



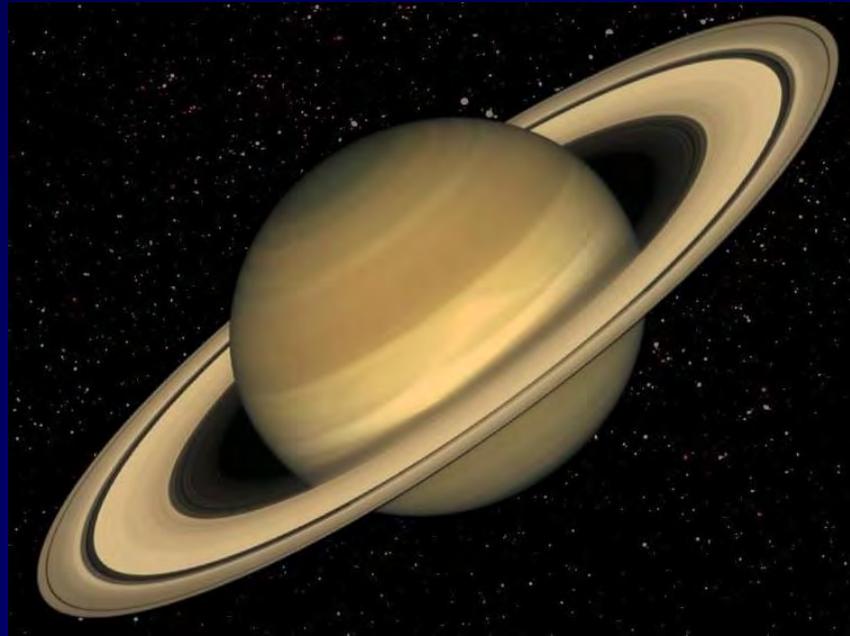
Granulomi: correlazioni clinico-istologiche

Giorgio Filosa

JESI

Definizione

Un processo infiammatorio caratterizzato principalmente dalla presenza di aggregati di istiociti viene definito come "granulomatoso" .



Definizione

Un pattern granulomatoso corrisponde ad un modello reattivo ad un agente immunogenetico che non puo' essere eliminato ed è solo degradato lentamente dal sistema immunitario

Le granulomatosi cutanee appartengono ad un gruppo di malattie che differiscono nella patogenesi e (a volte) nella presentazione clinica e nel profilo istologico.

Definizione

- La lesione elementare è rappresentata da una papula ben delimitata di colore roseo che confluisce per formare una placca di forma e grandezza diverse, diviene giallastro alla vitro pressione.
- Le forme sono localizzate e diffuse.

Cutaneous infections presenting with granulomatous infiltrates: a review of histopathological patterns

José Carlos Cardoso

Eduardo Calonje

DIAGNOSTIC HISTOPATHOLOGY
2013 by Elsevier Ltd.

The granulomatous pattern is characterized by the macrophages (histiocytes) which become epithelioid and form aggregates of multinucleated giant cells, lymphocytes, neutrophils and/or plasma cells. Necrosis may be present

A challenge to dermatopathologists due to various modes of presentation and frequent identical histological picture

The result of a complex interplay between invading organism or antigen, prolonged antigenaemia, macrophage activity, a Th1 cell response, B cell overactivity, circulating immune complexes and biological mediators.

The granuloma is an active site of numerous enzymes and cytokines

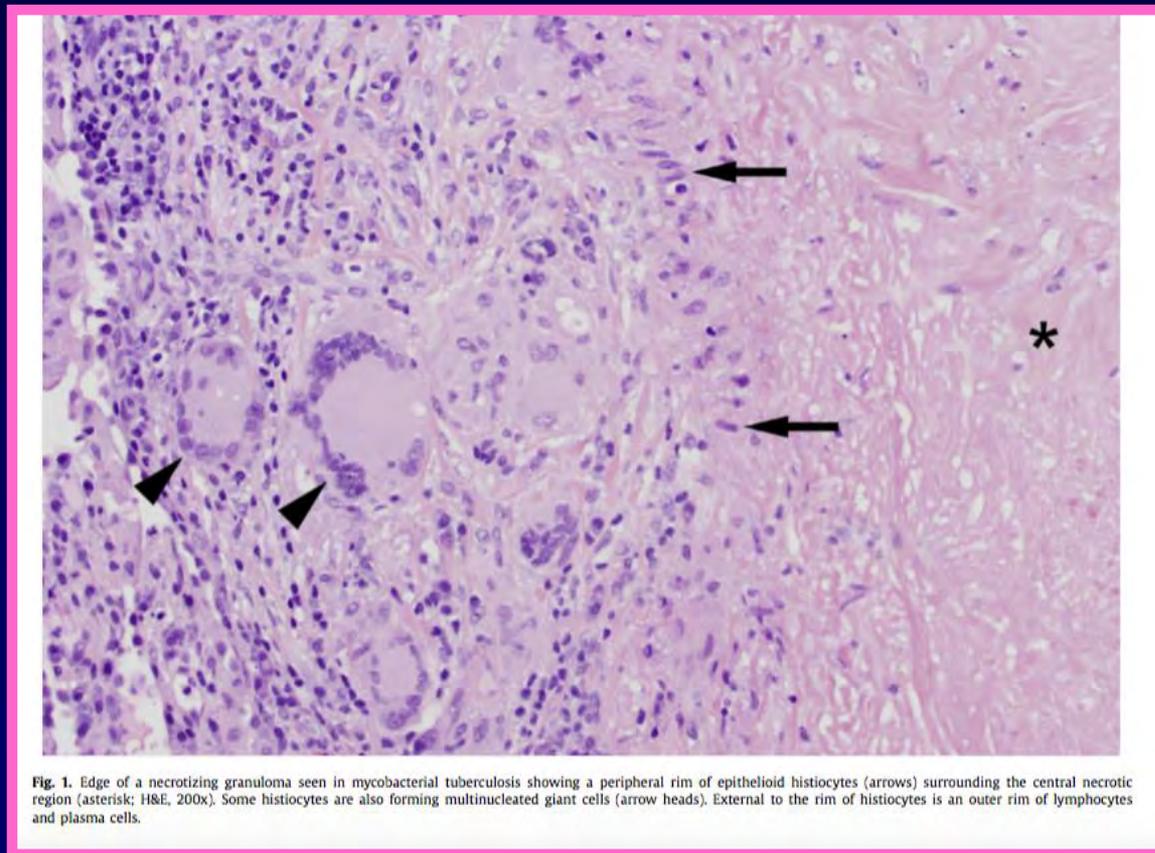


Fig. 1. Edge of a necrotizing granuloma seen in mycobacterial tuberculosis showing a peripheral rim of epithelioid histiocytes (arrows) surrounding the central necrotic region (asterisk; H&E, 200x). Some histiocytes are also forming multinucleated giant cells (arrow heads). External to the rim of histiocytes is an outer rim of lymphocytes and plasma cells.

A clinicopathological classification of granulomatous disorders

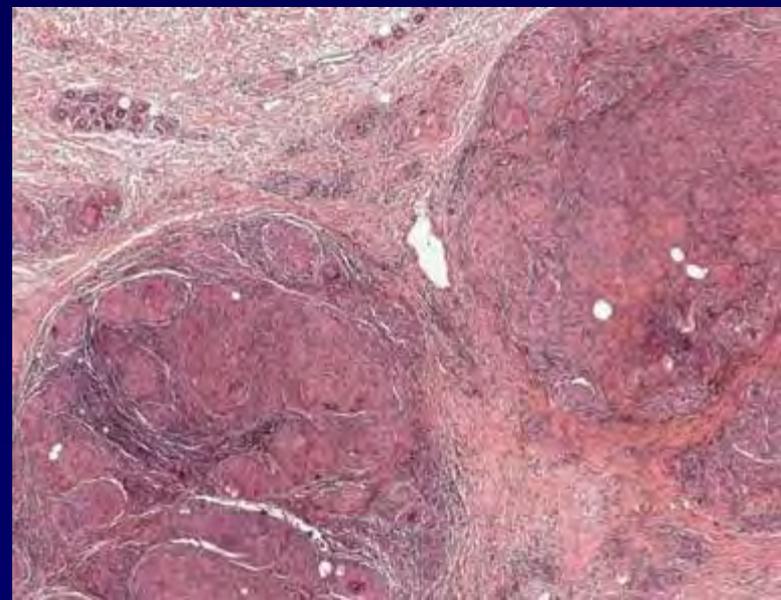
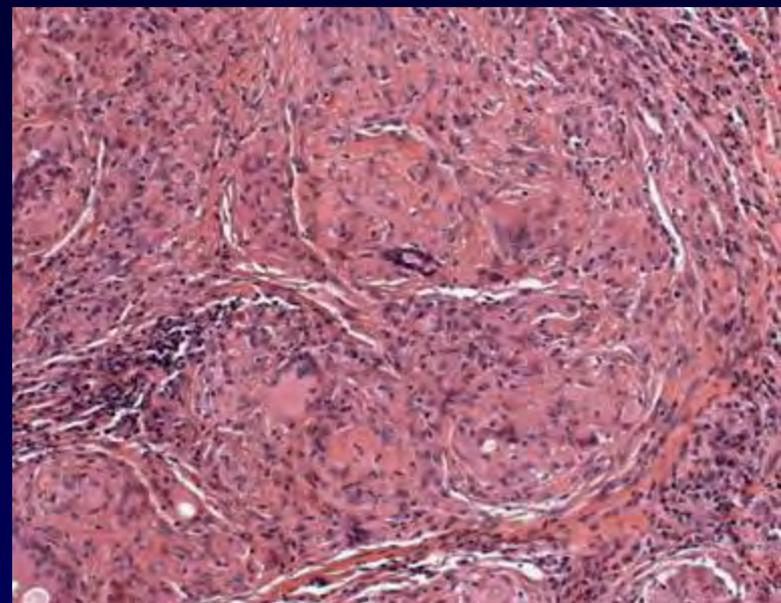
D Geraint James

Cutaneous granulomas are usually classified as infectious or non-infectious.

Table 1 Classification of granulomatous disorders

<i>(1) Infections</i>	<i>(2) Vasculitis</i>	<i>(5) Hypersensitivity Pneumonitis</i>
Fungi	Wegener's	Farmers' lung
Histoplasma	Necrotising sarcoidal	Bird fanciers'
Coccidioides	Churg-Strauss	Mushroom workers'
Blastomyces	Lymphomatoid	Suberosis (cork dust)
Sporothrix	Polyarteritis nodosa	Bagassosis
Aspergillus	Bronchocentric	Maple bark strippers'
Cryptococcus	Giant cell arteritis	Paprika splitters'
Protozoa	Systemic lupus erythematosus	Coffee bean
Toxoplasma		Spatlese lung
Leishmania	<i>(3) Immunological aberrations</i>	
Metazoa	Sarcoidosis	<i>(6) Chemicals</i>
Toxoplasma	Crohn's disease	Beryllium
Schistosoma	Primary biliary cirrhosis	Zirconium
Spirochaetes	Hepatic granulomatous disease	Silica
T pallidum	Langerhan's granulomatosis	Starch
T carateum	Orofacial granulomatosis	Talc
T pertenuis	Peyronie's disease	
Mycobacteria	Blau's syndrome	<i>(7) Neoplasia</i>
M tuberculosis	Hypogammaglobulinaemia	Carcinoma
M leprae	Histiocytosis X	Reticulosis
M kansasii	Immune complex disease	Pinealoma
M marinum		Dysgerminoma
M avian	<i>(4) Leucocyte oxidase defects</i>	Seminoma
BCG vaccine	Chronic granulomatous disease of childhood and adults	Reticulum cell sarcoma
Bacteria		Malignant nasal granuloma
Brucella		
Yersinia		<i>(8) Miscellaneous infections</i>
		Whipple's disease
		Cat scratch
		Lymphogranuloma
		Kikuchi
		Buruli ulcer

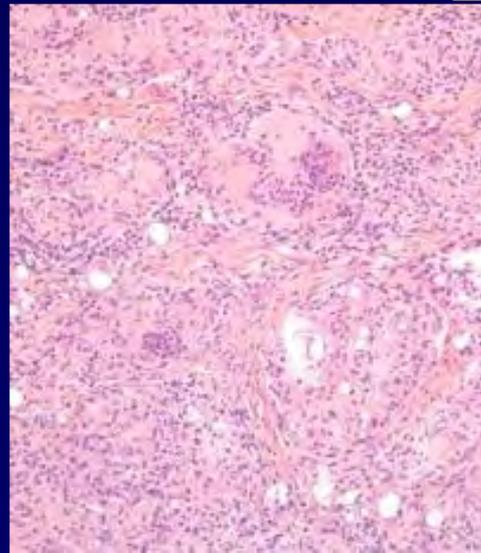
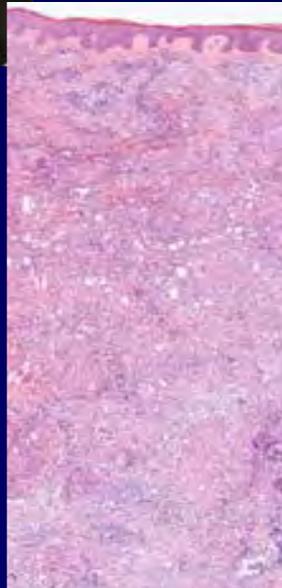
Etanercept-induced cutaneous and pulmonary sarcoid-like granulomas resolving with adalimumab



Biopsy of the mass showed sarcoidal type granulomatous inflammation with nodular aggregations of non-necrotizing epithelioid histiocytes in the subcutis

Granulomatous skin reactions after tumour vaccine in two patients

JEADV 2018, 32, e86-e121 © 2017

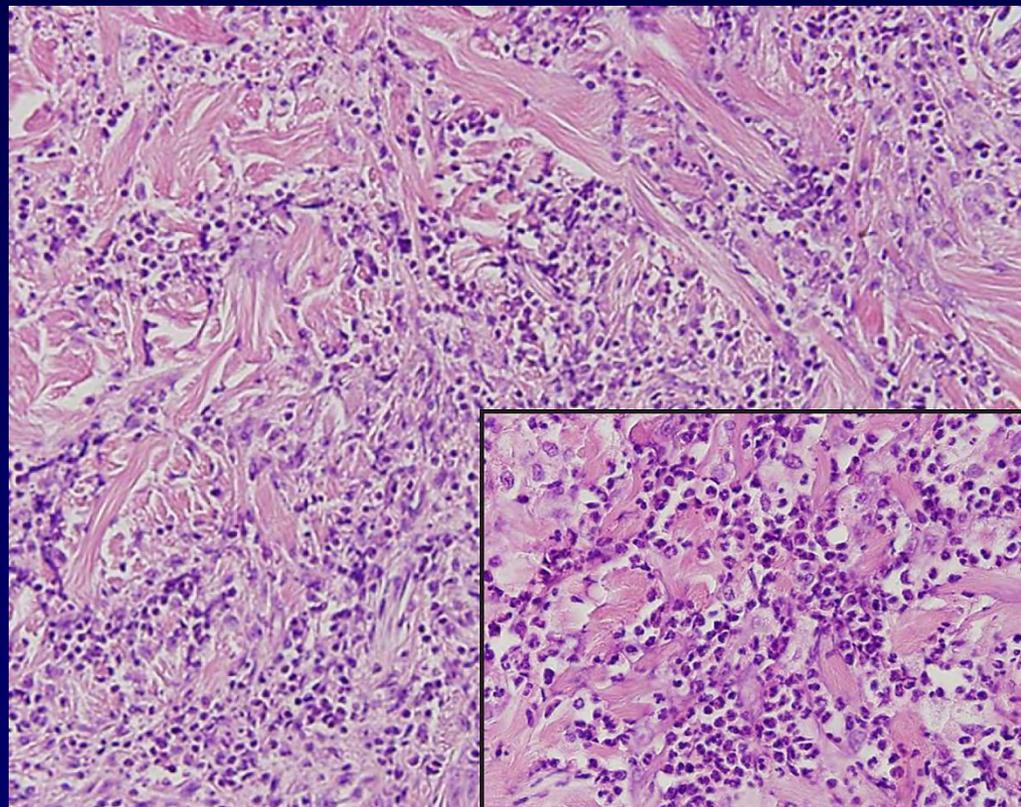




Palisaded Neutrophilic Granulomatous Dermatitis in a Patient with Systemic Sclerosis-Rheumatoid Arthritis Overlap Syndrome

Kyong-Hee Jung, Sangho Jeong, Seong-Ryul Kwon, Mie Jin Lim, Jiyeon Gwon, Jeonghyun Shin¹, Won Park

Division of Rheumatology, Department of Internal Medicine, ¹Department of Dermatology, Inha University, Incheon, Korea



Granulomatous & histiocytic dermatitides 34(2017)301–311

Mark R. Wick*

Histologic Classification of Cutaneous Granulomatous & Non-neoplastic Histiocytic Diseases

Necrobiotic/Necrotizing

- Granuloma annulare
- Necrobiosis lipoidica
- Rheumatoid nodules
- Lupus miliaris disseminatus faciei
(Variant of granulomatous rosacea)
- Infectious
 - Mycobacterial
 - Fungal
 - Parasitic
 - Luetic

Non-Necrobiotic/Necrotizing

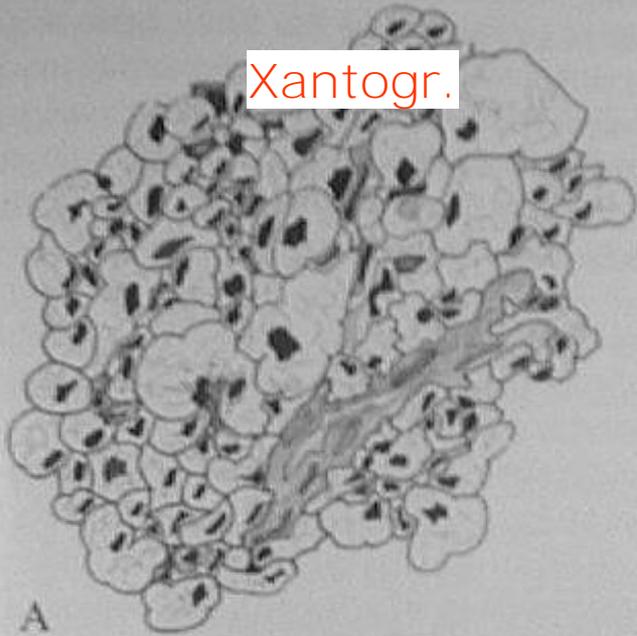
- Sarcoidosis
- Foreign body reactions
- Melkersson-Rosenthal syndrome
- Granulomatous rosacea
- Elastolytic granuloma
- Cutaneous Crohn disease
- Granulomatous pigmented purpura
- Interstitial granulomatous dermatitis
- Lichenoid & granulomatous dermatitis
- Blau syndrome
- Infections (mycobacterial, fungal, etc.)

Histiocytic but Non-Granulomatous*

- Malakoplakia
- Infectious
 - Leishmaniasis
 - Histoplasmosis
 - Lepromatous leprosy
 - Rhinoscleroma
 - Lymphogranuloma venereum
 - Granuloma inguinale

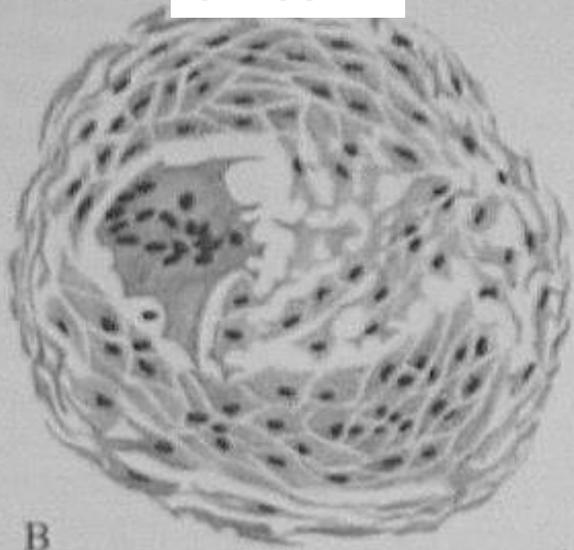
“necrobiotic” and “necrotizing”, actual the first refers to degenerative change, the second implies en masse cell death in the lesions. Necrosis often associates itself with infectious processes whereas necrobiosis does not

Xantogr.



