

ERYTHEMA NODOSUM AND ERYTHEMA INDURATUM

Clinicopathologic comparison of two panniculitides

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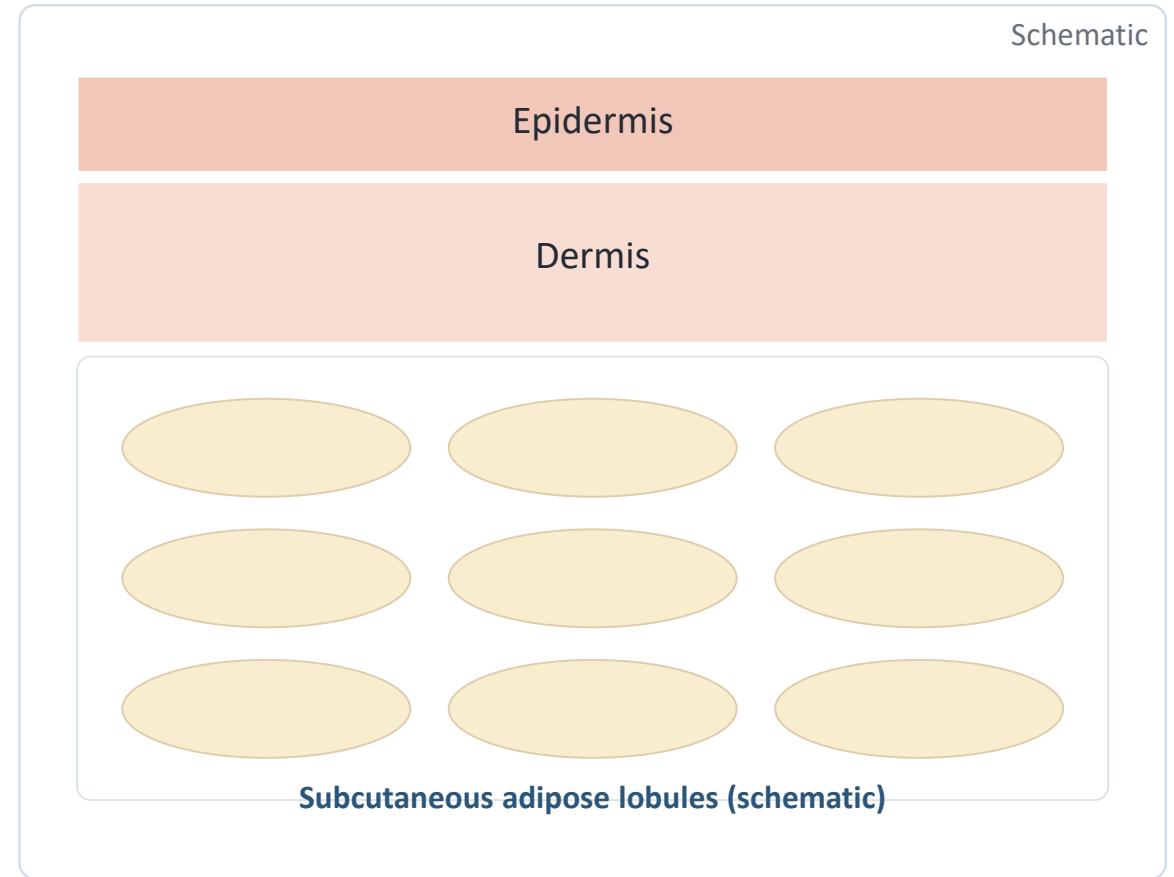
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Learning outcomes

- Localize inflammation to subcutaneous septa or fat lobules.
- Distinguish the clinical course of erythema nodosum from erythema induratum.
- Interpret key histologic features, particularly vasculitis and necrosis.
- Select a sufficiently deep biopsy and integrate systemic associations.

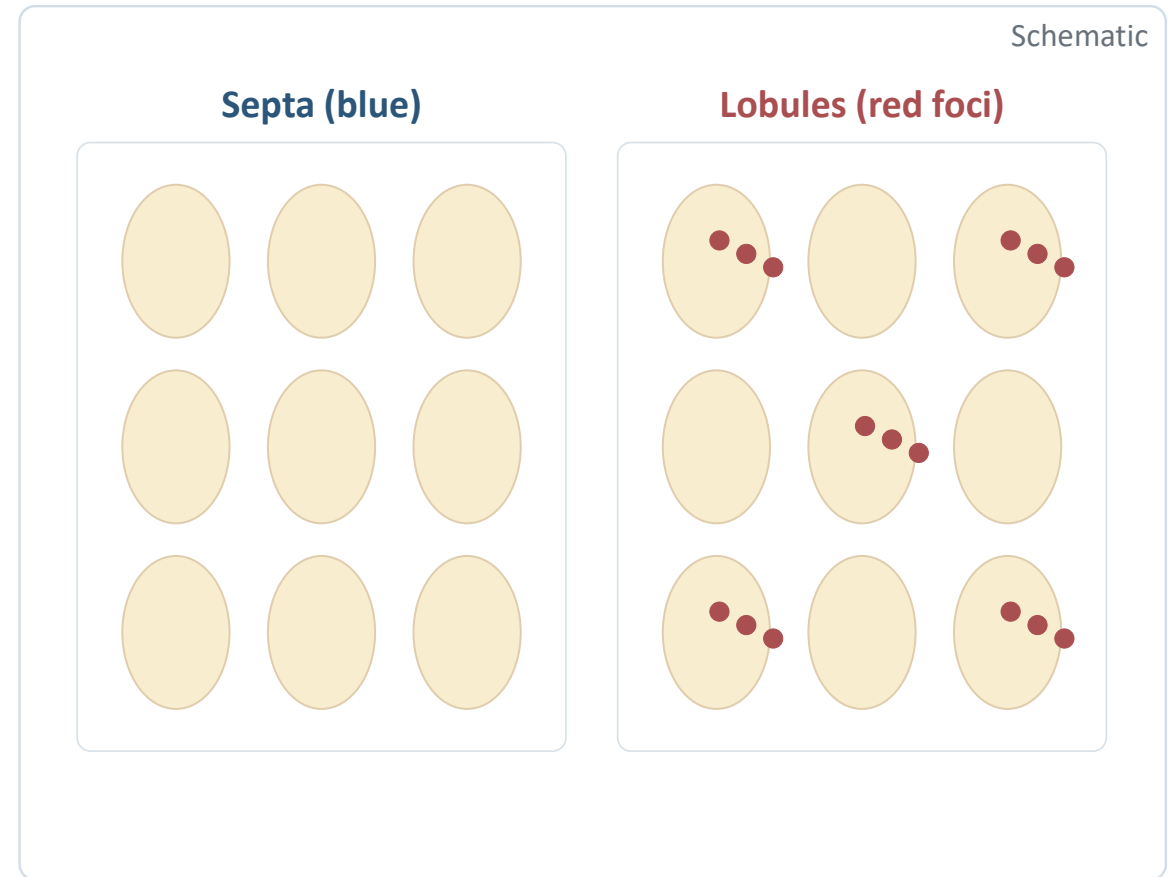
Panniculitis is inflammation of the subcutis

- Subcutaneous adipose tissue is the primary inflammatory compartment.
- Inflammation may be centered on fat lobules or their connective-tissue septa.
- This compartmental pattern is a starting point for histologic classification.



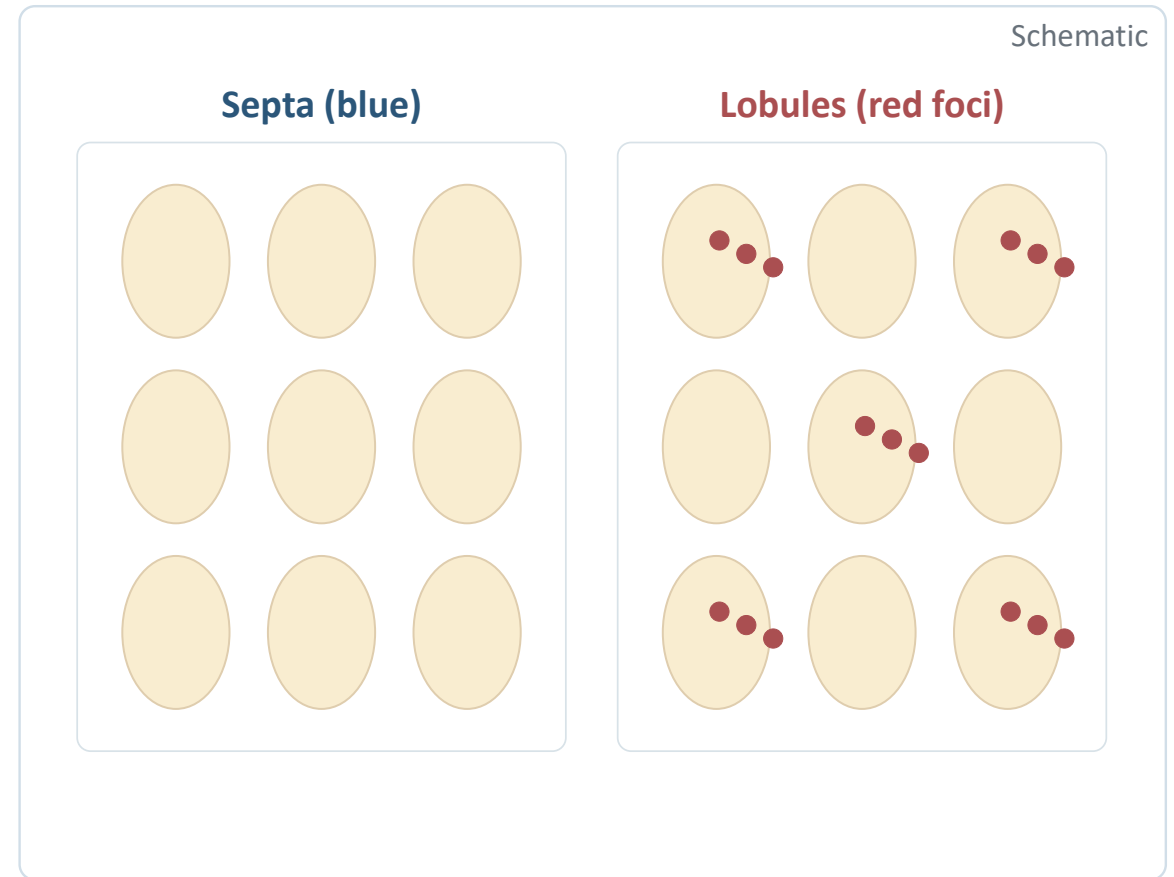
A fat lobule is separated by fibrous septa

- Adipocytes form lobular aggregates within the subcutaneous layer.
- Connective-tissue septa partition lobules and contain vessels.
- Diagnosis requires enough subcutis to evaluate both compartments.



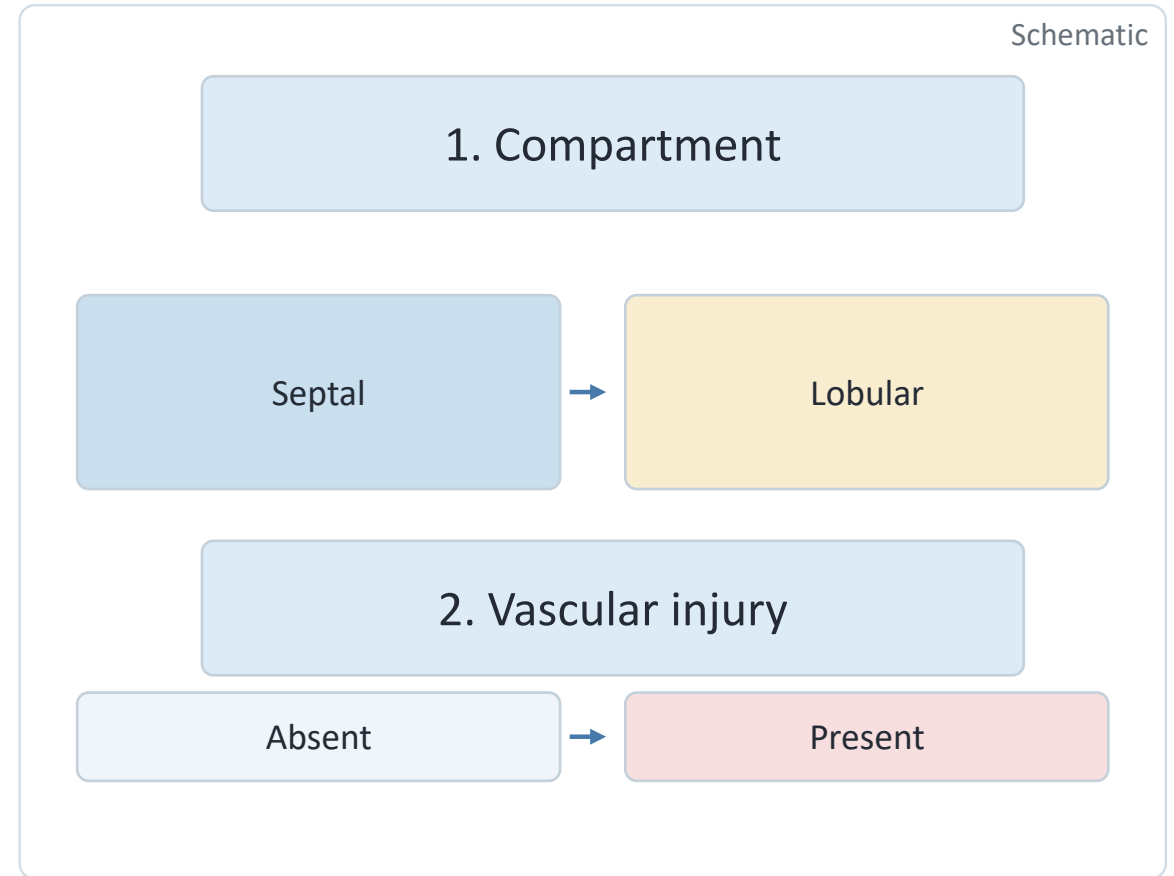
Septal and lobular patterns are not interchangeable

- Septal panniculitis: Inflammation predominates between lobules.
- Lobular panniculitis: Inflammation predominates inside lobules.
- A mixed lesion requires identification of its dominant pattern.



