CLINICAL ASPECTS AND DIAGNOSIS OF LEPROSY

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Agenda

- Transmission
- Risk factors
- Common clinical findings
- Rare clinical forms
- Ocular and mucosal lesions
- Leprosy reactions
- Diagnosis of leprosy
- Differential diagnosis

Introduction

- Leprosy is a chronic infectious granulomatous disease caused by *Mycobacterium leprae or mycobacterium lepromatosis* an intracytoplasmic parasite for macrophages and Schwan cells.
- Armauer Hansen discovered *M leprae*, in 1873
- The disease primarily affects the superficial peripheral nervous system and the skin, but it also may involve the upper respiratory tract mucosa, the eyes, bones, and testes.

Kundakci N et al. Clinics in Dermatology (2019) 37, 200–212

Talhari C et al. Clinics in Dermatology 2015, 33; 26-37.

Transmission

- The mechanism of transmission is dependent on the infectivity of the host and the proximity, frequency, and duration of contact.

- Upper respiratory secretions are the most common route of transmission, though skin contamination and vertical transmission have been rarely reported.

- The incubation period typically range from 3 to 5 years for tuberculoid leprosy and 9 to 12 years for lepromatous leprosy.

- Most individuals exposed to the organisms do not develop clinical symptoms.

Risk Factors

- Close contact with a recently diagnosed patient, especially patients with polar lepromatous leprosy (LL)/multibacillary leprosy (MB).

- Humans are the primary carriers of infection *with M leprae,* apart from the Americas, where the armadillo also serves as a zoonotic reservoir.

Armadillo

Risk factors

- Age between 5 to 15 years and >30 years at the time of exposure.
- Immunosuppression and immunodeficiency.
- Genetic predisposition.

Maymone MBC et al. J Am Acad Dermatol 2020;83:1-14

COMMON CLINICAL FINDINGS

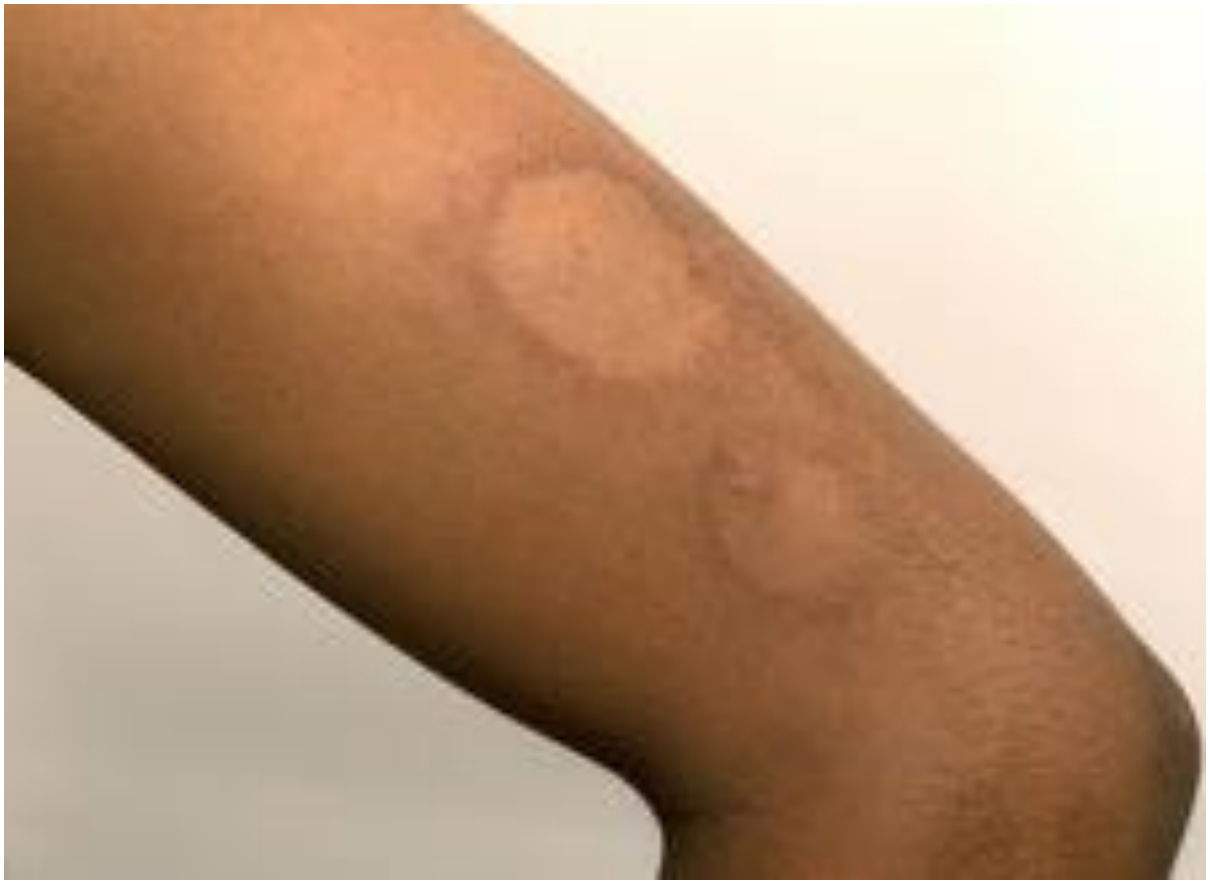
CLASSIFICATION OF LEPROSY						
Clinical findings	LL	BL	BB	BT	TT	I
Type of lesions	Macules, papules, nodules, diffuse infiltration	Macules, papules, plaques, infiltration	Plaques and dome-shaped, punched-out lesions	Infiltrated plaques	Infiltrated plaques, often hypopigmented	Macules, often hypopigmented
Number of lesions	Numerous	Many	Many	Single, usually with satellite lesions, to more than 5	One or few (up to 5)	One or few
Distribution	Symmetric	Tendency to symmetry	Evident asymmetry	Asymmetric	Localized, asymmetric	Variable
Definition	Vague, difficult to distinguish normal versus affected skin	Less well-defined borders	Less well-defined borders	Well-defined, sharp borders	Well-defined, sharp borders	Not always defined
Sensation	Not affected	Diminished	Diminished	Absent	Absent	Impaired
Bacilli in skin lesions	Many (globi)	Many	Many	Few (1+), if any, detected	None detected	Usually none detected

Tuberculoid Leprosy

- In general, patients with TT have a robust cell-mediated (TH1) response against the M leprae complex and therefore a less severe disease course.

- TT is characterized by the presence of a single or few hypopigmented, hairless, hypo- or anesthetic, well-defined macules or plaques.