A

SARCOID



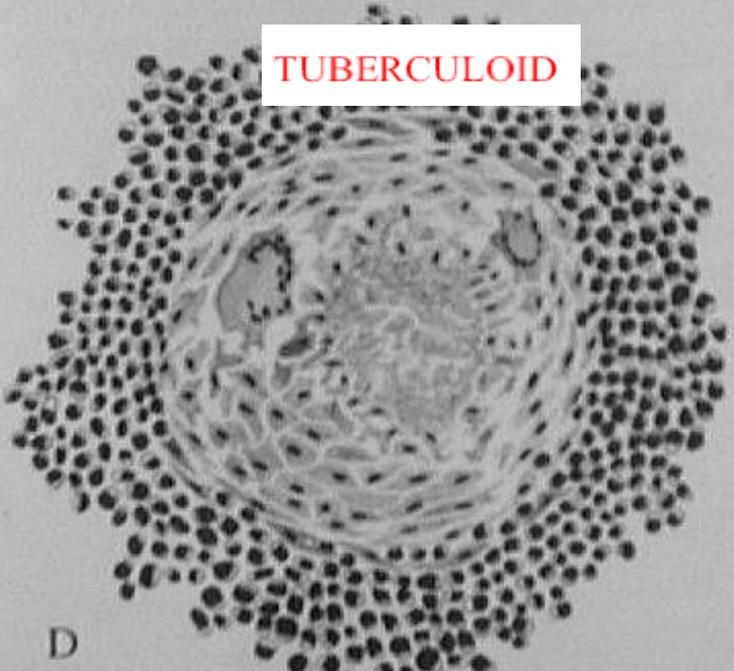
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Corpo estr



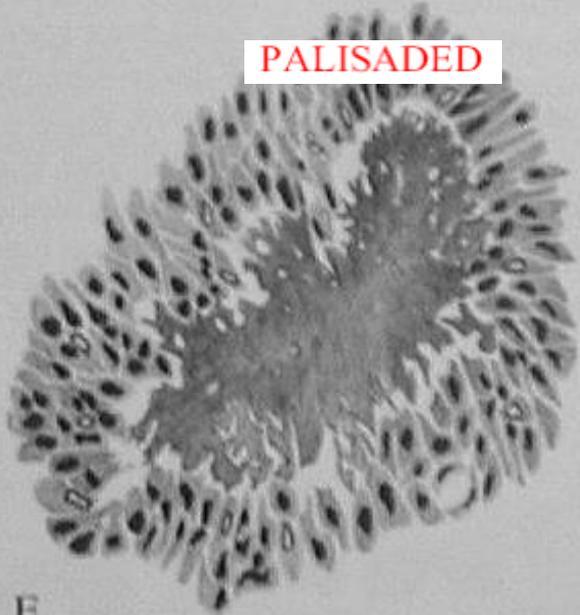
C

TUBERCULOID



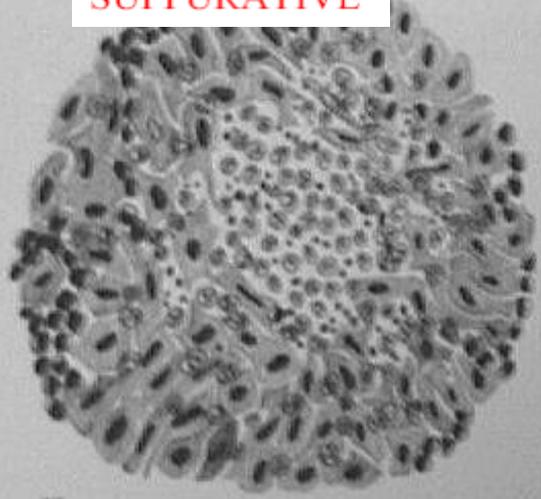
D

PALISADED



E

SUPPURATIVE



F

Micrograph A. Xanthogranuloma. B. Sarcoid granuloma. C. Corpus luteum. D. Tubercloid granuloma.

Cutaneous infections presenting with granulomatous infiltrates: a review of histopathological patterns

José Carlos Cardoso

Eduardo Calonje

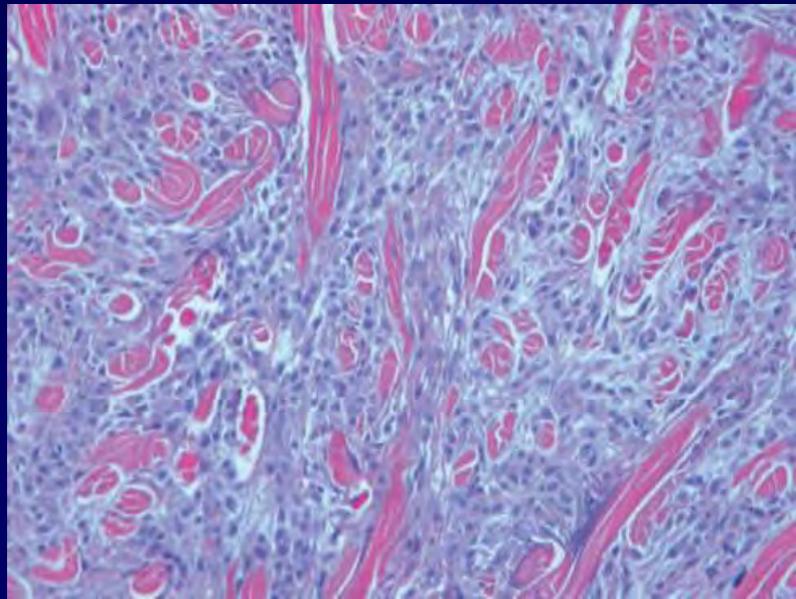
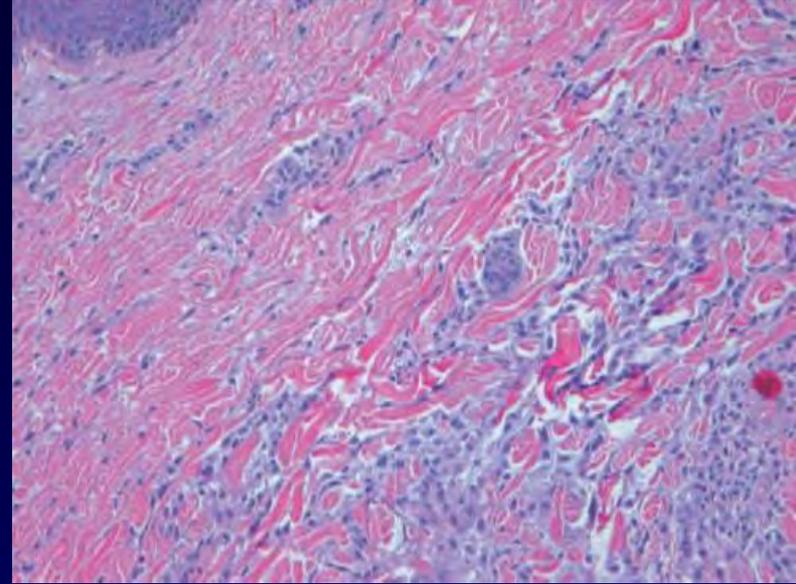
Consider in this classification **histiocytic granulomas**: parasitized histiocytes infiltrate the dermis in a diffuse pattern, without forming well defined granulomas.

Some infections may present this pattern:
leprosy, leishmaniasis or histoplasmosis.

The rope sign: a case of interstitial granulomatous dermatitis with arthritis

Francesco SAVOIA ¹, Caterina STINCHI ¹, Giuseppe GADDONI ¹, Annalisa PATRIZI ²
Giulia ODORICI ^{2*}, Vera TENGATTINI ², Pierluigi CATALETA ³, Silvia ZAGO ⁴

Giornale Italiano di Dermatologia e Venereologia





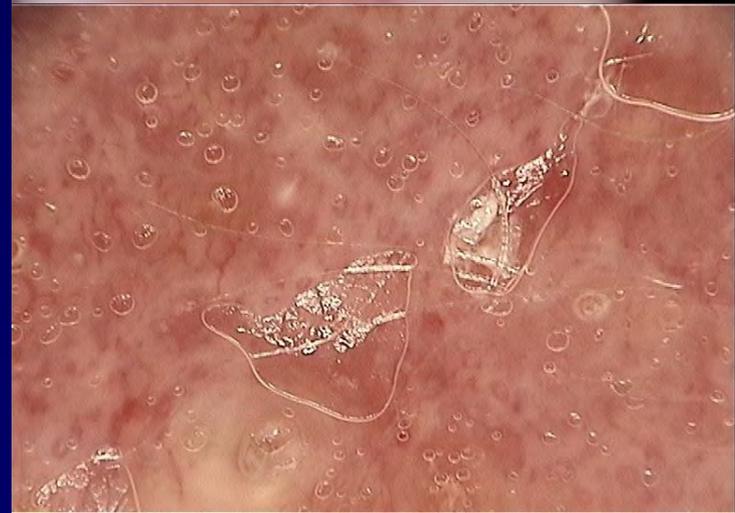
Dermoscopy could be useful in differentiating sarcoidosis from necrobiotic granulomas even after treatment with systemic steroids

Shahira Ramadan¹, Dalia Hossam¹, Marwah A. Saleh¹

Necrobiosis lipoidica
arborizing blood vessels with
mixed pink, white and
yellowish background



Sarcoidosis:
linear vessels with
translucent orange areas,
white scar-like
depigmentation and white
scales



Dermoscopy in General Dermatology: A Practical Overview

Enzo Errichetti · Giuseppe Stinco



Granulomatous Skin Diseases: Sarcoidosis, Cutaneous Leishmaniasis and Lupus Vulgaris;

structureless orange-yellowish areas associated with focussed linear or branching vessels, hairpin, comma-shaped, glomerular-like

Milia-like cysts, whitish lines or structureless areas, follicular plugs, dilated follicles, white and/or yellow scales.

Lupus Vulgaris

The etiologic agent of tuberculosis, *M. tuberculosis*, is clinically one of the most common microbial causes of granulomas

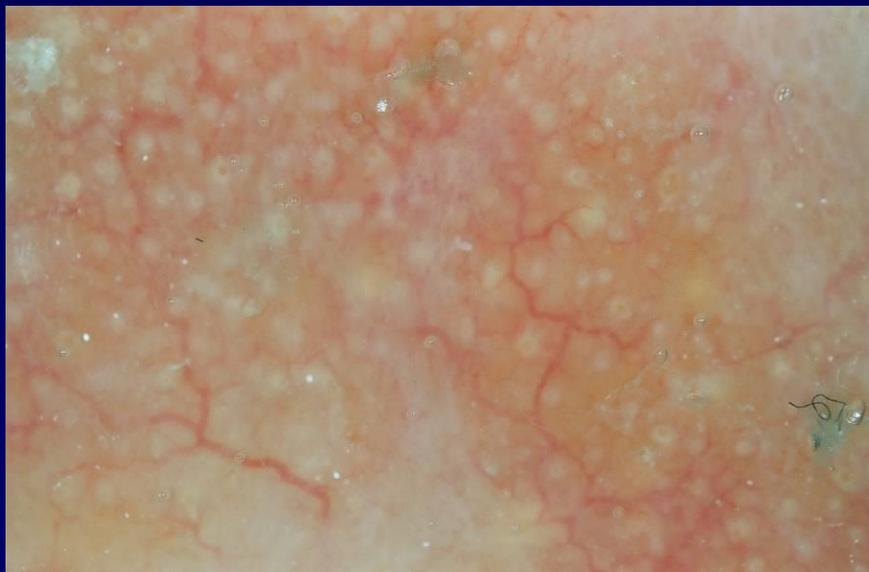


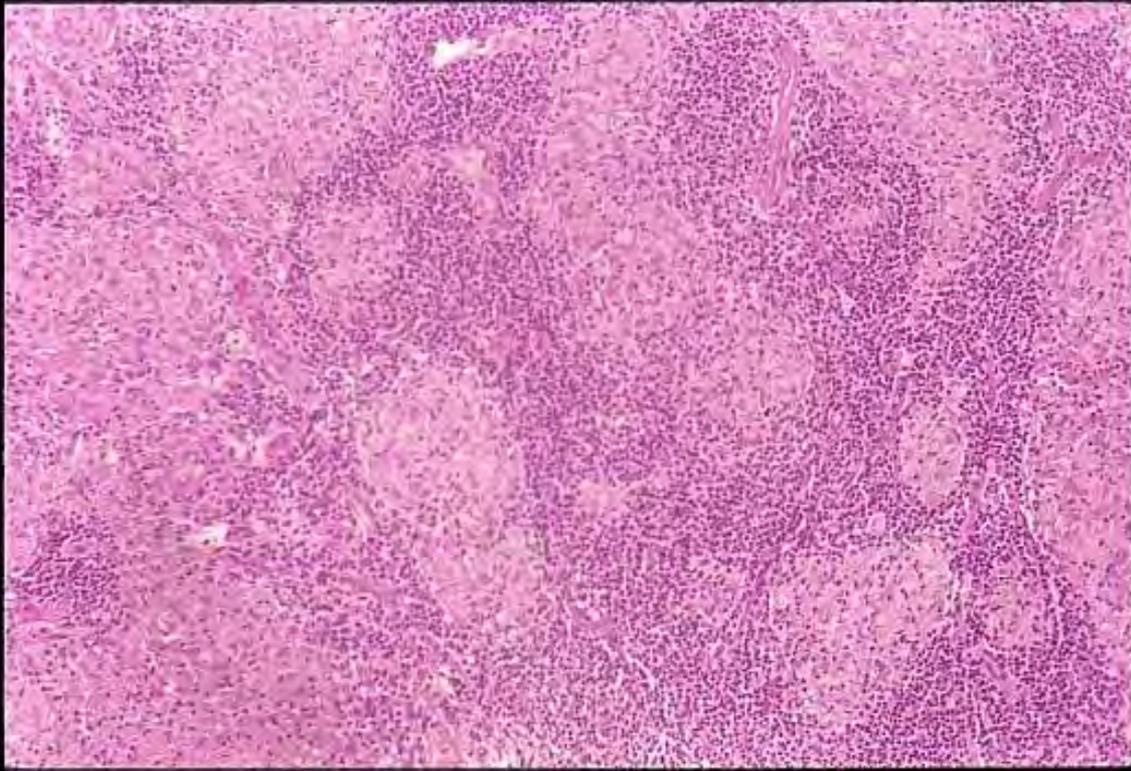
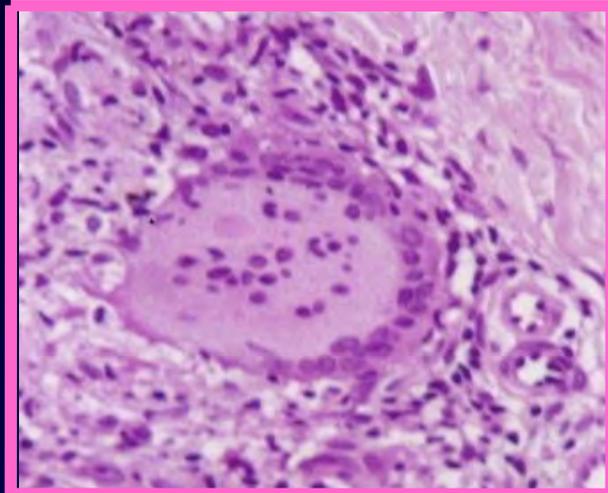
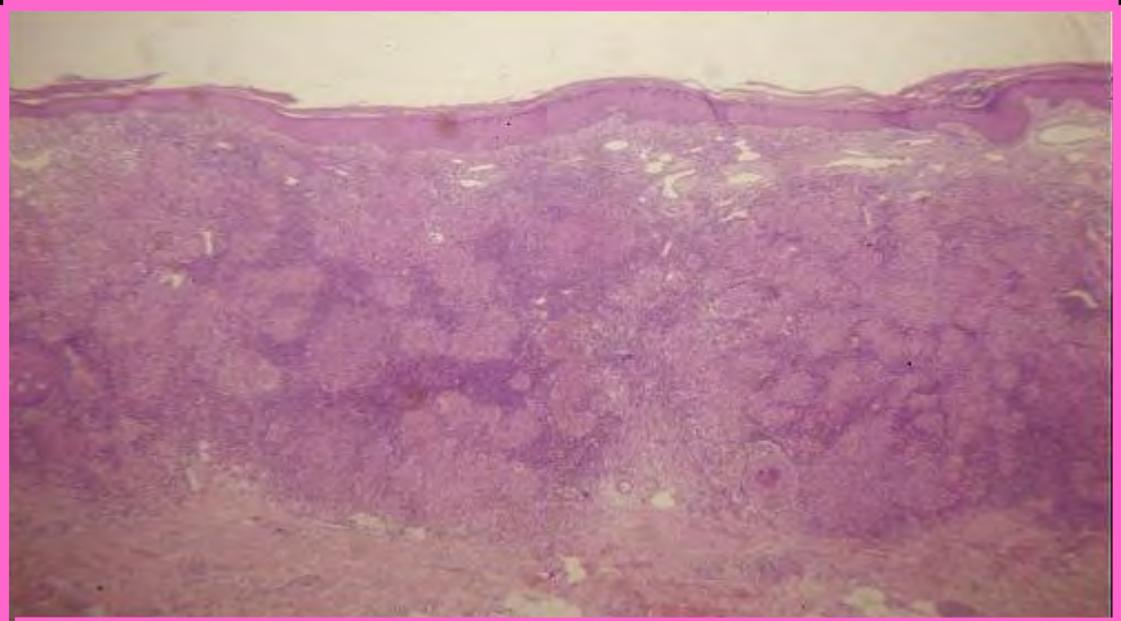


Lupus Vulgaris: A New Look at an Old Symptom – The Lupoma Observed with Dermoscopy

Marcella Brasiello^a, Iris Zalaudek^c, Gerardo Ferrara^b,
Jean-Yves Gourhant^d, Patrizio Capoluongo^a, Paolo Roma^a,
Giuseppe Argenziano^a