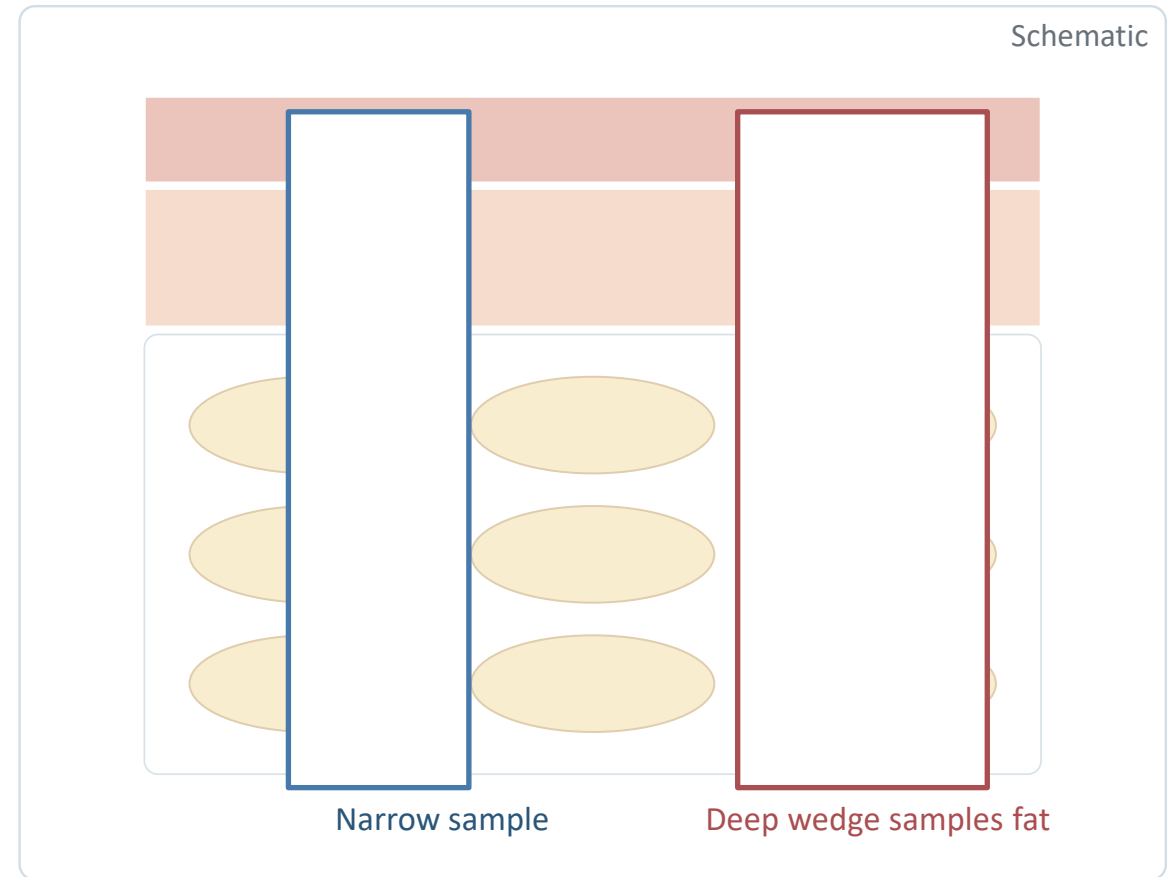
Vasculitis is a second diagnostic axis

- Classify the compartment: Septal versus lobular.
- Assess whether vascular walls show inflammation and destruction.
- The combination narrows the differential more than either feature alone.



Deep sampling determines whether the pattern is visible

- A superficial sample may contain dermis but too little adipose tissue.
- A deep wedge or incisional biopsy helps demonstrate septa, lobules, and vessels.
- Inadequate sampling may misclassify panniculitis or overlook vasculitis.

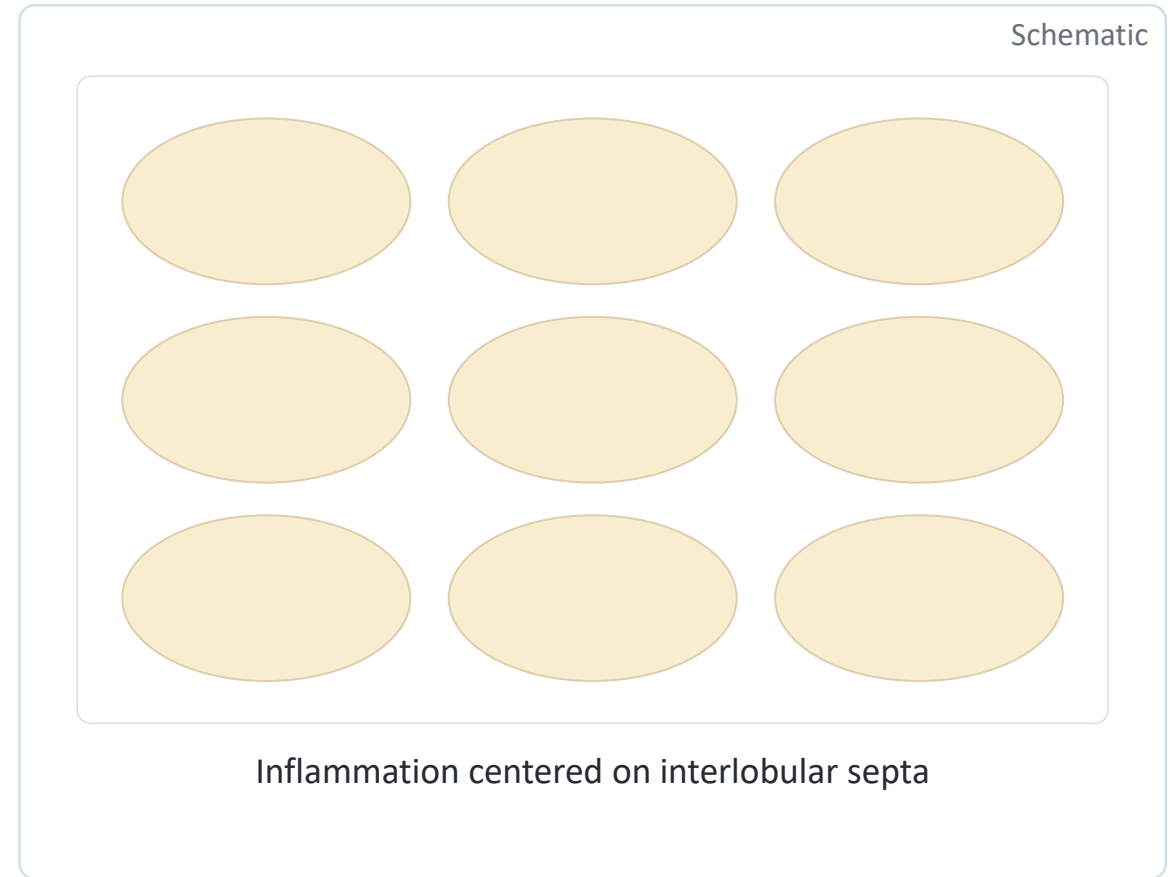


Two diseases: One tissue, different primary patterns

Characteristic	Erythema nodosum	Erythema induratum
Dominant site	Fibrous septa	Fat lobules
Vasculitis	Classically absent	Deep necrotizing vasculitis
Necrosis	Not defining	Fat and sometimes caseous necrosis
Typical course	Bruise-like fading; no scar	Nodules often ulcerate

Erythema nodosum: The prototypical septal panniculitis

- Most common form of panniculitis in the Robbins account.
- Usually has a subacute presentation involving the lower legs.
- Its recognizable clinical and histologic signatures are complementary.



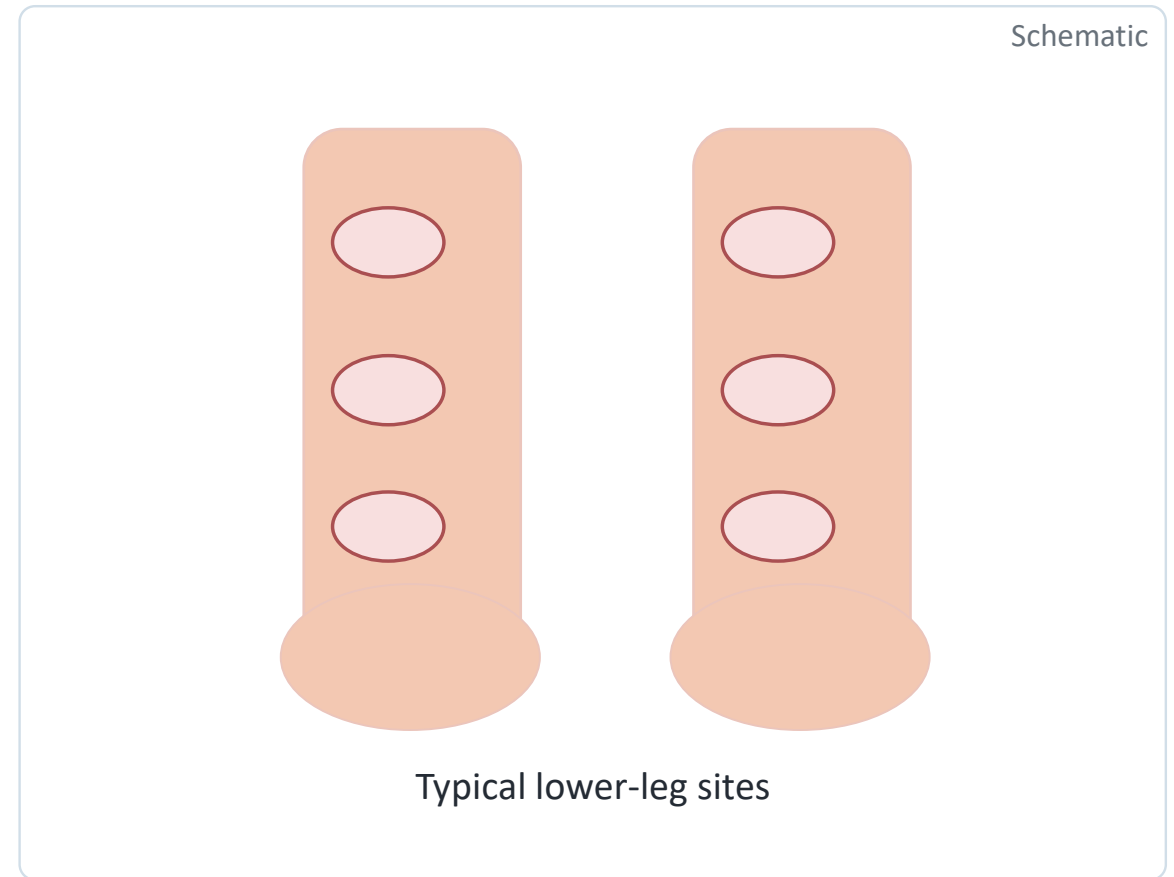
A lesion may be easier to feel than to see

- Poorly defined, erythematous plaques and nodules are characteristic.
- Lesions are often deep enough to be identified by palpation.
- Severe tenderness is a distinctive clinical clue.

Clinical recognition begins with palpation, not merely surface color.

Lower-leg distribution is a major clue

- Panniculitis often affects the lower legs.
- Erythema nodosum commonly presents as tender nodules on the anterior shins.
- Distribution increases suspicion but does not establish etiology.



The pain reflects an inflamed deep compartment

- Exquisite tenderness is a prominent feature of erythema nodosum.
- The palpable nodule is located in inflamed subcutaneous tissue.
- A normal-looking overlying surface does not exclude substantial pathology.

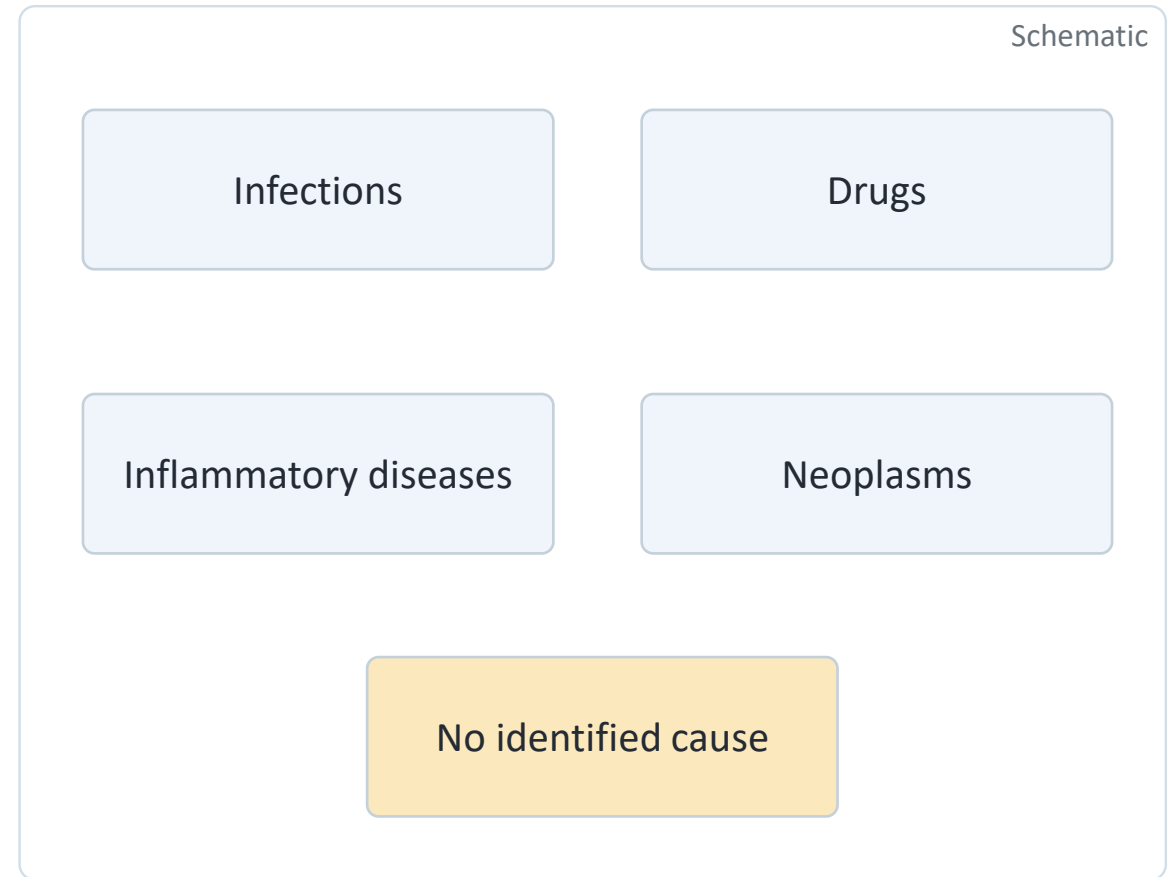
Interpret this as a clinicopathologic relation; It is not a validated pain mechanism.

Constitutional symptoms may accompany skin findings

- Fever and malaise can accompany the eruption.
- Skin lesions may therefore signal a process beyond the skin.
- Clinical history should search for systemic and exposure-related clues.

Erythema nodosum has several categories of association

- Infections, medication exposure, and systemic inflammatory disease.
- Some malignant neoplasms also occur in association.
- An etiologic association is not the same as a proven cause in an individual.



Streptococcal infection is a recognized association

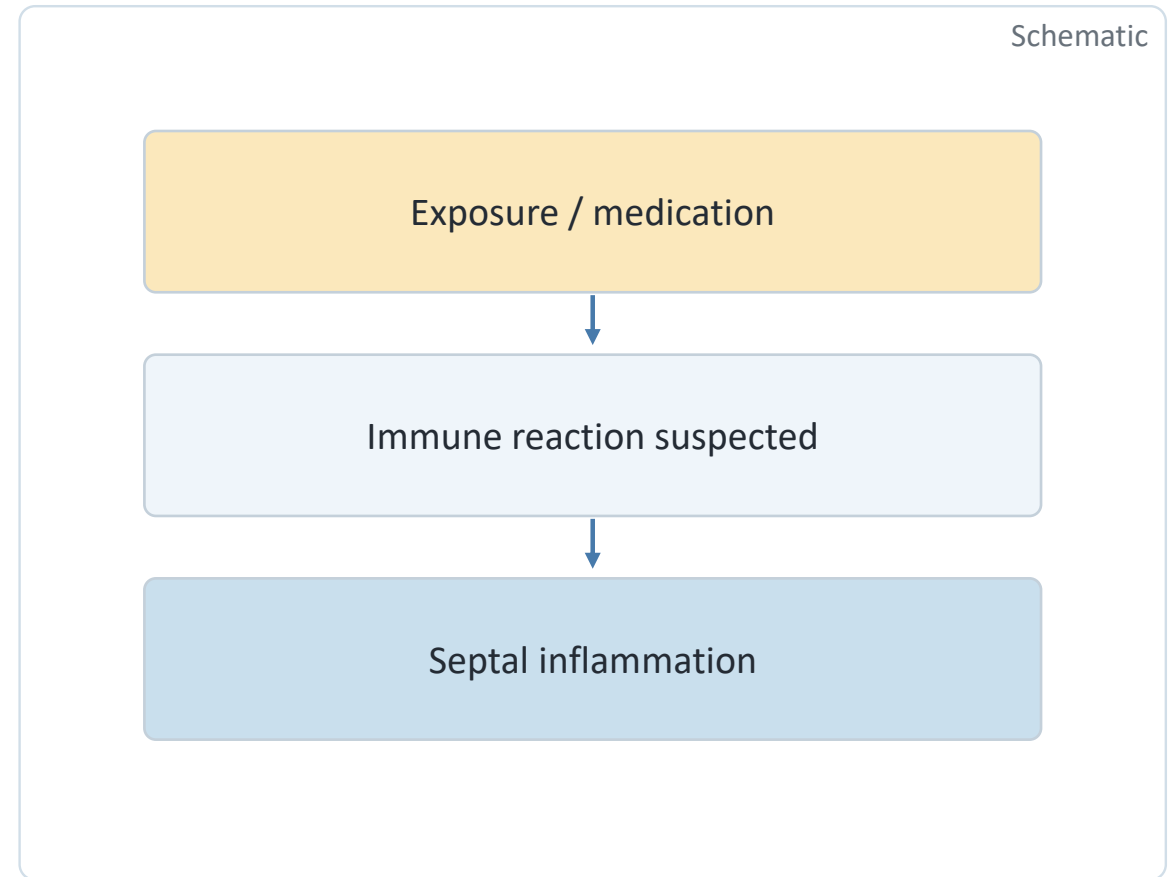
- β -hemolytic streptococci among triggers.
- A recent history of pharyngitis or infection can guide evaluation.
- Document chronology before attributing the eruption to an infection.