Tuberculoid leprosy



Bordeline tuberculoid leprosy

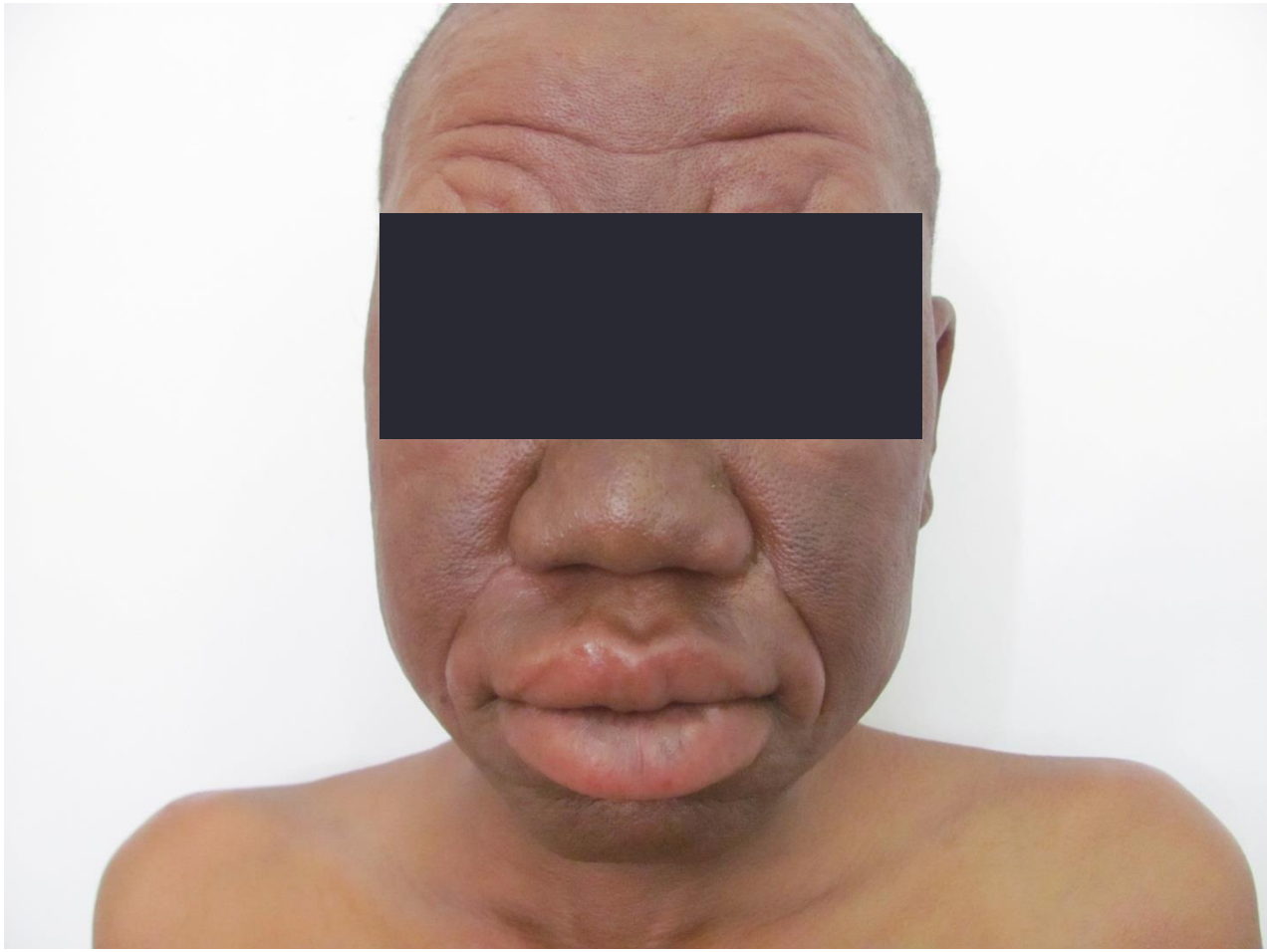
- BT is an immunologically unstable state in between TT and LL disease. This group includes BT, BB, and BL, with the vast majority of patients with leprosy falling within this category.

Lepromatous leprosy

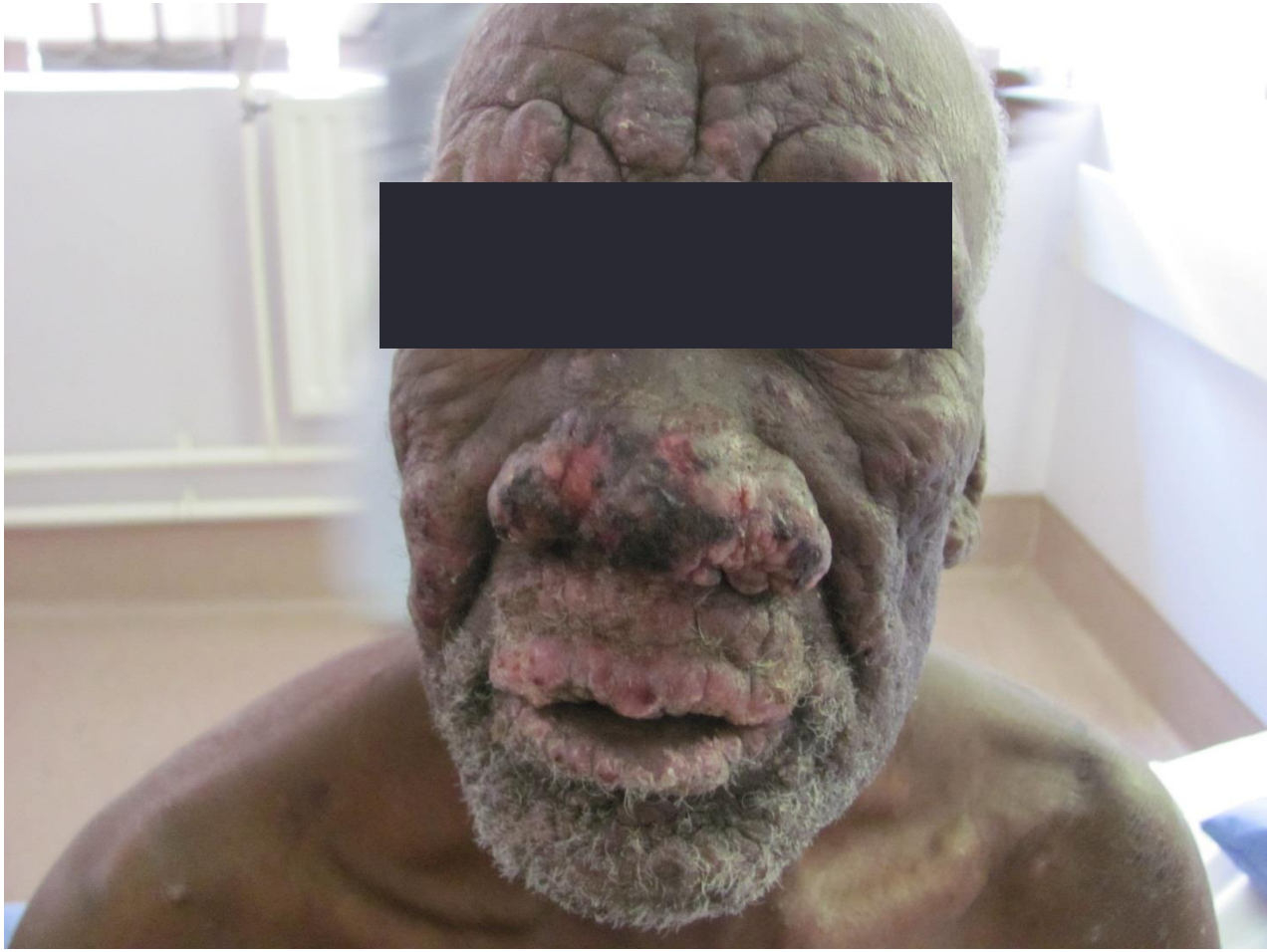
- At the end of the spectrum, patients with LL seemingly lack a cellular-immune response to the M leprae complex, leading to widespread disease and numerous lesions that may affect multiple organ systems, including the kidney and testes.