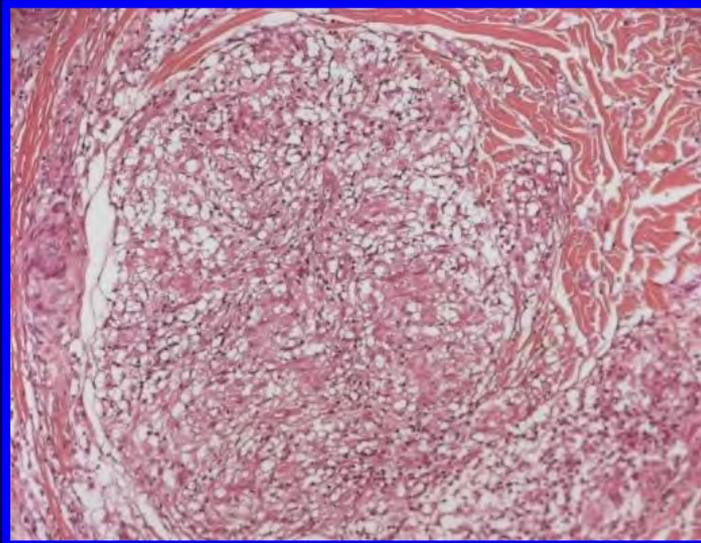
Dermatology 2009;218:172–174

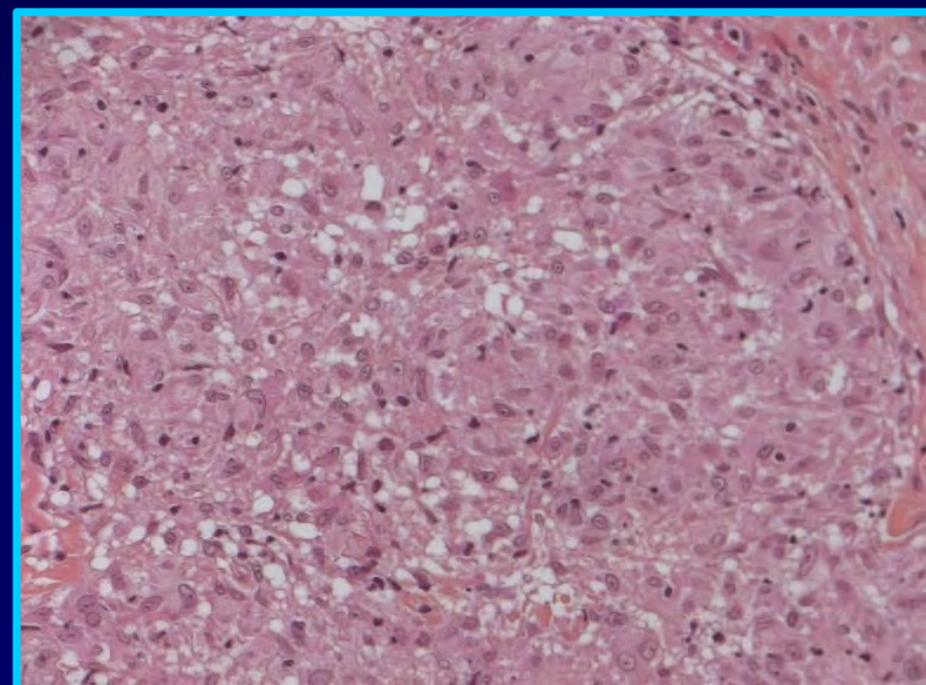
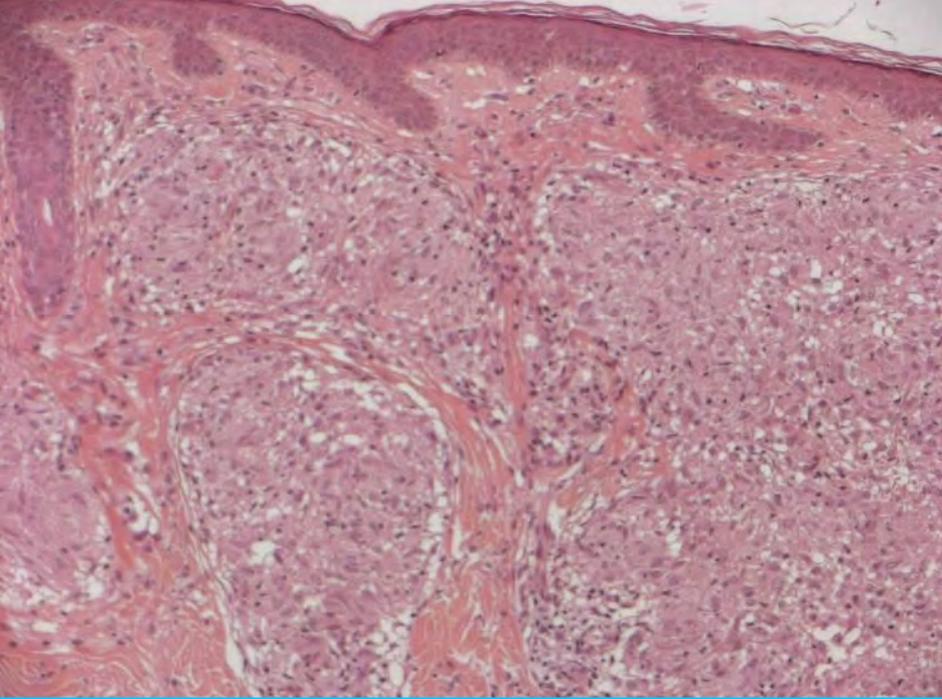






Sarcoidosis





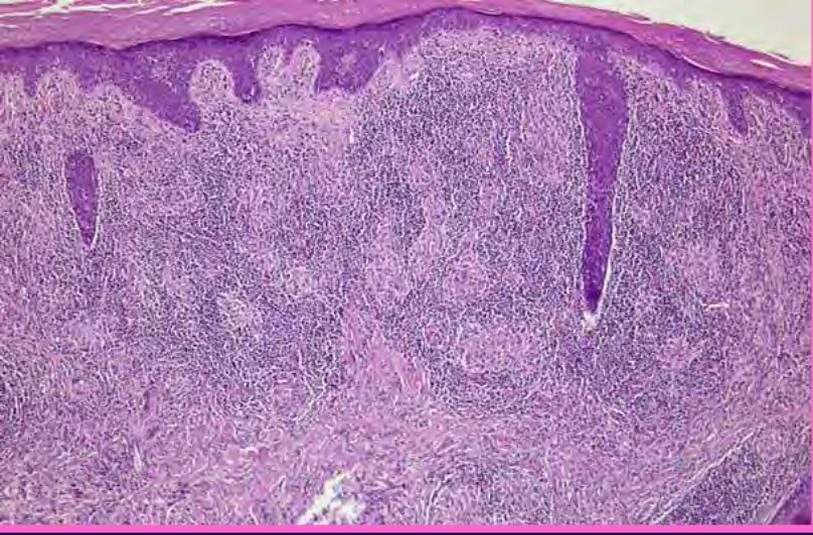
Leishmania



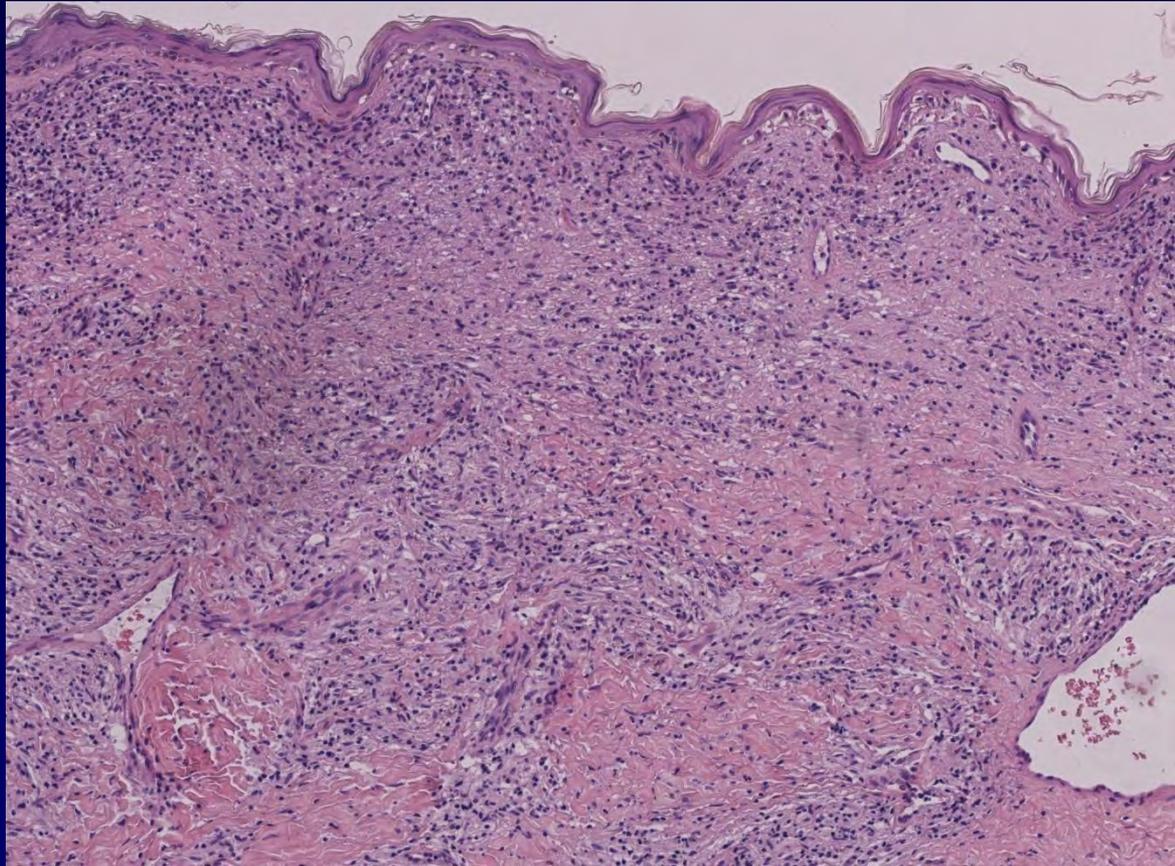
Leishmaniasis:

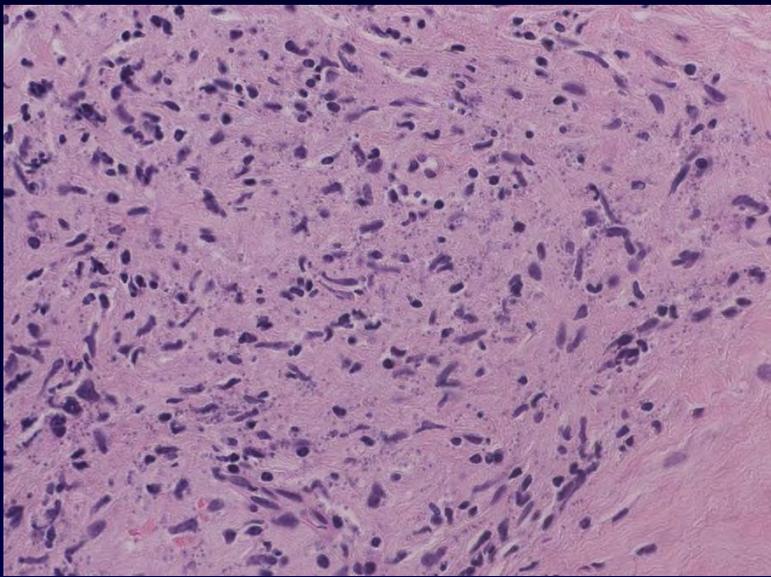
Spectrum of clinical disease caused by the protozoan Leishmania . This parasite is transmitted by phlebotomine sandflies, and the disease presents in three clinical forms: cutaneous, mucocutaneous, and visceral. Granulomatous responses are a feature of cutaneous and mucocutaneous leishmaniasis.

iperplasia pseudo-epiteliomatosa

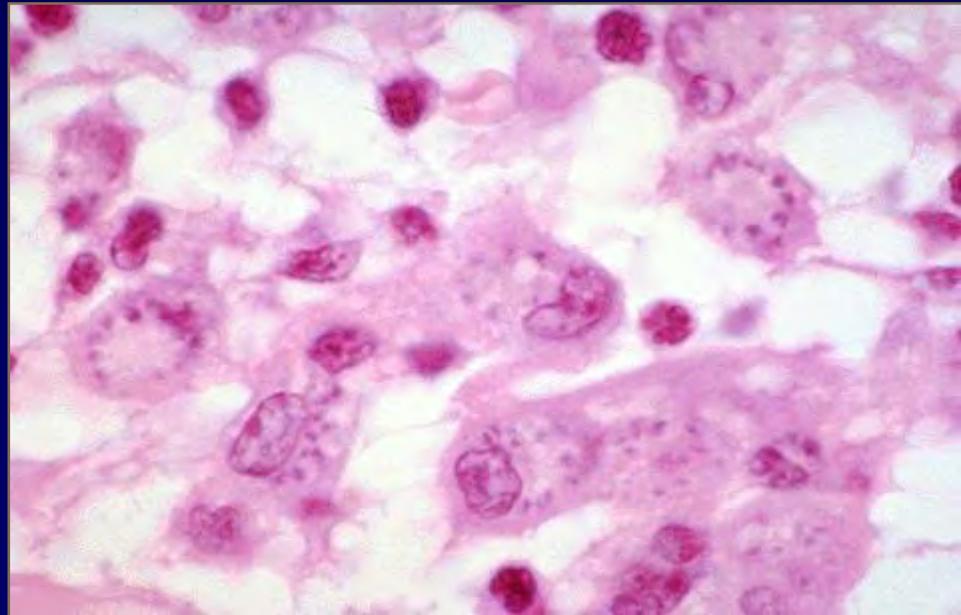
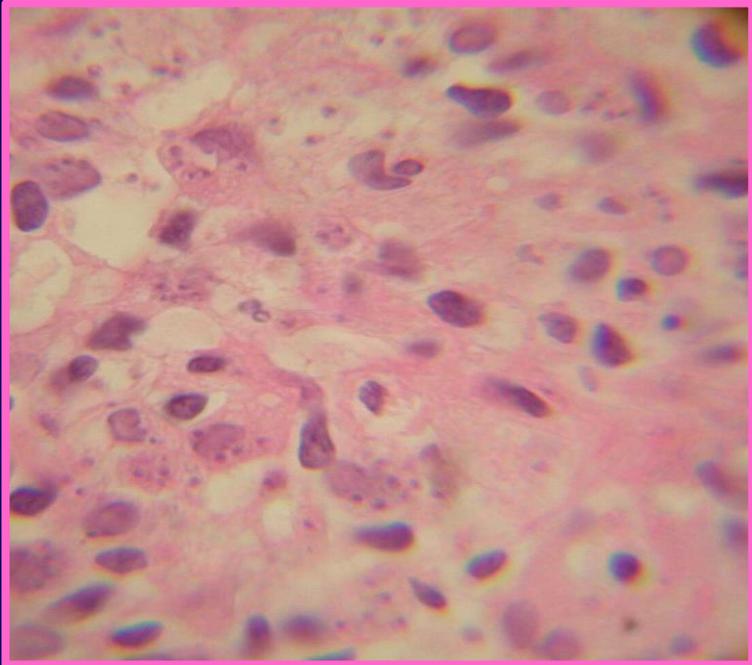


Nodular pattern



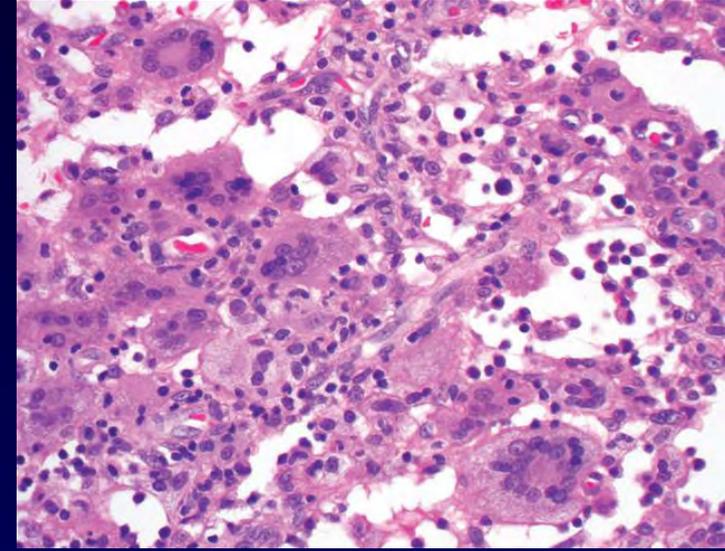


**micro-ascensualizzazione
granulomi ("Corpi di Leishman-Donovan")**

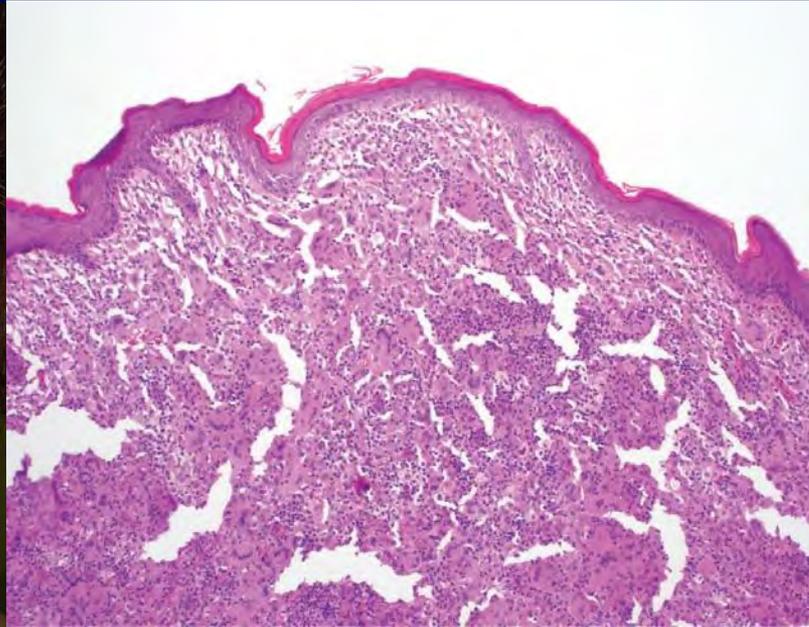


Granulomi necrobiotici

- Anulare
- Necrobiosi
- Xantogranuloma
- Reumatoide

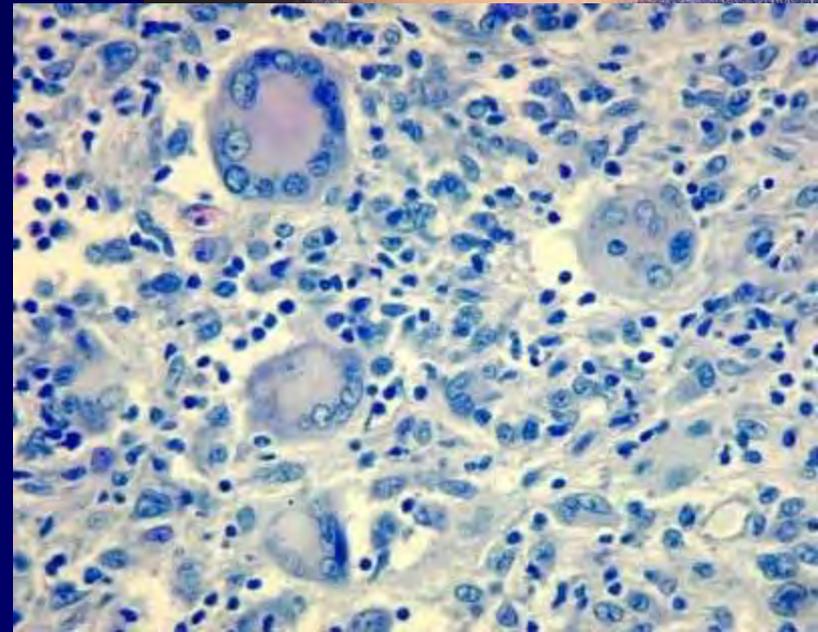


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Predominant histiocytic infiltrate with Touton giant cells and some eosinophils (H-E 40X).