Tuberculosis and selected deep infections are relevant

Infectious group	Examples in Robbins	Interpretation
Commonly highlighted	β -hemolytic streptococci; tuberculosis	Investigate when relevant
Less common	Coccidioidomycosis; histoplasmosis	Context/exposure dependent
Other	Leprosy	Clinical and epidemiologic context

Medication exposure belongs in the history

- Sulfonamides are among the textbook-listed drug associations.
- Oral contraceptives are also specifically cited.
- Time of initiation and cessation helps evaluate plausibility.



Sarcoidosis is an important systemic association

- Sarcoidosis can be accompanied by erythema nodosum.
- The panniculitis pattern does not itself identify the systemic disorder.
- Investigate systemic manifestations when the clinical setting suggests them.

Inflammatory bowel disease is another association

- Inflammatory bowel disease is specifically listed.
- Gastrointestinal history may provide a useful etiologic clue.
- The skin lesion alone cannot distinguish the underlying bowel condition.

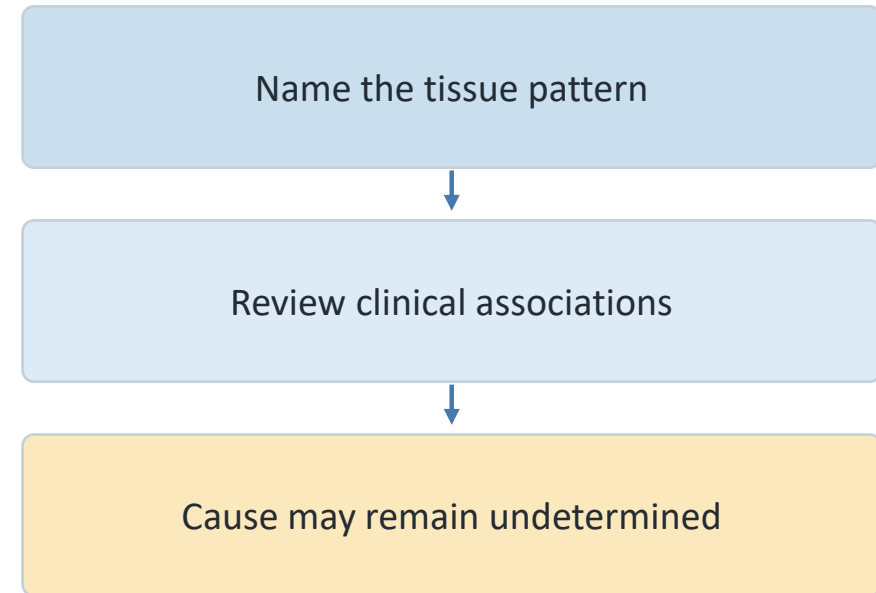
Malignancy is a possible but nonspecific association

- Certain malignant neoplasms among associations.
- No specific tumor type or screening threshold is provided in this section.
- Avoid implying cancer when the clinical evaluation does not support it.

Many cases remain without an identified trigger

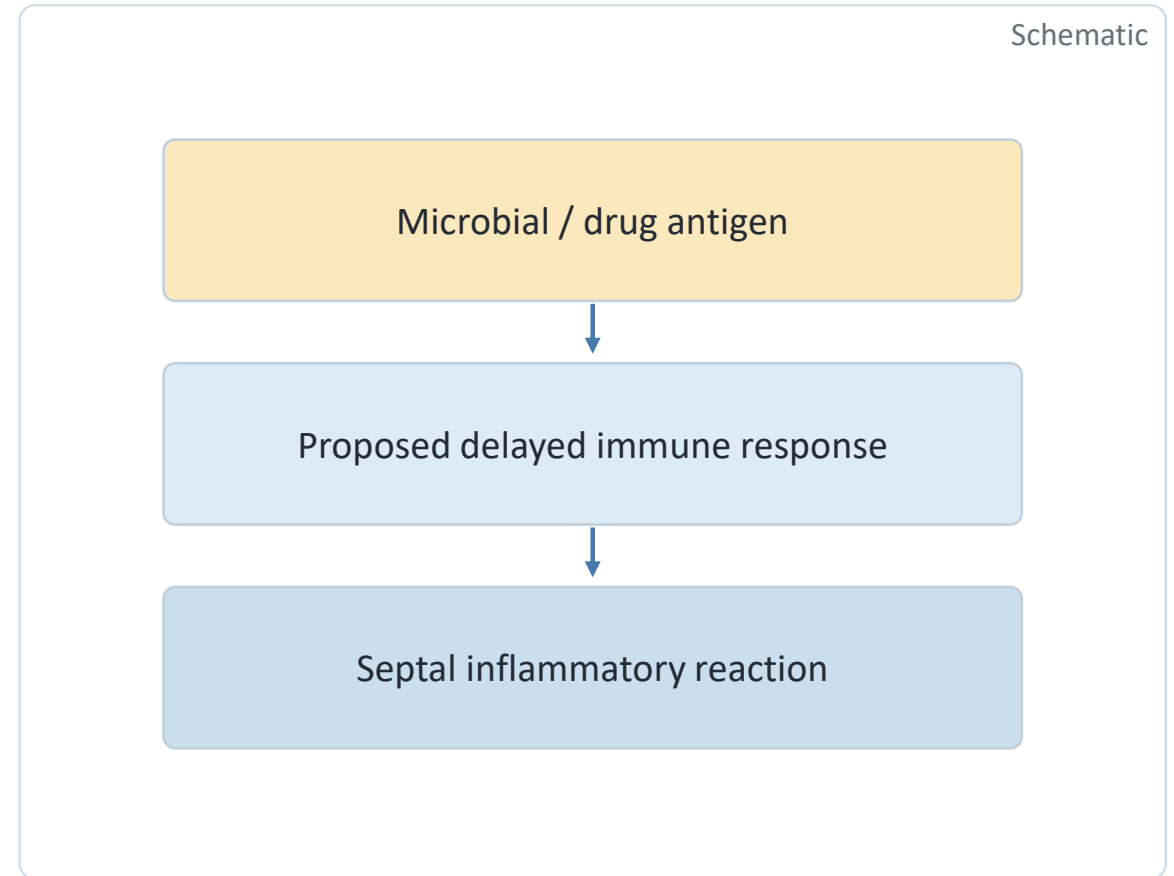
- The chapter explicitly notes that a cause often cannot be found.
- A negative etiologic work-up does not automatically refute the morphology.
- Separate the diagnosis of panniculitis from certainty about its trigger.

Schematic



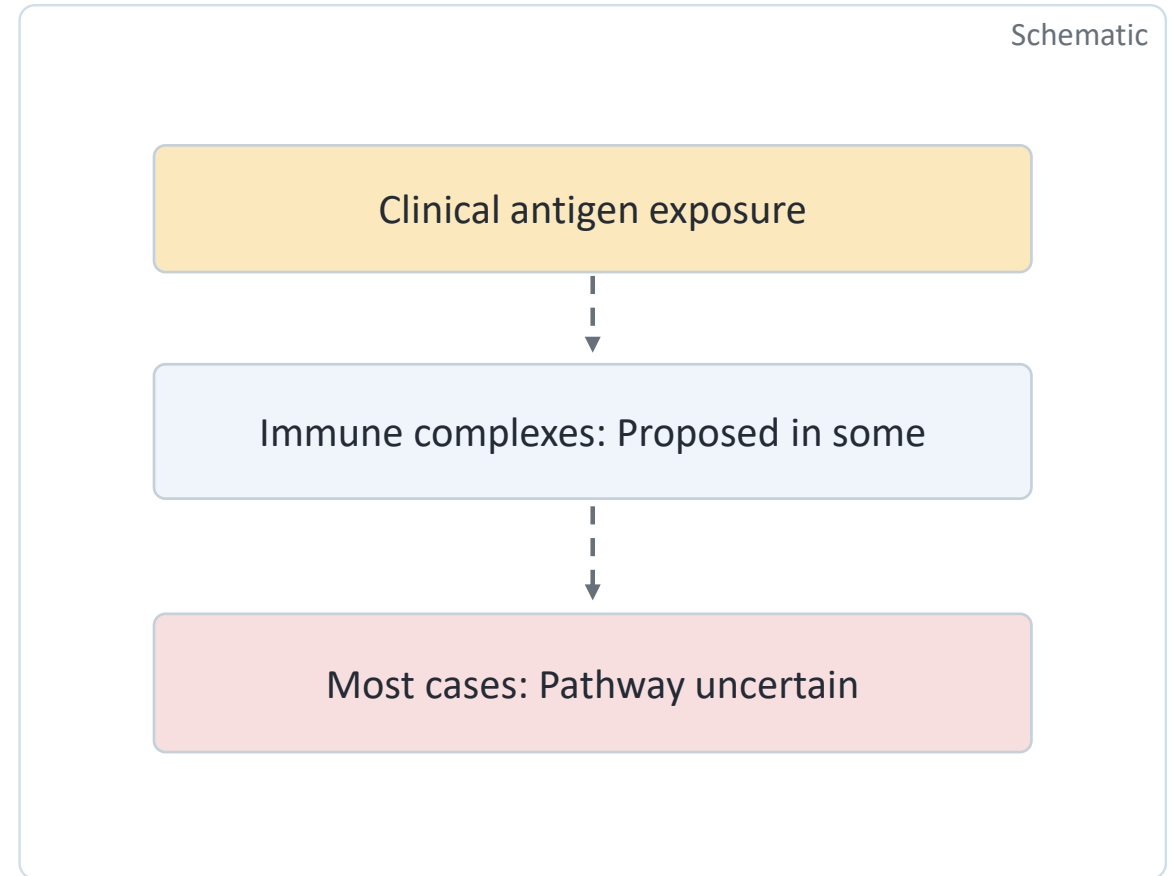
Delayed hypersensitivity is the proposed mechanism

- A proposed delayed response to microbial or drug antigens.
- This is a mechanistic hypothesis, not a demonstrated pathway in every patient.
- Different initiating antigens may converge on a similar septal pattern.



Immune complexes have been implicated in some cases

- Immune complex participation is reported for a subset of cases.
- Its presence should not be assumed for every lesion.
- The account explicitly emphasizes that pathogenesis is mostly unresolved.



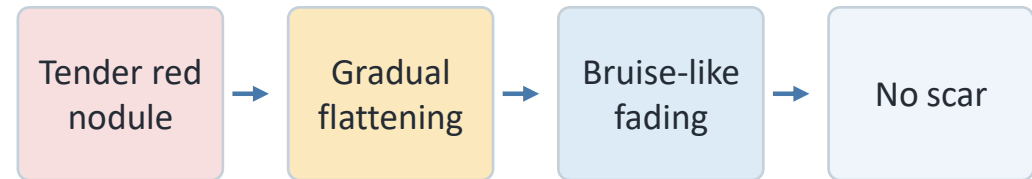
The same morphology does not prove the same trigger

- Different exposures and systemic diseases can be associated with nodules.
- The reaction pattern summarizes tissue injury, not a single pathogen.
- Etiologic attribution requires clinical evidence outside the skin specimen.

Erythema nodosum changes over weeks

- Inflamed tender nodules gradually flatten.
- Resolving lesions take on a bruise-like appearance.
- New lesions may emerge while older ones are regressing.

Schematic

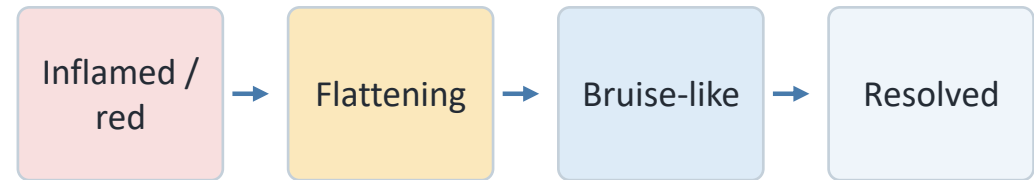


Evolution over weeks; Not a measured time scale

Bruise-like fading is a useful evolution clue

- Early: Erythematous tender plaques or nodules.
- Later: Flattening and bruise-like discoloration.
- An isolated mature lesion may look different from a newly erupted one.

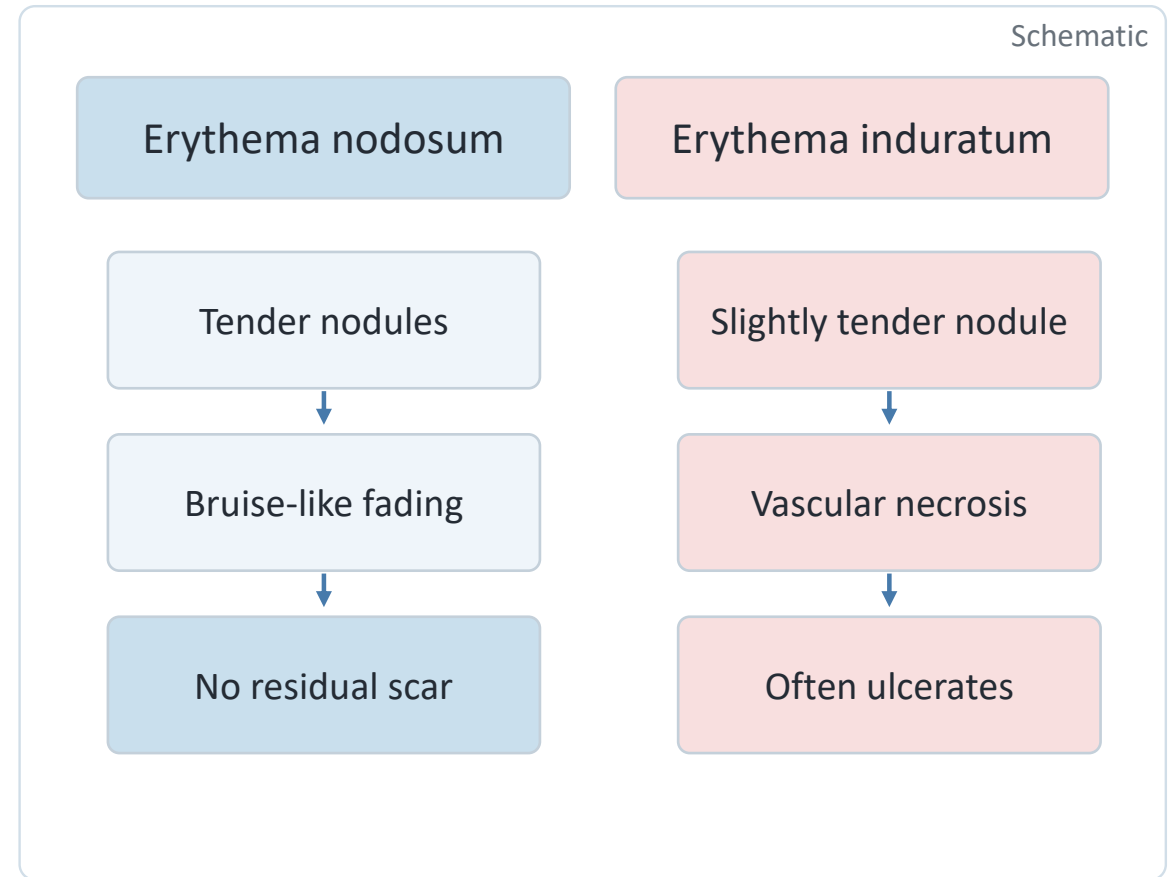
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Evolution over weeks; Not a measured time scale

Individual nodules usually resolve without scarring

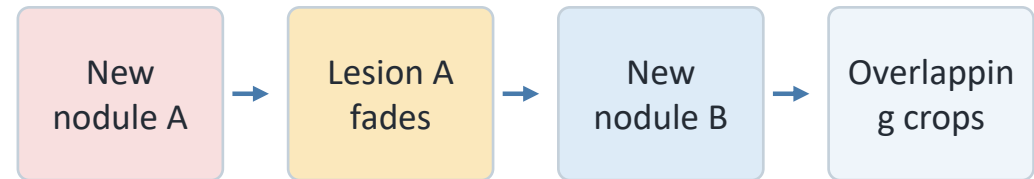
- Resolution without residual scar.
- The absence of ulcerative tissue destruction helps contrast erythema induratum.
- Interpret the overall eruption over time, not just a single observation.