- Additional signs and late sequelae include madarosis, saddle nose, infiltration of both earlobes, and acquired ichthyosis on the lower extremities.

Lepromatous leprosy



Lepromatous leprosy



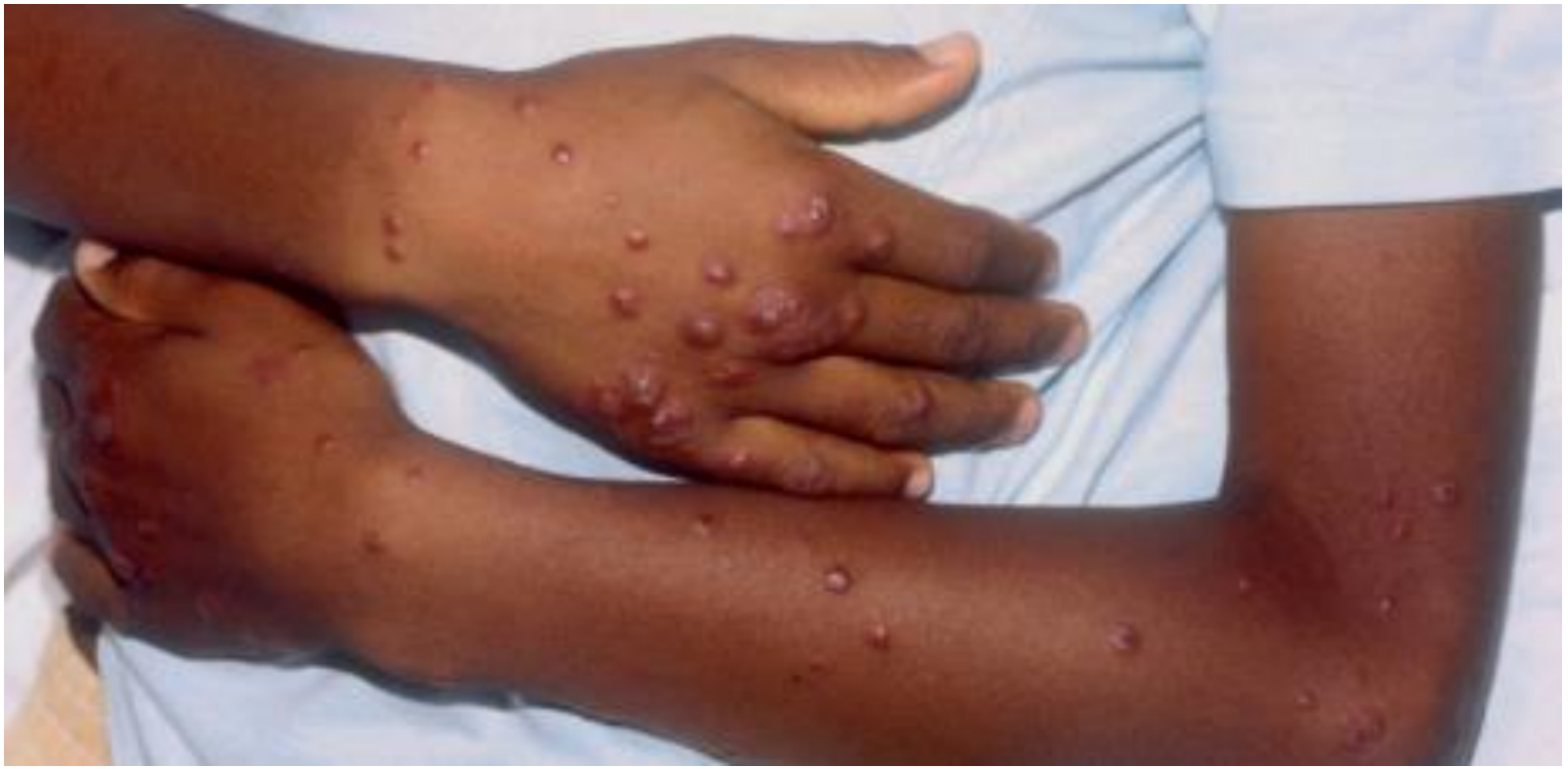
RARE CLINICAL FORMS

Histoid leprosy

- Present with bright copper-reddish nodules usually located in unconventional areas, such as the lower back, axilla, waist, chest, and neck.
- Histoid leprosy is seen during relapses in patients successfully treated with dapsone for a long period.
- The bacilli in these lesions are dapsone resistant.
- Rarely, histoid nodules can occur in patients who have not previously been treated.

Kundakci N et al. Clinics in Dermatology (2019) 37, 200–212

Histoid leprosy



Lucio leprosy

- The entire body has a uniform, diffuse, and bright infiltration.
- When the disease progresses, diffuse thickening of the eyelids gives the patient a sleepy or sad appearance.
- The first clinical manifestation is often madarosis.
- There may be mild anemia, numbness and edema of the hands and feet, nasal congestion, epistaxis, and hoarseness.
- This type of leprosy is associated with the Lucio phenomenon.

Pure neural-type leprosy

- Leprosy can sometimes appear with only peripheral neuropathy without any skin signs.

- This very rare type of leprosy is called neural-type leprosy or pure neural leprosy.

- Because there are no other skin lesions, the diagnosis is difficult and is usually made by biopsy of sensorial nerves, such as the sural and superficial radial nerves.

Goulart IMB et al. Dermatol Res (2008) 300:269–290

OCULAR AND MUCOSAL LESIONS

Ocular involvement

- Can lead to significant ocular complications, the most common being diminished lid closure (lagophthalmos) exposure keratitis (facial nerve involvement), impaired corneal sensation, cataracts, and iris atrophy (direct invasion by bacilli and its sequels).

- Patients with lepromatous leprosy (BL or LL) appear to have greater chance of developing ocular complications when compared with those classified as BB, BT, or TT.

Nasal and oral mucosal involvement

- The nasal mucosa is commonly involved during lepromatous disease and is often the entryway of the M leprae complex.
- Symptoms include nasal obstruction, epistaxis, septal perforation, and saddle nose deformity, which are more often seen in patients with LL.
- Oral mucosal lesions in leprosy are thought to be secondary to respiratory tract transmission and the prevalence varies among studies from 11.5% to 57%.
- Oral lesions. are nonspecific, manifesting as asymptomatic, erythematous macules, papules or nodules that eventually ulcerate, involving the soft and hard palate, posterior tongue, and gingivae.

de Abreu MA, Michalany NS, Weckx LL et al. Braz J Otorhinolaryngol. 2006;72:312-316.