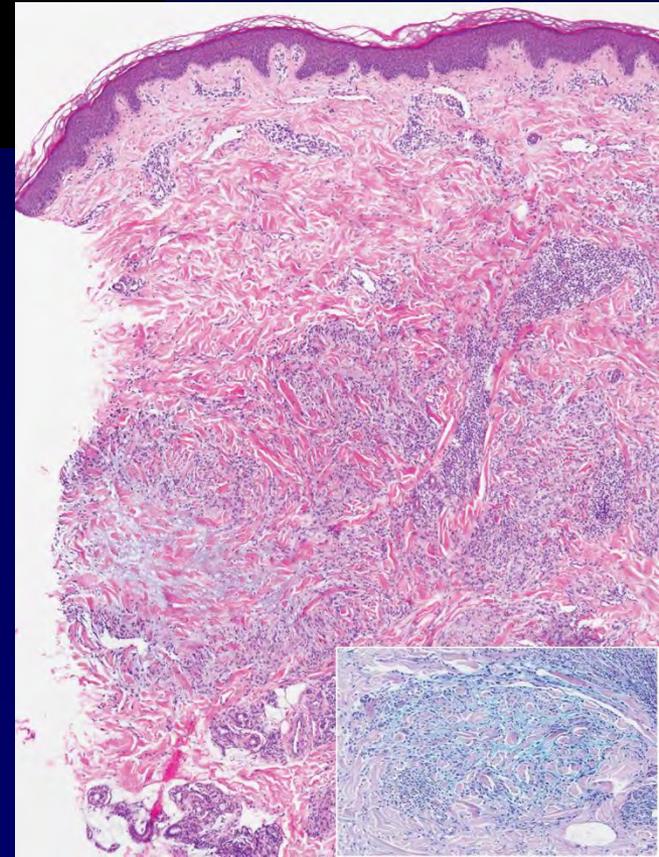
ORIGINAL ARTICLES

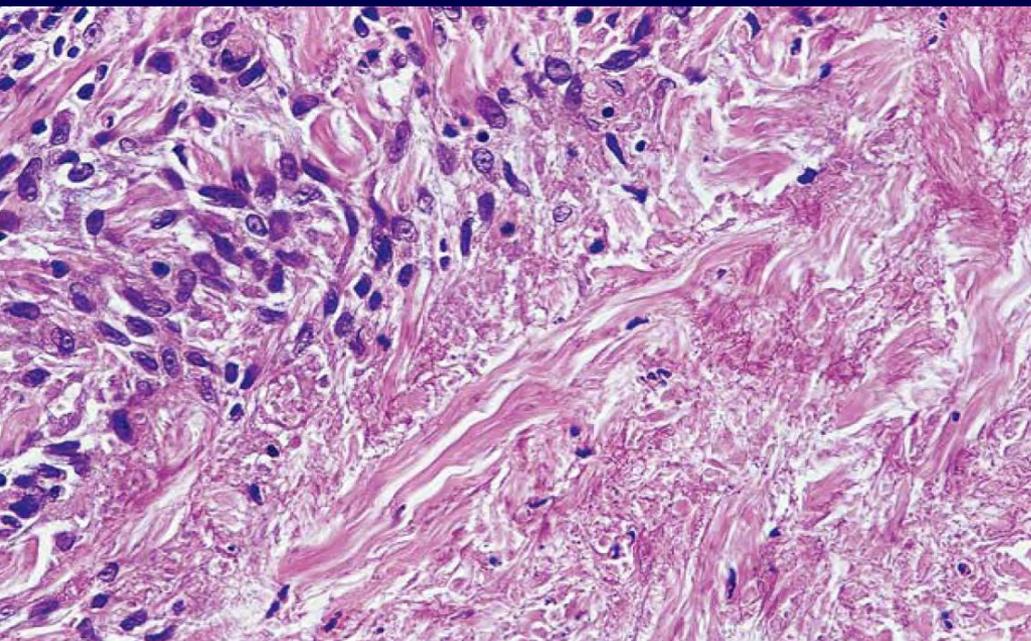
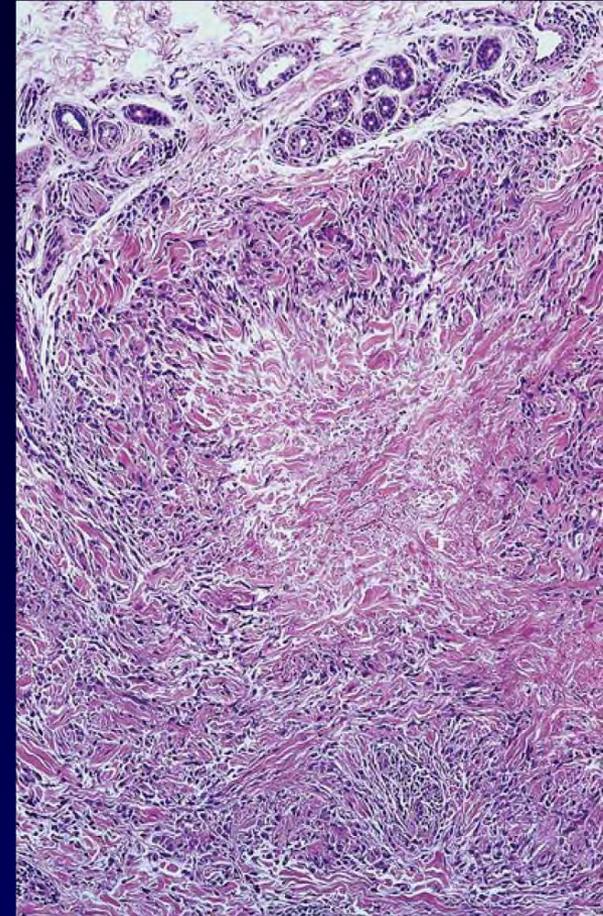
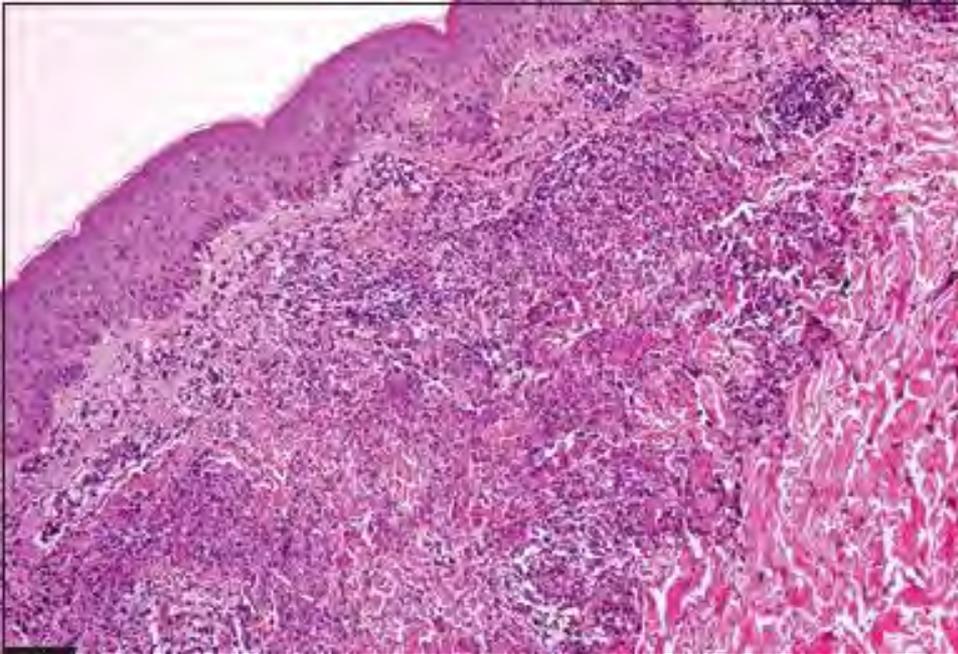
Juvenile xanthogranuloma: experience in a Children's Hospital

María Marta Buján¹, Graciela Sosa², Andrea Bettina Cervini³, Amelia Laterza⁴,
Adrián Martín Pierini⁵

Granuloma annulare

- Unknown etiology and pathogenesis
- Three main histopathologic patterns:
 - **palisaded (biopsy of a fully papule)**
 - interstitial (most frequent)
 - sarcoidal/tuberculoid (less common)
 - perforating (? result of scratching)





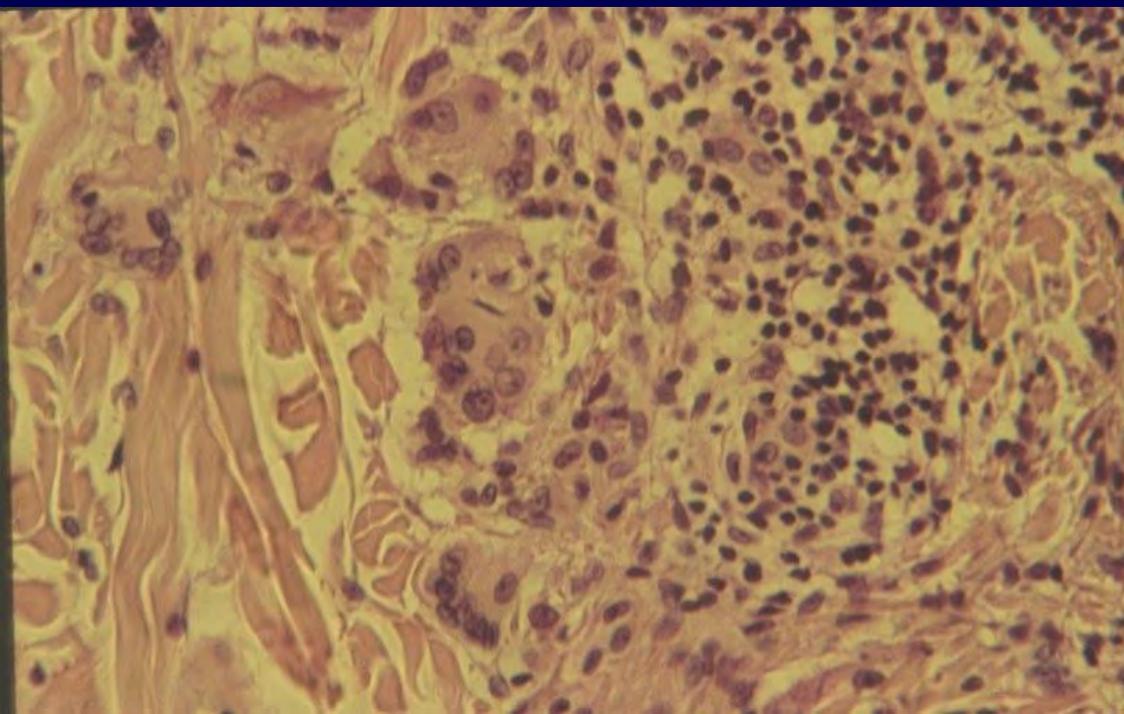
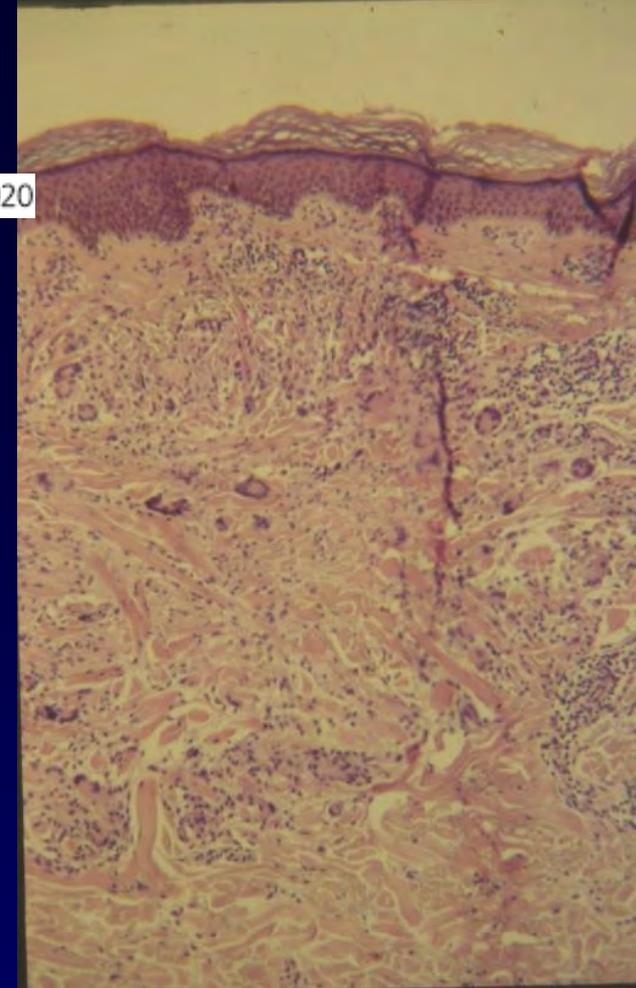
McKee

Localized GA: the characteristic appearance of a well-circumscribed palisading GA consisting of a necrobiotic center surrounded by a cellular infiltrate

the collagen is fragmented granular. peripheral palisade of histiocytes, lymphocytes and fibroblasts.

Annular elastolytic giant cell granuloma associated with diabetes mellitus: a case report and review of the Japanese literature

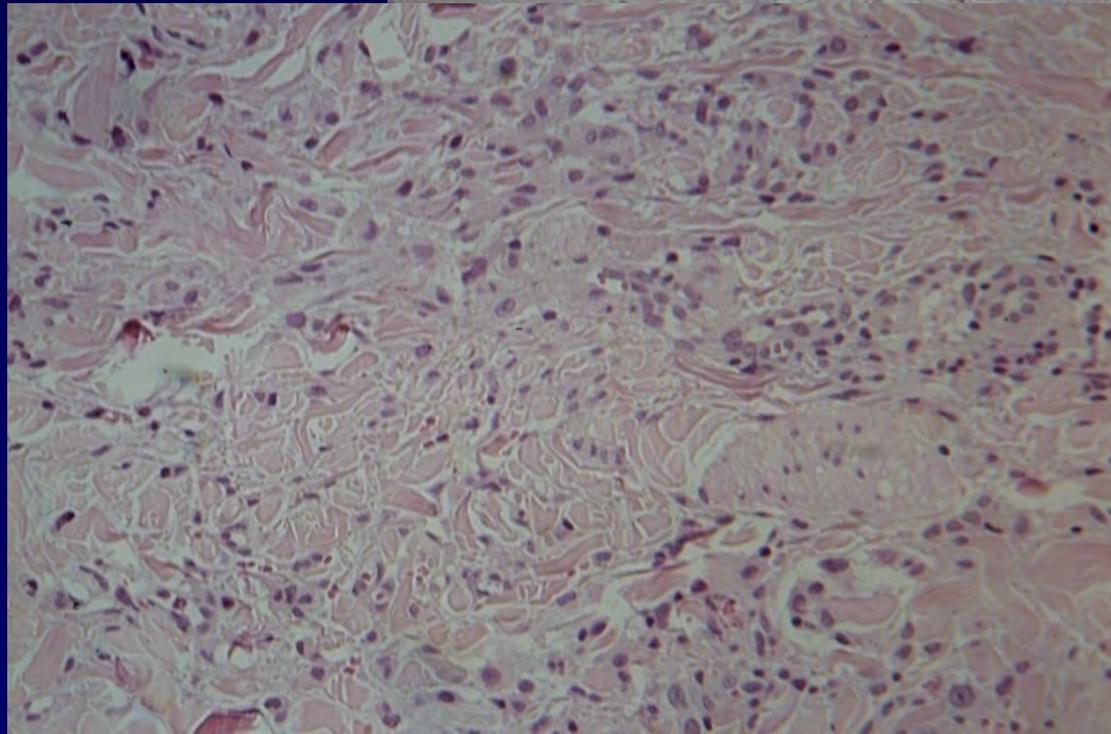
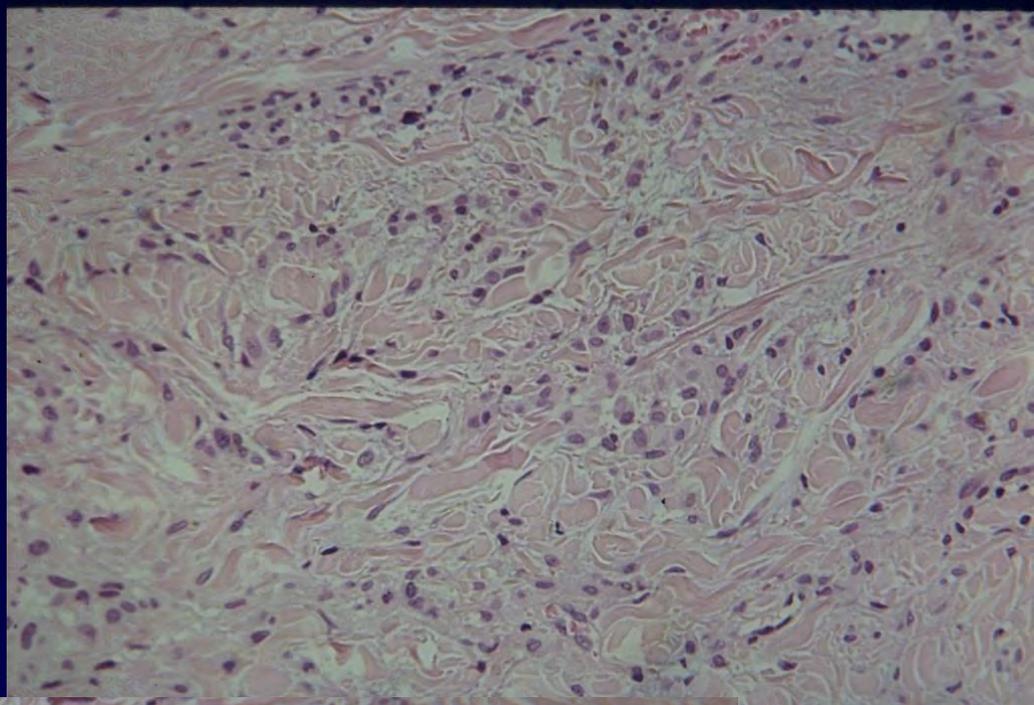
2011 British Association of Dermatologists • *Clinical and Experimental Dermatology*, 36, 915–920



**Annular elastolytic
granuloma**



**Anular disseminated granuloma
in diabetic patient**



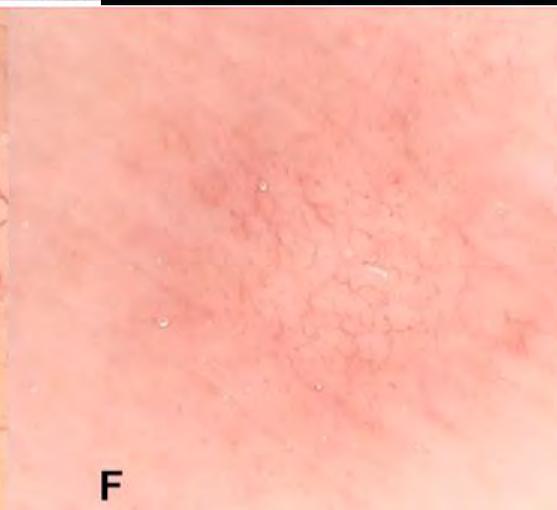
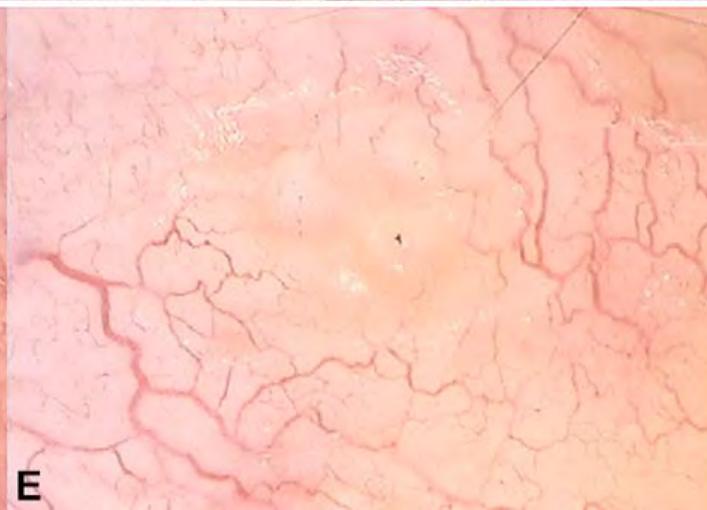
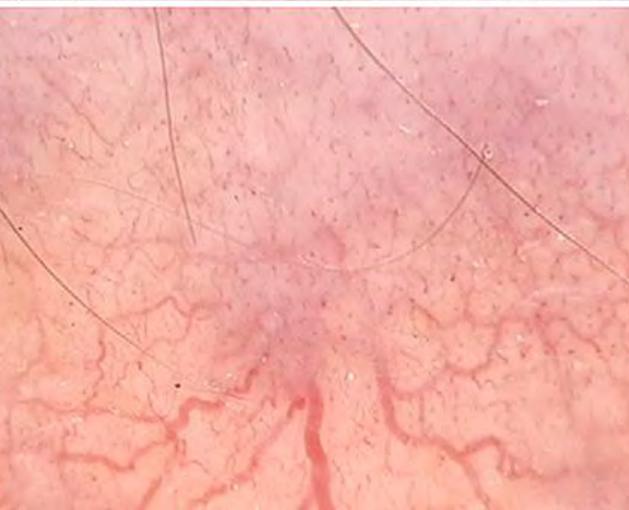
Necrobiosis lipoidica

