Rakel RE, editor. Saunders Manual of Medical Practice. 2nd edition. WB Saunders; 2000

263 Leprosy

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Etiology and Epidemiology

1. Geographic: Although discovered by Hansen in Norway in 1873, the acid-fast bacillus *Mycobacterium leprae* now is transmitted mainly in developing nations. Leprosy is seen in immigrants from such countries and occasionally in U.S.-born persons from Hawaii and the Gulf Coast states. About 150 to 200 new cases are diagnosed in the United States each year, adding to the 5000 to 6000 previously diagnosed persons living in the United States.
2. Agent-host interaction: Three "basic science" facts about *M. leprae*, along with the spectrum of human immunologic response to it, determine clinical findings in leprosy:
   a. Slow growth, with a "doubling time" of 12 to 21 days
   b. Optimal growth at 82° F (28° C), favoring invasion of cooler body areas
   c. Affinity for nerves, especially in these cooler areas
3. Transmission from upper airways of untreated multibacillary cases results in secondary cases 2 to 8 or more years later in 5 to 7 per cent of close household contacts. Conversely, most new cases of leprosy have no obvious source case.

Symptoms

1. Leprosy should be considered in any person from an endemic area who has persistent unexplained findings in skin, upper airways, eyes, or peripheral nerves, especially in the limbs. All of these are cooler areas of the body.
2. These findings vary considerably, determined by the patient's placement on a five-type clinical continuum from multibacillary (lepromatous; LL) to paucibacillary (tuberculoid; TT) (see Table 263–1).
   a. Multibacillary patients have poor cell-mediated immune (CMI) responses specific to *M. leprae*. This is probably genetic but does not imply a broad-spectrum immune deficit.
   b. Paucibacillary patients have good CMI responses, yet this CMI response can cause early and severe damage to large nerves, especially in type I reactions (see below).

Key Symptoms

- Prior residence in developing nation (or U.S. Gulf Coast, Hawaii)
- Anesthetic skin lesion(s)
- Certain persistent unexplained skin lesions
- Numb, weak, or painful nerve in limb
- Unexplained ulcers, burns, deformities in limbs

Clinical Findings

1. *Multibacillary (LL, BL, BB) leprosy*
   a. Often presents with multiple, infiltrated (raised), poorly marginated plaques or with nodules.
   b. Early in lepromatous disease, there may be only mild "stocking and glove" sensory loss. Often there is no motor nerve loss, even in advanced disease.
   c. Eye, ear, nose, and throat (EENT) lesions are common, including earlobe thickening, iritis or keratitis, and chronic nasal infiltration that may slowly progress to septal perforation.
2. *Borderline cases*, especially BB, show mixed features and are most susceptible to type I reactions, which can be an emergency.
3. *Paucibacillary (BT, TT) leprosy*
   a. Usually presents with only a few, well-marginated macules or plaques. These lesions nearly always show mild to profound anesthesia.
   b. Cutaneous or regional nerves are commonly enlarged, with associated sensory and often motor loss.
   c. If a motor nerve shows tenderness and acute loss of function, type I reaction should be suspected and steroids begun.
   d. The "pure neural" form of paucibacillary leprosy (i.e., without skin lesions) is rare in the United States.
4. The anesthesia in all types of leprosy, especially if progressive or untreated, leads to neuropathic injuries, ulcerations and the classic—but pre-

TABLE 263–1. COMPARISON OF CLINICAL ASPECTS OF MULTIBACILLARY AND PAUCIBACILLARY LEPROSY (HANSEN'S DISEASE)