LEPROSY REACTIONS

Leprosy reactions

- In about half of the patients, inflammatory conditions called “reactions” develop during the clinical course of the disease.

- These inflammatory reactions are due to the immunologic response of the host to the bacilli.

Type I leprosy reaction (reversal reaction)

- This type of reaction is related to delayed type hypersensitivity and is seen in TT and borderline (BT, BB, or BL) leprosy patients with immunologic recovery during or after treatment.

- Clinical manifestations include thickening of the nerves, neuralgia, edema on the face and extremities, exacerbation of preexisting skin lesions, and emergence of new skin lesions.

- Acute neuritis can cause loss of nerve functions.

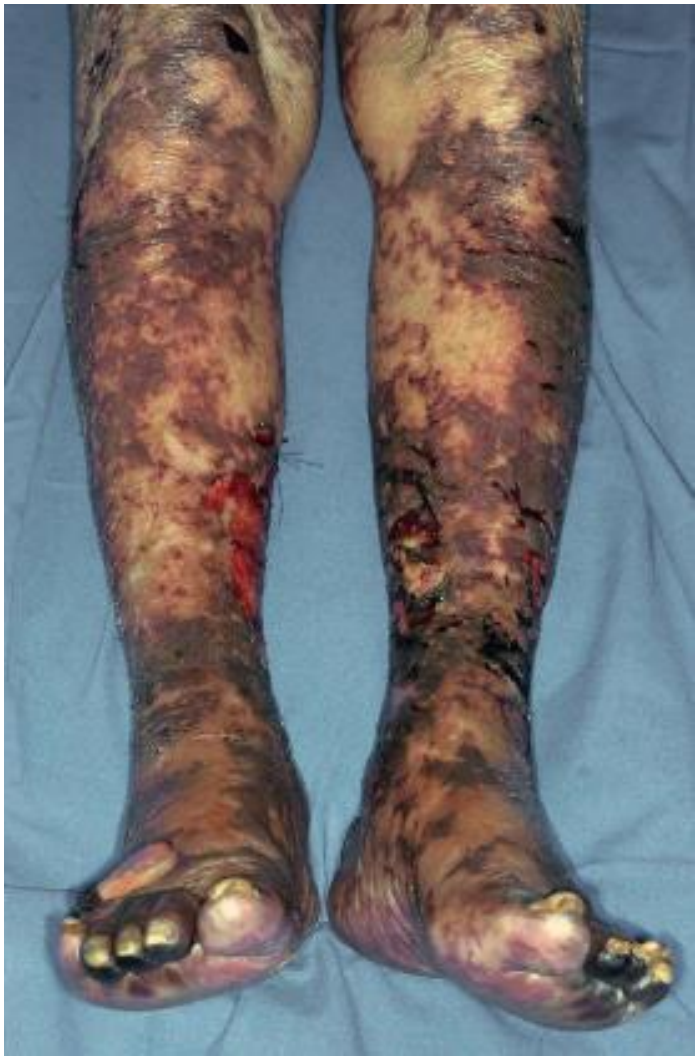
Type one leprosy reaction

Type II leprosy reaction (erythema nodosum leprosum reaction)

- Type II leprosy reaction (T2 R) is seen in LL and BL patients under treatment.
- The mechanism involves cytokine pattern and formation of immune complexes and may be accompanied by cell-mediated immunity.
- T2 R is a cutaneous and systemic small-cell vasculitis and can affect any tissue containing leprosy antigens.
- Fever, malaise, arthralgia or arthritis, erythemanodosum-like skin lesions, iridocyclitis, glomerulonephritis, epididymoorchitis, lymphadenitis, and hepatosplenomegaly are the main clinical manifestations.

Type III reaction (Lucio's phenomenon)

- Patients with diffuse lepromatous leprosy (Lucio leprosy), seen in Central and South America, may develop the Lucio phenomenon, a thrombotic phenomenon, in addition to small vessel vasculitis.



Three cardinal diagnostic criteria for leprosy

1. Hypopigmented or reddish skin lesions with loss of sensation

2. Involvement of the peripheral nerves, as demonstrated by their thickening and associated loss of sensation

3. Skin-smear positive for acid-fast bacilli

Guidelines for the diagnosis, treatment and prevention of leprosy ISBN: 978 92 9022 638 3

Leprosy diagnosis

- There is no laboratory test that alone can make a diagnosis of leprosy.

- Patient history
- Clinical examination,
- Assessment of peripheral nerve damage
- Laboratory evaluations

Patient history

- For the diagnosis of leprosy, history of contact with a lepromatous patient has vital importance.

- Taking a thorough history, including travel to or residence in a country where leprosy is endemic, is crucial when considering a diagnosis of leprosy.

Skin lesions

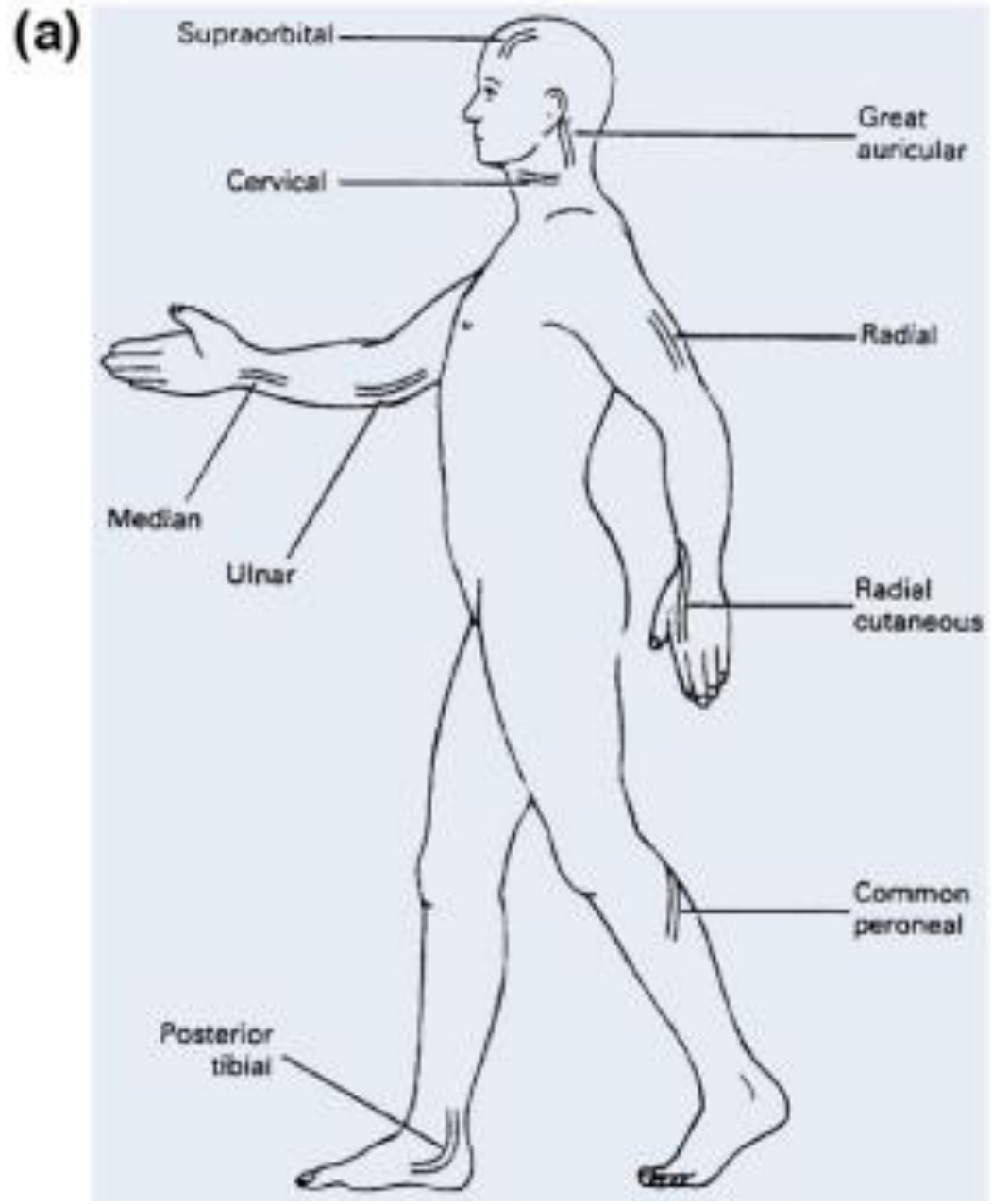
- Skin lesions are present in all clinical forms. These are macular, papulo-nodular, or plaque-type lepromatous lesions.

