Leprosy and Buruli ulcer: Similarities and differences

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Geographic distribution

**Leprosy**
- Second most common mycobacterial disease (after tuberculosis)
  - In > 90 countries
  - Worldwide (esp. Brazil, India, Indonesia)

**Buruli ulcer**
- Third most common mycobacterial disease (after tuberculosis and leprosy)
  - In > 30 countries
  - Mainly in the tropics (esp. Benin, Côte d’Ivoire, Ghana)
Endemicity
Red: high;
Yellow: moderate;
Green: low;
*: suspected cases
(Walsh et al, Dermatol Clin 2011; 29: 1-8)
Problem of underreporting

**Leprosy**
- New cases in 2011: > 200,000
- Between 2010 and 2011: Increasing number of new cases except in Americas and Africa
- Africa: Low number of submitted reports

**Buruli ulcer**
- Reported cases: 5,000 -> 6,000 annually
- Underreporting: Major challenge in many countries
Geographic distribution of Buruli ulcer: 3 remarks

1. Enormous variations between different countries!

<table>
<thead>
<tr>
<th>Year Range</th>
<th>Country</th>
<th>Number</th>
<th>Diagnosis Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002-2012</td>
<td>Côte d’Ivoire</td>
<td>7,000</td>
<td>Clinical diagnosis</td>
</tr>
<tr>
<td>2004-2012</td>
<td>Australia</td>
<td>101</td>
<td>Lab confirmation</td>
</tr>
<tr>
<td>1982-2012</td>
<td>Japan</td>
<td>36</td>
<td>Lab confirmation</td>
</tr>
<tr>
<td>1968-2012</td>
<td>Peru</td>
<td>15</td>
<td>Lab confirmation</td>
</tr>
</tbody>
</table>

2. Underreporting: major challenge in many countries.

3. Reported cases are not always confirmed cases!
Clinical aspects

Leprosy

Affect cooler body areas primary with skin lesions

- Skin patches, papules, plaques, nodules, nerve thickening
- Internal organs: testes, eyes
- Incubation period: 5 → 7 years (→ 20 years)

Buruli ulcer

- Skin nodules, plaques, oedemas, ulcers
- Bone involvement in ≈10% of African cases
- Incubation period: ≈ 3 months (shorter in case of reactivation)
Nodule
Oedema
Ulcer
(Courtesy of A Kibadi Kapay)
Ulcer
(Courtesy of WM Meyers)
Osteomyelitis
(Courtesy of WM Meyers)
Leprosy and Buruli ulcer coinfections

- Lower Congo (DRC) (Dr. W.M. Meyers, AFIP, Washington DC)
- Cohort of patients with:
  - leprosy: 1061
  - Buruli ulcer: 180
- Both diseases in 6 patients
  Indeterminate or tuberculoid leprosy
Patient MM
(Kivuvu, Lower Congo):
BU lesion on the eye
(Courtesy of WM Meyers)
Patient MM: Leprosy lesion on her left elbow (Courtesy of WM Meyers)
Patient JA (Kivuvu, Lower Congo)
Large BU lesion on his diaphragm area and leprosy lesions visible on left shoulder
(Courtesy of WM Meyers)
Tuberculosis coinfection

Leprosy
• Very rare
  - No cases of cutaneous TB
  - A few cases of leprosy patients with history of pulmonary TB

Buruli ulcer
• Very uncommon
  - Cutaneous TB and BU in the same lesion:
    3 / > 5,000 BU cases
  - Pulmonary TB after BU successful treatment:
    1 / > 5,000 BU cases
HIV coinfection

**Leprosy**
- Does not alter incidence and clinical aspect

**Buruli ulcer**
- Higher incidence in HIV+ patients
- More severe forms in HIV+ patients (disseminated forms, osteomyelitis)
Transmission

Leprosy
• Communicable disease
• Zoonosis? (armadillos)
• Nasal droplets from infected untreated persons (*M. leprae* shedding from skin)

Buruli ulcer
• Noncommunicable
• Directly related to environmental factors
• Minor trauma to the skin (Insects bites???)
Leprosy and Buruli ulcer in animals

Leprosy
• Wild armadillos
  (Southern USA, Mexico, Argentina)
• Imported monkeys
  - Mangabeys
    (from Nigeria → Louisiana)
  - Chimpanzees
    (from Africa → USA, Japan)

Buruli ulcer
• Wild and domestic animals
  (only south eastern Australia)
• Wild animals:
  Koalas, possums, potoroos, rats
• Domestic animals:
  Horses, dogs, cat, alpacas (zoo)
Leprosy in newly captured armadillos from Louisiana (Portaels et al 1987)
Chimpanzee with lepromatous leprosy (*Sierra Leone) after 30 years in Japan (Suzuki et al 2010)
Koala with BU
(Courtesy of J Hayman)
Common Ringtail Possum with BU
(Courtesy of Janet Fyfe)
(Fyfe et al., 2010)
Long-footed Potoroo with BU
(Courtesy of Tony Mitchell)
Long-footed Potoroo with BU
(Courtesy of Tony Mitchell)
Alpaca with BU
(Courtesy of Ewen McMillan)
(O’Brien et al., 2013)
Horse with BU  
(Courtesy of Albert van Zyl)  
(van Zyl et al., 2010)
Dog with BU
(Courtesy of Ewen McMillan)
(O’Brien et al., 2011)
Microbiology

Leprosy

- **M. leprae**: Obligate intracellular

- **Genome sequencing**
  - 3.3 million bp
  - Protein coding genes: 50%

- **In vivo growth**: (nude) mice, monkeys, armadillos

- **Generation time**: 12 → 14 days

Buruli ulcer

- **M. ulcerans**: Intracellular and extracellular

- **Genome sequencing**
  - 5.8 million bp (0.17bp in plasmid)
  - Protein coding genes: 70%

- **In vivo growth**: (nude) mice, rats, guinea pigs, armadillos

- **Generation time**: ≃ 20 hours

- **Toxin** production (mycolactone) (plasmid)
Diagnosis

**Leprosy**
- **Clinical diagnosis**
- **PCR sensitivity:**
  - MB 95%
  - PB 55%

**Buruli ulcer**
- **Clinical and laboratory diagnosis**
- **IS2404-PCR sensitivity:**
  >95% (>200 copies in genome)

Direct smear examination, PCR and histopathology (differential diagnosis)
Treatment

Leprosy
• Rifampin, dapsone, clofazimine
• Drug resistance to rifampin, dapsone

Buruli ulcer
• Rifampin + streptomycin (since 2004) + surgery for large lesions and bone lesions (WHO 2012)
• No drug resistance

Prevention of disability
Conclusion

Similarities in terms of control of both diseases

- **In countries where both diseases are endemic:**
  - control should be performed under the **same national program**
  - combined public health activities should be put in place

- **Improvement of:**
  - early detection
  - treatment outcome and prevention of disabilities
  - financial burden for countries and NGO’s
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