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<th>Disease</th>
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<td><strong>Sarcoidosis</strong></td>
<td>Bimodal: ages 25-35 and 45-65; more often in African-Americans, esp. women; children may develop before age 4 or at ages 8-14</td>
<td>Th1 CD4+ pattern upregulated following antigen stimulation; unknown antigen (perhaps infection due to seasonality); HLA-DRB1,-DQB1 good prognosis</td>
<td>25% with skin involvement; red-brown papules/plaques on head, neck, upper trunk/arms; hypopigmentation, nodules, alopecia; erythema nodosum A/W good prognosis; may koebnerize with trauma</td>
<td>Superficial and deep collections of epithelioid histocytes with sparse lymphocytic infiltrate; Langhans giant cells possibly containing asteroid Schaumann bodies</td>
<td>Coriolisercoids (topical, IL systemic) Antimalarials Tetracyclines PVA Methotrexate MIF-alpha inhibitors</td>
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<td><strong>Granuloma annulare</strong></td>
<td>2:1 female to male affected; 2/3 younger than 30 years old; no racial predilection; Classic: children, young adults; Generalized: middle-aged females; SubQ: children (boys &gt; girls) &lt; 8 years old</td>
<td>Unknown: possibly incited by infection, trauma, UV light; Th1-type inflammation; can exhibit Koebner response; possible relationship to HLA-Bw35</td>
<td>Classic: annular plaque on dorsal hands/feet, arms, legs and trunk; Generalized: 10-100s small coalescing papules on trunk/symmetric extremities; A/W lipid abnormalities; Perforating: papules with umbilication; SubQ: deep nodules common on dorsal foot</td>
<td>Two patterns: 1. Palsied histocytes + lymphocytes around central altered collagen in superficial and deep dermis; mucin present 2. Interstitial: histocytes, monocytes + mucin amongst altered collagen</td>
<td>Observation Topical/IL steroids Topical calcineurin inhibitors Cryosurgery PVA/PUVA IL-10/γ-gamma For systemic: Antimalarials Isotretinoin Triplet antibiotics with rifampin, ofloxacin, minocycline</td>
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<td><strong>Necrobiotic lipoidica</strong></td>
<td>&gt;50% of patients have diabetes/glucose intolerance; 3:1 female to male ratio</td>
<td>Unknown: possibly vascular disease resulting from immunoreactors or microangiopathic change seen in glucose intolerance</td>
<td>Red-brown papules that coalesce and become yellowish, atrophic plaques with elevated border usually in pretibial region; rarely A/W squamous cell carcinoma, ulceration</td>
<td>Square punch with palisaded alternating tiers of epithelioid histocytes and degenerated collagen: superficial and deep perivascular mixed infiltrate with plasma cells; mucin rare</td>
<td>First-line: Topical/IL/oral steroids Second-line: Pentoxifylline ASA + dipyridamole Antimalarials PVA/PUVA/1 Thalidomide Surgery for severe lesions</td>
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<td><strong>Annular elastolytic giant cell granuloma</strong> (Miescher's granuloma, actinic granuloma of O'Brien)</td>
<td>Uncommon: middle-aged women (&gt;40); however, children can also be affected</td>
<td>Unknown: may be variant of GA, possible cell-mediated response to antigen on actinically-damaged elastic fibers</td>
<td>Sun-exposed sites (head, neck, upper extremities): annular plaques with atrophic center and raised, erythematous border; multiple small papules usually &lt; 10mm and fewer than 10 lesions that coalesce on sun-exposed skin</td>