Crops can overlap in time

- New nodules may develop while older nodules flatten.
- A patient can have lesions at different stages simultaneously.
- Biopsy interpretation should take the lesion's age into account.

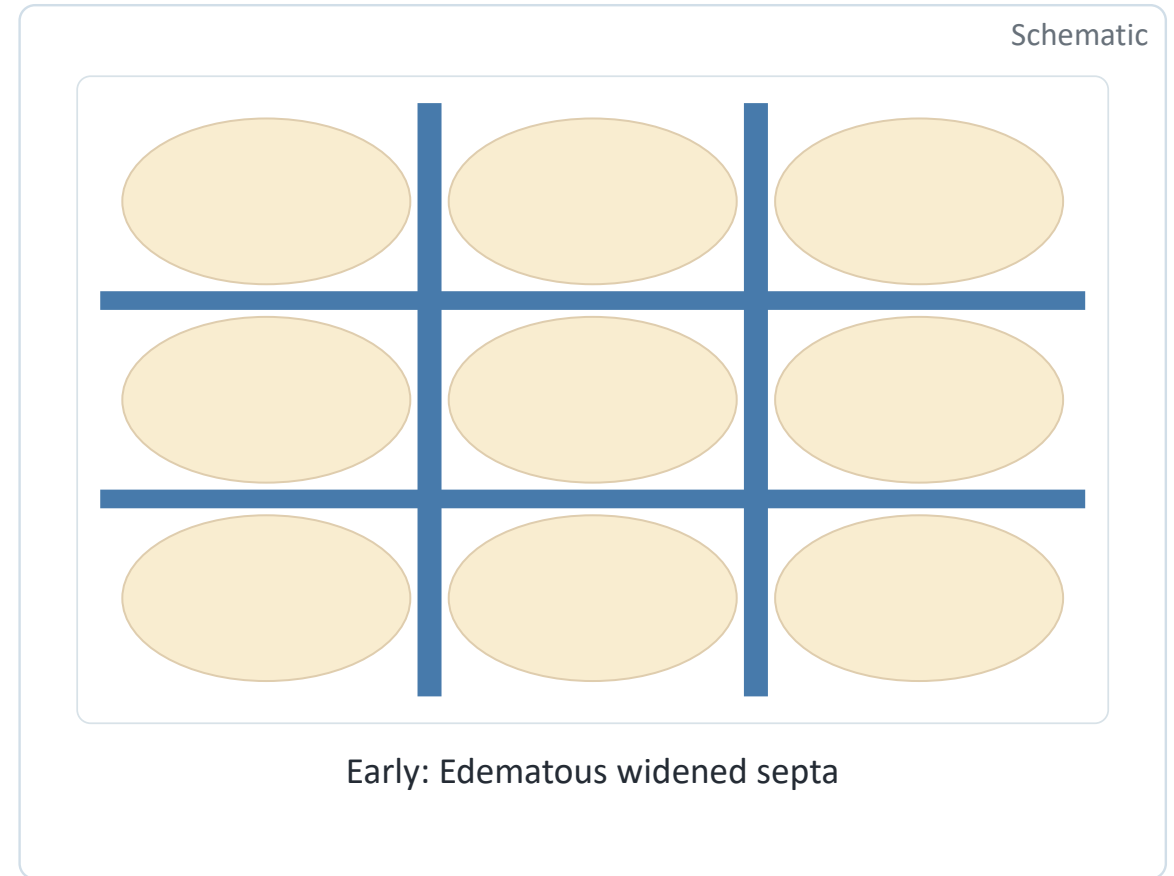
Schematic



Different lesions may have different ages

Histology: The earliest finding is septal expansion

- Early erythema nodosum widens the fibrous septa.
- Edema is a principal reason for the increase in septal thickness.
- The predominant anatomic center remains interlobular connective tissue.

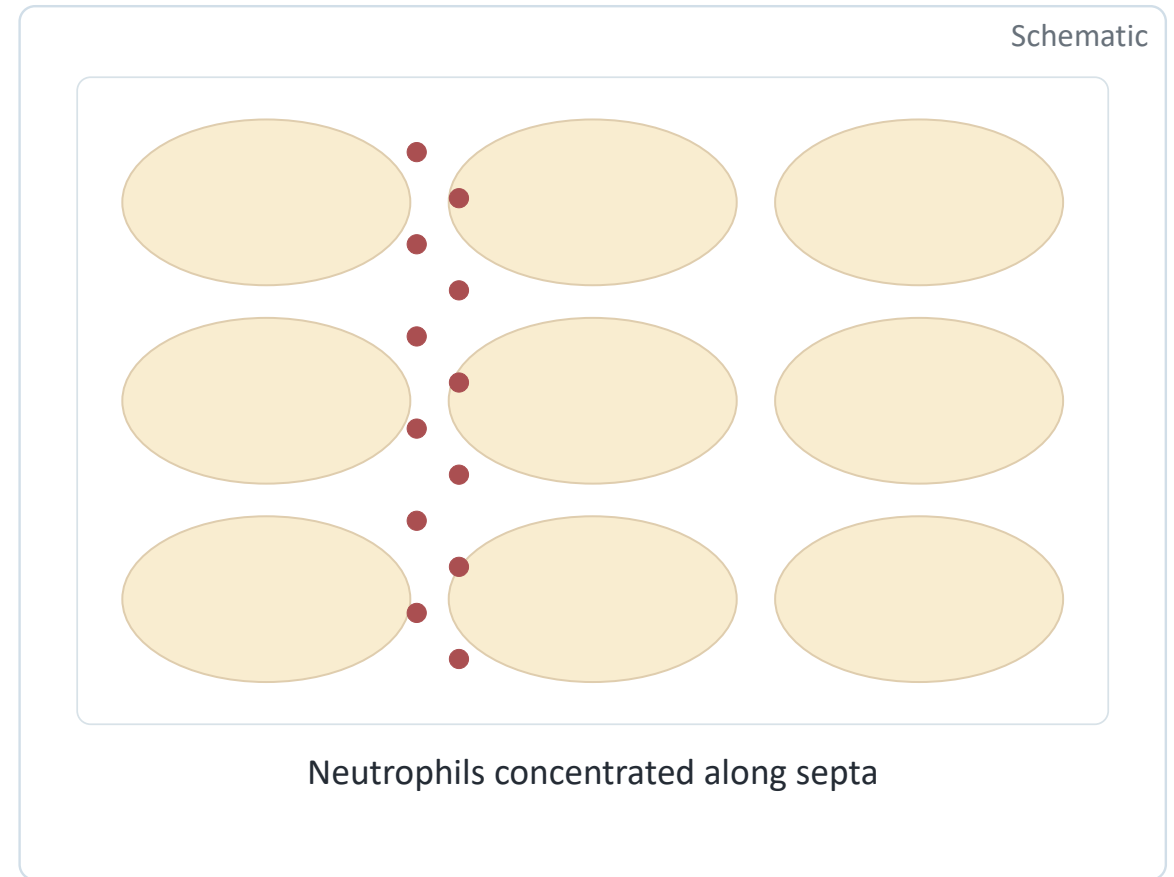


Fibrinous exudate accompanies early inflammation

- Fibrin exudation in early lesions.
- Interpret fibrin in the context of edematous inflamed septa.
- Do not confuse septal exudation with necrotizing vascular injury.

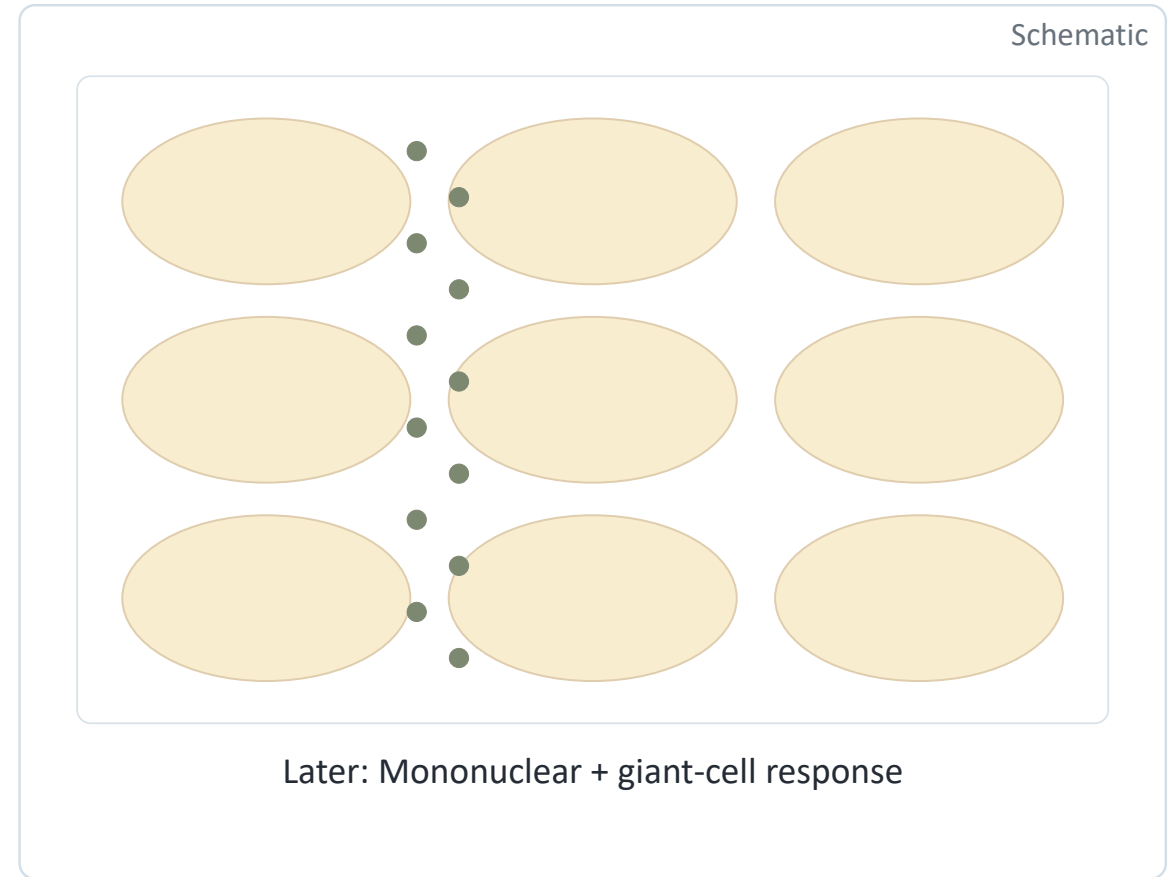
Early erythema nodosum is often neutrophil rich

- Neutrophilic infiltration is an early histologic component.
- A neutrophil-rich septum must be evaluated with the lesion age in mind.
- Superficial or very early sampling can obscure the complete pattern.



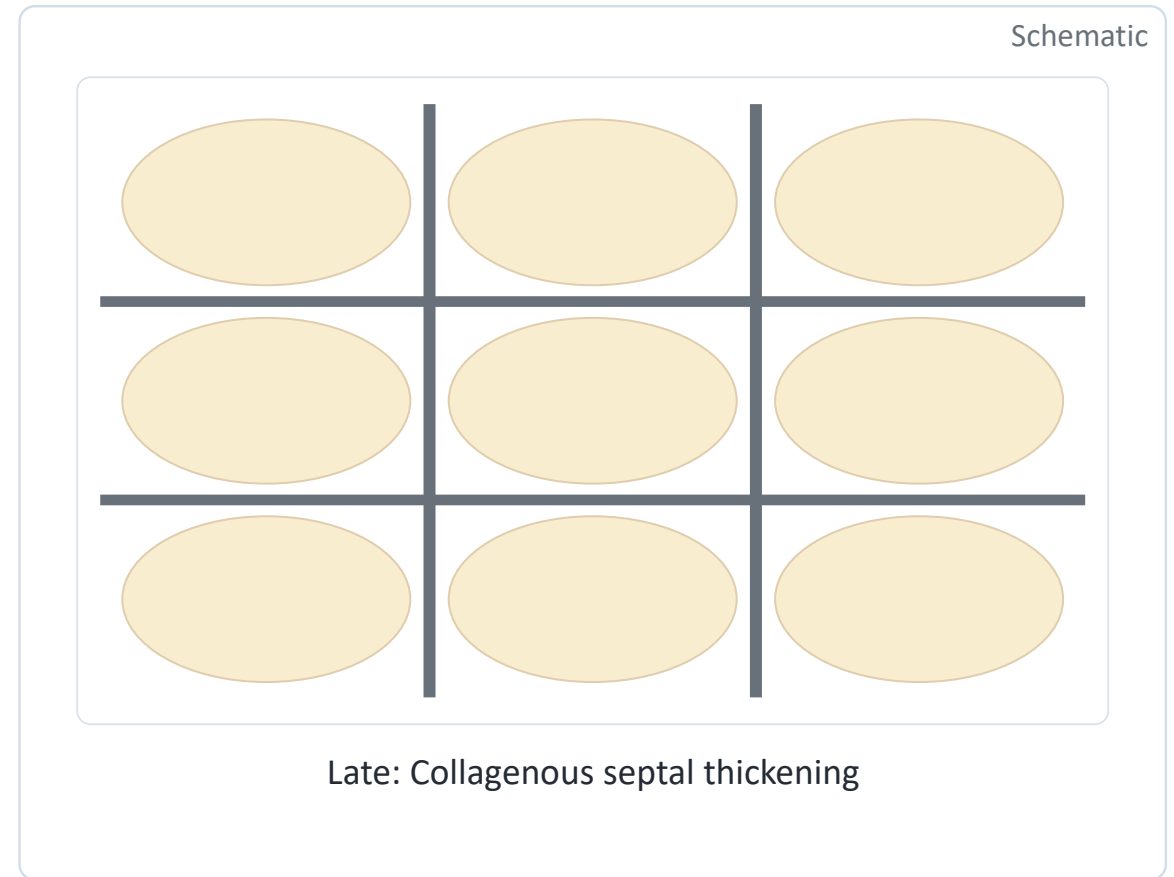
The infiltrate changes as lesions mature

- Lymphocytes and macrophages become prominent later.
- Multinucleated giant cells may accompany the later response.
- Occasional eosinophils are described in the chapter.