- The most prominent features of skin lesions are dryness, loss of sweating, hair loss, and sensory loss.

- *M leprae* has an affinity for cooler body parts, a distribution that is localized to digits, extremities, earlobes, the central face, or the extensor surfaces of the forearms or thighs is more indicative of leprosy.

Findings of peripheral nerve involvement

- Leprosy primarily affects the peripheral nerves.
- Assessment of peripheral nerve thickening and loss of sensation both on skin lesions and on the skin areas that are innervated by the peripheral nerves.


(a)
Supraorbital
Great auricular
Cervical
Radial
Median
Ulnar
Radial cutaneous
Common peroneal
Posterior tibial

Radiologic examinations

- Radiologic examinations, such as, ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI), and electroneuromyography, can be used to evaluate peripheral neural involvement.

- Nerve biopsies (sural nerve biopsy) can be performed for the diagnosis of primary neural leprosy.

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Skin smear microscopy

- M leprae multiplies more easily in the cooler parts of body.
    - the outer parts of the eyebrows, chin, and ear lobes
    - outer surface of the fingers and toes
    - relatively cold skin areas such as elbows, knees, and nasal mucosa

Skin smear microscopy

- At the outset, the skin area is wiped with an alcoholic cotton, and a skinfold is gripped firmly between thumb and index finger to prevent bleeding.
- An incision of 5 mm in length and 3 mm in depth is made with a scalpel, and the blade is turned at the right angle several times within the incision.
- Dermal tissue collected on the blade is smeared on a glass slide.
- For nasal mucosa, nasal swabs can be obtained by the aid of a curette or dry swab cotton.
- The smear is fixed and stained with Modified-Ziehl-Neelson (EZN).

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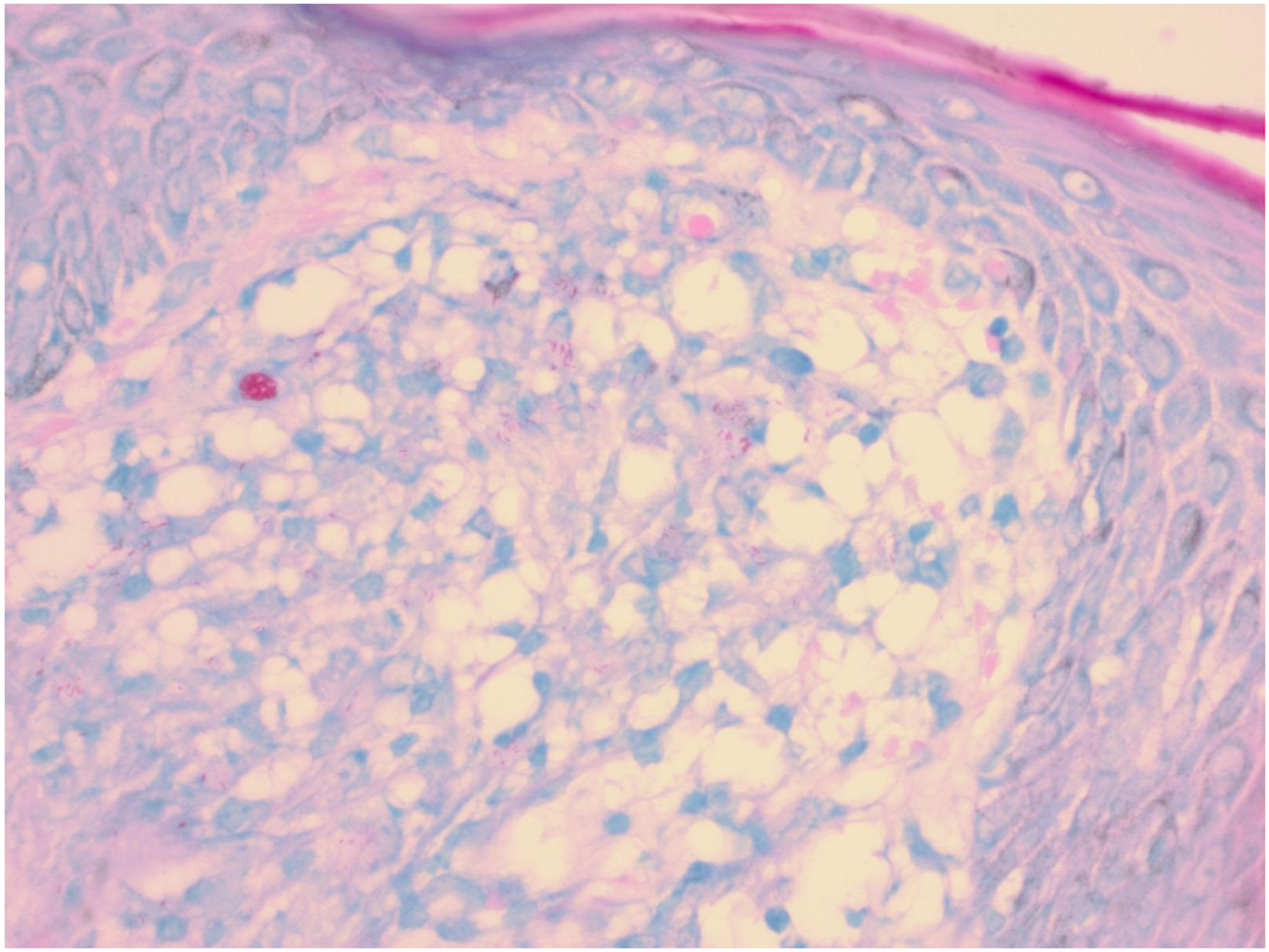
Dermatopathologic diagnosis

- Histopathologic features can be extremely useful in classifying the type of leprosy and identifying the presence of a leprosy reaction.

