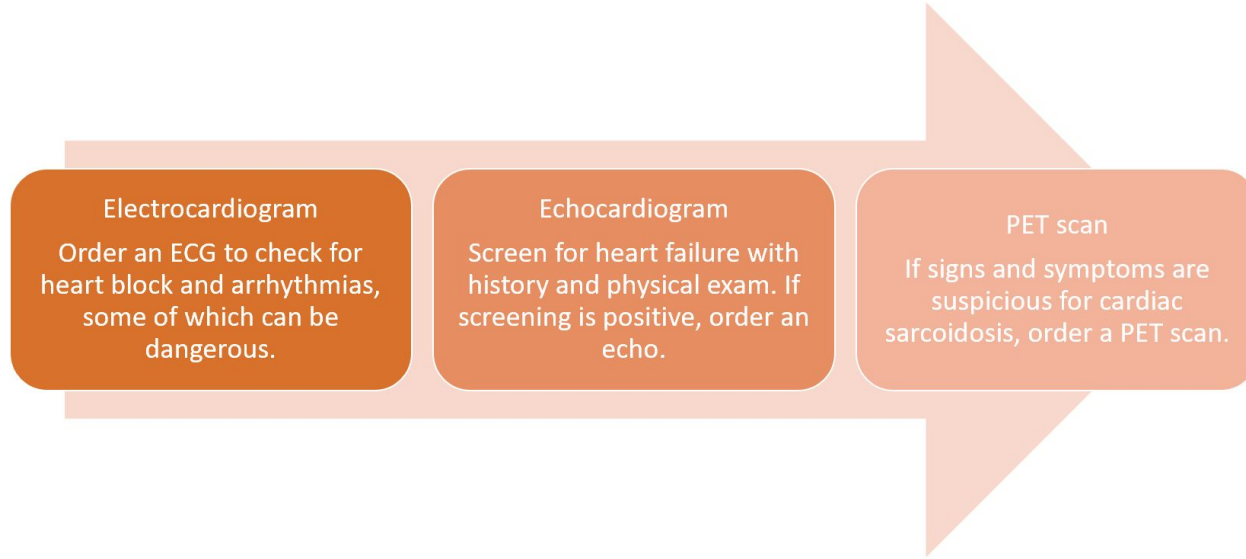
Symptoms: Cough, dyspnea

Workup of Sarcoidosis: Pulmonary Function Tests (PFTs)

- ↓ vital capacity (normal: 3-5 L)
- ↓ total capacity (normal: 4-6 L)
- ↓ diffusion capacity (normal >75%)

Symptom: Shortness of breath

Workup of Sarcoidosis: Cardiac



Symptoms:
Palpitations
Presyncope/syncope

Symptoms:
Fatigue
Dyspnea
Orthopnea

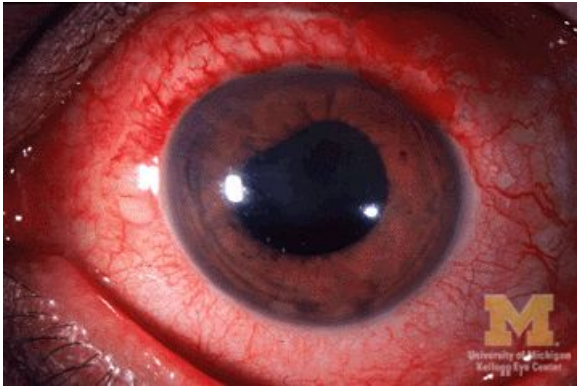
Key clinical manifestations of cardiac sarcoidosis:
Conduction system disease
Tachyarrhythmias
Heart failure
Cardiomyopathy

Workup of Sarcoidosis: Labs

- Complete blood count (CBC)
 - Anemia: uncommon
 - Leukopenia: 5-10% of patients
 - Eosinophilia: 3% of patients
 - Thrombocytopenia: rare
- Liver function tests (LFTs)
 - ↑ Serum alkaline phosphatase
- Renal function tests
 - ↑ Blood urea nitrogen (BUN)
 - ↑ Creatinine
- Serum calcium and elevated 24-hour urine calcium
 - Hypercalciuria is more common than hypercalcemia.

Workup of Sarcoidosis: Eye Exam

Uveitis:



[Anterior uveitis](#) by Dr. Jonathan Trobe is distributed under a [CC BY 3.0 license](#).