<td>Upper-mid dermis with histocytes, giant cells, lymphocytes with occasional palisading and no altered collagen; giant cells engulf elastin (elastophagocytosis) and stain positive with elasin stains; lack of elastin within granulomatous regions characteristic; no mucin</td>
<td>Difficult to treat: responds poorly to Topical/IL steroids PVA Antimalarials Retinoids Arcedololot reports: Cyclosporine Chloroquine</td>
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<td><strong>Cutaneous Crohn's disease</strong> (metastatic Crohn's forms non-casing granulomas while other cutaneous findings do not necessarily)</td>
<td>20-45% of patients with Crohn's will develop cutaneous disease; 2/3 are female</td>
<td>Th-1, Th-17 cytokines elevated; thought to be immunologic response to enteric bacteria</td>
<td>Genital lesions include labial/scrotal swelling, perianal lesions (fistulas, ulcers); non-gonital lesions include oral/leg ulcers, non-describe erythematous papules/nodules in other locations</td>
<td>Epithelioid granulomas with surrounding lymphocytes, non-casing, superficial and deep dermis involved</td>
<td>Difficult to treat: no effect RA treatment usually has no effect</td>
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<td><strong>Foreign body reaction</strong></td>
<td>Non-biologic foreign bodies include: tattoo, paraffin, silicone, silica, aluminum, beryllium, talc</td>
<td>First have infiltrate of neutrophils followed by macrophages that engulf foreign material; then may form multinucleated giant cells</td>
<td>Acute erythema/inflammation initially followed by chronic inflammation manifested most commonly as red-brown papules, nodules or plaques at site of injury</td>
<td>Several patterns possible: lichenoid, pseudolymphomatous and granulomatous; in latter, may have predominance of either epithelioid histocytes or Langhans-type giant cells which may contain incising particles in cytoplasm</td>
<td>Depends on inciting agent: Tattoo reaction: IL/topical steroids, surgical excision, lasers Other non-biologic agents: excision Fillers reaction: hyaluroni-dase/IL steroids</td>
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<td><strong>Necrobiotic xanthogranuloma</strong></td>
<td>Rare condition affecting men and women equally; average age is sixth decade</td>
<td>Strongly associated with monoclonal gammopathy (lgGκ) and lymphoproliferative disorders (usually not aggressive): may elicit giant cell granulomatous response</td>
<td>Cutaneous findings include: yellow periorbital papules and plaques; trunk may form red-yellow annular plaques with atrophic center</td>
<td>In mid-dermis or subcutis, palisading granulomas composed of histiocytes, foam cells, giant cells surrounding zone of altered collagen; cholesterol clefts present</td>
<td>Treatment of underlying paraproteinemia: Chlorambucil, melphalan or cyclophosphamide Systemic corticosteroids Radiation CO2 laser Plasmapheresis</td>
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<td><strong>Rheumatoid nodule</strong></td>
<td>20% of rheumatoid arthritis patients affected; associated with moderate to high titer RF</td>
<td>Interplay of genetic and environmental factors; link to HLA-DR4; aggregates of immune complexes consisting of RF may contribute</td>
<td>Skin colored, nontender nodules millimeters to centimeters in size over extensor joints, commonly elbows and dorsal hands; rapid appearance of multiple nodules A/W metachromatizedTNF inhibitors</td>
<td>In deep dermis/subcutis are palpated histiocytes around fibrin; no mucin is present</td>
<td>Excision (often recur) Antimalarials can reduce size RA treatment usually has no effect</td>
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### Granulomas (cont.)