Lepromatous leprosy



Polymerase chain reaction (PCR)

- PCR is typically used to support a clinical diagnosis of leprosy, in most endemic countries it is an expensive and labor-intensive technique and is not routinely performed.

Other laboratory investigations

- The antibody titre against phenolic glycolipid 1(PGL-1) a cell wall species-specific glycolipid, is useful in MB leprosy. However, this test may be positive in contacts and negative in PB leprosy. It helps to classify leprosy into PB and MB and it can be used to follow the effect of treatment in MB patients and to detect relapses.

- Lymphocyte transformation or Interleukin (IL)-c or IL- 2 release essays against different antigenic determinants have been a disappointment up to now, at least for diagnostic purposes.

- The lepromin test (Mitsuda), an old test, is positive in PB leprosy and negative in MB leprosy. However, it can be positive and negative in healthy people. Thus, it helps only with the classification.

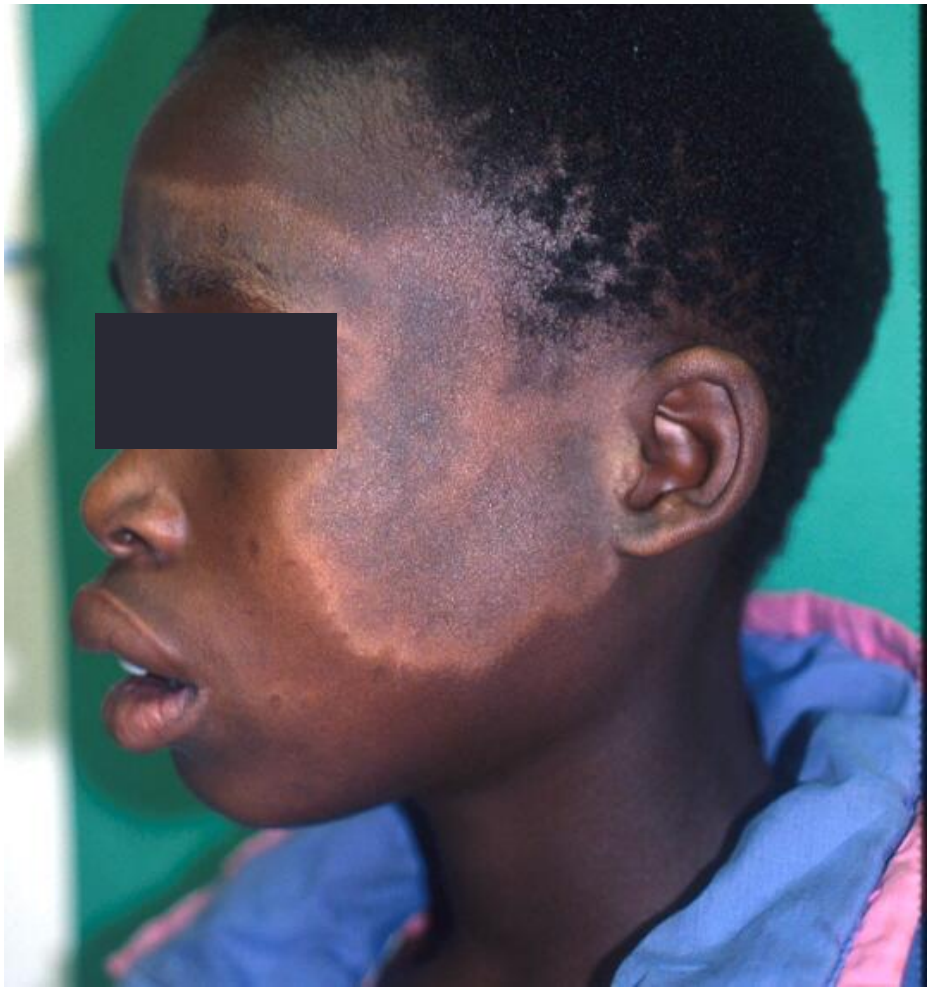
Alemu Belachew WM et alJEADV 2019, 33, 1205–1213

DIFFERENTIAL DIAGNOSIS

Differential diagnosis of Indeterminate and tuberculoid leprosy

- Pityriasis alba
- Segmental vitiligo
- Acquired postinflammatory hypopigmentation,
- Nummular eczema,
- Tinea versicolor