Conjunctival granulomas:

[Sarcoid granulomas of the palpebral conjunctiva.](#)

VisualDx. Updated August 02, 2022. Accessed September 20, 2022.

Symptoms: Dry eyes, blurry vision, redness, pain, photophobia

Workup of Sarcoidosis: Skin Biopsy

[Bone marrow biopsy in sarcoidosis at 10x](#). VisualDx.
Updated August 02, 2022.
Accessed September 20, 2022.

While the photo cited above depicts a bone sample, the non-caseating granulomas (as shown by the yellow arrows) are similar to those that would be seen in skin biopsies from patients with specific cutaneous sarcoidosis.

The diagnosis of sarcoidosis is confirmed by a skin biopsy showing **non-caseating granulomas**.

Cutaneous Sarcoidosis: Papules, Nodules, and Plaques

Papules

Red to brown violaceous papules not associated with scarring

[Close up of annularly arranged papules.](#) VisualDx. Updated August 02, 2022. Accessed September 20, 2022.

[Micropapules along the eyelid.](#) VisualDx. Updated August 02, 2022. Accessed September 20, 2022.

[Close up of confluent papules.](#) VisualDx. Updated August 02, 2022. Accessed September 20, 2022.

Nodules

Red to flesh colored nodules that can have overlying telangiectasias (on nose)

[Multiple nodules on the knuckles.](#) VisualDx. Updated August 02, 2022. Accessed September 20, 2022.

[Multiple nodules on the central face.](#) VisualDx. Updated August 02, 2022. Accessed September 20, 2022.

[Peau d'orange nodules on the lip.](#) VisualDx. Updated August 02, 2022. Accessed September 20, 2022.

Plaques

Circular well circumscribed ovoid plaques commonly found on extensor surfaces

[Close up of two confluent plaques.](#) VisualDx. Updated August 02, 2022. Accessed September 20, 2022.

[Infiltrating plaques on the lateral face.](#) VisualDx. Updated August 02, 2022. Accessed September 20, 2022.

[Plaques with scale forming an annulus.](#) VisualDx. Updated August 02, 2022. Accessed September 20, 2022.

Cutaneous Sarcoidosis: Nails and Scalp

Nails (may manifest as **dactylitis and dystrophy**):

[Sausage digits and nail dystrophy in sarcoidosis.](#)

VisualDx. Updated August 02, 2022. Accessed September 20, 2022.

Scalp (may manifest as **alopecia**):

[Scarring alopecia on scalp.](#)

VisualDx. Updated August 02, 2022. Accessed September 20, 2022.



Syed 2021

Case #2

AM is a 24 year old female (she/her/hers) who complains of tender red “bumps” on her bilateral distal extremities for the past week. She first noticed one or two of the bumps on her right leg while she was shaving in the shower, but now they have gradually appeared all over both shins. She’s tried taking ibuprofen for the pain, but it’s only mildly helpful. She denies any recent trauma to the area. However a few days before she noticed the bumps, she reports having some arthralgias and feeling febrile and fatigued.

[Violaceous papules and plaques on the lower extremities.](#)

VisualDx. Updated August 02, 2022. Accessed September 20, 2022.

Medications

- Ibuprofen PRN, for pain
- Cetirizine (2nd gen antihistamine) daily, for seasonal allergies

Medical Hx

- Chickenpox (age 5)
- Seasonal allergies

Social Hx

- Diet: Variety of meats, vegetables/fruit, grains, and dairy
- EtOH: Two 12 oz glasses of wine/day on weekends
- Drugs/Tobacco: Denies

Family Hx

- Mother: Grave’s Disease

Rest of Physical Exam & ROS:

- **Pulmonary:** Mild dyspnea; No cough, sputum or hemoptysis, wheezing, or sore throat
- **Cardiac:** No chest pain, palpitations, or rubs/murmurs
- **GI:** No constipation, diarrhea, N/V, hematochezia, or hepatosplenomegaly
- **MSK:** Ankles swollen and sore bilaterally with full ROM
- **Neuro:** No focal deficits
- **Ophthalmology:** Mildly injected conjunctiva bilaterally
- **Skin:** No other rashes/skin findings or mucosal ulcers