- The exact pathogenesis of necrobiosis lipoidica is still unknown. Well-known association with diabetes mellitus, enhanced glycosylation of dermal collagen and increased collagen cross-linking have been discussed



Dermatoscopy of early-onset necrobiosis lipoidica

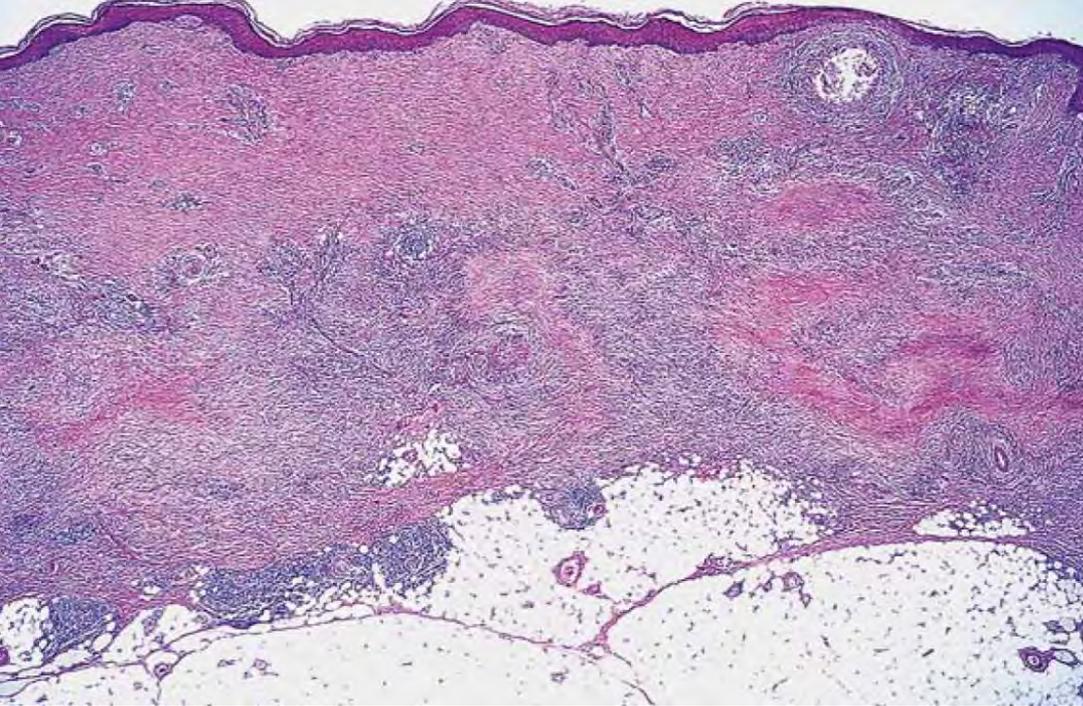
*Renato Marchiori Bakos, MD, PhD,^a André Cartell,
MD,^b and Lucio Bakos, MD, PhD^a*



B

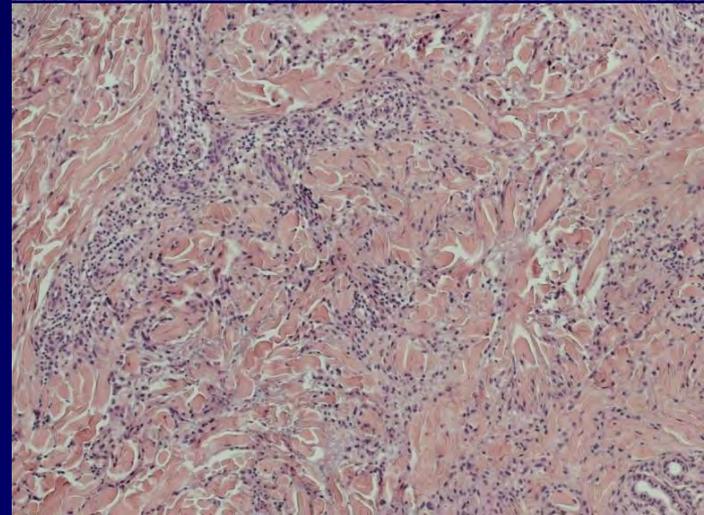
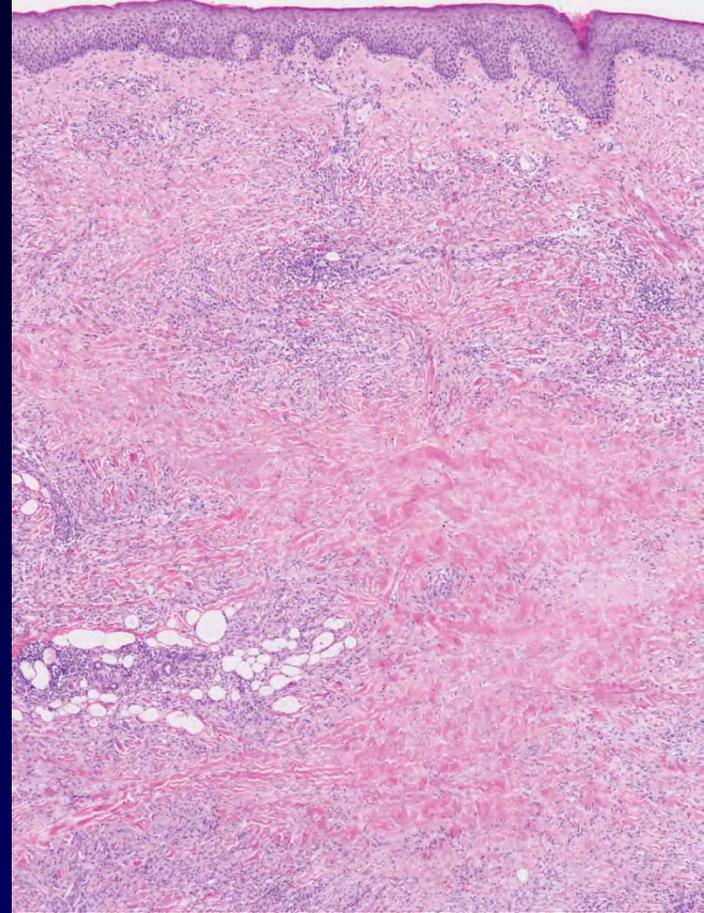
E

F



McKee

Necrobiosis lipoidica: the degenerate collagen is surrounded by a palisade of histiocytes, lymphocytes and fibroblasts. sandwich"or"wedding cake"-like appearance

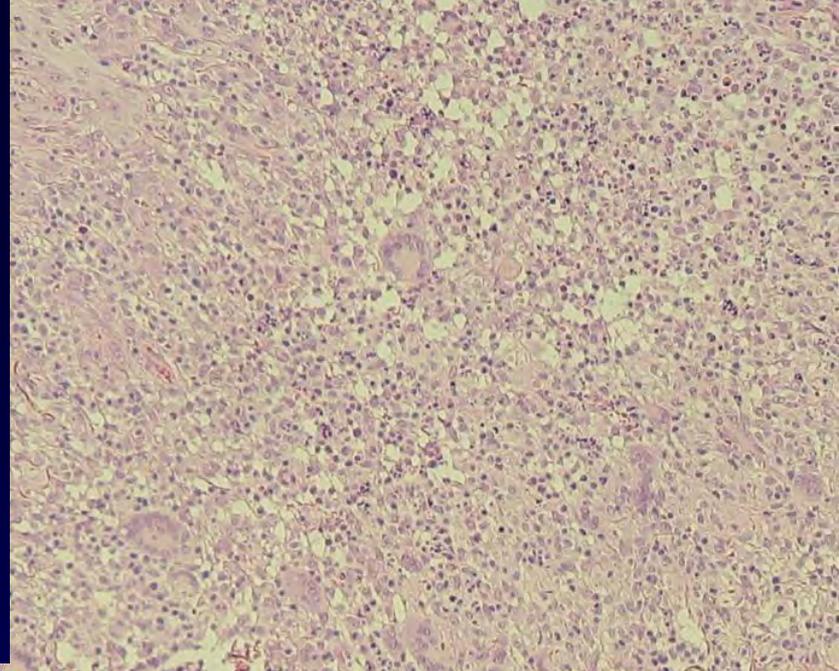
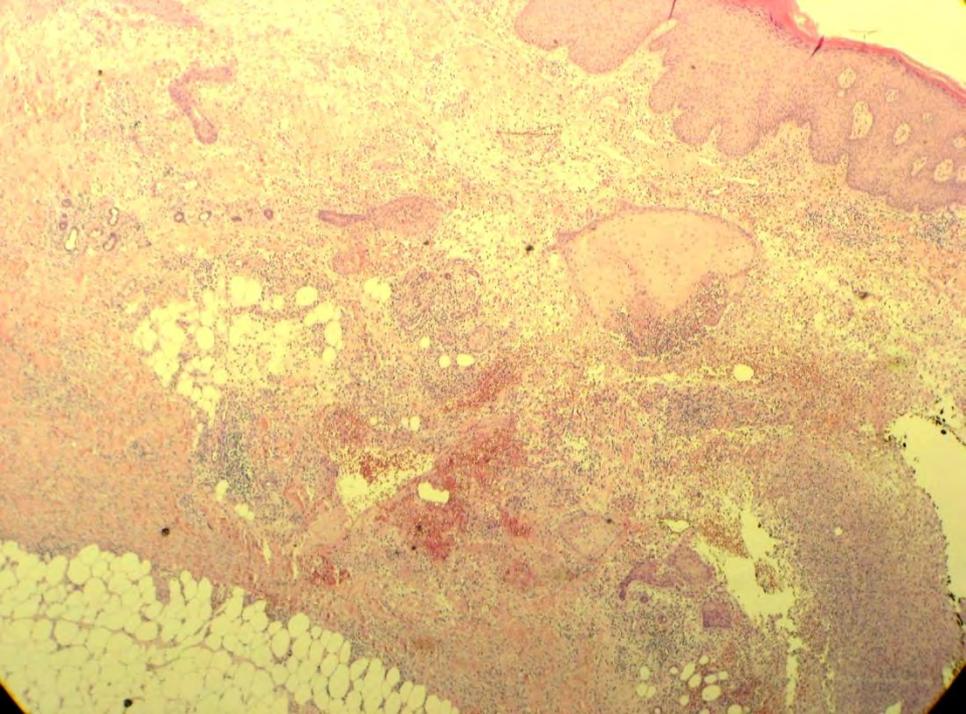


Crohn's disease

- ▣ 10-20%
- ▣ Onset precedes symptoms of bowel disease
- ▣ No correlation with severity of activity
- ▣ The presence of granulomas has been called metastatic Crohn.

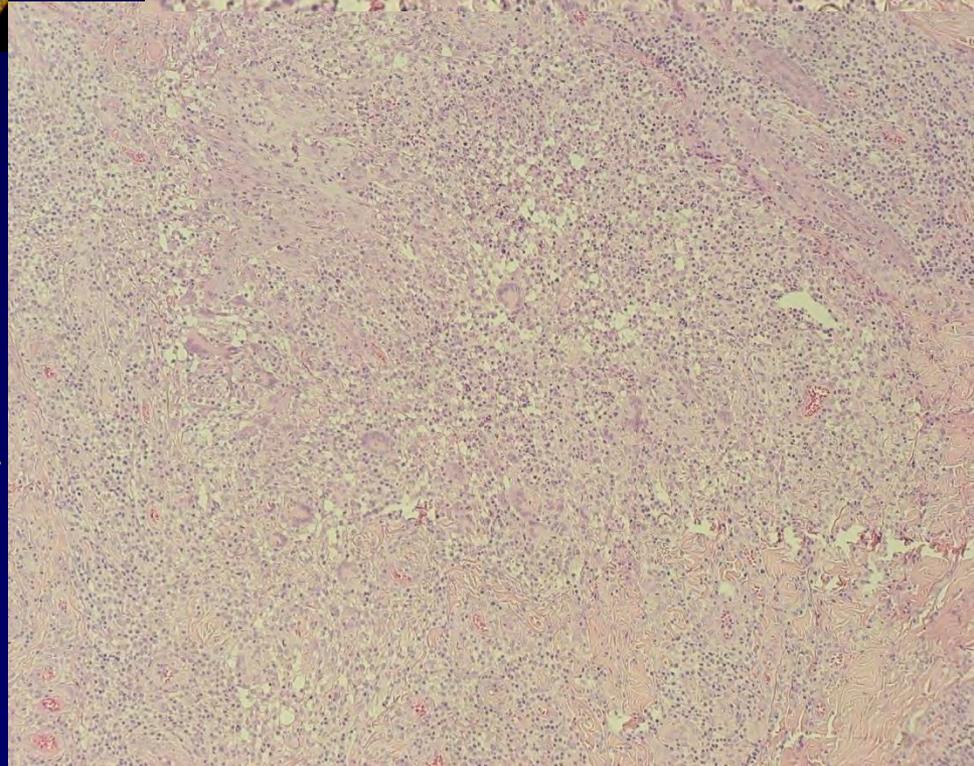


Cortesia Prof Papini



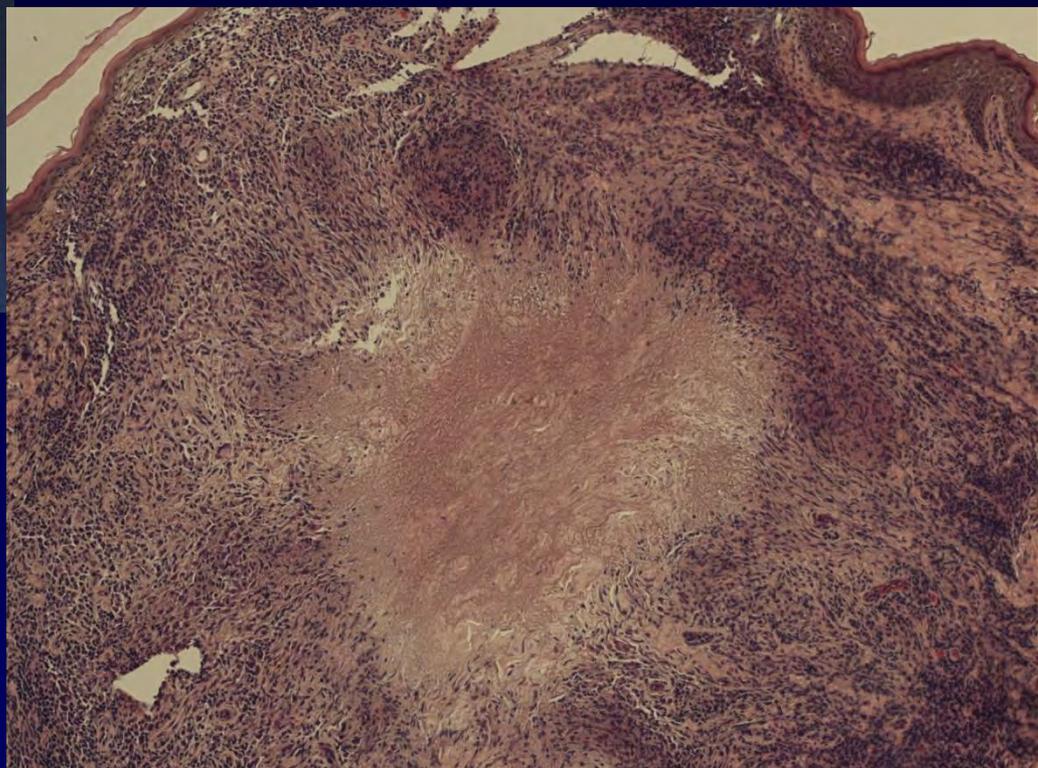
Cortesia Prof Papini

**Ill defined granulomatous infiltrate
Giant cells in the deep reticular dermis,
sometimes swollen endothelial cells**





Nodulo reumatoide





Original Article

Granulomatous lesions of the skin

Gautam K¹, Pai RR², Bhat S²

Infections are important cause of granulomatous skin lesions with leprosy as the leading etiology.

Various modes of presentation.

Skin biopsies definitely help for a diagnosis.

Special stains play a supporting role in diagnosis.

Culture and PCR are indicated in certain cases.

Table 1. Classification of granulomatous infections and associated pathogens.

Group number, type of causal agents	Granulomatous disorders
Group 1	
Well recognized	
Mycobacteria	Tuberculosis, leprosy, Buruli ulcer, swimming pool (fish tank) granuloma
Bacteria	Brucellosis, melioidosis, actinomycosis, nocardiosis, granuloma inguinale, listeriosis, tularemia
Spirochetes	Syphilis, pinta, yaws
Fungi	Mycoses (see table 3)
Protozoa	Leishmaniasis, toxoplasmosis
Nematodes	Visceral larva migrans (toxocariasis)
Trematodes	Schistosomiasis, paragonimiasis, fascioliasis, clonorchiasis
<i>Chlamydia</i> species	Lymphogranuloma venereum, trachoma
Rickettsia	Q fever (<i>Coxiella burnetii</i> infection)
Viruses	Infectious mononucleosis, cytomegalovirus infection, measles, mumps
Group 2	
Recently recognized	
Bacterium	Cat-scratch disease (<i>Bartonella henselae</i> infection)
Actinomyces	Whipple's disease (<i>Tropheryma whippelii</i> infection)
Group 3	
Suspected but not established	
Measles virus	Crohn's disease
Mycobacterium	Primary biliary cirrhosis
? (see table 4)	Sarcoidosis
Viral	Kikuchi's disease
?	Chronic granulomatous disease of childhood
?	Langerhans granulomatosis

[View issue TOC](#)

Volume 44, Issue 5

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Pages 433–443

ORIGINAL ARTICLE

Clinical and histopathological features of cutaneous nontuberculous mycobacterial infection: a review of 13 cases

Jing Jing Li , Rohan Beresford, Janet Fyfe, Christopher Henderson

The **immunocompetent** patients: localized lesions on the extremities, pseudoepitheliomatous hyperplasia, intraepithelial abscesses, transepidermal elimination and dermal granulomatous inflammation with necrosis and suppuration.

The **immunocompromised** patients: disseminated suppurative inflammation with little granuloma formation and numerous acid-fast bacilli.

Granuloma infettivo

Sarcoideo

(perineurale) lebbra t.

