Leprosy in the United States

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I have no relevant disclosures.
LEPROSY

- Present on every continent except Antarctica
- The countries with the highest numbers of patients are **India**, Brazil, and Indonesia
- 150 – 200 new cases of leprosy per year in the U.S.
LEPROSY

- *Mycobacterium leprae*
- Main route of transmission is human respiratory droplets
- Less frequent route of transmission: contact with nine-banded armadillo
- 95% of the population has complete resistance to this organism
LEPROSY

- Disease primarily of peripheral nerves and skin
- Long incubation
- Slowly-progressive mycobacterial infection
Most cases in the U.S. occur in immigrants. The majority of leprosy patients in the U.S. are Hispanic and Asian/Indian.

Some cases are armadillo-related. Leprosy is endemic in LA and TX.
SPECTRUM OF DISEASE

- **Tuberculoid leprosy**
  - High, but not complete, resistance
  - High macrophage activity against the bacillus
  - 2 – 3 skin lesions; few bacilli on skin biopsy

- **Lepromatous leprosy**
  - Low resistance
  - *Mycobacteremia*, heavy load in skin and nerves
  - Many skin lesions

- **Borderline leprosy**
Polar tuberculoid

Borderline leprosy

Polar lepromatous

Relatively high immunologic resistance to *M. leprae*

Low bacterial load in skin and peripheral nerves

Low immunologic resistance to *M. leprae*

High bacterial load in skin and peripheral nerves
LEPROMATOUS LEPROSY

- Poor host resistance to *M. leprae*; normal resistance to other mycobacteria
- Disease of skin and peripheral nerves (also URT, eyes, testicles)
LEPROMATOUS LEPROSY

- Pink and hypopigmented macules, plaques, and nodules; not anesthetic in early stages
- Skin lesions are widespread and symmetrically distributed
- Any cutaneous surface except warm areas (e.g. axillae, inguinal folds)
LEPROMATOUS LEPROSY

- Late stage:
  - Massive bacterial infiltration of the dermis
  - Thickened skin of the face with furrows ("leonine facies")
  - Collapse of the nasal bridge
  - Thickening of earlobes
  - Loss of eyebrows and lashes
LEPROMATOUS LEPROSY

- Bacterium enters Schwann cells and causes slow demyelination of the peripheral nerves
- Affects small cutaneous nerves and nerve trunks; does not affect CNS
LEPROMATOUS LEPROSY

- Slow progression towards sensory and motor neuropathy of the hands and feet
- This is one of many mechanisms of nerve disease in leprosy patients
LEPROMATOUS LEPROSY

- At least 2 years of oral antibiotic therapy, until there is complete clinical and histologic clearance of the organism
- Standard therapy in the US: daily doses of Dapsone 100 mg, Rifampin 600 mg, and Clofazamine 50 mg
- Other possible substitutes: daily doses of Minocycline 100 mg, Levofloxacin 500 mg, or Clarithromycin 500 mg
LEPROSY

- Main cause of nerve damage in this population is autoimmune reactional states
- Two main reactional states:
  - Type I reaction
  - Erythema nodosum leprosum
- During active reactions, permanent peripheral nerve damage may occur within weeks
- Nerve damage in the absence of reactions is very slow and smoldering
LEPROMATOUS LEPROSY

- Of these two reactional states, polar lepromatous patients *may* develop ENL.
LEPROMATOUS LEPROSY – ERYTHEMA NODOSUM LEPROSUM

- Immune complex disorder
- Deposition of immune complexes in skin, nerves, synovia of joints, and vascular endothelia
- Painful red dermal nodules in previously-unaffected skin (forearms, legs, face, trunk)
- Fever
- Arthralgias of hands, knees, and feet
- Uveitis
- This reaction may persist for months or years
LEPROMATOUS LEPROSY – ERYTHEMA NODOSUM LEPROSUM

- Inflammation of the facial, ulnar, median, common peroneal, and posterior tibial nerves

- Possible consequences:
  - Lagophthalmos
  - Paresthesias in the fingers and toes
  - Decreased sensation in hands and feet
  - Wrist drop, paralysis of fingers
  - Foot drop, claw foot
THERAPY FOR ENL

- For patients with active neuritis:
  - Prednisone 1 mg/kg/day
  - Slow taper

- ENL without neuritis:
  - Thalidomide for men and non-childbearing women

- Some patients require both prednisone and thalidomide

- Clofazamine as an adjuvant
ENL occurs in about 40% of all patients with lepromatous leprosy
BORDERLINE LEPROSY

- Immunologically unstable form of leprosy
- May upgrade towards tuberculoid pole, or may downgrade towards lepromatous pole
- These patients have a significant bacterial load in skin and peripheral nerves, but less than in polar lepromatous patients
Polar Tuberculoid

Borderline Leprosy

Polar Lepromatous

Relatively high immunologic resistance to *M. leprae*

Low bacterial load in skin and peripheral nerves

Low immunologic resistance to *M. leprae*

High bacterial load in skin and peripheral nerves
BORDERLINE LEPROSY

- Macules and **annular plaques with central clearing**
  - Pink or hypopigmented
- Skin lesions are widespread and asymmetrically distributed
**BORDERLINE LEPROSY**