(Some) Possible Etiologies of EN

- **Sarcoidosis**
 - Likely: Dyspnea, Uveitis, Prodrome of fever/fatigue/arthritis
 - No cardiac involvement or lupus pernio
- **Inflammatory Bowel Disease**
 - Likely: Fever, Fatigue, Uveitis, Arthritis
 - No diarrhea, abdominal pain, other rashes, or weight loss
- **Behcet Syndrome:**
 - Likely: Uveitis, Arthritis, Family hx of autoimmunity
 - No aphthous/genital ulcers, acneiform rash
- **Sweet Syndrome**
 - Likely: Uveitis, Arthritis
 - No hx of systemic disease, inciting medications, or recent infections
- **Streptococcus Infection**
 - Likely: Fever, Most common infectious cause
 - No sore throat or lymphadenopathy
- **Disseminated Tuberculosis**
 - Likely: Dyspnea, Fever
 - No sputum/hemoptysis, constitutional sx
- **Histoplasmosis/Coccidioidomycosis**
 - Likely: Dyspnea, Arthritis, Fever
 - No hepatosplenomegaly or sputum

Erythema Nodosum (EN) Overview

- Form of **septal panniculitis**
 - May be a **Type IV (cell-mediated/delayed) hypersensitivity reaction** (immune complexes in venules of subcutaneous fat → inflammation, neutrophil recruitment → non-caseating granuloma formation)
 - **Infectious, systemic, autoimmune, hormonal, and drug/medication-related etiologies**
 - More common in **white patients** than **Black patients** with **sarcoidosis**
 - Females > Males (3-6:1)
 - Age: 20-30's
- Typically a ***clinical*** diagnosis; Suspicion supported by:
 - **Acute** onset
 - **Tender, erythematous/violaceous nodules** or plaques 3-20 cm in diameter
 - Classically on the **shins**, but may also occur on ankles, thighs, arms, buttocks, or face
 - May follow **prodrome** of fever, fatigue, and arthralgia
 - Ulcerations, pustules/vesicles, and/or crusting should be ***absent***

Erythema Nodosum (EN) Overview

- Usually **spontaneously resolves** within 8 weeks
 - Turns from red → yellow-brown or blue-green (resembles bruises) = “**Erythema Contusiformis**,”
then heals without scarring or with hypo-/hyper-pigmentation

[Erythema nodosum in coccidiomycosis.](#)

VisualDx. Updated August 02, 2022.

Accessed September 20, 2022.

[Contusiform plaques.](#) VisualDx. Updated

August 02, 2022. Accessed September

20, 2022.

[Contusiform nodule on thigh.](#) VisualDx.

Updated August 02, 2022. Accessed

September 20, 2022.

Example Images of EN:

[Erythema nodosum on legs.](#) VisualDx.
Updated August 02, 2022. Accessed
September 20, 2022.

[Erythema nodosum on knees.](#) VisualDx.
Updated August 02, 2022. Accessed
September 20, 2022.

[Erythema nodosum on calves.](#) VisualDx.
Updated August 02, 2022. Accessed
September 20, 2022.

Dermatologic Features: Often pretibial nodules or plaques; Erythematous/violaceous (red/purple); Poorly demarcated (no clear margin); Irregular borders; Tender; Non-pruritic (not itchy); Warm to touch

Nodules = *raised, solid* lesions >0.5 cm

[Close-up of erythema nodosum.](#) VisualDx.
Updated August 02, 2022. Accessed
September 20, 2022.

[Close-up of an erythematous nodule.](#)
VisualDx. Updated August 02, 2022.
Accessed September 20, 2022.

Plaques = *raised, flat-topped* lesion with
distinct borders up to 0.5 cm

[Dusky erythematous plaque.](#) VisualDx.
Updated August 02, 2022. Accessed
September 20, 2022.

[Confluent erythematous plaques.](#)
VisualDx. Updated August 02, 2022.
Accessed September 20, 2022.

Additional Examples of EN:

[Erythema nodosum on lower legs.](#)

VisualDx. Updated August 02, 2022.

Accessed September 20, 2022.

[Erythematous plaques on legs.](#) VisualDx.

Updated August 02, 2022. Accessed

September 20, 2022.

[Close up of erythema nodosum nodule.](#)

VisualDx. Updated August 02, 2022.

Accessed September 20, 2022.

[Large erythematous plaque.](#) VisualDx.

Updated August 02, 2022. Accessed

September 20, 2022.

Less Common Sites for EN:

Forearms:

[Violaceous plaques on the arms.](#)

VisualDx. Updated August 02, 2022.

Accessed September 20, 2022.