Clinical Aspect	Multibacillary (Lepromatous)			Paucibacillary (Tuberculoid)	
	←	Borderline		→	
Ridley-Jopling type*	LL	BL	BB	BT	TT
Immunity (cell mediated, *M. leprae* specific)	Absent	Low	Moderate	High	Strong
Infectiousness (untreated)	Moderate	Slight		Minimal	None
Clinical features					
Skin lesions	Many, small, raised	Variable size, number		3–5, larger	1–2, flat, dry
Sensation, sweating	Slow "stocking-glove" loss	Varies		Moderate loss	Marked loss (early)
Nerve enlargement	None and/or late	Slow, variable			Marked and/or early
"Systemic" invasion (EENT, testes, bone)	Common (if untreated)	Variable, moderate		Rare	None
Clinical suspicion if:	Skin or EENT lesions (± peripheral anesthesia)			Anesthetic lesion or thickened nerve	
Diagnostic confirmation					
Skin Biopsy	AFB in subdermal histiocytes and nerves			Skin granulomas, nerve infiltrates; AFB rarely seen	
Bacillary index (on slit-skin smear)	5–6+	4–5+	2–4+	0–2+	0–1+
Reaction susceptibility					
Type I ("reversal")		←		→	
Type II (ENL)	←	→			
Potential dermatologic differentials include (consider neuropathy differential also)	Kaposi's sarcoma; neurofibromatosis; pityriasis; granuloma multiforme; leishmaniasis; lichen simplex or planus; drug eruption; keloids; syphilis (LL may have false-positive VDRL); etc.			Tinea corporis or versicolor; atopic or contact dermatitis; sarcoid; mycosis fungoides; psoriasis or other plaques; skin TB; SLE; etc	

Abbreviations: AFB, acid-fast bacilli; EENT, eye, ear, nose, throat; ENL, erythema nodosum leprosum; SLE, systemic lupus erythematosus; TB, tuberculosis; VDRL, Venereal Disease Research Laboratory [test].

*LL, lepromatous leprosy; BL, borderline lepromatous; BB, borderline; BT, borderline tuberculoid; TT, tuberculoid leprosy.

Adapted from Pust RE, Campos-Outcalt D: Leprosy in the United States: risks, recognition, regimens, resources. Postgrad Med 1985; 77:151–159, with permission.

ventable—deformities. Motor paralysis may contribute to further, sometimes severe, loss of limb function.

Key Signs

- Anesthetic macules or plaques and/or stocking-glove hypesthesia
- Other typical persistent skin lesions (see Table 263–1)
- Enlarged or tender nerves
- Sensory or motor loss, especially in facial, ulnar, median, radial, peroneal, or posterior tibial nerves
- Ulcers and deformities resulting from damage to regions served by these anesthetic nerves
- Nasal or anterior eye damage, especially if other consistent findings

Acute Type I Reaction

- Tender swollen nerve(s) with acute loss of motor function—*treatment urgent*

Type II Reaction: Erythema Nodosum Leprosum (ENL)

- Tender subdermal nodules, arising acutely, especially on extensor surfaces

Laboratory Tests

1. The 4-mm punch skin biopsy is the most useful diagnostic test in the United States. The specimen must be deep enough to include subdermal fat. Submitted in 10% formalin, it should be labeled to indicate the possibility of leprosy; this will also alert the pathologist to perform acid-fast bacilli (AFB) stains on the histologic specimen. Histopathologists experienced in leprosy, such as those at the U.S. Public Health Service (USPHS) Hansen's Disease Program, can classify the biopsy in one of the five Ridley-Jopling (LL to TT) categories, thus confirming the clinical picture and determining appropriate chemotherapy regimens.
2. Much like the direct sputum smear in tuberculosis, slit-skin smears stained for AFB may confirm the diagnosis of multibacillary leprosy and

quantify the bacterial load. In practice, however, nonleprologists are seldom prepared to do this test. Smears are not necessary to make the diagnosis in developed countries, where histopathology is readily available.

3. Numerous sophisticated diagnostic tests are proposed, including polymerase chain reaction, but so far none have proven as useful as clinical examination, punch biopsy, and slit-skin smears.

Key Tests

- Thorough EENT, skin, and limb examination is the best "test."
- Punch biopsy of skin lesion (mailed to USPHS Hansen's Disease Program)
- Slit-skin smears (not needed for initial diagnosis)

Differential Diagnosis

1. Skin
   a. The classic findings are virtually pathognomonic: Paucibacillary patients have skin lesions that are anesthetic; multibacillary cases have skin biopsies or smears showing AFB. In either type, nerve enlargement adds to the certainty of the diagnosis.
   b. Skin diseases that may be initially confused with leprosy include those in Table 263–1; however, none of these causes anesthesia.
2. Peripheral neuropathies
   a. Only peripheral nerves—never the central nervous system—are involved in leprosy.
   b. Leprosy and diabetes are the most common of the several causes of limb neuropathy in the world. However, in leprosy the clinician will virtually always find some of leprosy's other classic features.
3. EENT
   a. Perforation of the nasal septum can be found in congenital syphilis, Wegener's granulomatosis, or cocaine abusers.
   b. When chronic EENT changes suggest lepromatous leprosy, the clinician should examine the nerves and biopsy the skin.