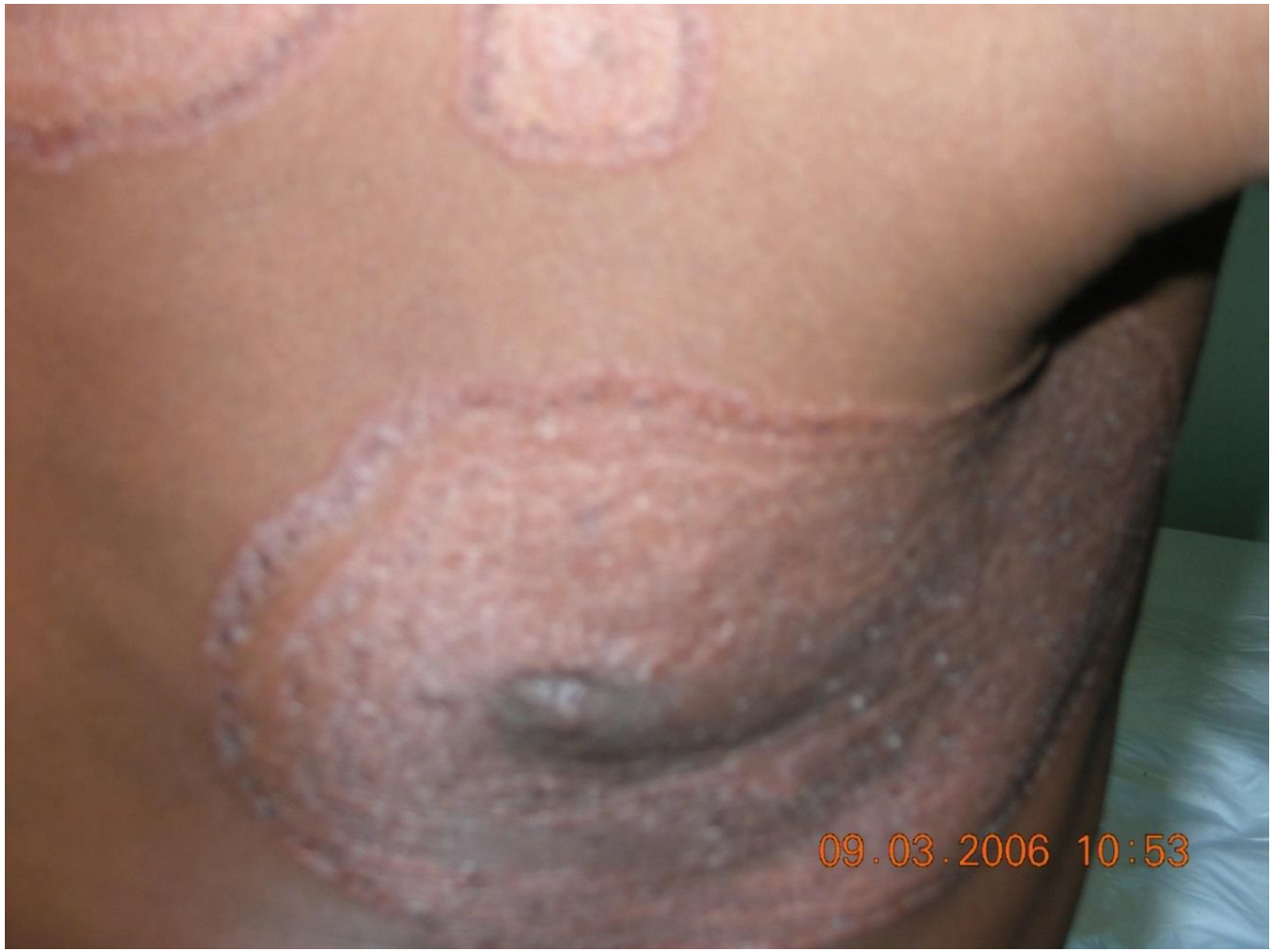
Pityriasis alba



Differential diagnosis of Borderline tuberculoid

- Granuloma annulare
- Sarcoidosis
- Tinea corporis
- Psoriasiform eruptions
- Erythema annulare centrifugum

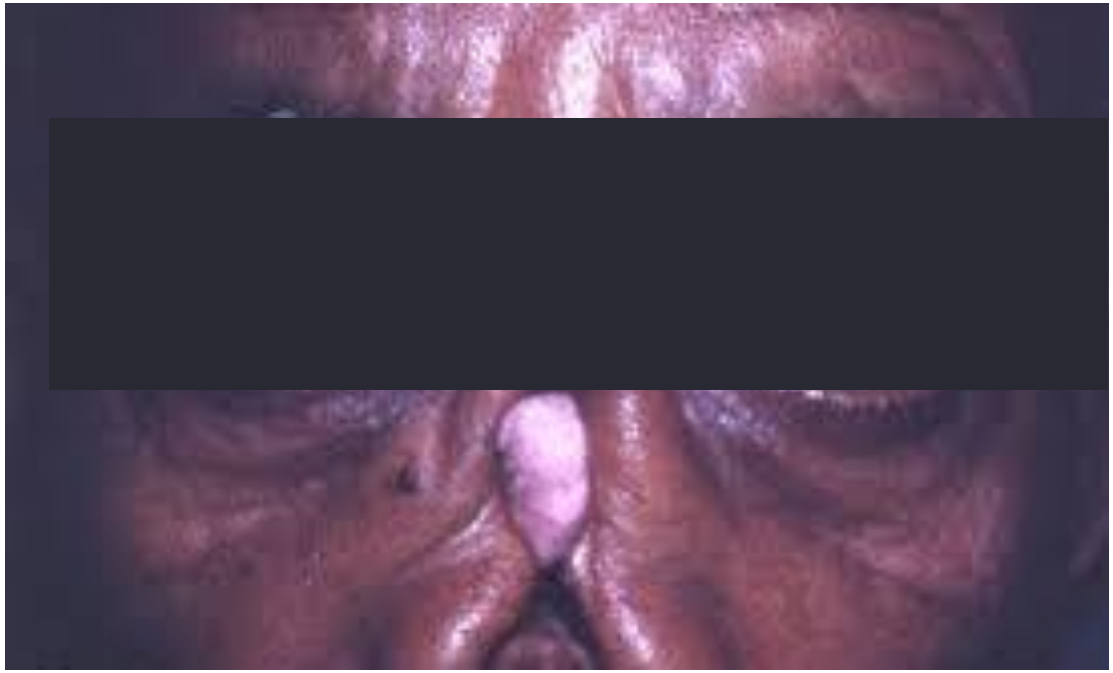
Tinea corporis

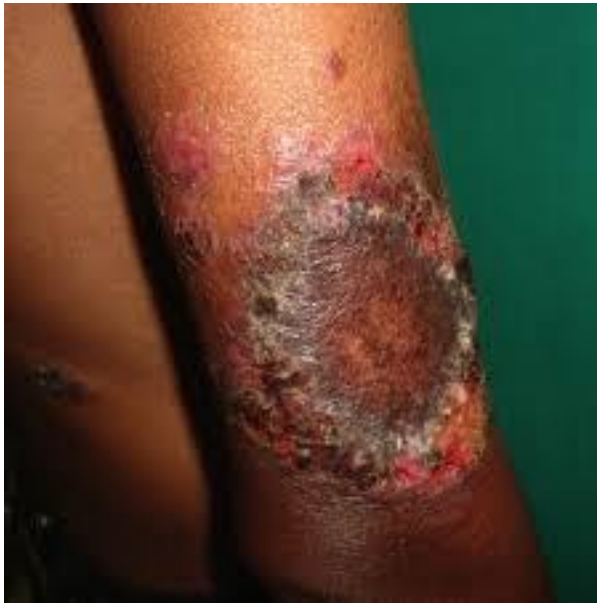


Differential diagnosis of Mid-borderline, borderline and polar lepromatous leprosy

