Current management of Leprosy

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Contrast with TB

- Effective antibiotic treatment
- Drug resistance is not a problem
- Diagnosis may be more difficult
- Inflammation
  - Skin & nerves
  - Treatment with steroids
  - Difficult to switch off
- Stigma
Key Facts

• Leprosy caused by *Mycobacterium leprae*
• Type of disease determined by host immune response
• Skin and nerves
• 250,000 new cases per year
• 16 million completed treatment
• >3 million with permanent disability
• 194,000 disability adjusted life years
• Women disproportionately affected
Leprosy Spectrum

CMI Ab

Type 1
Type 2

Reversal reactions
Tuberculoid    Borderline      Borderline    Lepromatous
Tuberculoid    borderline    lepromatous    leprosy

TYPE 1 REACTIONS

TYPE 2 REACTIONS
Nerve Damage

Motor and Sensory function lost
Claw hand, foot drop, inability to close eyes
Neuropathic injuries
Diagnosis

- Clinical
  - Skin lesions, peripheral nerve thickening
- Serological tests
  - PGL-1 antibody
  - Specificity ~ 60%
- T cell tests
  - Proving difficult to identify *M. leprae* specific antigens
- No skin tests
MDT Success Story

- Combination Rifampicin/Dapsone/Clofazimine
  - 2 or 3 drugs 6 or 12 months
- 16 million patients treated since 1982 (Novartis provider)
- Low relapse rates 1%
- Some molecular evidence of drug resistance
  - Rifampicin and Dapsone
- No clinical evidence of resistance being a problem
- Evidence of adverse affects and poor compliance
  - Haemolysis, skin pigmentation
- Need to develop alternative regimens
- Single monthly dose of Rifampicin, Ofloxacin,
  - RCT against WHO-MDT - 6and 12 mà
  - Trial could be done in African centres, add in biomarkers
Chemoprophylaxis

- Single dose of Rifampicin
- Protection only for wider community
- Not household
- Not multibacillary leprosy
- Only lasted 2 yrs
- Consistent with small effect against low bacterial load
Nerve Function Impairment

- Motor and sensory loss
- Before, during and after treatment
  - Cohort studies Ethiopia, Bangladesh, India
  - 30 - 56% impairment at diagnosis
- Delay in diagnosis important, > 6 m 60%
- On going studies to identify most sensitive test
  - Temperature
Incidence of outcome episodes in the INFIR Cohort ($n=188$)
Treating Nerve damage and reactions

- Prednisolone 30-60 mg
- 12-24 weeks treatment time, no good data on dose or duration
- Cochrane review only 3 trials could be included

Outcomes
- Skin - 80% improvement
- Nerves
  - sensory improvement about 50%
  - Motor improvement about 40%
- Relapse rate - 35-50 %
- TENLEP
  1. Comparing 20 vs 32 weeks steroid treatment for nerve damage
  2. Treating patients with subclinical nerve damage.

Tenlep- multicentre, India, Nepal, Bangladesh. Recruiting finished Oct 2013
T1R – Second Line agents

- Needed for patients who do not respond to steroids
- Patients who have adverse effects from steroids
- Methylprednisolone 1 gm x 3 days then Pred
  - No benefit
- Azathioprine
  - RCT in TLM Hosp N India, placebo, 24, 36 or 48 weeks aza
  - No benefit added to steroids from adding in azathioprine
- Cyclosporin
  - RCT in Ethiopia about to report
- Need for new immuno-suppressants
  - biologics
Neuropathic Pain in leprosy

- 18-25% patients attending leprosy clinics
- Significant cause of depression
- No treatment assessed
- Amytriptyline needs assessing.
ENL is a multisystem immune complex and T cell disorder

- fever, malaise
- Painful nodules.
- Bone pain, neuritis
- Orchitis, iritis,

ENL during or after multi-drug therapy (MDT)

- treatment with Prednisolone or Thalidomide
- ENL is recurrent, lasts years
- Death due to steroid adverse effects (Addis Ababa series)
Aims of ENLIST

– Improve understanding of mechanisms causing ENL
– Gather evidence for treatment
– Improve access to treatments

• Prospective data collection (7 centres, four continents)
  – Almost 300 patients enrolled
  – Basis for future studies
  – Scientific collaboration, multicentre RCTs
Challenges

- Ongoing transmission despite 30 years of effective MDT
- Opportunity RCT of new Multi-Drug Therapy
- Chronic inflammation
- Nerve damage
  - Simple tests
- Predicting which patients will develop nerve damage and reactions
- Immunosuppressants
  - Steroids, identifying which patients respond
- ENL- ENLIST model of global and south-south collaboration
- Stigma
- Early diagnosis still elusive
Thanks
## Impact of HIV-1 on leprosy

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HIV/Leprosy Summary

- HIV infection does not appear to impair local immune response to *M. leprae*
- Patients may present with typical leprosy lesions
- When on HAART then excess BT cases
- Higher risk of Type 1 reactions
- Presentation with IRD
- Treat with MDT
- Long immunosuppression may be needed
Reviews

Cochrane Reviews


• WHO Expert Committee Leprosy Oct 2010
References

Leprosy Epidemiology

- Leprosy technically eliminated as a public health problem 2002 (<1 case per 10 000)
- Under-reporting of cases to meet elimination targets
- Leprosy case figures stabilising in major countries
- Surveys done - many undiagnosed cases
  - Bangladesh PUL 13 /10 000 (Moet 2008)
  - India 3 - 9/10 000, 30% children (Shetty 2009)
  - Hyper-endemic foci

- Policy Implications
  - Ongoing transmission
  - Leprosy resistant to elimination
Incidence of leprosy in Brazil 1980 - 2008

Year: 1980 - 2008

Number of new cases detected:

- 1980: 15,000
- 1981: 16,000
- 1982: 17,000
- 1983: 18,000
- 1984: 19,000
- 1985: 20,000
- 1986: 21,000
- 1987: 22,000
- 1988: 23,000
- 1989: 24,000
- 1990: 25,000
- 1991: 26,000
- 1992: 27,000
- 1993: 28,000
- 1994: 29,000
- 1995: 30,000
- 1996: 31,000
- 1997: 32,000
- 1998: 33,000
- 1999: 34,000
- 2000: 35,000
- 2001: 36,000
- 2002: 37,000
- 2003: 38,000
- 2004: 39,000
- 2005: 40,000
- 2006: 41,000
- 2007: 42,000
- 2008: 43,000