Relapse and drug resistance in leprosy

Paul R. Saunderson,
Medical Director,
American Leprosy Missions
Introduction – historical aspects

- Dapsone (4,4’-diaminodiphenylsulfone, or DDS)
  - Synthesized in 1908, but only used in leprosy in 1940s
  - Initially very effective as monotherapy
  - Resistance developed during 1950s
  - Proven in 1964 by Shepard in the mouse-foot-pad
  - Became increasingly serious during 1970s, with an increasing number of relapse cases
  - Primary resistance first confirmed in Ethiopia in 1977
Introduction - MDT

- Both rifampicin and clofazimine known from 1960s
- Recommended two MDT regimens (MB and PB)
- Successful treatment for leprosy for > 30 years
Relapse in the MDT era

• Cases previously treated only with DDS
  – Can be treated with MDT

• Definition of true relapse after MDT:
  – Documented completion of first course of MDT
  – Presence of new skin lesion(s), without Type 1 reaction
  – In MB cases, (increase in) BI of 2+
Relapse in the MDT era

- Rates vary from 0/1000 PYAR to 20.4/1000 PYAR after 2 years MDT
- Even after 12 months MDT, relapse rates are low
- Relapse or reinfection?
  Hawaii......Rio de Janeiro (Rocha A et al, 2011)
Surveillance for drug resistance

• Program set up by WHO in 2006
• Initially funded by TNF, now by ILEP members (FRF & ALM)
• Molecular methods rather than MFP
  – Easy (incl. transport of specimens), reliable and quick
  – Mutations in folP1 gene relate to dapsone res.
    \[ rpoB \] gene relate to rifampicin res.
    \[ gyrA \] gene relate to fluoroquinolone res.
  – Samples with a BI of 2 or more
Surveillance for drug resistance

• Network of 11 reference labs (in 7 countries)
  – DNA sequencing
• In 2012, samples came from 11 endemic countries
• In 2011, 648 samples were processed (516 – Brazil)
  – 16 dapsone resistance
  – 16 rifampicin resistance (all in Brazil)
  – 8 fluoroquinolone resistance (5 in India, 3 in Brazil)
Management of drug resistant cases

• Advice from WHO’s 8th Expert Committee on Leprosy (2012) for proven rifampicin resistance:
  – Daily treatment for 6 months, comprising:
    • Clofazimine 50mg and any two of the following:
      • Ofloxacin 400mg
      • Minocycline 100mg
      • Clarithromycin 500mg
  – Followed by daily treatment for 18 months, with:
    • Clofazimine 50mg and
    • Either: Ofloxacin 400mg or Minocycline 100mg
Conclusions

• Dapsone resistance is still present, but is not of clinical importance
• Rifampicin resistance is still rare but small foci need to be monitored and managed accordingly
• Fluoroquinolone resistance is worrying
• Surveillance should continue, with the addition of more samples from new cases, and any not responding to standard MDT
Thank you!