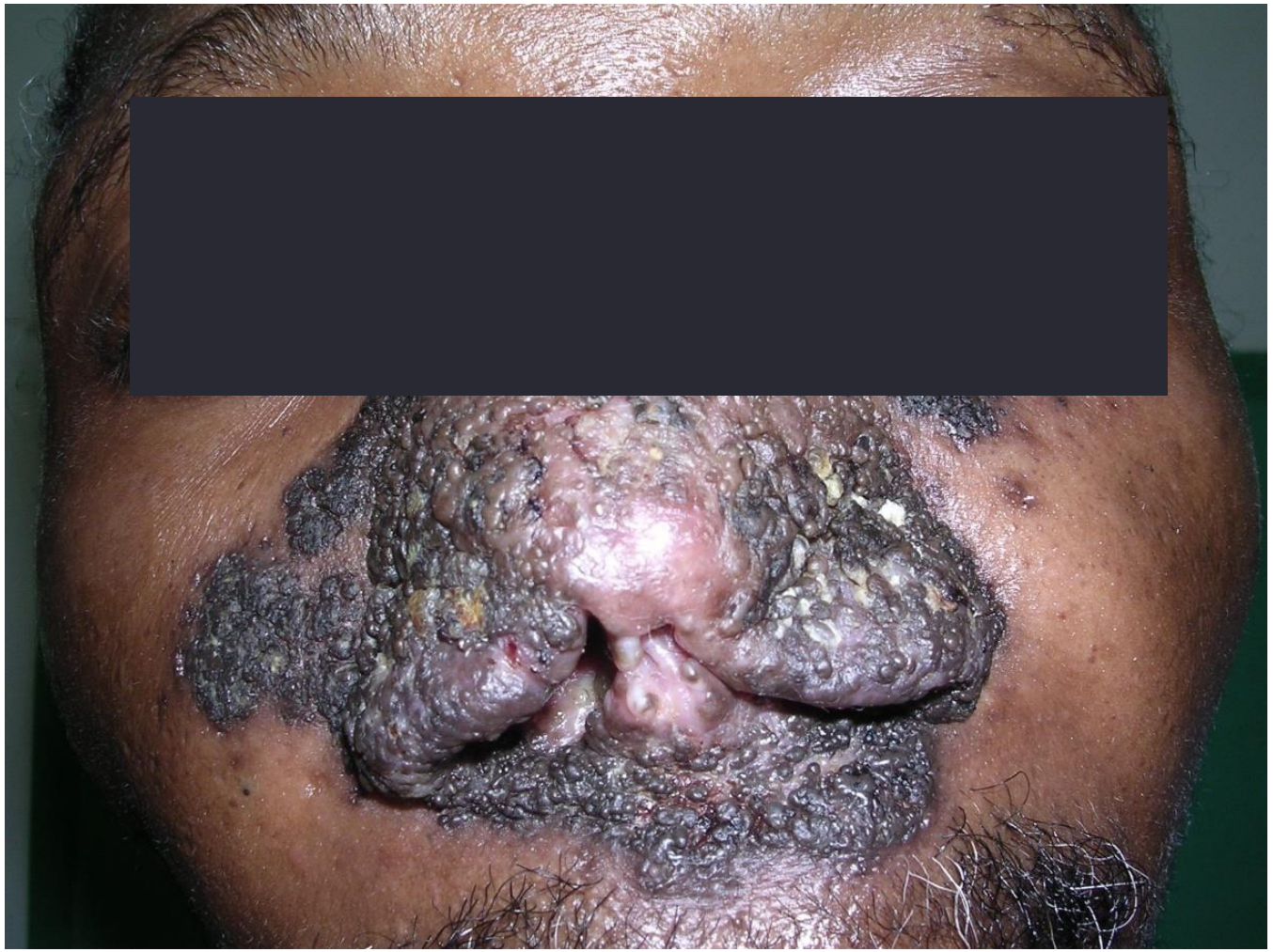
- Necrobiotic xanthogranuloma,
- Late syphilis
- Mycosis fungoides
- Juvenile xanthogranulomatosis,
- Leishmaniasis
- Tuberculosis
- Sarcoidosis

Tertiary syphilis

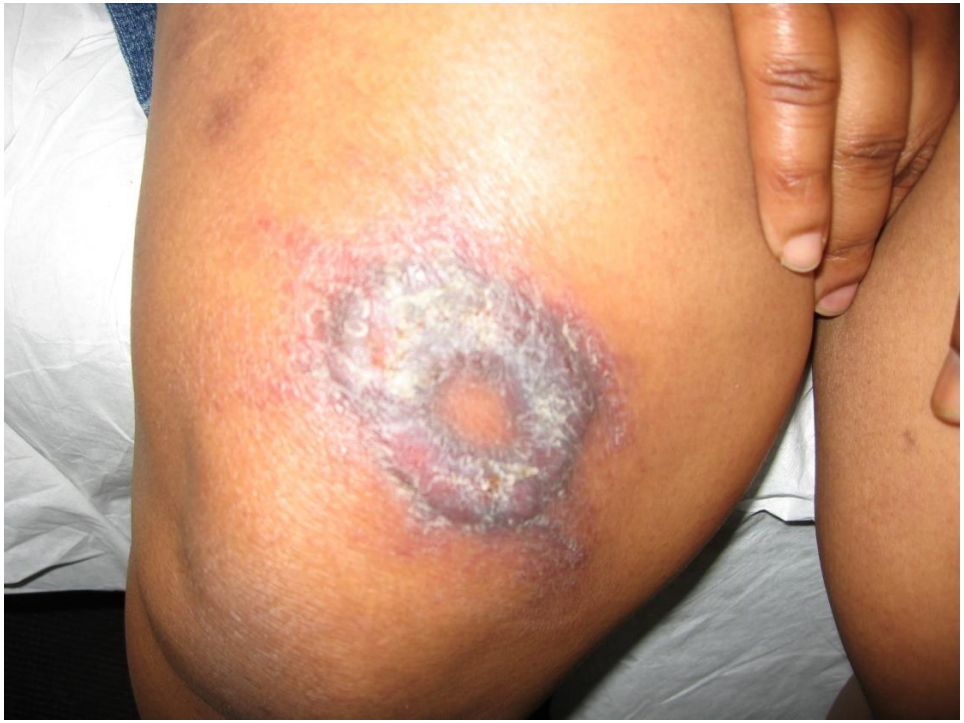


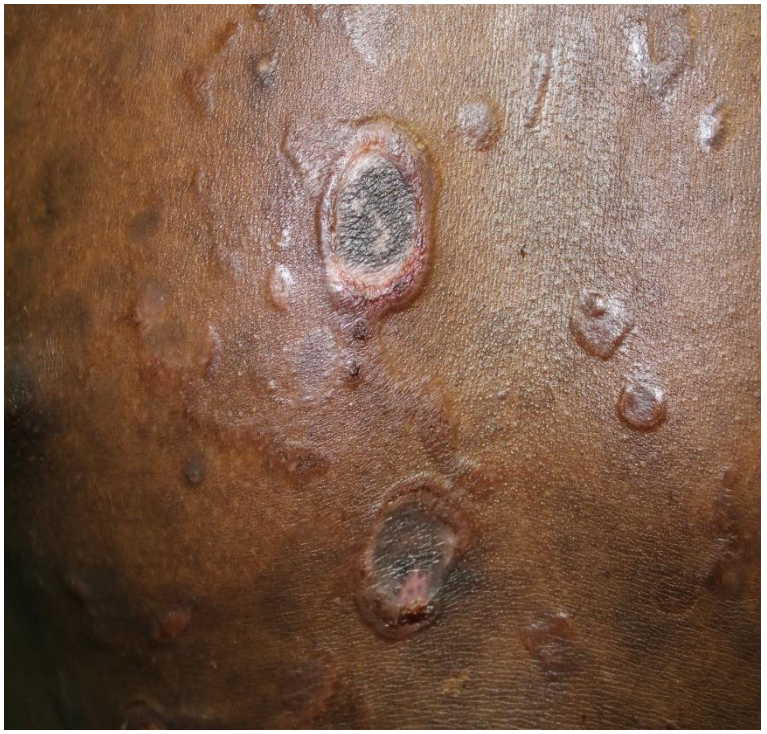


Lupus vulgaris- Cutaneos TB



Cutaneous T cell lymphoma





Differential diagnosis of Pure neural leprosy

- **Differential diagnosis in a single nerve destruction** Surgical trauma, bone fractures, nerve tumors, compression neuropathies compression (carpal tunnel syndrome, cervicobrachial syndrome and others)

- **Differential diagnosis in multiple nerve destruction** Hereditary sensory neuropathy (Thevenard's syndrome), Dejerines Sottas disease, neurogenic musculoskeletal atrophy (Tooth-Charcot-Hoffman), syringomyelia, Gullian Barre syndrome, primary amyloidosis of nerves, other polyneuropathies.

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Conclusion

- Leprosy is a mutilating and stigmatizing disease with a low rate of infectivity and a wide range of clinical presentations.
- Keep in mind the “many faces of leprosy” to prevent misdiagnosis.
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Thank you