- *M. leprae* may cause slowly progressive damage to peripheral nerves by direct infiltration
- Main cause of nerve damage is autoimmune reactional states
- Both ENL and Type I reactions may occur in borderline leprosy
**TYPE I REACTIONS**

- Cell-mediated immune reaction; CD4(+) T lymphocytes
- Acute increase in the immune response to the antigens of *M. leprae* that are in the skin and nerves
- *Does* increase the clearing of bacilli from tissues
- Causes sudden inflammation of peripheral nerves that may lead within weeks to permanent neurologic deficits (if not appropriately treated)
- Type I reactions usually occur during the first year of antibiotic therapy
TYPE I REACTIONS

- Nerve damage in Type I reactions is more rapid and severe than in ENL.
TYPE I REACTIONS

- Inflammation of facial, ulnar, median, common peroneal, and posterior tibial nerves

- Possible consequences:
  - Lagophthalmos, paralysis of other facial muscles
  - Decreased sensation in hands and feet, and paresthesias
  - Wrist drop, paralysis of fingers
  - Foot drop, claw foot
TYPE I REACTION

- Existing skin lesions become red, edematous, and painful
- Edema of the hands and feet
TYPE I REACTION

- For patients with active neuritis:
  - Prednisone 1 mg/kg/day
  - Very slow taper
- Close followup to monitor improvement of neurologic disease
- May need physical therapy
- Clofazamine as an adjunct
- Continue antibiotic therapy
TUBERCULOID LEPROSY

- High, but not complete, resistance to *M. leprae*
- Granulomatous response to the organism
- One or two skin lesions
- Pink or hypopigmented plaque or macule. Sharply marginated. May become annular. Hairless and anesthetic.
- Any cutaneous surface, except warm areas
TUBERCULOID LEPROSY

- Few or no organisms on skin biopsy
- Slit smears negative
ENL and Type I reactions do not occur in polar tuberculoid leprosy. Immunologically stable.

Nerve damage mainly occurs to those peripheral nerves in the vicinity of a tuberculoid lesion.

The nerve damage is granulomatous and may be rapid. Sensory or motor deficiencies may occur.

May affect small sensory nerves, or more important structures (ulnar nerve, branches of the facial nerve).
TUBERCULOID LEPROSY

- Standard therapy in the US: daily doses of Dapsone 100 mg and Rifampin 600 mg. One year.
PERMANENT SEQUELAE

1. Cranial nerve palsies, especially CN V and VII
2. Loss of pain and temperature sensation in hands and feet → unrealized traumatic injuries and/or recurrent cellulitis

This may lead to loss of digits and ulcers of the feet, lower legs, and hands
3. Partial loss of motor function in hands →
difficulty with fine movements (typing, buttons, keys, cutlery)
PERMANENT SEQUELAE

4. Advanced loss of motor function and complete atrophy of the muscles of the hands and feet → non-functioning hands and feet, difficulty with walking and other ADLs
PERMANENT SEQUELAE – PREVENTION AND THERAPY

- Antibiotic therapy; prompt treatment of Type I reactions and ENL
- Patients with insensate hands and feet should perform self-examination daily, and obtain treatment for ulcers and infections
- Shoes
- Protection of hands in industrial workers
- Occupational therapy, physical therapy
- Corrective surgery for permanent deformities
Gram-positive, acid-fast bacillus

Obligate intracellular parasite

Grows best at 27 – 33° centigrade

Will not grow *in vitro* on any culture medium

Will grow experimentally in armadillos, mouse foot pads, and certain monkeys

The genome has been sequenced
MICROBIOLOGY

- Incubation period is 3 - 5 years
- Doubling time is 12 days; slowest-growing bacterial pathogen in humans
- Only bacterial pathogen known to invade peripheral nerves
- Patient susceptibility to this organism is only to this organism
- The role of Toll-like receptors on antigen-presenting cells
Reservoir: humans and nine-banded armadillos

Leprosy is present in 15% of wild nine-banded armadillos in the Southern U.S.

Some evidence suggests that in the Southern U.S., humans do in fact contract leprosy from armadillos

The 9-banded armadillo, *Dasypus novemcinctus*, is common across parts of many southern states.
LEPROSY IN THE U.S.

- 150 – 200 new cases per year
- TX, LA, CA, FL, NY, and HI
- In 2008, 82% of new patients were born outside the U.S., especially: Brazil, India, Mexico, Philippines
LEPROSY IN THE U.S.

- The center for leprosy research is the National Hansen’s Disease Program in Baton Rouge, LA. The NHDP is part of the US Public Health Service.
- There are 14 Federally-supported leprosy clinics in the U.S.: AZ, CA, FL, IL, NY, PR, TX, WA.
- NHDP will accept the transfer of leprosy patients with complex clinical courses. NHDP also provides pathology and PCR services.
THE END