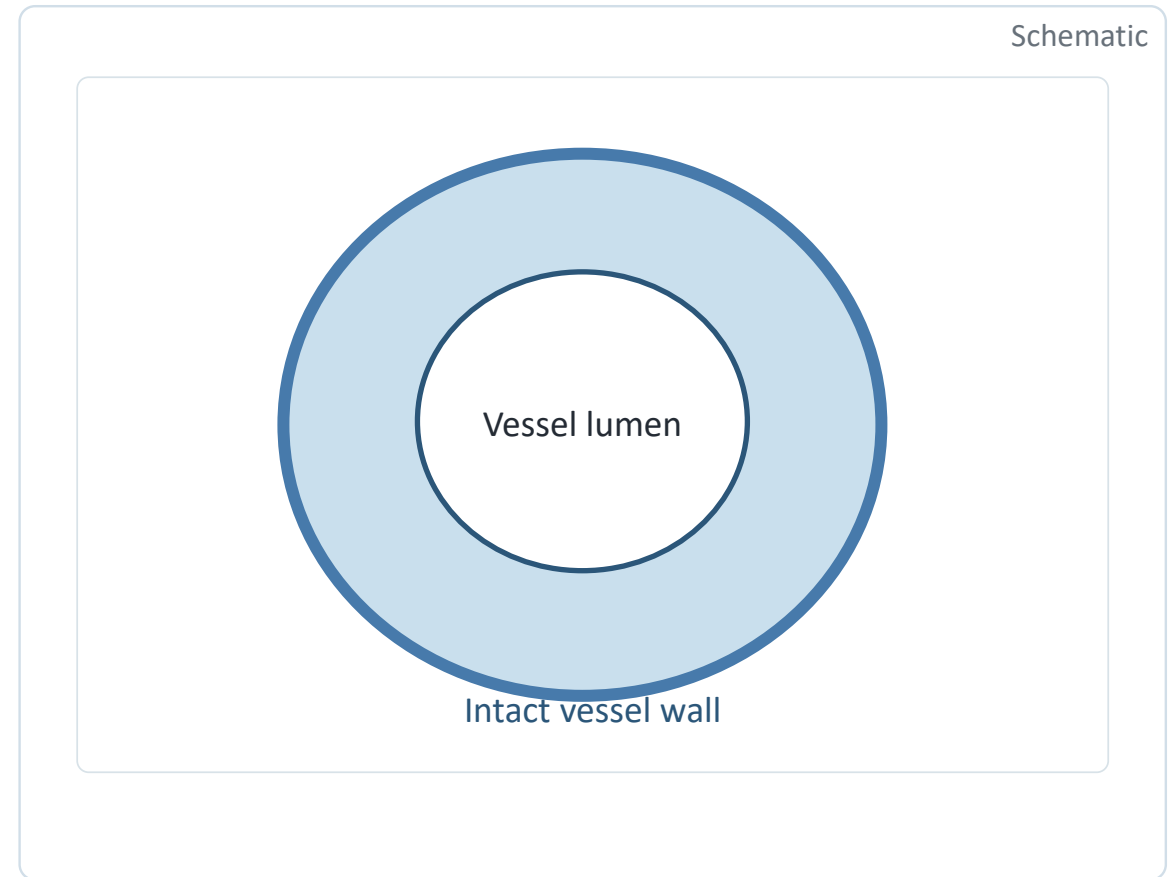
Septal fibrosis marks a later stage

- Later lesions show fibrosis within the affected septa.
- Inflammatory composition changes alongside connective-tissue remodeling.
- The histology of a late nodule should not be expected to mimic a fresh one.



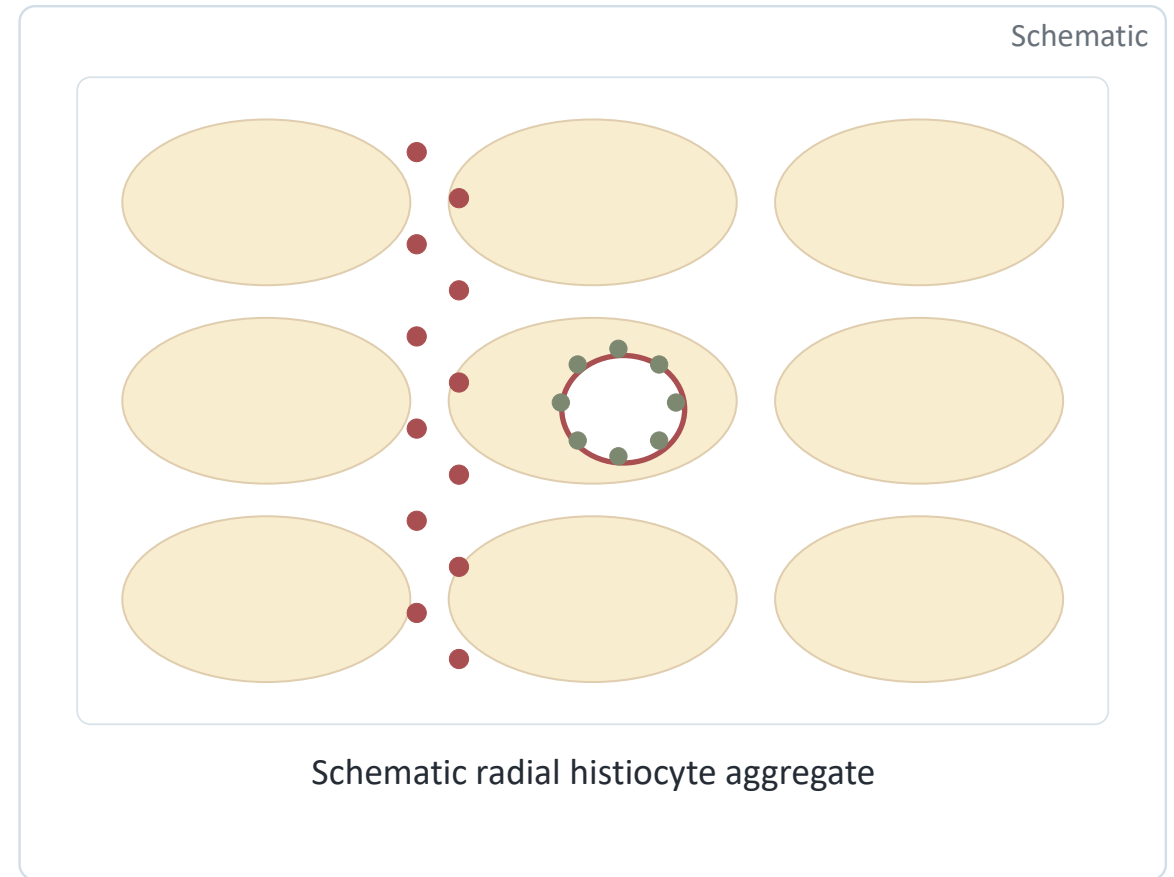
Classic erythema nodosum lacks necrotizing vasculitis

- , vasculitis is absent in the characteristic morphology.
- This is a powerful contrast with erythema induratum.
- Pathology reporting should specify vascular-wall findings rather than use vague “inflammation” terminology.



Miescher radial granulomas: A supplementary clue

- Small histiocyte aggregates may form around a central cleft in septa.
- They support an erythema-nodosum pattern when present.
- Published reviews caution that they are not absolutely pathognomonic.

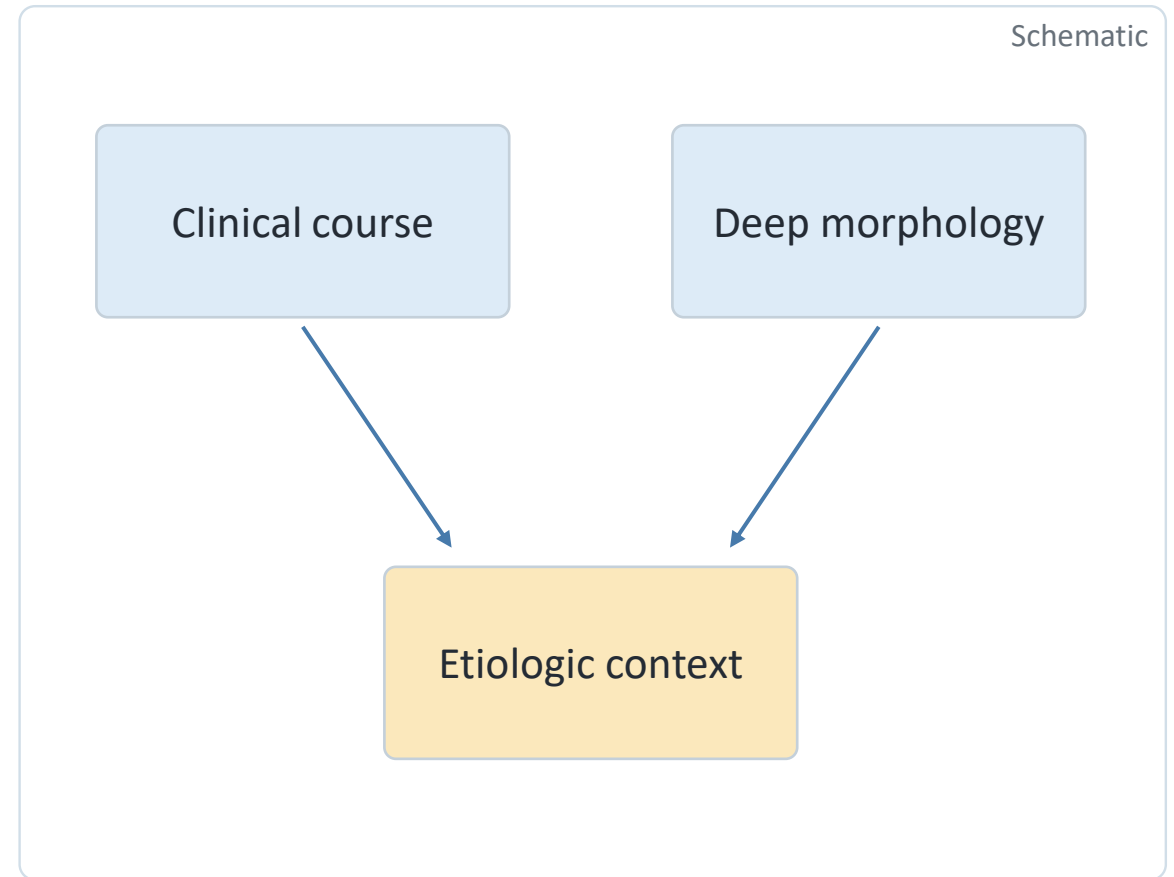


A lesion's age determines what the pathologist sees

Feature	Early erythema nodosum	Later erythema nodosum
Septa	Edematous and widened	Fibrotic and thickened
Inflammatory cells	Neutrophils prominent	Lymphocytes; macrophages; giant cells
Additional elements	Fibrin exudation	Occasional eosinophils
Vasculitis	Classically absent	Classically absent

Clinical diagnosis and biopsy answer different questions

- Clinical history establishes distribution, tenderness, and time course.
- Deep histology localizes inflammation and assesses vessel injury.
- History and targeted testing help assign a possible underlying trigger.



A directed etiologic evaluation is preferable

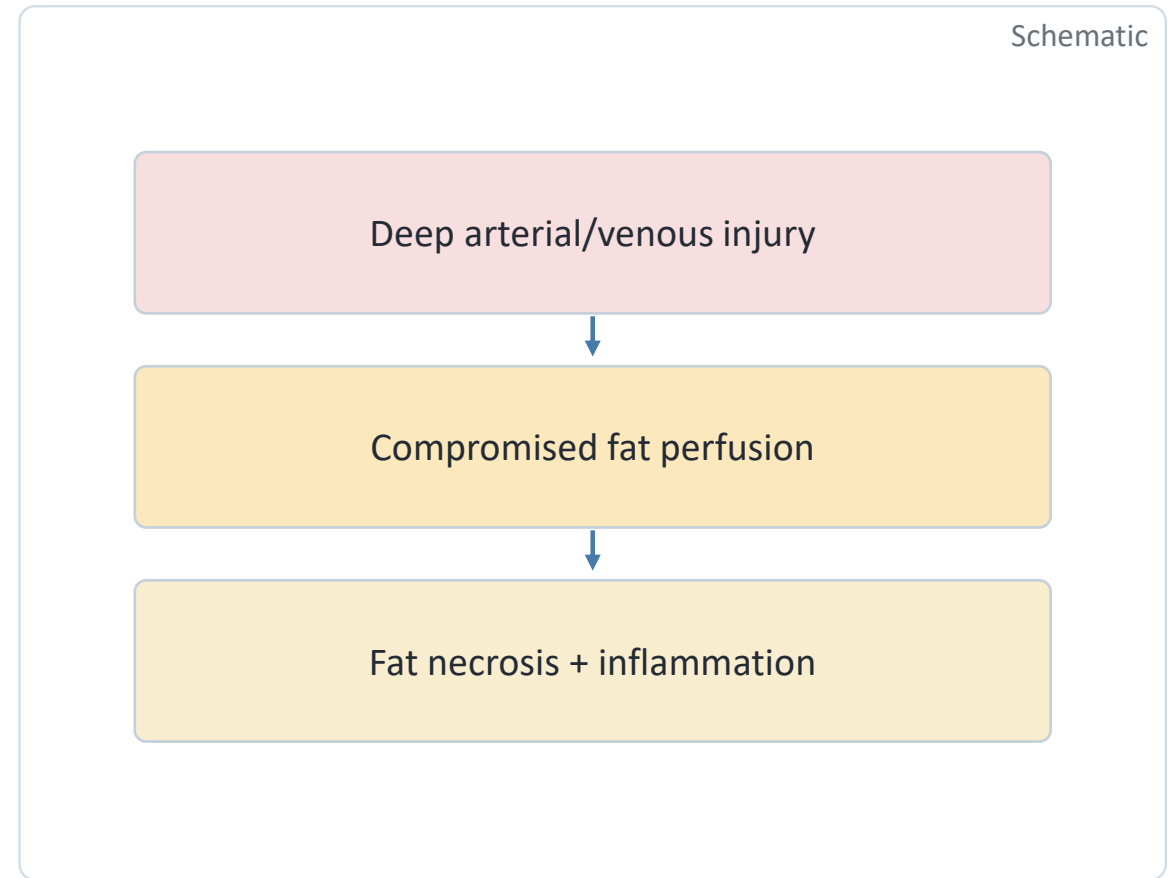
- Review recent infection, drug exposure, and systemic inflammatory symptoms.
- Investigations are guided by risks and findings, not a universal test panel.
- Examples in clinical reviews: Inflammatory markers, streptococcal testing, TB assessment or chest imaging when indicated.

Do not treat a clinical association as histologic proof

- An erythema-nodosum biopsy does not identify streptococci, sarcoidosis, or IBD.
- The same septal pattern can arise across multiple clinical contexts.
- Reports should state the morphologic diagnosis and separately note clinical correlations.

Erythema induratum: An uncommon vasculitic panniculitis

- It as an uncommon form of panniculitis.
- Its characteristic target is the deep vascular supply of subcutaneous fat.
- Vascular compromise leads to fat necrosis and inflammation.



Population pattern is descriptive, not diagnostic

- Adolescents and menopausal females.
- Demographic patterns cannot replace tissue diagnosis.
- In a compatible lesion, consider the disease beyond a strict age group.