Tubercoloide

Tubercolosi (lupus v, primaria)
Leishmaniosi, Lue, Brucellosi

Suppurativo

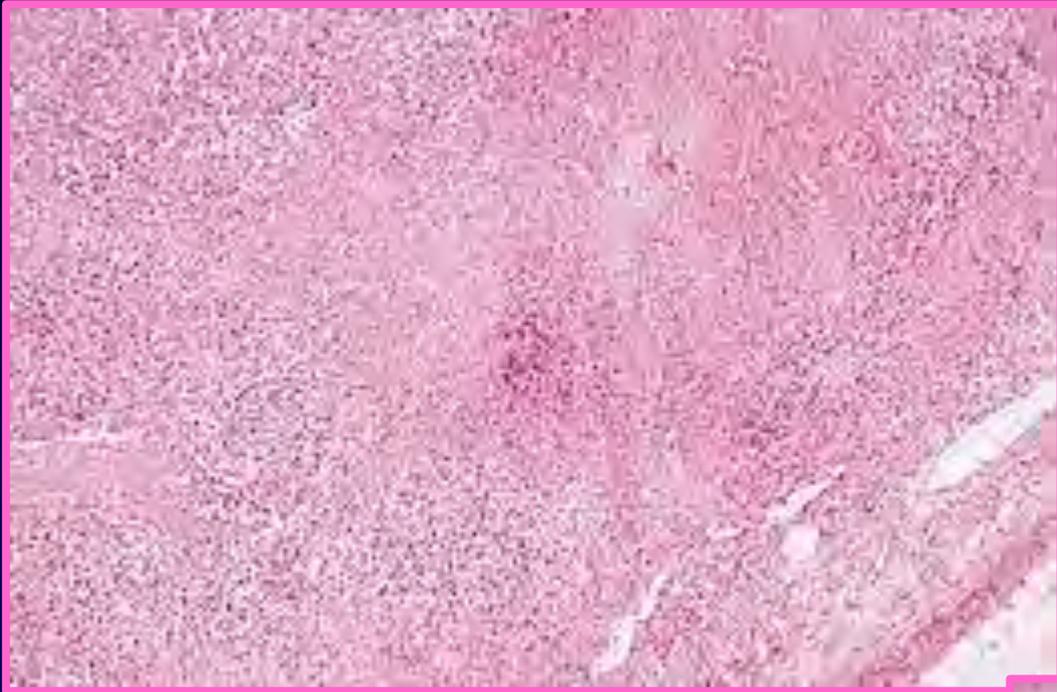
Mal. Batteriche
Micobatteriosi at./Tbc (Scrofuloderma)
Actinomicosi
Micosi profonde/superficiali
Candidosi Parassitosi

A palizzata



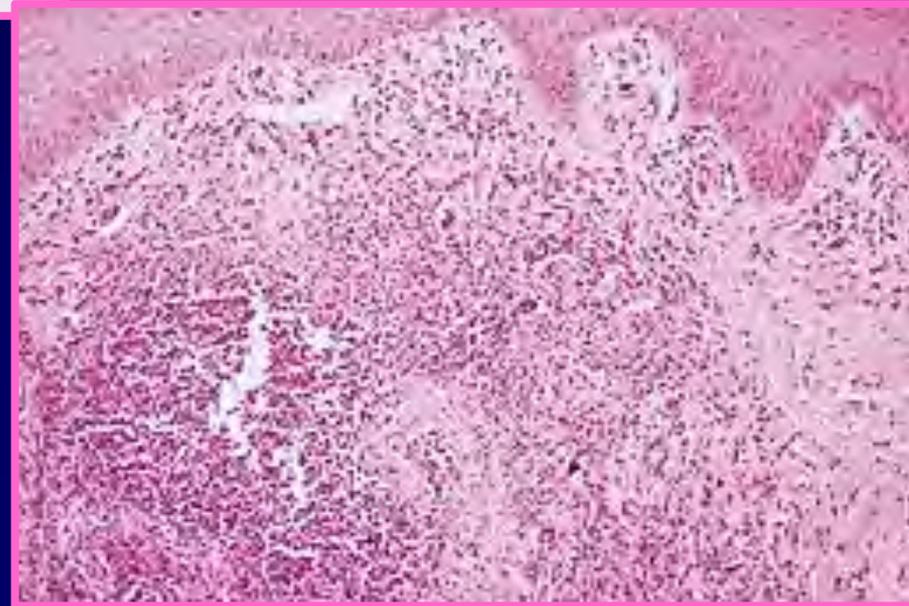
Malattia da graffio di gatto

Malattia da graffio di gatto



The histopathologic features are not diagnostic. Warthin Starry silver staining is used to detect *Bartonella henselae*, present in the early phase of the disease. Mostly neutrophils and eosinophils

Cat-scratch disease or fever is also known as benign lymphoreticulosis or regional granulomatous lymphadenitis, histopathological features of cat scratch disease are not diagnostic



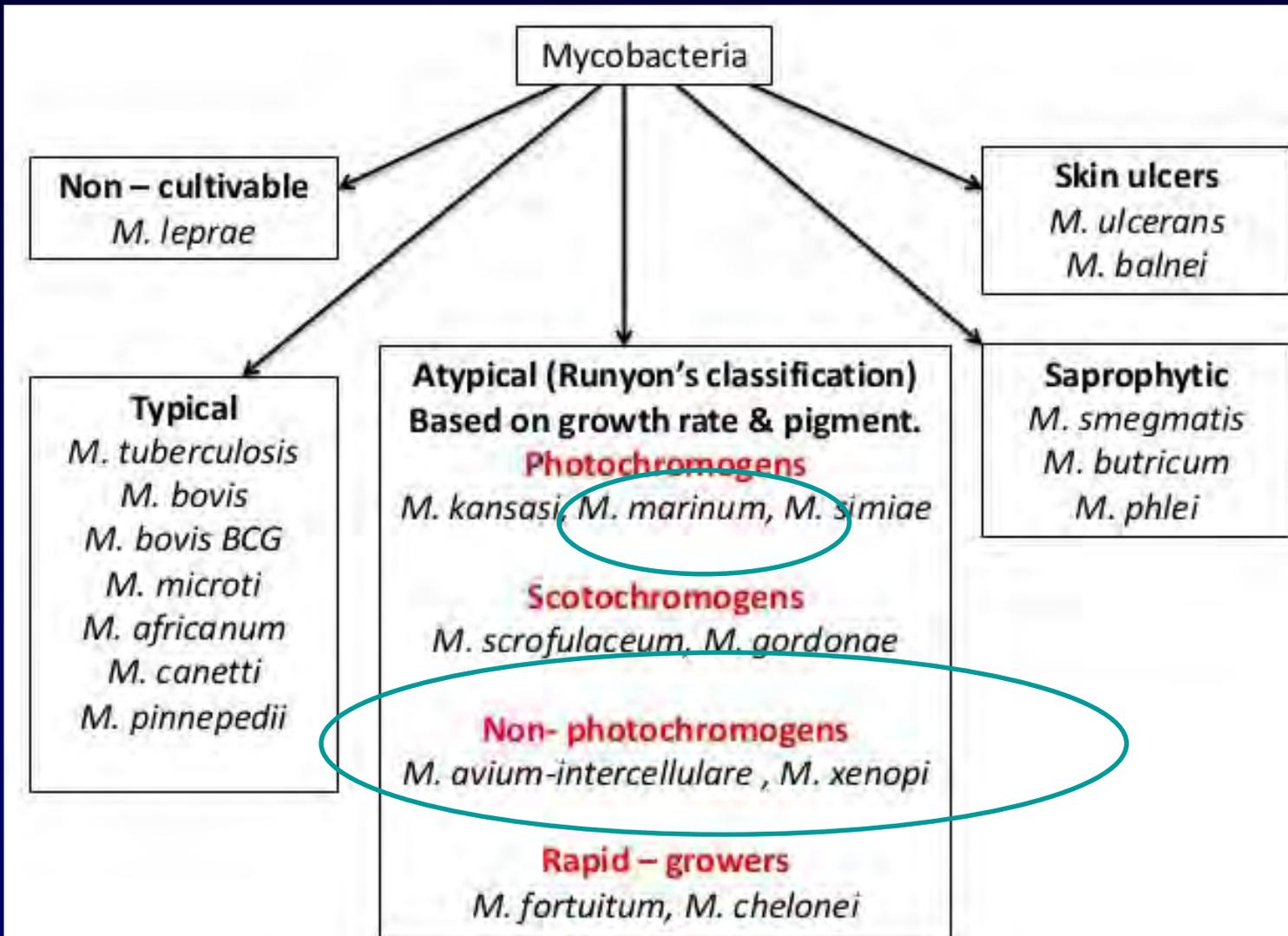
Mycobacteria

- Mycobacteria are the most common etiologies of necrotizing granulomas, granulomatous response limits the extent of inflammation, activates histiocytes, and forms a rim of histiocytes and peripheral lymphocytes around a necrotic center (Ghon focus).
- Mycobacteria are a large group comprising *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Mycobacterium avium* complex, *Mycobacterium ulcerans*, *Mycobacterium marinum*.
- several opportunistic mycobacteria

Lupus Vulgaris



Micobacteriosi Atipica



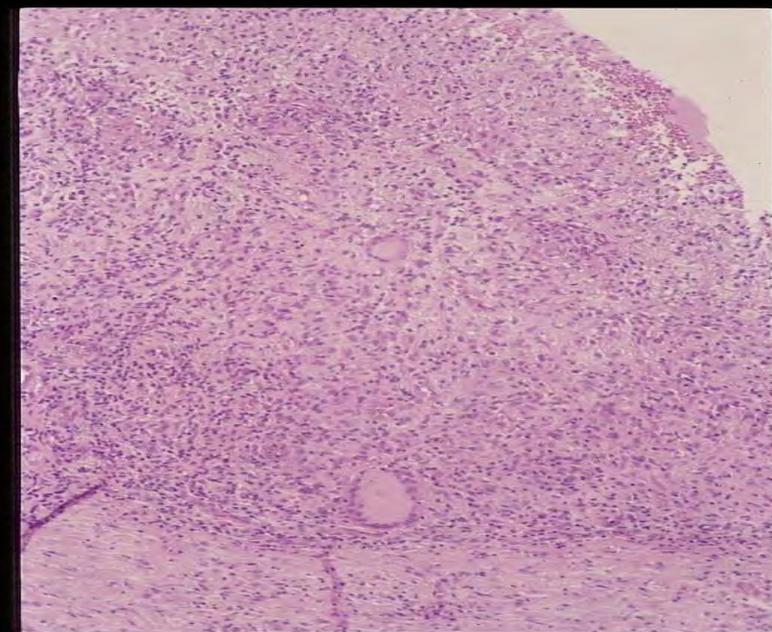
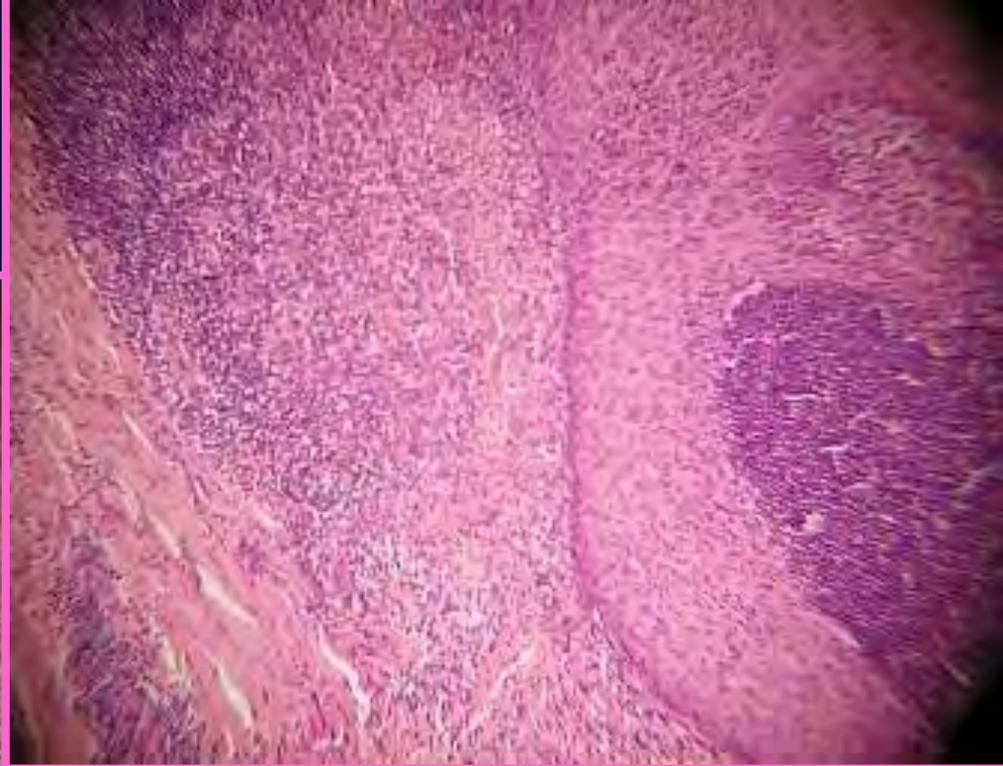
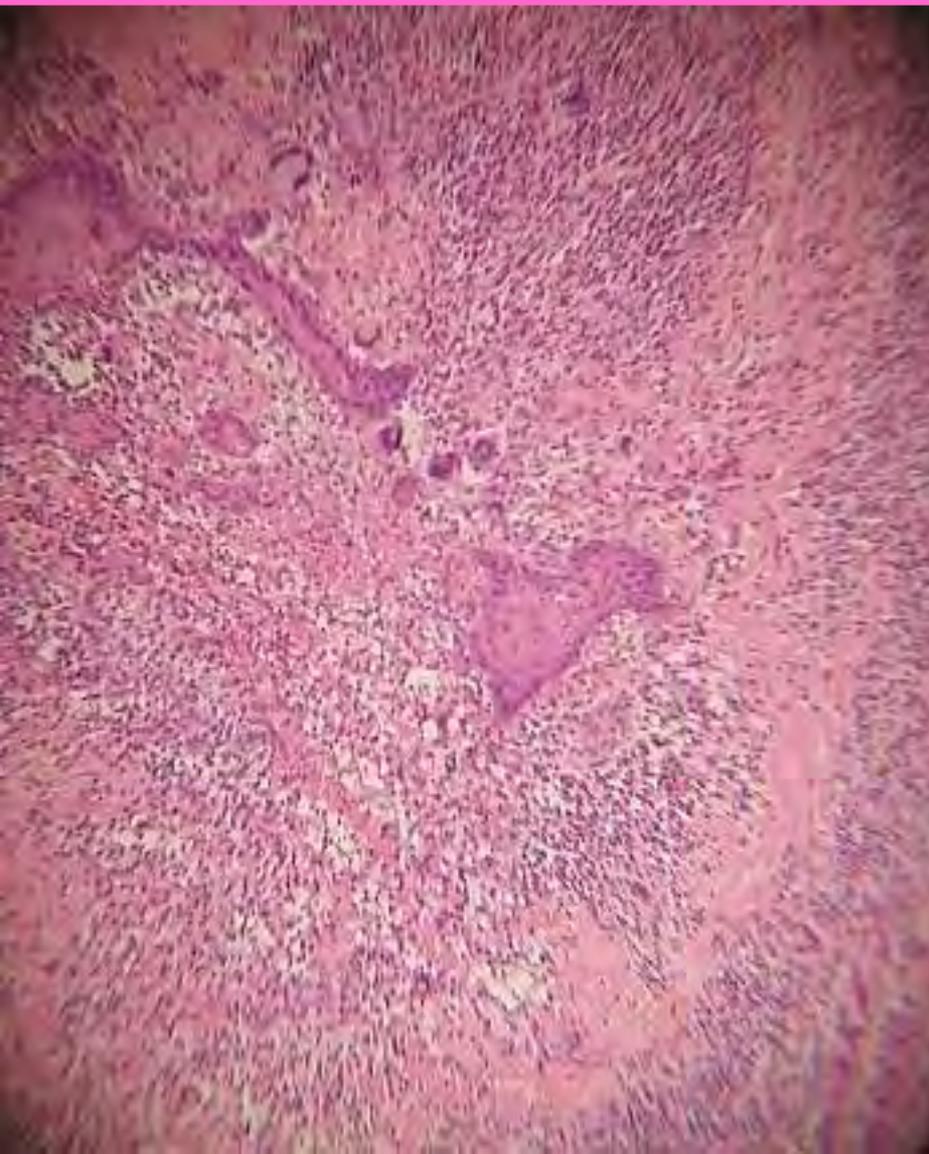
Atypical Mycobacteria

Mycobacterium marinum

- “Swimming pool/fish tank” granuloma
- Ulcerating lesions in skin at site of abrasions incurred in swimming pools about 2-3 wks. after inoculation
- Single nodules, typically on hands, may ulcerate and suppurate with sporotrichoid ascending spread
- Fresh and salt water
- Tx with Minocycline 100 mg bid
- Heals spont. w.in 1-2 yrs. w/residual scarring

