Tuberculosis and Leprosy
Classical Granulomatous Diseases in the Twenty-First Century

David M. Scollard, MD, PhD[a,*], Mara M. Dacso, MD, MS[b,c], Ma. Luisa Abad-Venida, MD, FPDS[d]

KEYWORDS

• Granuloma • Atypical mycobacteria • Tuberculosis • Lupus vulgaris • Leprosy • Hansen disease • Leprosy reaction • Cell-mediated immunity

KEY POINTS

- Cutaneous lesions are rare in tuberculosis but are common in leprosy.
- *Mycobacterium tuberculosis* is cultivable; *Mycobacterium leprae* is not.
- Both infections are curable, but optimal multidrug regimens for them are different.
- Standard Ziehl-Neelsen staining may fail to stain many *M leprae,* because they are weakly acid-fast compared with *M tuberculosis.*
- A delay or failure to diagnose cutaneous tuberculosis may be associated with mortality if there is concomitant systemic disease; delay or failure to diagnose leprosy is associated with a high risk of peripheral neuropathy and disability.
- Hypoesthesia and intraneural or perineural localization of granulomas are helpful in distinguishing leprosy from tuberculosis clinically and histologically.

INTRODUCTION

Tuberculosis (TB) and leprosy, the 2 major mycobacterial infections of humans, are classic granulomatous diseases that still affect millions of people. Both infections are now curable, but no highly effective vaccine is yet available for either of them. Both are ancient scourges with a wide range of cutaneous manifestations, and both are infamous for their ability to mimic other diseases and sometimes fool even the most skilled diagnostician.

Etiopathogenesis

TB and leprosy are both chronic infections, but they are very different diseases (**Table 1**). *Mycobacterium tuberculosis* is cultivable; *Mycobacterium leprae* is not. *M leprae* infects peripheral nerves; *M tuberculosis* does not. Untreated tuberculosis has a high mortality; untreated leprosy has a high disability rate due to peripheral neuropathy. Cutaneous lesions are typical of leprosy, but rare in tuberculosis.

The cell-mediated immune response (CMI) to these agents is the critical determinant in individual susceptibility to these infections and in the range of clinical and histologic appearances of their cutaneous lesions (**Fig. 1**). The organisms express pathogen-associated molecular patterns on their surfaces, which are recognized by pattern recognition receptors of macrophages and

All authors declare that they have no conflicts of interest.
[a] National Hansen's Disease Programs, 1770 Physician Park Drive, Baton Rouge, LA 70816, USA; [b] Center for Dermatology and Cosmetic Laser Surgery, 5026 Tennyson Parkway, Plano, TX 75024, USA; [c] Department of Dermatology, University of Texas Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas, TX 75390-9069, USA; [d] Department of Dermatology, Jose R. Reyes Memorial Medical Center, Rizal Avenue, Manila 1008, Philippines
* Corresponding author.
E-mail address: dscollard@hrsa.gov

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Table 1
A comparison of tuberculosis and leprosy

	TB	Leprosy
Etiologic agent	*M tuberculosis*	*M leprae*
Acid-fastness	Strong (Ziehl-Neelsen stain)	Weak (Fite stain preferred)
Growth in tissue	Extracellular or in macrophages	Obligate intracellular pathogen, in macrophages and Schwann cells
Cultivable	Yes	No
Growth temperature	37°C	33°C
Number of protein genes	3993	1614
Number of pseudogenes	6	1133
Transmission	Airborne droplets	Probably airborne
Initial site of infection	Periphery of lung	Nose and nasopharynx
Cutaneous infection	Uncommon	Typical, very common
Infection of peripheral nerves	No	Yes
Infection is curable	Yes	Yes
CMI	Mainly 2 polar types; strong and weak CMI	Full spectrum from strong to none
Outcome if untreated	High mortality	Very low mortality; high disability rate from peripheral neuropathy
Vaccine	BCG (variable protection)	BCG (variable protection)

dendritic cells, facilitating phagocytosis.[1] Innate immunity to mycobacteria is mediated by macrophages and dendritic cells, including Langerhans cells in the skin, and may be sufficient to prevent further progression of the infection.

If innate immunity is insufficient, mycobacterial antigens are presented to CD4+ T cells, initiating the acquired CMI.[2] Based largely on inherited immunologic capabilities, CMI in most individuals will be driven by activated CD4+ T lymphocytes

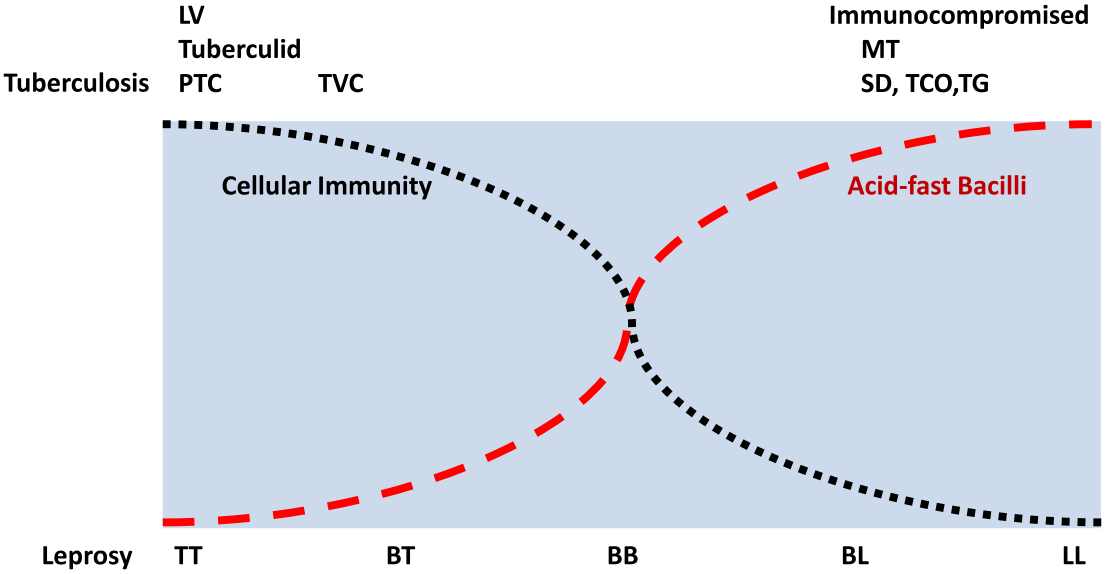

Fig. 1. Immunopathologic patterns of cutaneous tuberculosis and leprosy. The cellular immune status and bacterial load of different forms of cutaneous tuberculosis compared with the broad, continuous spectrum in leprosy. Cutaneous tuberculosis: MT, miliary tuberculosis; PTC, primary tuberculous chancre; SD, scrofuloderma; TCO, tuberculosis cutis orifacialis; TG, tuberculous gumma.