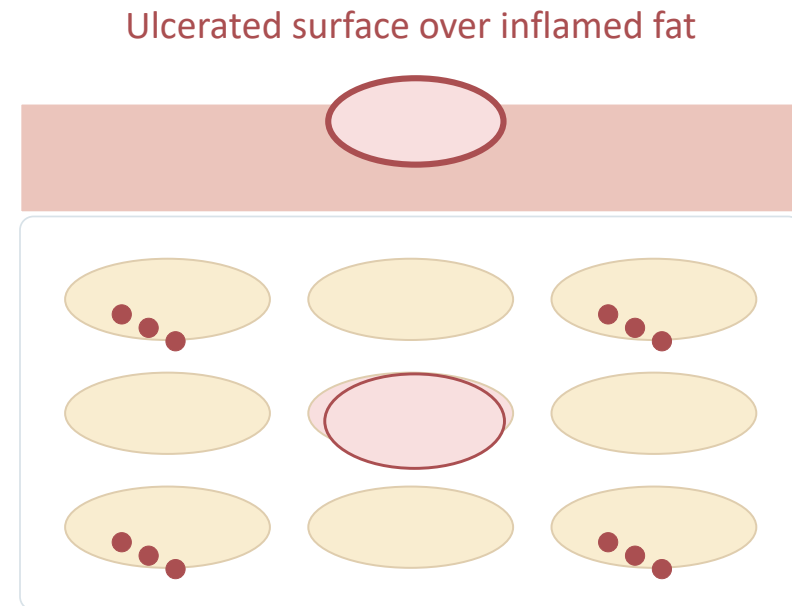
The clinical nodule is less exquisitely tender

- Erythema induratum presents as an erythematous nodule.
- It is typically described as slightly tender, compared with intense tenderness in erythema nodosum.
- Depth and ulceration are more discriminating than redness alone.

Ulceration strongly shifts the differential

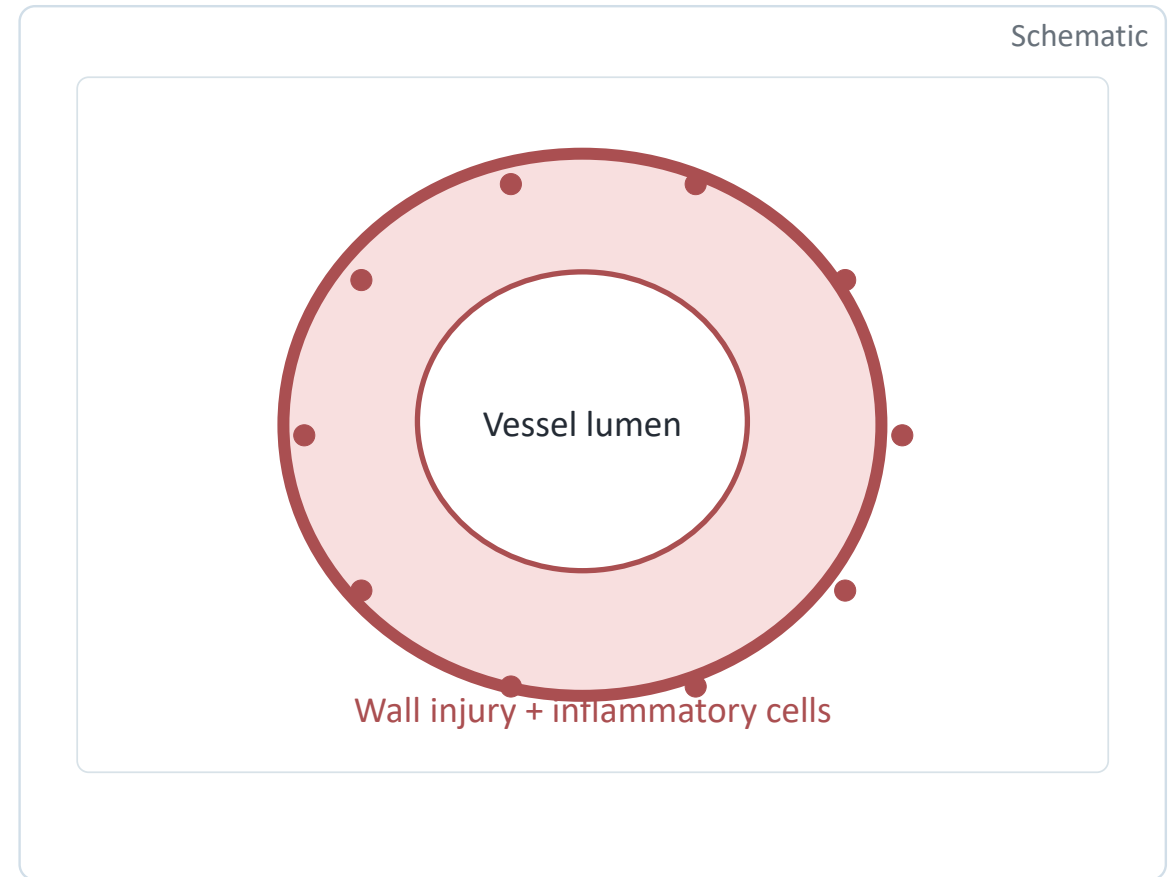
- Erythema-induratum nodules usually ulcerate.
- Erythema nodosum typically fades without a residual scar.
- An ulcerating deep nodule warrants assessment for vascular injury or another destructive process.

Schematic



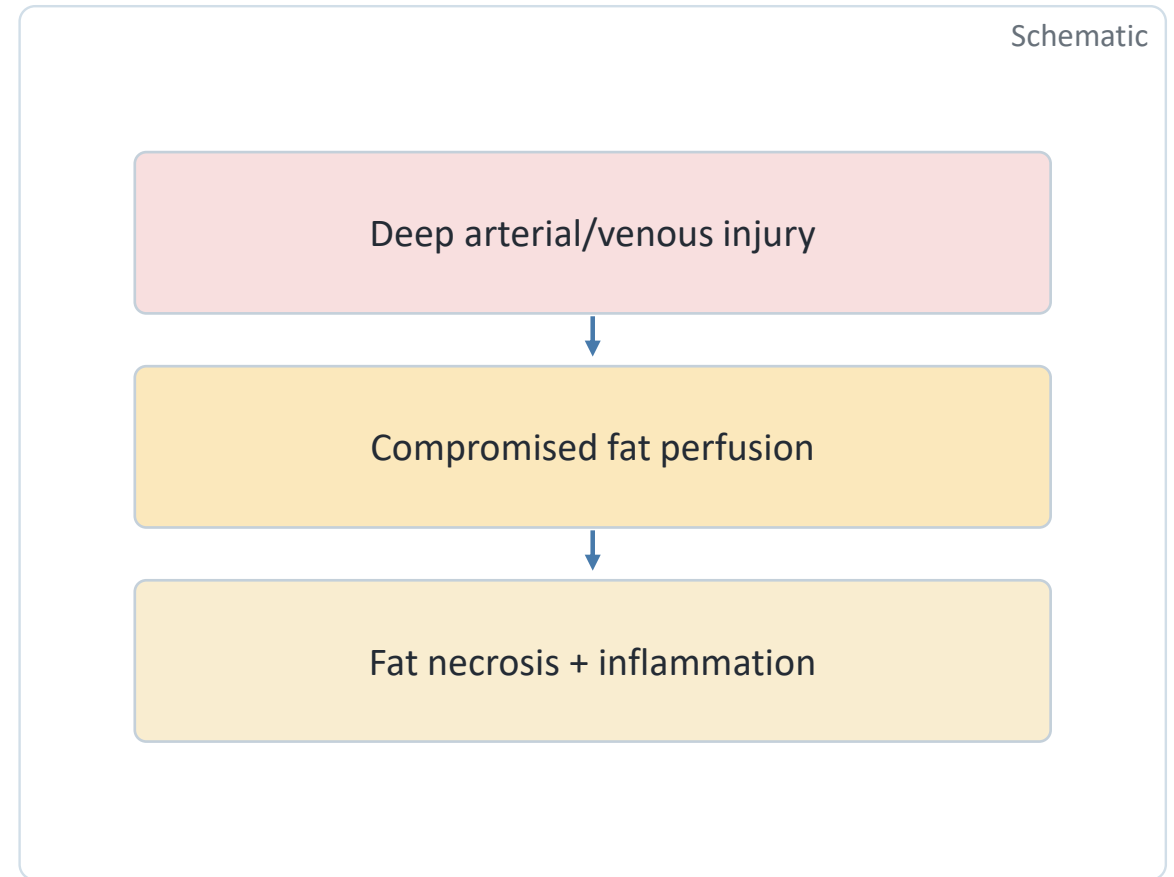
The proposed initiating event is deep-vessel vasculitis

- Erythema induratum as primarily vascular in origin.
- Deep vessels supplying the subcutaneous fat lobules are involved.
- The early vascular lesion helps explain subsequent parenchymal injury.



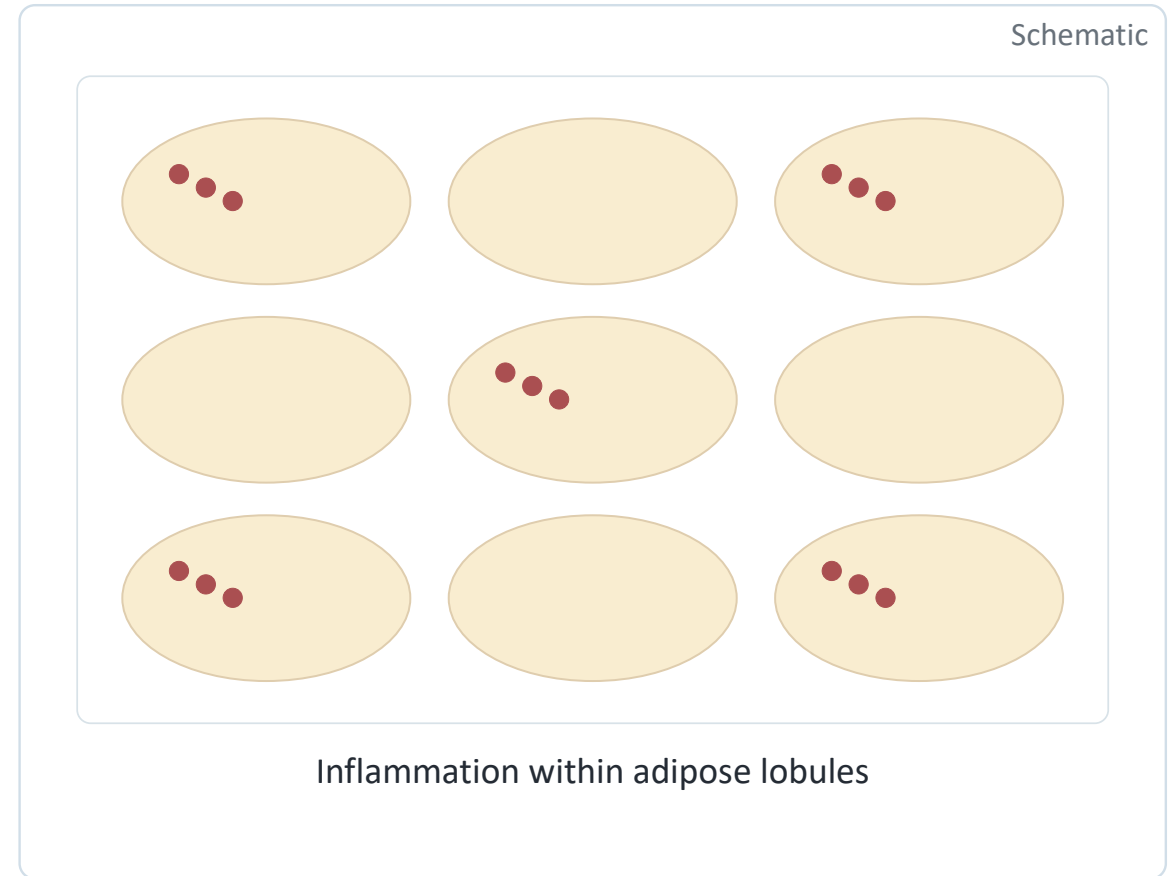
Vascular injury compromises lobular perfusion

- Damage to deep vessels can reduce blood supply to the surrounding fat.
- Fat necrosis and an inflammatory response follow vascular compromise.
- This pathogenesis is a textbook interpretation, not a universally proved initiating sequence.



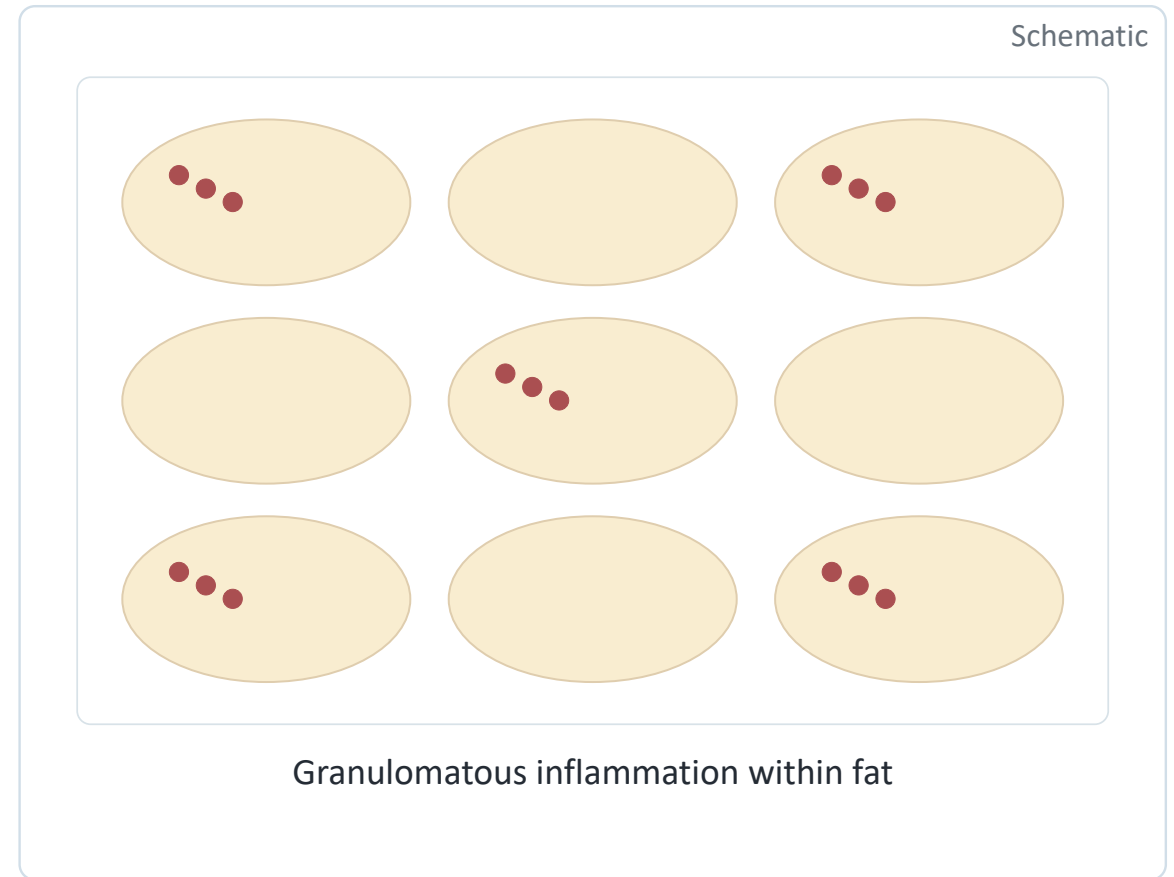
Fat-lobule injury produces the lobular pattern

- Erythema induratum is centered on the adipose lobules.
- The accompanying inflammatory reaction differs from primarily septal erythema nodosum.
- Map the affected fat compartment before evaluating individual cell types.