Mycobacterium marinum

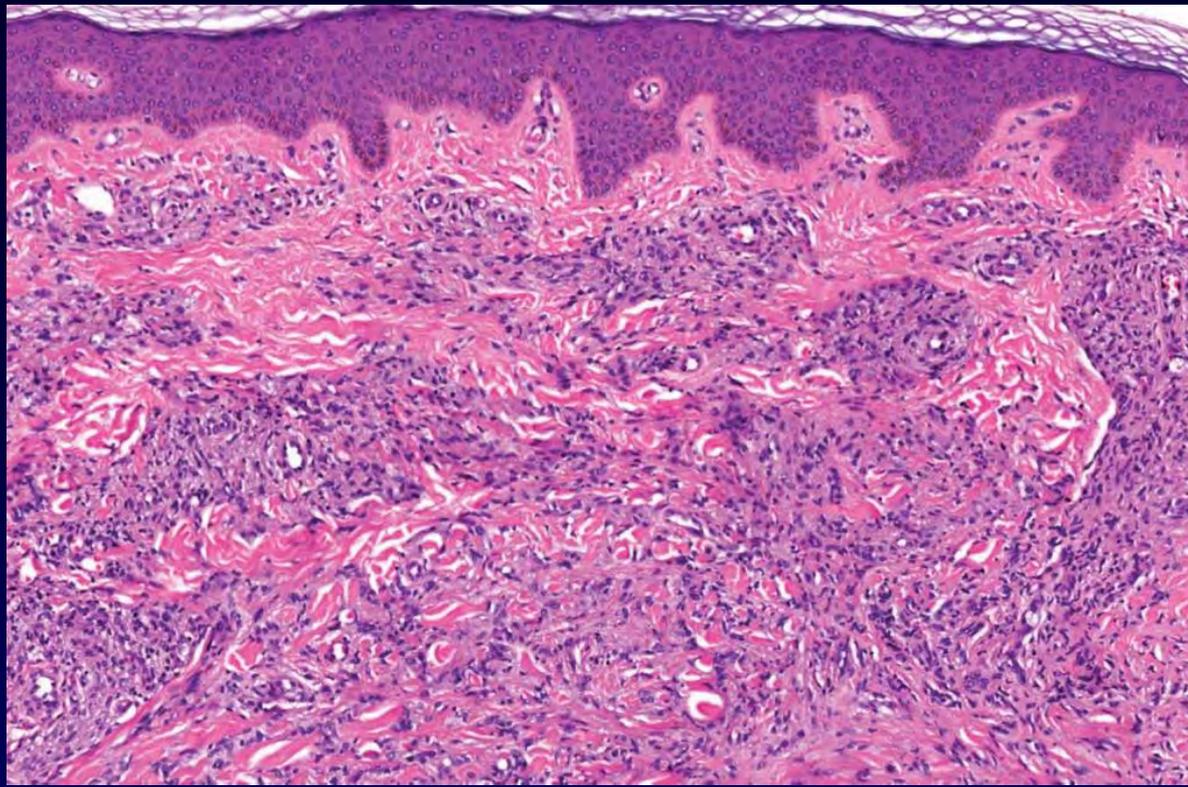




Lebbra



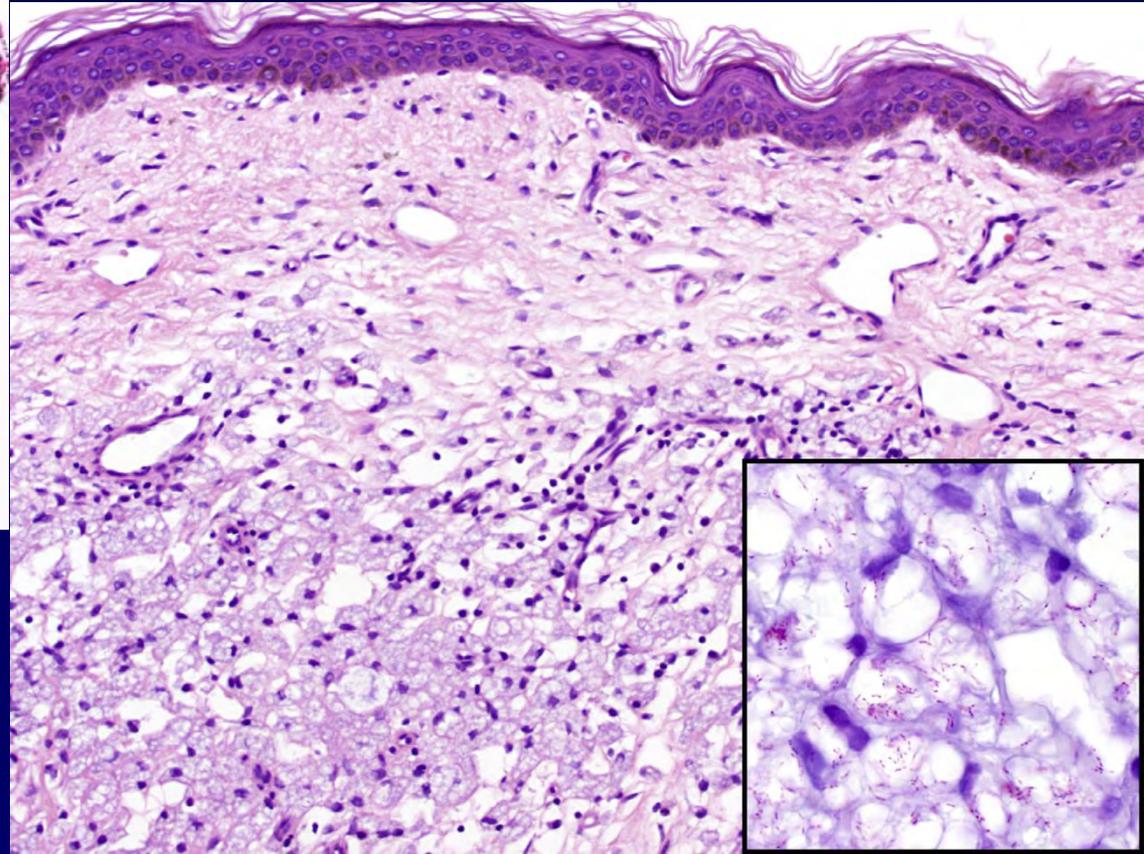
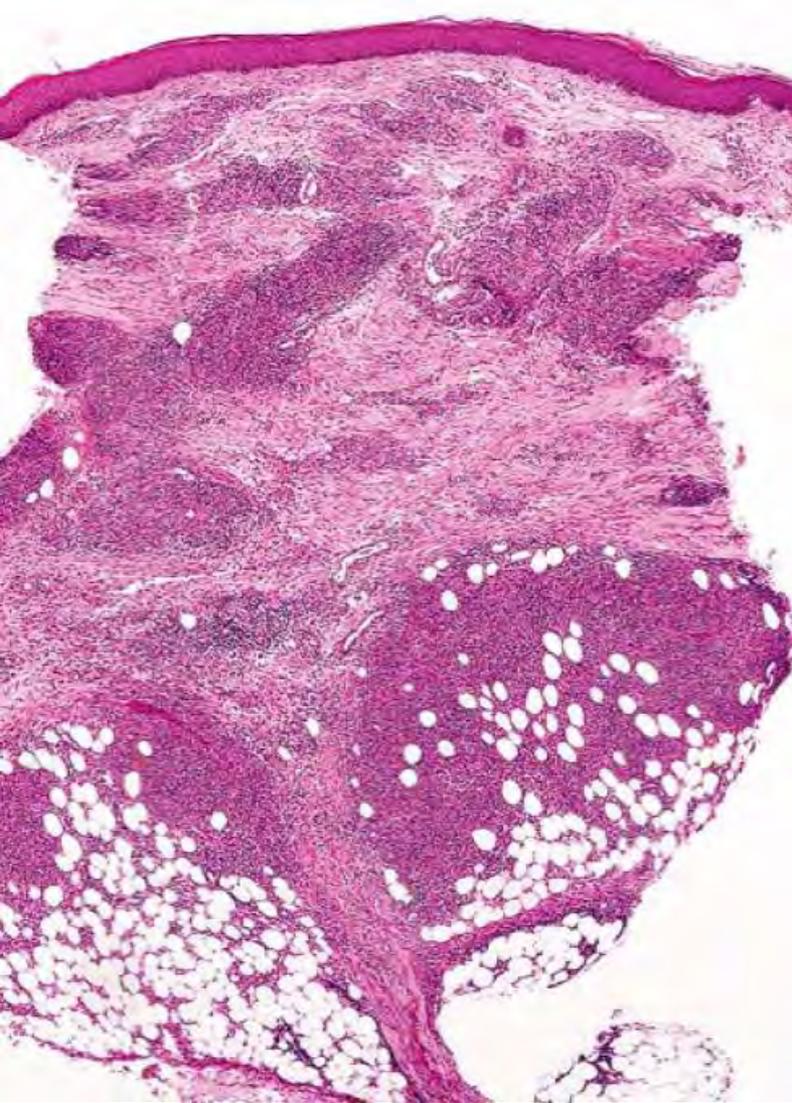
Mycobacterium leprae, otherwise known as Hansen's disease, is primarily a tropical, mycobacterial infection which most of ten affects skin, nerves, and nasal mucosa. **Mycobacterium leprae** is an obligate intracellular gram positive, partially acid fast bacillus

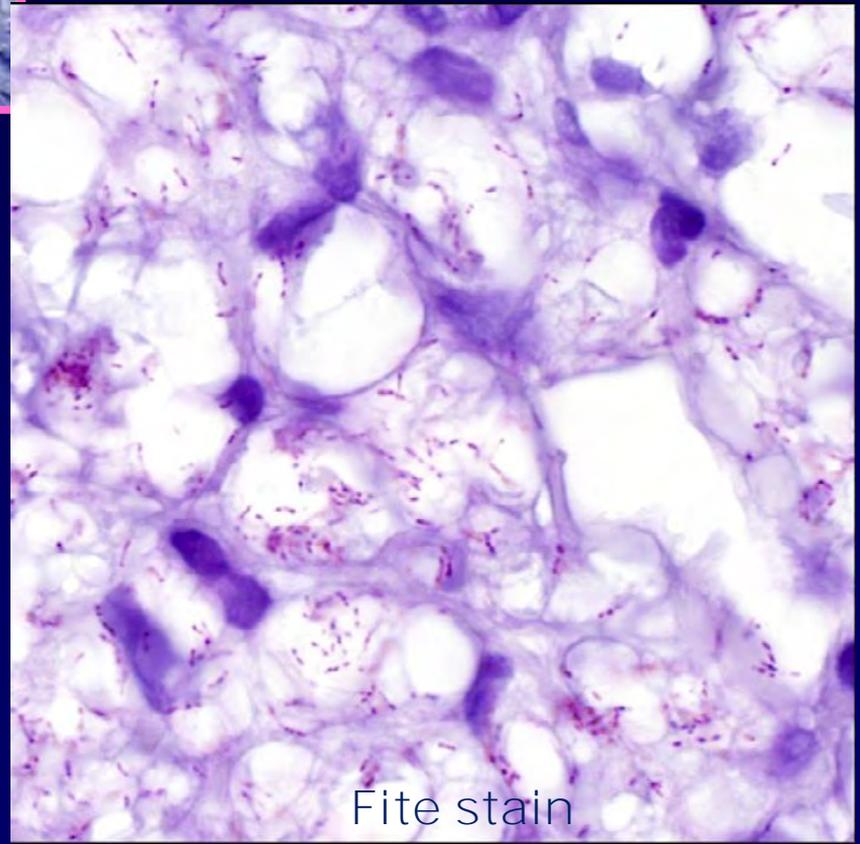
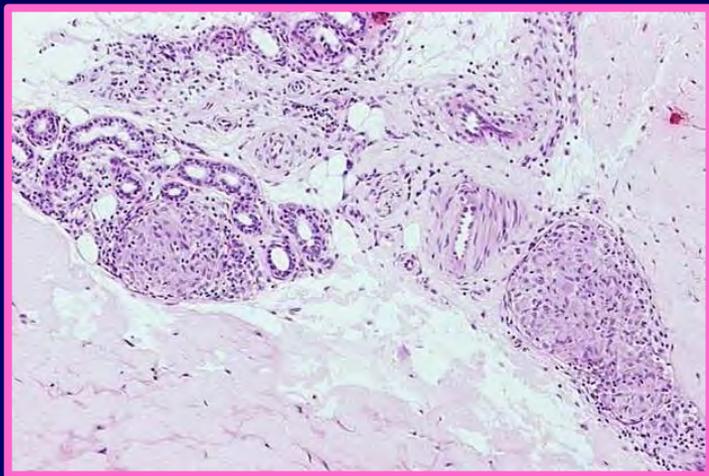
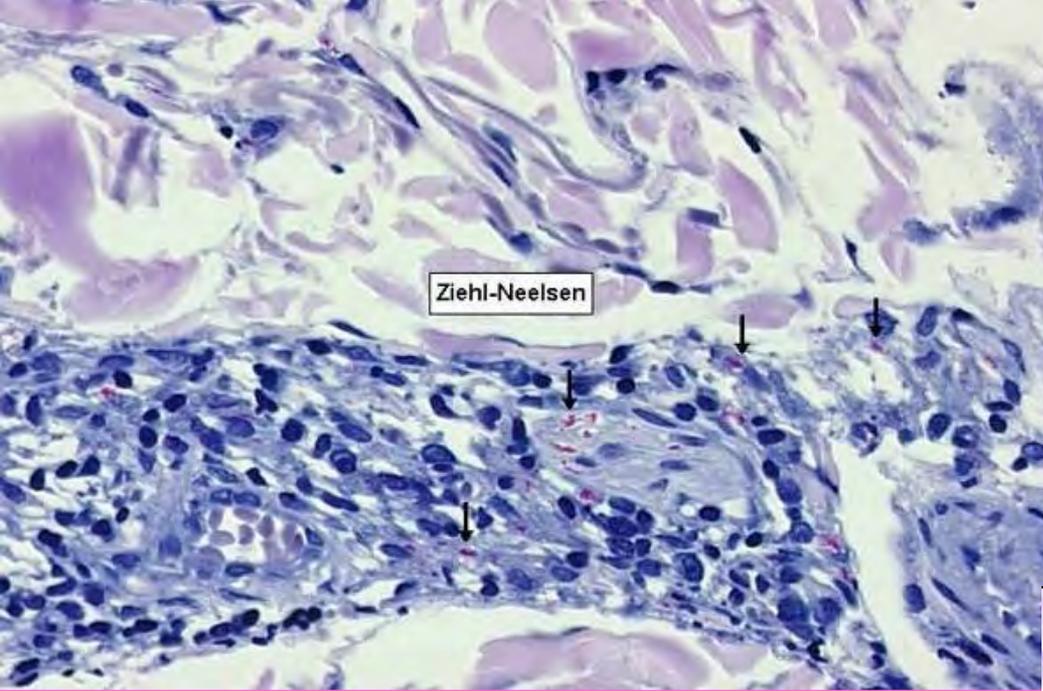


McKee

Histologically, wellformed noncaseating tuberculoid granulomas typically elongated throughout the dermis following cutaneous nerves, arrector pili muscles and sweat glands. Bacilli are absent or very scanty in the tissue.

**Erythema nodosum
leprosum: an intense
inflammatory cell infiltrate
outlines the dermal
vasculature and extends
into the subcutaneous fat.**



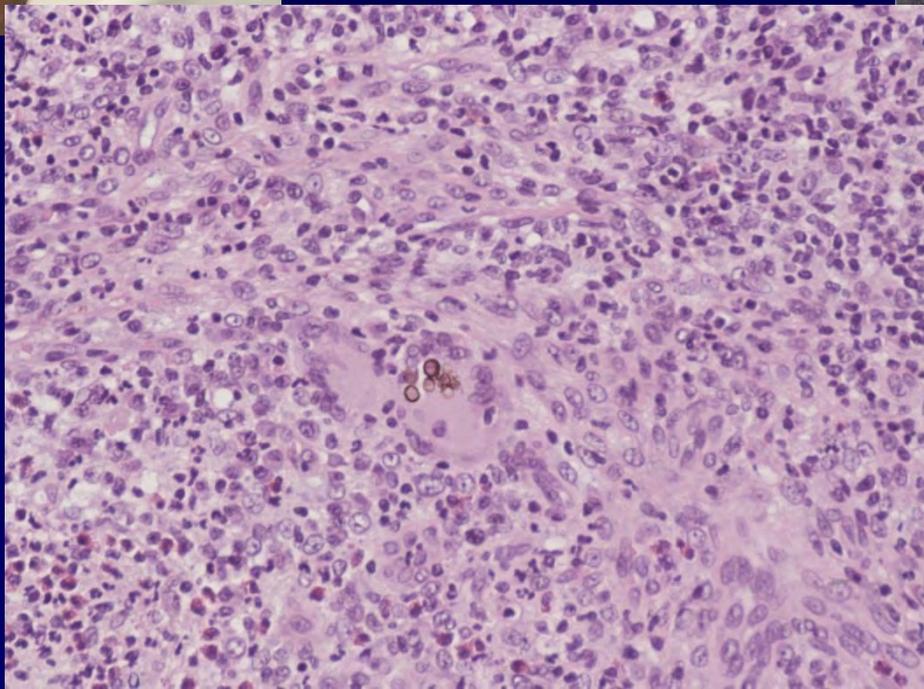


Subcutaneous fungal granulomas

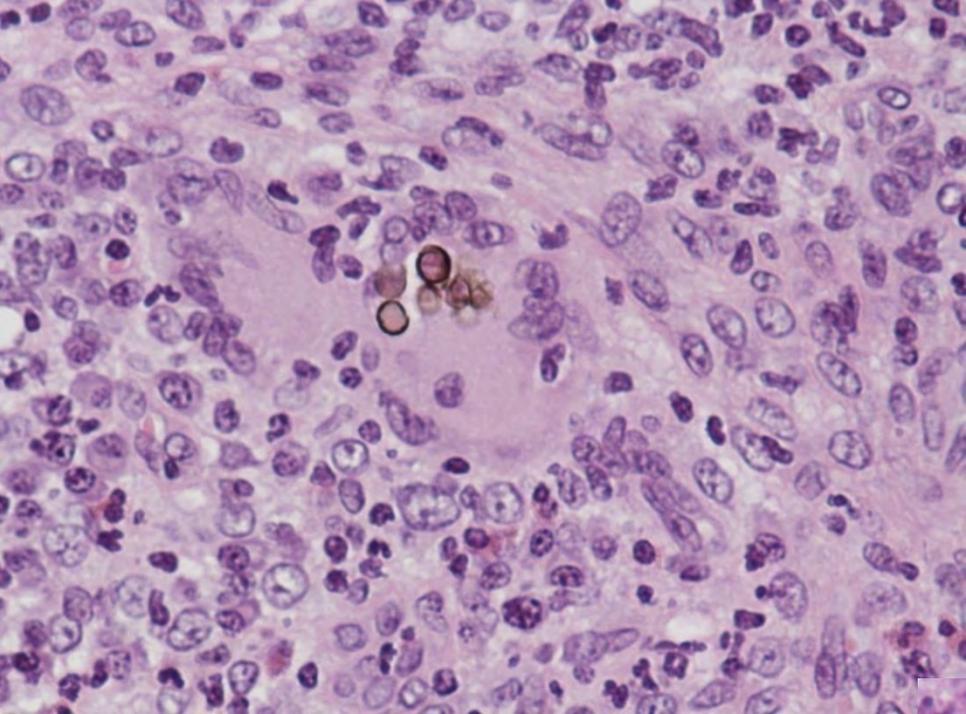
A wide variety of entities with several common histopathological features are included in this group.

Common histopathological findings include, in addition to the characteristic suppurative granulomas the presence of overlying epidermal acanthosis, pseudoepitheliomatous hyperplasia and frequent intraepidermal abscesses