Hands:

[Nodules on the hand.](#) VisualDx. Updated

August 02, 2022. Accessed September

20, 2022.

Wrists:

[Nodules on the distal forearm.](#) VisualDx.

Updated August 02, 2022. Accessed

September 20, 2022.

Cubital Region:

[Erythematous nodules on the elbow.](#)

VisualDx. Updated August 02, 2022.

Accessed September 20, 2022.

[Resolving nodule on the forearm.](#)

VisualDx. Updated August 02, 2022.
Accessed September 20, 2022.

[Hyperpigmented plaques on arm.](#)

VisualDx. Updated August 02, 2022.
Accessed September 20, 2022.

[Resolving plaque on leg.](#) VisualDx.

Updated August 02, 2022. Accessed
September 20, 2022.

Examples of hyperpigmentation caused by resolved EN

[Deep gray and brown nodule on ankle.](#)

VisualDx. Updated August 02, 2022.
Accessed September 20, 2022.

[Hyperpigmented plaques on shin.](#)

VisualDx. Updated August 02, 2022.
Accessed September 20, 2022.

Clinical Pearl:

Erythema Nodosum is a form of acute panniculitis (inflammation of subcutaneous fat) that presents as **warm, red/purple, tender nodules** typically on the **pretibial surface**. It can be a symptom of various systemic infections, autoimmune and inflammatory conditions, hormonal changes, or drug reactions.

Diagnostic Algorithm for EN

Note: This flowchart is *not* meant to be memorized! Rather, it is to help get you thinking about the diagnostic framework for EN. Some of the most common etiologies are included (however, keep in mind that there are still other, rarer causes)!

Suspected EN

Initial Work-Up

(Should depend on medical history & clinical findings)

- Labs
 - CBC
 - ESR & CRP
 - Pregnancy test for individuals of child-bearing capacity
- Chest X-Ray (CXR)
- Skin Biopsy

Comprehensive Medical History

- HPI, PMHx, & ROS
- Medications (esp. **OCP's, Sulfonamides, Halides, & Sulfonylureas**)
- Recent travel/exposures

Yes, and no other findings

Drug-Induced

Cough, Dyspnea, Fatigue, Fever, Arthralgia, Uveitis, Rash

CXR: Lymphadenopathy & Nodular Opacities

Sarcoidosis

Diarrhea, Abdominal Pain, Uveitis, Malabsorption

ASCA, p-ANCA, Abdominal X-Ray, Colonoscopy

Inflammatory Bowel Disease

Recurrent oral & genital ulcers, Ocular lesions, Rash

Demonstrates Pathergy

Behcet's Disease

Upper Respiratory Symptoms, Exudative Pharyngitis, Fever

Antistreptococcal O Titers, Throat Swab Culture

Streptococcal Infection

Cough, Dyspnea, Arthralgias, Fever, Night Sweats

CXR: Lymphadenopathy & Consolidations, IgM

Coccidiomycosis

Cough, Dyspnea, Hepatosplenomegaly, Fever, Oral ulcers

CXR: Lymphadenopathy & Nodular Opacities, Urine Antigen

Histoplasmosis

Cough, Dyspnea, Fevers, Night Sweats, Weight Loss

CXR: Lymphadenopathy & Cavities, TST Skin Test, IFN- γ Blood Test

Tuberculosis

Summary

- Sarcoidosis is a multisystemic inflammatory disorder characterized by **granulomas**, most commonly in **skin** and **lungs**.
- A basic workup of sarcoidosis involves a chest x-ray, ECG, CBC, CMP, and eye exam.
- The diagnostic test for sarcoidosis is a **biopsy** showing non-caseating granulomas.
- **Cutaneous manifestations** of sarcoidosis include: papules, plaques, nodules, lupus pernio, and erythema nodosum.
- **Lupus pernio** is specific to sarcoidosis and involves reddish-purple papules and plaques on **nose**, cheeks, and ears.

Summary

- Erythema nodosum (EN) is a form of **septal panniculitis**, characterized by multiple tender, warm, red to purple nodules.
- The most common site is the **shins**.
- It is thought to be due to a **Type IV HS** reaction.
- It is a manifestation of an **underlying condition**; the most common etiologies are **drug-induced, infection, or autoimmune/inflammatory conditions**.
- While the diagnosis of EN itself is **clinical**, the workup of the underlying cause should include a thorough history, review of systems, and medication profile.

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