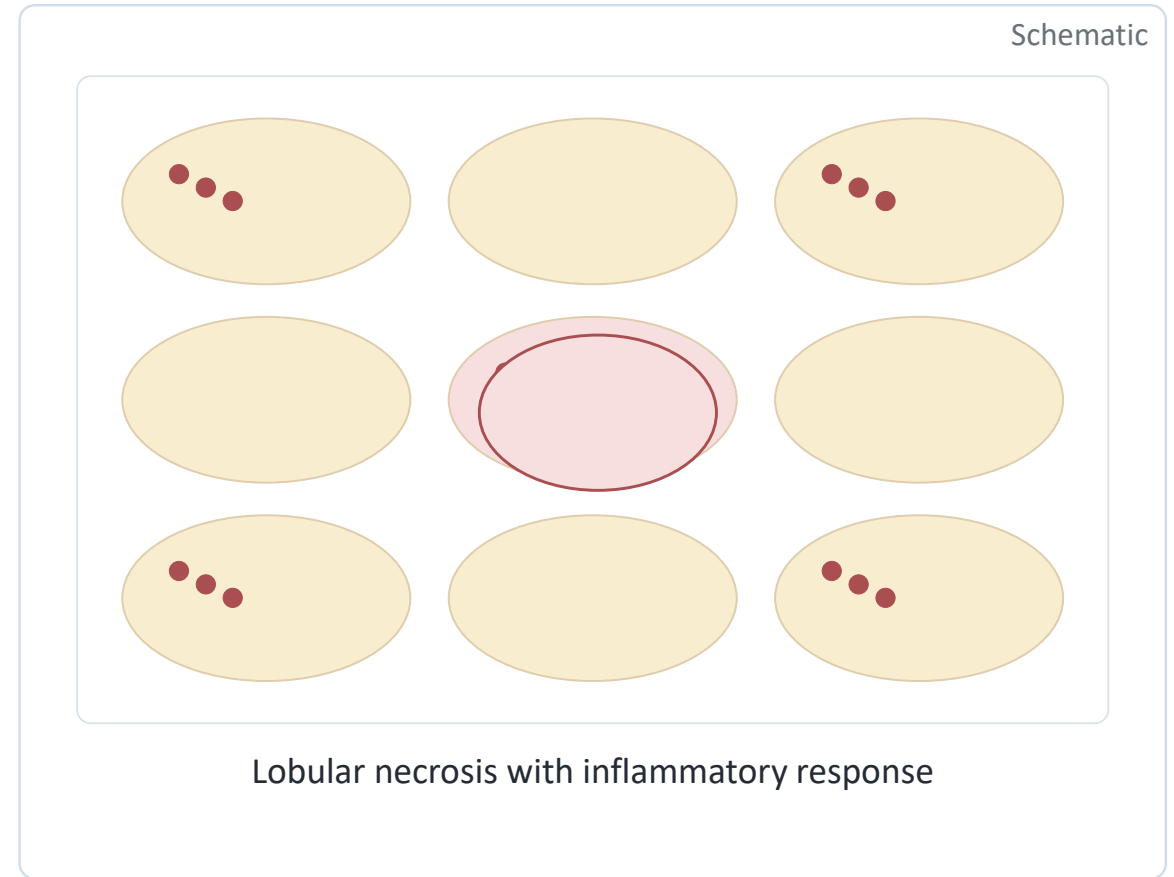
Granulomatous inflammation is characteristic

- Granulomatous reaction involves the fat lobules.
- The histologic pattern reflects a macrophage-rich inflammatory response.
- The pattern is not by itself a specific microbiologic diagnosis.



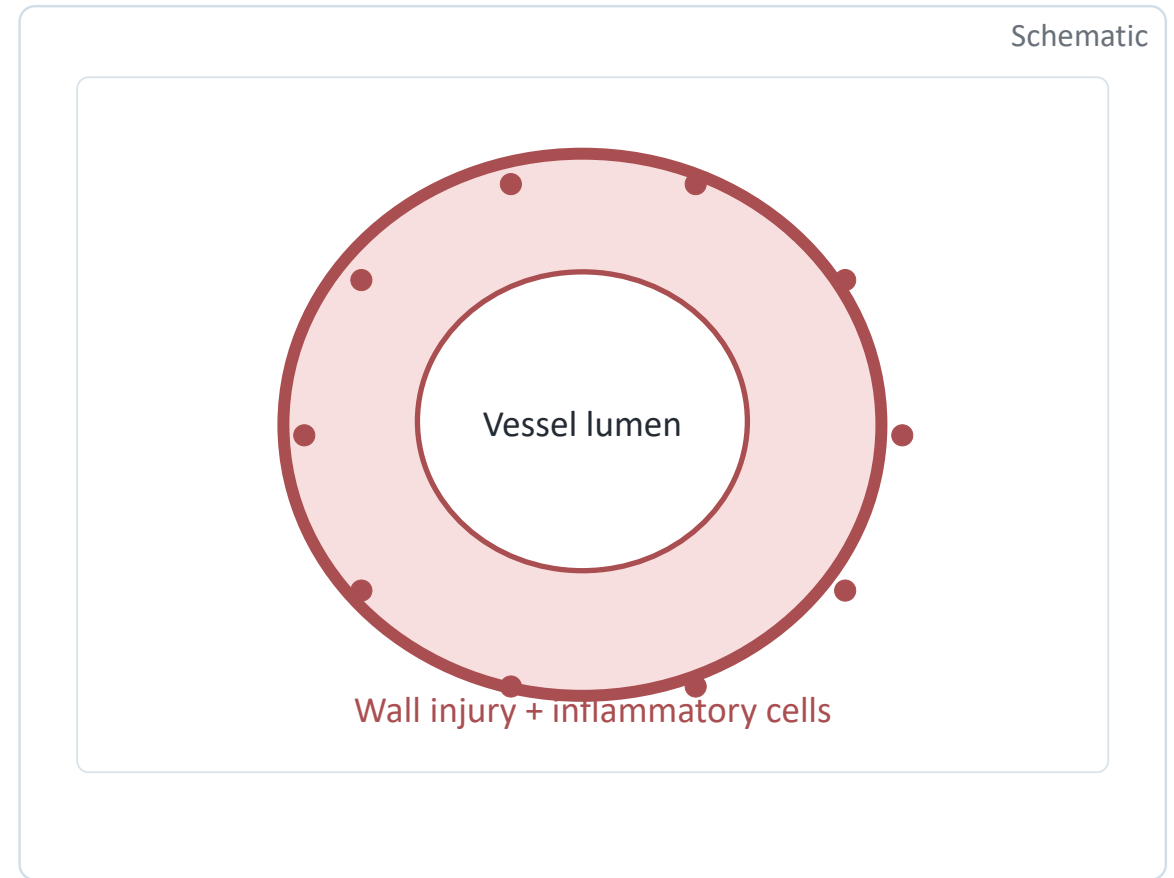
Caseous necrosis is described within fat lobules

- Zones of caseous necrosis in erythema induratum.
- This finding must be interpreted alongside granulomas and vascular injury.
- Caseation alone cannot establish active tuberculosis in a skin biopsy.



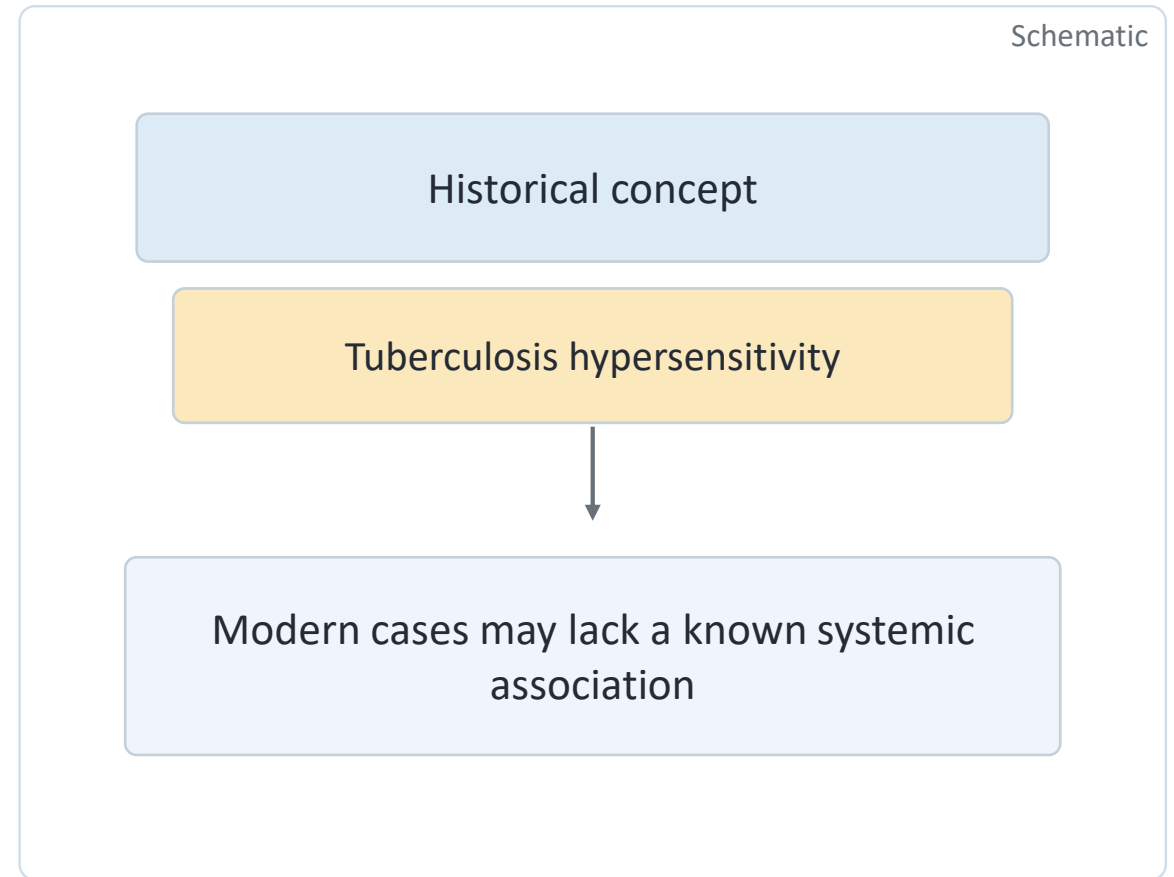
Early vessel changes affect arteries and veins

- Small- to medium-sized arteries and veins may show necrotizing vasculitis.
- Affected vessels lie in the deep dermis and subcutis.
- Both the caliber and anatomical level of involved vessels matter.



Tuberculosis: Historical association, variable today

- Erythema induratum was originally considered a hypersensitivity response to tuberculosis.
- Cases now commonly lack identifiable underlying disease.
- Clinical evidence is needed to determine whether tuberculosis is implicated.



Nodular vasculitis and erythema induratum: Terminology

Term	Common contemporary usage	Diagnostic caution
Erythema induratum of Bazin	Tuberculosis-associated nodular vasculitis	Requires clinical association
Nodular vasculitis	Similar deep vasculitic panniculitis without proven TB	Not defined by biopsy alone
Erythema induratum (Robbins)	Broader clinical-pathologic entity	Historical usage overlaps

Tuberculosis assessment is contextual

- Clinical history, local epidemiology, exposure, and systemic findings guide assessment.
- TB testing or chest investigations may be appropriate in a compatible setting.
- Negative organism stains in skin do not alone establish or refute a TB-associated process.

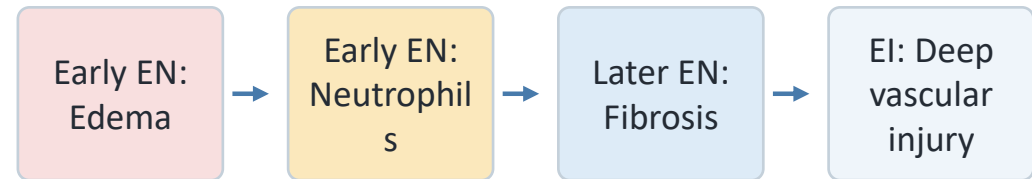
The diagnostic contrast begins at low power

Low-power clue	Erythema nodosum	Erythema induratum
Primary compartment	Septa	Lobules
Architecture	Widened septa; later fibrosis	Lobular inflammation and fat necrosis
Vascular involvement	Classically no destructive vasculitis	Early deep necrotizing vasculitis
Granulomatous element	May have giant cells / radial nodules	Granulomatous lobular reaction

Early and late biopsies tell different stories

- Early erythema nodosum: Edema, fibrin, neutrophils in septa.
- Later erythema nodosum: Mononuclear infiltrate and septal fibrosis.
- Early erythema induratum: Necrotizing deep-vessel inflammation; Lobular necrosis and granulomas are also key features.