Treatment

1. Regimens recommended in the United States since 1997 for chemotherapy of paucibacillary (TT and BT) and multibacillary (BB, BL, and LL) leprosy include rifampin, dapsone, and clofazimine.
   a. These same three drugs are the basis for the World Health Organization (WHO)–recommended regimens around the world. Although utilizing less frequent doses of rifampin, the WHO regimens are probably as effective as the U.S. regimens.
   b. Drug regimens of choice in the United States in 1999 are shown in Table 263–1 and in the Key Treatment box.
2. Treatment of *leprosy reactions* (see Key Treatment box)
   a. *Many patients first present to clinicians when they are in reaction.* All reactions except the most mild should be started on treatment with high-dose daily oral steroids.
   b. The only common "emergency" in leprosy is the acute motor neuropathy induced by a serious type I reaction. Prednisone will also control type II (ENL) reactions; thus it is not absolutely necessary for the nonleprologist to distinguish type I from type II in the emergency situation.
   c. An ENL reaction may persist for several months to a few years; in this situation thalidomide is also highly effective and avoids the complications of long-term steroids. Decisions about thalidomide use can be made later, in consultation with a physician authorized to prescribe it through the USPHS Hansen's Disease Program and/or Celgene Company, the U.S. manufacturer of thalidomide (Thalomid).

Key Treatment (Adult Doses)

Paucibacillary Leprosy (TT and BT)

- One year of daily rifampin (Rifadin), 600 mg, plus dapsone, 100 mg

Multibacillary Leprosy (BB, BL, LL)

- Two years of daily rifampin (Rifadin), 600 mg, plus dapsone, 100 mg, plus clofazimine (Lamprene), 50 mg

Acute Type I or II Leprosy Reactions

- Continue above regimen, consult with USPHS Hansen's Program, and *add* for
- Mildest reactions (no nerve pain or function loss or fever): hydroxychloroquine sulfate (Plaquenil) or nonsteroidal anti-inflammatory drugs
- All other reactions
  –Begin 60 to 80 mg prednisone daily; consider slow taper after 1 week.
  –Consider thalidomide (under proper precautions) for prolonged or recurrent type II (ENL) reactions.

Prognosis

1. With early diagnosis and recommended treatment, all forms of leprosy have an excellent prognosis. Skin lesions may become barely visible. Nerve and EENT damage is usually arrested but is rarely reversed by treatment. The clear exception is the full or partial recovery from acute motor neuropathy by prompt steroid treatment of type I reactions.
2. Physical therapists, orthotists, and podiatrists play crucial roles in tertiary prevention and in restoration of limb function.
3. Eye and ENT specialists contribute to the care of lepromatous complications.

Follow-Up

1. Leprosy patients should be seen every 1 to 3 months during their 1 to 2 years of chemotherapy, more often if in reaction. Intensity of long-term follow-up is determined by the complications of motor and sensory loss; this in turn requires patient education for prevention and treatment of secondary infections and limb or eye dysfunctions.
2. The USPHS Hansen's Disease Program is eager to be of assistance to any U.S. clinician. Their services include telephone clinical consultation about diagnosis and treatment, histopathology and slit-skin smear interpretation, provision of the recommended drugs (see Key Treatment box), professional and patient education, and, in some circumstances, acute hospitalization. The phone number is 1-504-642-7771 or toll-free 1-800-642-2477 in Carville or Baton Rouge, LA (U.S. central time zone). The American Leprosy Mission, 1 ALM Way, Greenville, SC 29601, is a nongovernmental international agency that also supplies clinical education materials in the United States.
3. Patients with leprosy who reside in the United States thus have available to them through these channels all of the resources needed for diagnosis, treatment, education, and follow-up.

Journals and Internet Sites Devoted to Leprosy

- *International Journal of Leprosy: http://www.allenpress.com/catalogue/index/lepr/index.html*
- *Leprosy Review* (British Leprosy Relief Association): *http://www.lepra.org.uk*
- American Leprosy Mission: *http://www.leprosy.org/*
- Netherlands Leprosy Relief Association (INFOLEP): *http://infolep.twinfo.nl/infolep*

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