**Disease** | **Epidemiology** | **Pathogenesis** | **Clinical features** | **Histopathology** | **Treatment**
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**Primary inoculation tuberculosis**<br>(cutaneous primary complex) | Worldwide distribution, but commonly seen in developing and impoverished populations, less than 10% of infection leads to clinical disease | M. tuberculosis infection and interaction with T lymphocytes/mycobacterial antigens \(\rightarrow\) increased MHC II antigens and IL-2 \(\rightarrow\) macrophages accumulate and granulomas are formed. (patient with no immunity to bacteria) | Inoculation into skin/mucosa \(\rightarrow\) painless, firm, red/brown papule develops 2-4 weeks after inoculation \(\rightarrow\) erosions to sharply demarcated ulcer \(\rightarrow\) spontaneous healing in 3-12 months with residual atrophic scar | Initial lesions may have a suppurative mixed dermal infiltrate (neutrophils, lymphocytes, plasma cells) and subsequently become granulomatous with necrosis, ulceration and caseation (weeks); AFB may be isolated | First line: Rifampin + isoniazid + pyrazinamide + ethambutol, Streptomycin
Second line: Thiacetazone Streptomycin Amikacin Quinolones

**Tuberculosis** | Similar geographic distribution as primary inoculation tuberculosis | Immune reaction in skin due to hematogenous dissemination of M. tuberculosis antigens from an internal focus; (patient with high cell-mediated immunity to bacteria) | 1. *Erythema induratum*: subcutaneous, erythematous nodules on bilateral calves \(\rightarrow\) involvement creating ulcers that heal with scarring
2. Lichen scrofulosorum: peri-follicular, clustered nodules, yellow-brown, firm papules with scale; spontaneous resolution without scar
3. Papulonecrotic tuberculid: symmetric, widely scattered, dusky red papules and papulopustules +/- central necrosis; extensor surfaces and buttocks; spontaneous resolution with scar | 1. *Erythema induratum*: tubular panniculitis, may see extension of tuberculid granulomas into deeper dermis
2. Lichen scrofulosorum: non-casing tuberculosis granulomas present in the upper dermis around hair follicles and sweat ducts
3. Papulonecrotic tuberculid: pitting histiocytes surrounding ulceration and areas of necrosis, leukocytoclastic vasculitis | First line: Rifampin + isoniazid + pyrazinamide + ethambutol, Streptomycin
Second line: Thiacetazone Streptomycin Amikacin Quinolones

**Legrosy**<br>(tuberculosis legrosy - TT bordeline tuberculosis- BT bordeline- BB bordeline)

**Granulomas**

**Late syphilis**<br>(tertiary syphilis) | Prevalent in tropical environments, including India, Asia, Central Africa, Central and South America | Incubation period from months to years; bacilli affects peripheral nervous system, lymph nodes, membranes, bones and viscera | Clinical presentation highly dependent on immunologic status of infected patient | Paucibacillary (>5 lesions): single dose rifampin, ofloxacin and minocycline
Paucibacillary (<5 lesions): rifampin monthly and dapson daily over 6-9 months
Multibacillary (>5 lesions): rifampin monthly, clofazimine monthly, dapson daily over 12-18 months | Penicillin G is the treatment of choice for all stages of syphilis

**Cutaneous leishmaniasis**

**Old World**: MIDDLE EAST: Eastern Mediterranean, North Africa, Asia; most common in mervall races<br>**New World**: Central and South America; Texas; most common in mervall races | Small number of organisms and high cellular immune reactivity to treponema \(\rightarrow\) infection of skin, CNS, CVS | Clinical presentation highly dependent on immunologic status of infected patient | Dermal infiltrate of lymphocytes, plasma cells and histiocytes \(\rightarrow\) satellite lymphoid follicles \(\rightarrow\) ulceration and caseation (weeks); AFB may be isolated | Rifampin + isoniazid + pyrazinamide + ethambutol, Streptomycin
Second line: Thiacetazone Streptomycin Amikacin Quinolones

**Rosalcea** | Far-skinned individuals, reported in both adults and children; also in association with HIV | Unknown: granuloma formation may be in response to Demodex | Persistent erythema and telangiectasia of bilateral cheeks, less often chin, nose, forehead; +/- papules, pustules, rhinophyma | Infiltrate of lymphocytes, histiocytes, plasma cells and giant cells arranged into tuberculoid granulomas; granulomas may be centered around ruptured hair follicles; necrosis not only in 11% of cases | Topical: metronidazole, azelaic acid, tretinoin
Oral: tetracyclines, TSM/SMX, isotretonin

**Poriforral dermatititis**

Young females; also reported in children | Unknown: may be variant of rosacea | Erythematous papules, pustules and occasionally vesicles arranged symmetrically around mouth, chin and nasolabial folds; characteristic sparing of immediate perioral area | Stark parakeratosis surrounding follicular ostia, spongiosis and acanthosis characterizes the epidermis, associated perivascular lymphohistiocytic infiltrate; occasional tuberculoid granuloma noted in several cases | Topical: metronidazole, azelaic acid, tretinoin
Oral: tetracyclines, TSM/SMX, isotretonin

**Lupus miliaris disseminatus faciei**

Males and females equally affected | Unknown: may be related to rosacea | Discrete red to yellow/brown papules localized over central face and periorbital region; lesions may last for months, then heal with scarring | Demarcated area of dermal caseation necrosis surrounded by multinucleated giant cells and lymphocytes; more often than not associated with ruptured pilosebaceous units, granulomas indicative of established lesions | Topical: metronidazole, azelaic acid, tretinoin
Oral: tetracyclines, TSM/SMX, isotretonin

### References


www.aad.org/DIR Directions, where a new chart is published each quarter. The latest online Boards’ Fodder is Comprehensive Laboratory Disease Workups by Paul M. Graham, DO; Sara Wilchowski, PA-C; and David Fivenson, MD. To view, download, or print every Boards’ Fodder ever published, check out the archives at www.aad.org/boardsfodder.