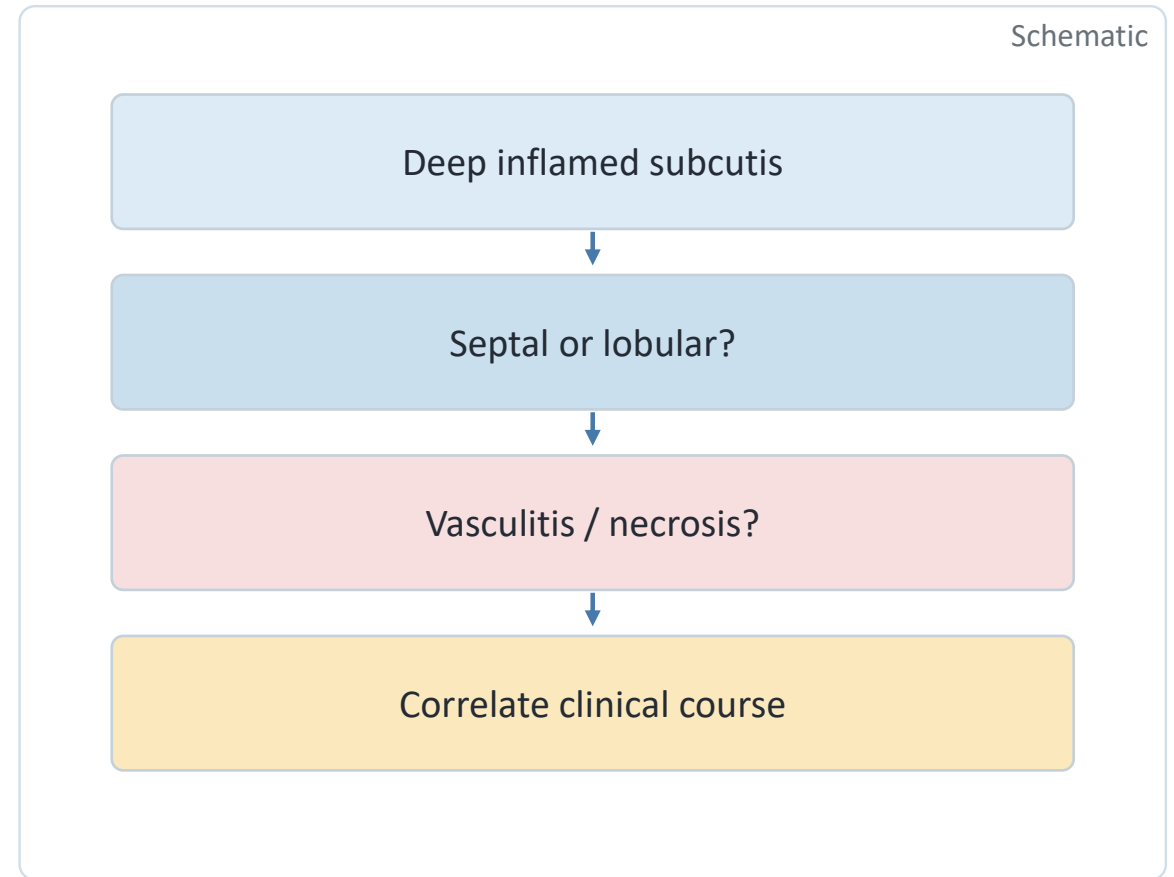
Schematic



Compare lesion age and vascular pattern

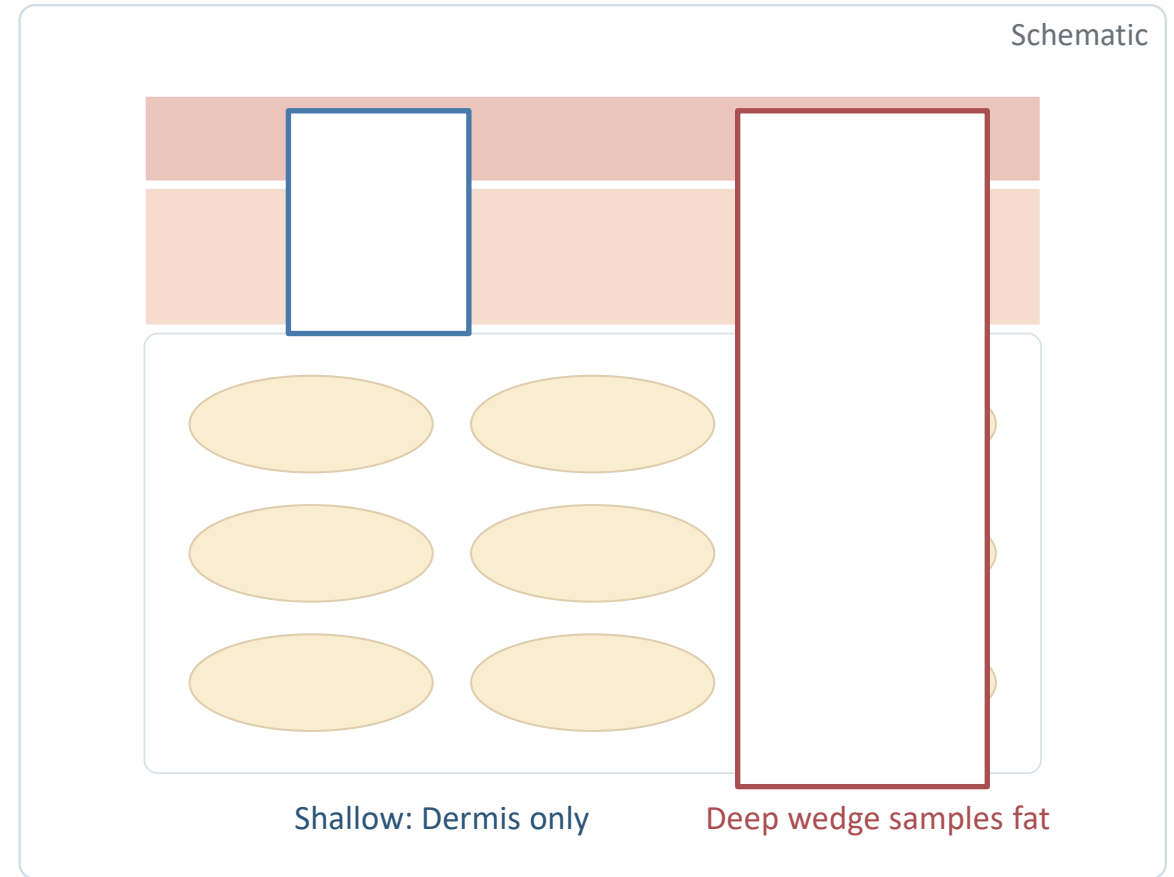
A practical classification pathway

- First: Confirm a subcutaneous inflammatory lesion.
- Second: Distinguish septal from lobular predominance.
- Third: Evaluate deep vessels, necrosis, and granulomatous reaction.
- Finally: Integrate site, ulceration, timing, and clinical associations.



When the biopsy is too shallow, diagnosis suffers

- Little or no subcutis prevents confident compartment assignment.
- Deep vasculitis may lie below the sampled dermis.
- A nondiagnostic superficial sample is not equivalent to a negative panniculitis evaluation.



Other panniculitides are meaningful differentials

Mimic from adjacent section	Why it matters
Factitial panniculitis	Trauma/injection can cause secondary inflammation
Lupus-associated panniculitis	Systemic autoimmunity may involve subcutis
Subcutaneous T-cell lymphoma	Neoplastic cells can mimic fat inflammation
Weber–Christian disease	Separate lobular, nonvasculitic pattern

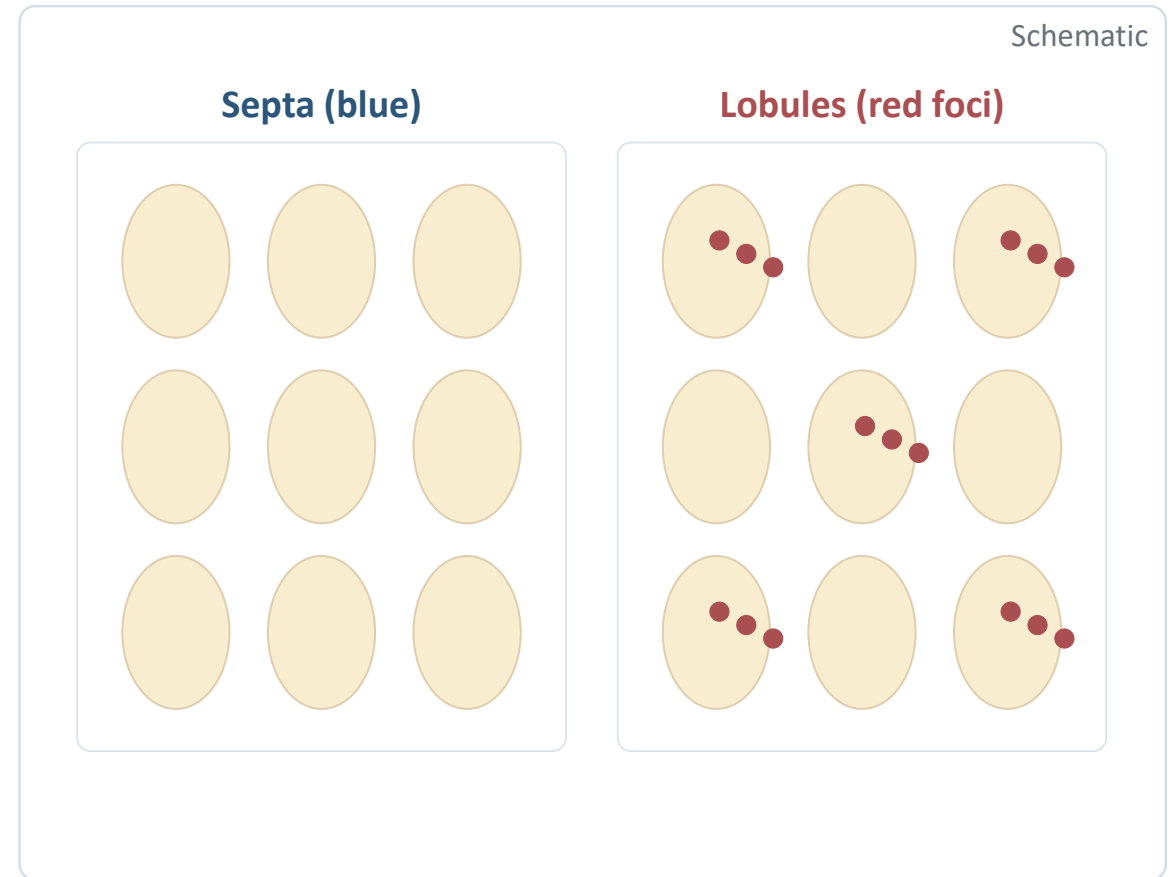
Case 1: Acute, exquisitely tender lower-leg nodules

ILLUSTRATIVE CASE

- A patient develops multiple painful erythematous nodules on the shins.
- Over subsequent weeks, earlier nodules flatten and become bruise-like.
- What compartment and vascular pattern would best fit?

Case 1: Expected histologic pattern

- Septal widening with edema and early neutrophilic inflammation.
- Evolving lesions may show lymphocytes, macrophages and septal fibrosis.
- Classic pattern: No necrotizing vasculitis.



Most likely pattern: Erythema nodosum.

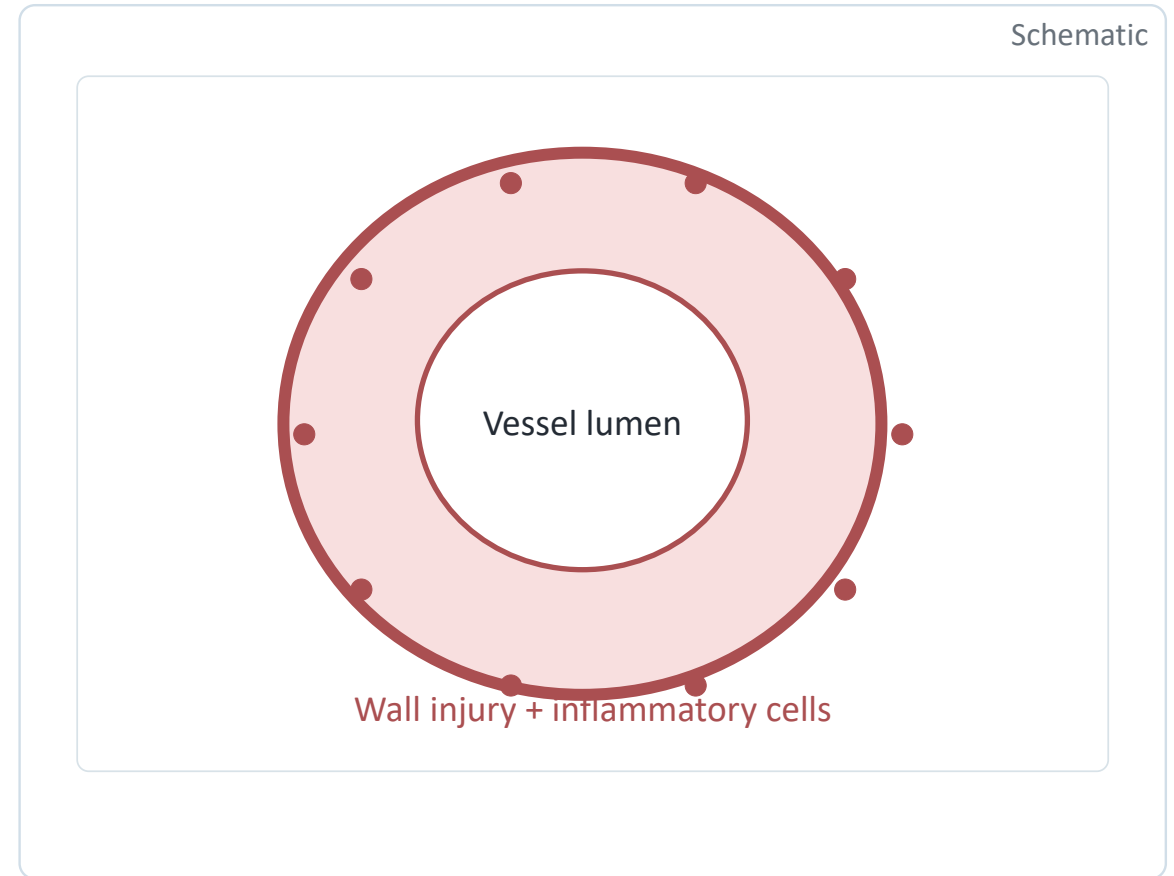
Case 2: A deep nodule progresses to ulceration

ILLUSTRATIVE CASE

- A slightly tender lower-leg nodule becomes ulcerated.
- Deep biopsy shows fat-lobule inflammation and necrosis.
- What additional histologic feature is especially discriminating?

Case 2: Inspect the deep arterial and venous walls

- Necrotizing vasculitis in small- and medium-sized deep vessels supports the pattern.
- Lobular granulomatous inflammation and caseous necrosis may coexist.
- Then assess whether an underlying TB association can be established clinically.



Most likely pattern: Erythema induratum / nodular vasculitis.

Case 3: A source-identification pitfall

ILLUSTRATIVE CASE

- A biopsy shows classic erythema-nodosum morphology.
- The patient reports no recent drug exposure or infectious symptoms.
- The histology supports a reaction pattern, not a specific trigger.
- An unidentified cause remains compatible with the Robbins account.

Report the morphology before speculating on etiology

- State dominant compartment: Septal, lobular, or mixed.
- Describe inflammation, fat necrosis, granulomatous change, and vessel injury.
- Note sample depth and lesion-age limitations if relevant.
- Reserve etiologic claims for an integrated clinical assessment.

Schematic

Anatomic compartment

Cellular pattern + necrosis

Vessel-wall injury

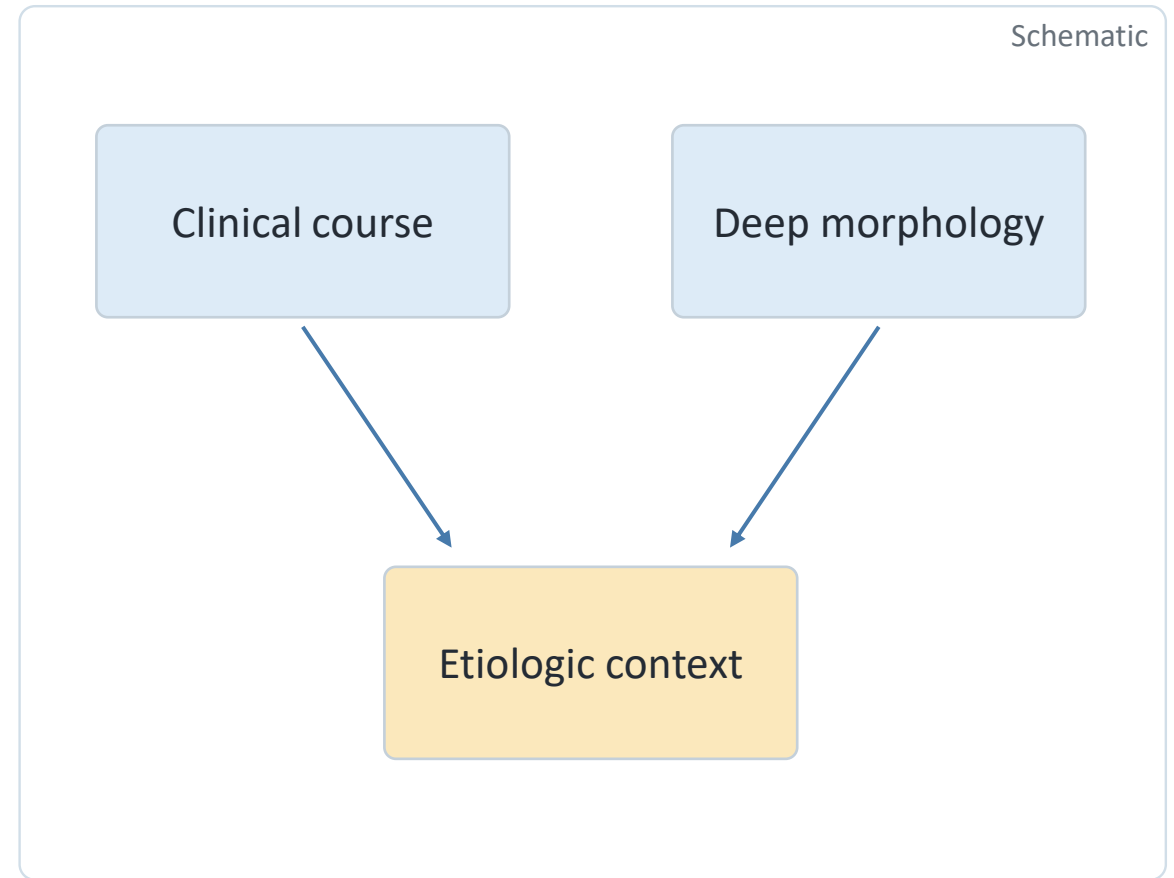
Adequacy + clinicopathologic correlation

Integrated comparison: Clinical and microscopic

Question	Erythema nodosum	Erythema induratum
Pain	Often exquisitely tender	Often slightly tender
Surface evolution	Bruise-like fading	Frequently ulcerates
Primary inflammation	Septa	Fat lobules
Deep vessels	No classic vasculitis	Necrotizing vasculitis
Late / associated change	Septal fibrosis	Granulomas; caseous necrosis

Three practical decisions

- Recognize the clinical pattern and lesion evolution.
- Sample deep enough to include representative septa, lobules, and vessels.
- Integrate the biopsy reaction pattern with possible systemic associations.



Selected sources and further reading

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