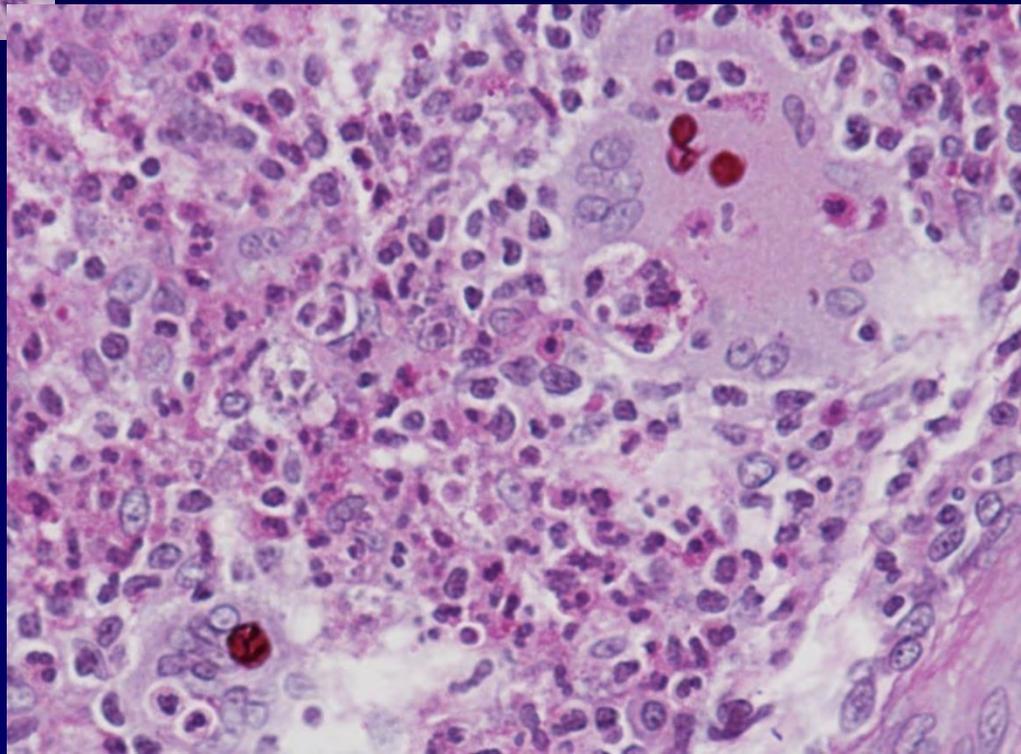
Chromoblastomycosis

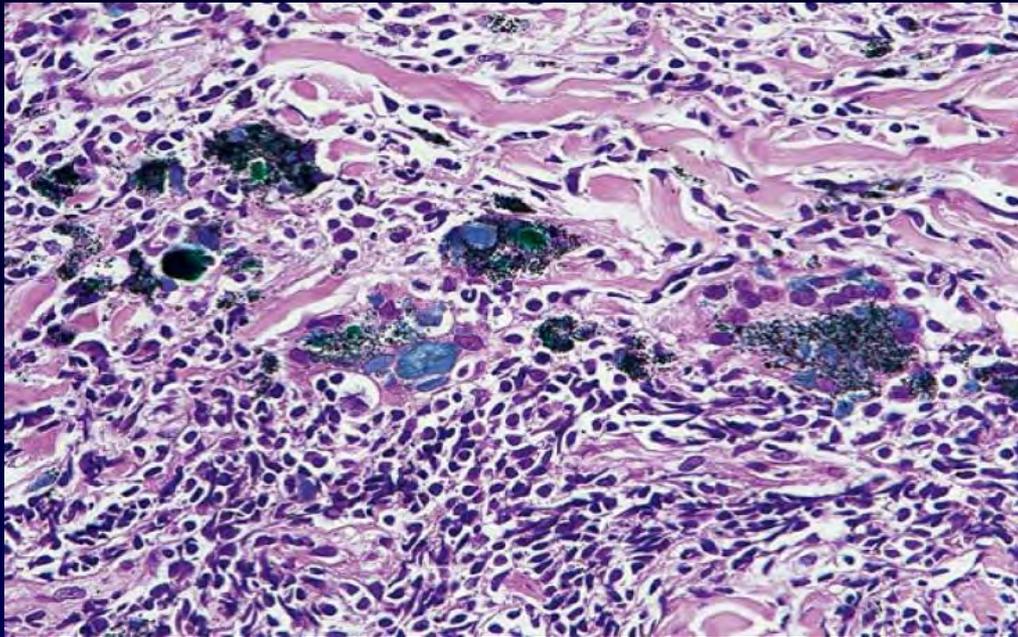


Cortesia Dott G.Soda

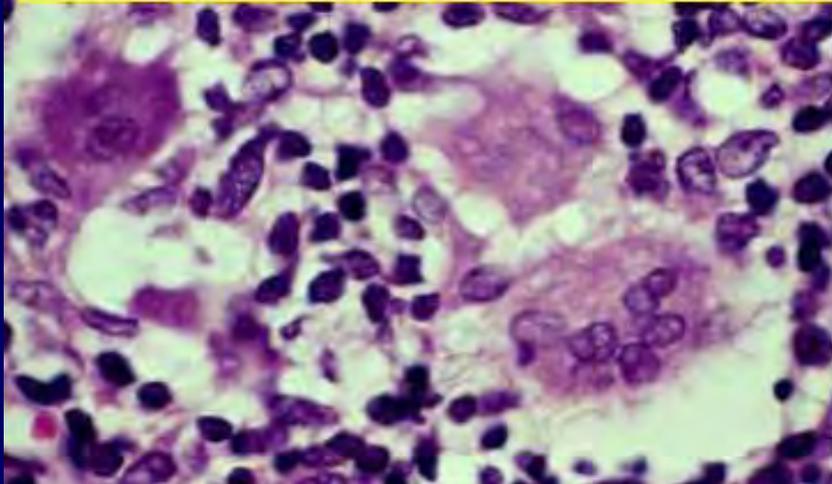


**Sclerotic bodies are
PAS positive**





Foreign body type giant cells

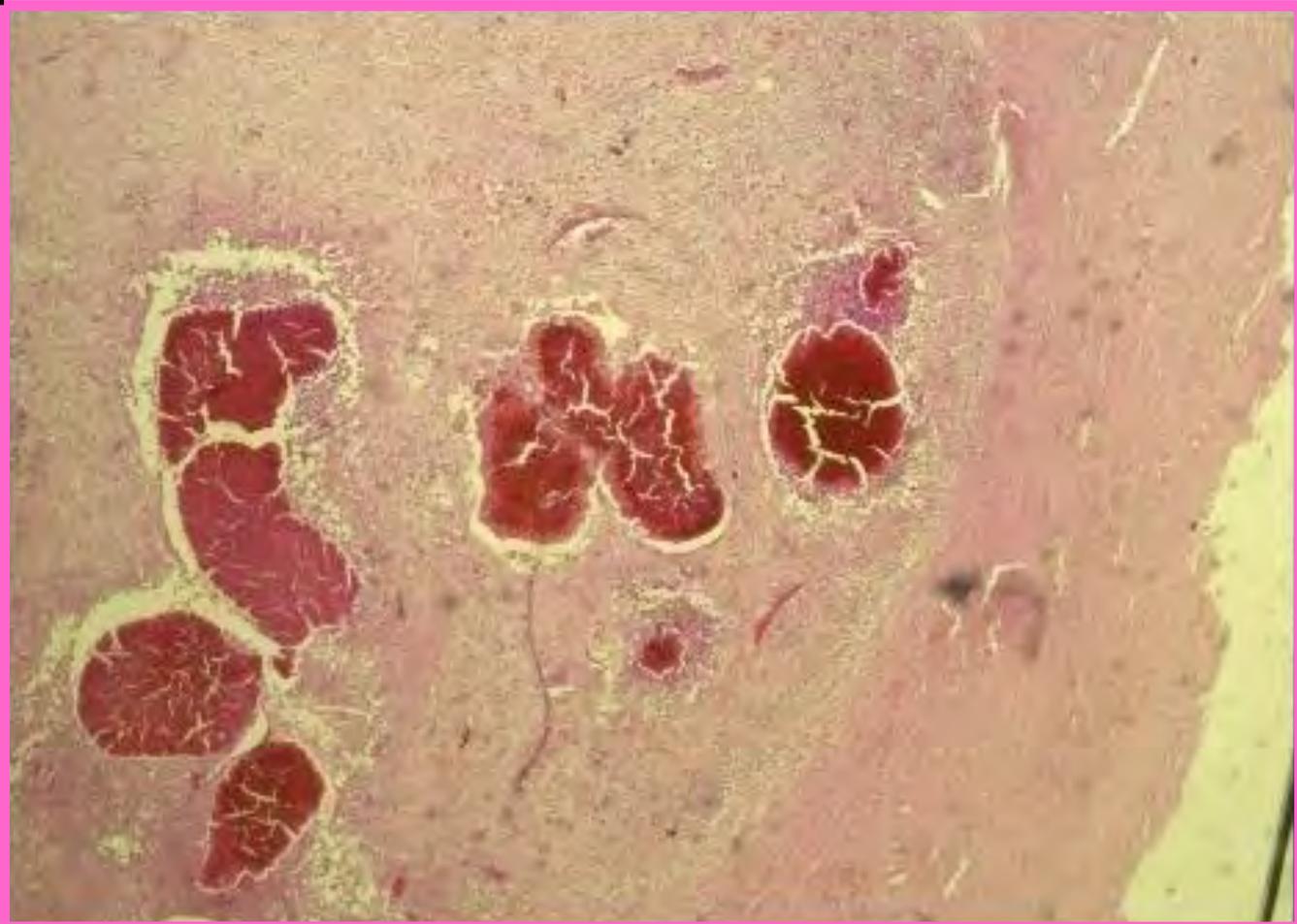


Maduromicosi

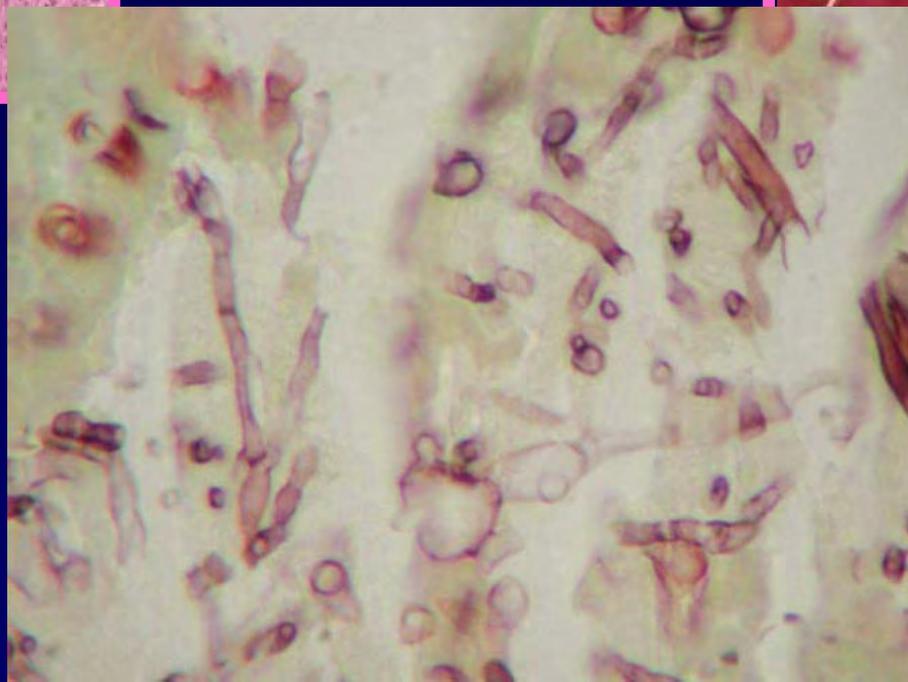
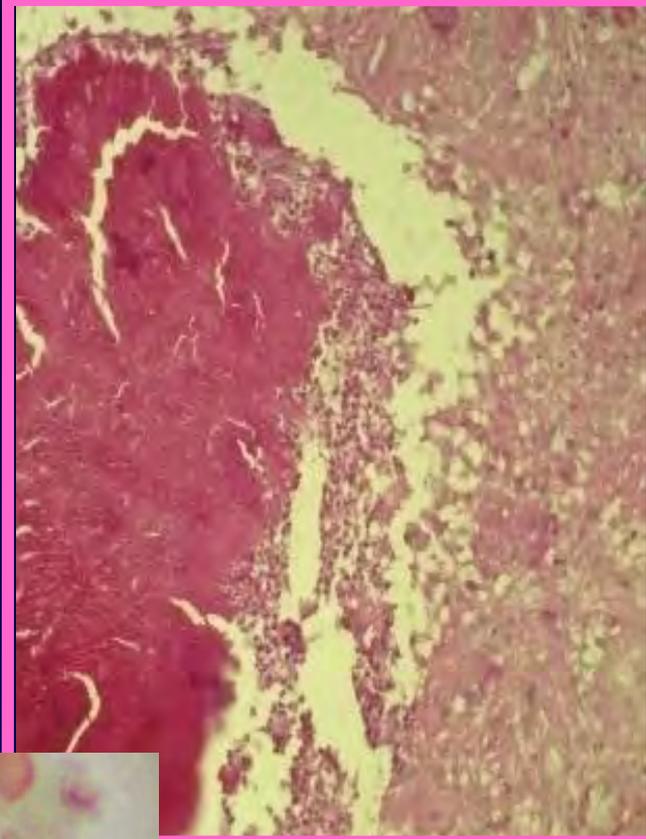
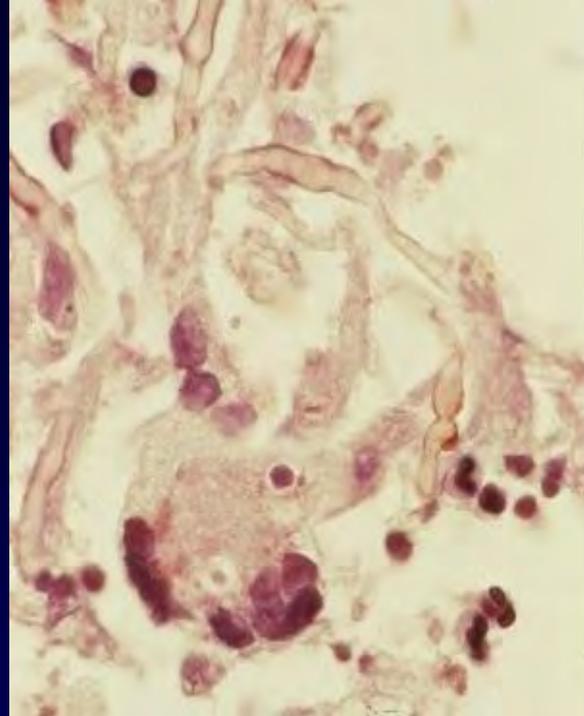


Mycetoma

- Mycetoma is a chronic, granulomatous, subcutaneous, inflammatory disease caused by true fungi (eumycetoma) or filamentous bacteria (actinomycetoma).
- Eumycetoma usually affects adult males involving limbs and other exposed body parts.
- Mycetoma due *Madurella mycetomatis* is diagnosed by clinician, and the organism was isolated from the discharging granules from the sinuses of foot.



Nodular pseudocapsulated lesion composed of lacunae filled with PAS Positive granules in the deep dermis

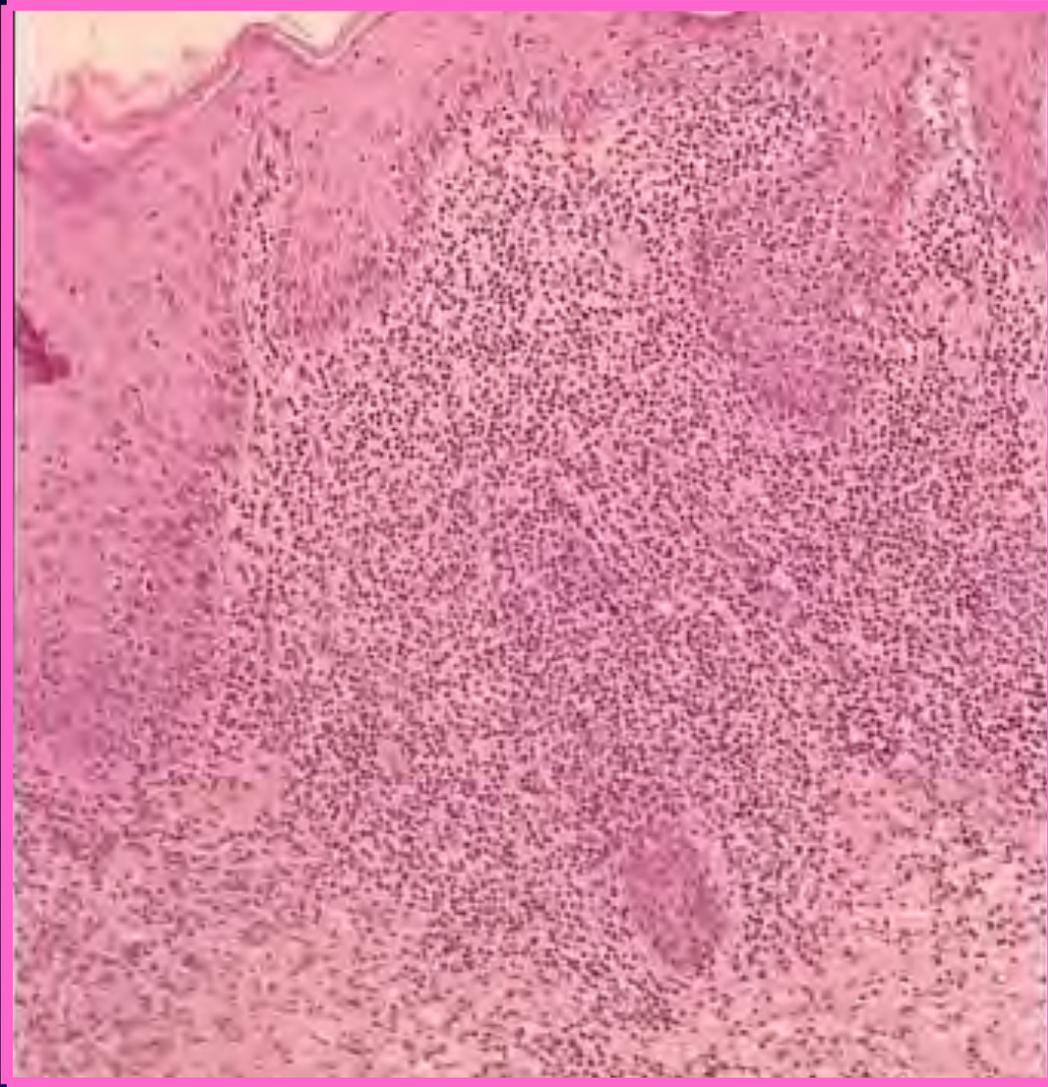


**Septate and
branching hyphae**

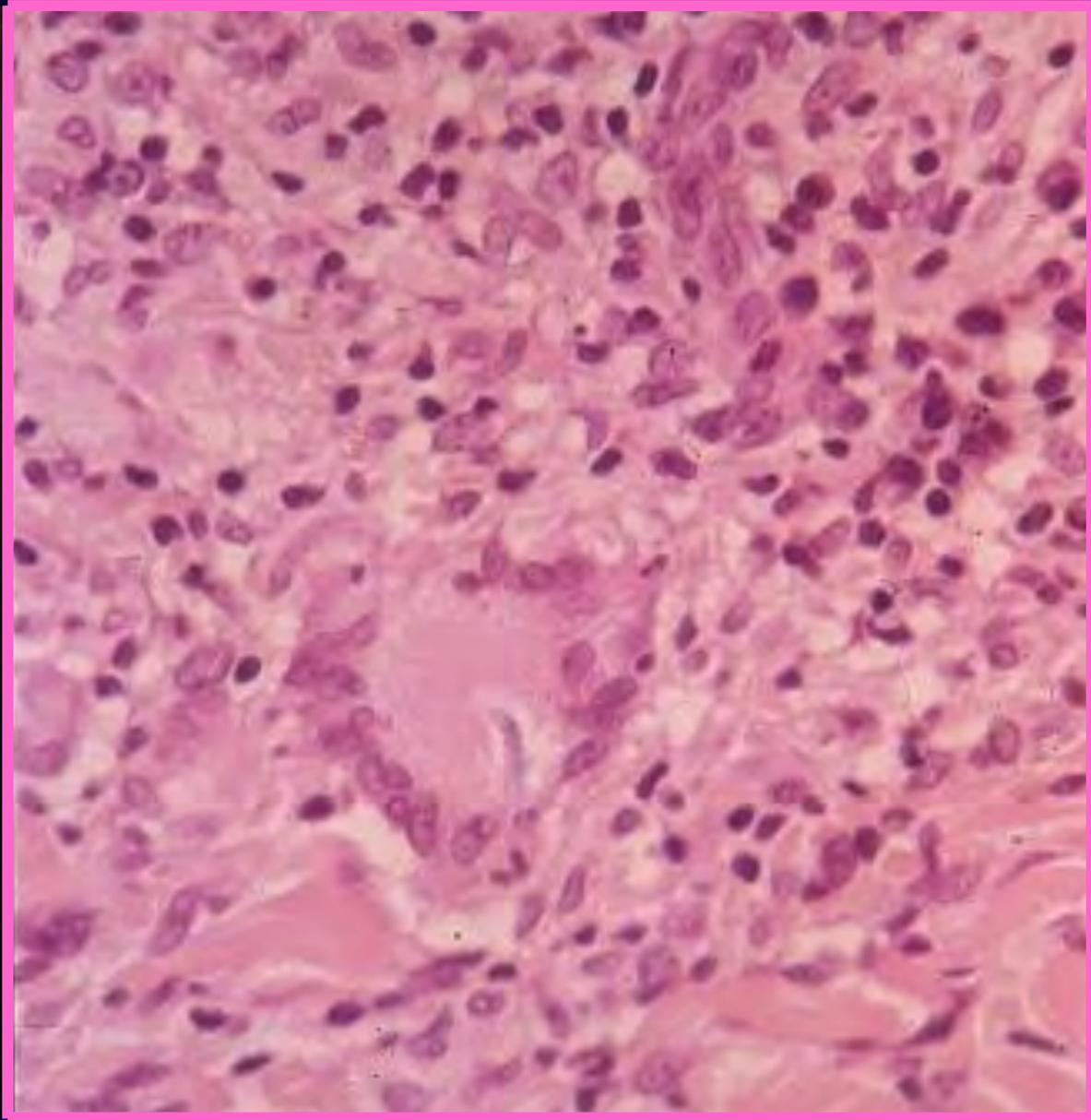
Sifilide

According to its protean spectrum of clinical manifestations, syphilis can also present a great variety of histological findings.









Plasmacells and giant cells

Conclusioni

Granulomatous skin lesions have various modes of presentation.

A classical clinical picture may not always be present.

Skin biopsies definitely help in arriving at a diagnosis, provided that a proper history and clinical correlation is available.

Special stains and dermoscopy play a supporting role.