Are tuberculin surveys in children useful to assess TB incidence?

Babis Sismanidis with acknowledgements to Brian Williams & Philippe Glaziou

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If the prevalence of tuberculous infection in children aged $A$ is $P$ then the annual risk of TB infection is (Styblo rule):

$$ARI = 1-(1-P)^{1/A}$$

We use infection prevalence in children to estimate disease incidence in adults (assuming infection constant over time)
First the good news...
Frequency distribution of induration sizes in Cape Town
Repeat surveys in South Korea

Halving every $\ln(2)/0.08 
\approx 10$ years

Rate of decline $= 7.8\%$/yr
Now the bad news...
Annual risk of tuberculous infection in the northern zone of India

A lot of 'noise'!
False test reactions due to environmental mycobacteria and (possibly) BCG

Prevalence of environmental mycobacteria seems to be very high around the equator, declining at very high and very low latitudes
Frequency distribution of induration sizes in Somalia.

- **red**: fitted
- **black**: environmental
- **green**: TB
Dependence on BCG (Somalia 2006)

Proportion positive with and without a BCG scar
Lack of clear method for establishing prevalence of infection and hence ARTI

Cut-off methods, mirror methods, model-based mixture methods, latent class analysis
Figure 2: Annual risk of tuberculous infection, as calculated using five methods, by country and age.

ARTI calculated based on different methods; Snanaube, PLoS ONE, 4;11:7749
Wide uncertainty of the process

Measurement error, time dependency with reading time
Clear digit preference
Dependence on testing day (Somalia 2006)

Proportion positive when the induration was read on three and four days after the placement
Low infection prevalence

As the incidence declines, the prevalence of infection declines and it gets much harder to measure it.
Changes in distribution patterns of induration size in Korea
Ethical considerations

• No (or little) benefit to surveyed individuals
• Most often done in children
• Ethical requirements:
  – Clearance from ethical committee
  – Informed consent from parents/guardians
  – Ascent from children
The way forward?

New generation of diagnostic tools; Interferon gamma release assays
Tuberculin skin test responses in household contacts of active TB cases
979 children, median age 7yr, Istanbul

Source: Bakir et al 2006
In summary

- Interpretation of PPD data can be problematic
- Diagnostic value of test difficult to establish
- Uncertainty about the relationship between prevalence of infection and disease incidence
- Uncertainty about time changes in the distribution of determinants of induration size
- Difficult to interpret time-changes in ARI

*Use of tuberculin surveys among children to estimate disease incidence is not recommended*