Tuberculosis in children in Europe
- the ptbnet

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• Significant Morbidity and Mortality
  1.4 million cases annually (95% developing countries)
  450,000 Deaths
  estimated 10-15% of global burden related to childhood TB
• Different clinical spectrum of disease
  5-10% < 2 yr meningitis
  disseminated disease more common
• Remains a diagnostic challenge
  paucibacillary, rarely culture confirmed:
  Sputum smear positive in 10.3% (10-14yr), 1.8% (5-9) and 1.6% (<5)
  Cultures positive 21% (10-14), 5% (5-9) and 4.2% (<5),
• Co infection with HIV - clinically very difficult to distinguish
Tuberculosis in children differs from adults

- Immune responses are
  
  Age-dependent: Following infection 40% < 2 yr, 25% 2-5 yr and 5-15% of older children will develop disease within 2 years

- Majority of disease results from progression of primary infection rather than reactivation

  might affect detectable immune responses

- More likely to be extrapulmonary and disseminated, particularly in infants

Newton, Kampmann *The Lancet Infectious Diseases*, August 2008; Vol 8: 498-510
Paediatric TB: Diagnostic challenges due to low bacillary load

- children less infectious
- lack of “gold standard”: microbiological confirmation exceptional
- difficulty in detecting resistance
Immunological

Host response

- skin test
- antigen-specific production of IFN \( \gamma \)
• of the 9 million annual TB cases, about 1 million (11%) occur in children (under 15 years of age).

• reported percentage of all TB cases occurring in children varies (from 3% to more than 25%)

• Children can present with TB at any age, but the most common age is between 1 and 4 years

• Most children will have a known household contact

• Chemoprophylaxis is a recommended intervention
Trends in incidence of TB in children under 15 years by ethnic group in London, 2001-2006

Percentage of TB cases of foreign origin, 2006
UK: Tuberculosis rates in persons born abroad by age

Development of TB in immigrant children

Children with TB at Imperial HCT

Ethnicity and country of birth:

- Black African: 47%
- Afro-Caribbean: 2%
- Caucasian: 7%
- SE Asian: 6%
- Mixed race: 4%
- Arab: 5%
- South Asian: 29%

Country of Birth:
- UK: 38%
- Non-UK: 62%

Travel to TB endemic countries:
- Yes: 56%
- No: 39%
- DK: 5%

Children with TB at Imperial HCT

Ethnicity and country of birth:
Issues for children with TB in Europe

- Incidence and prevalence vary depending on countries.
- Data on childhood TB are not recorded as systematically—no age-related reporting (0-14).
- Children are infected from adult contacts, but the contact details are not recorded.
- Clinical practice for prevention varies from country to country.
- Chemoprophylaxis protocols vary.
- Monitoring varies.
- No idea about MDR prevalence in children.
- Treatment/(MDR) protocols derived from adult practice.
ECDC- reported variables

Total No of cases and Notification rate/100 000

Sex ratio

Median age group- nationals and non-nationals

New (never treated)

Foreign born

Culture positive

pTB

HIV positive TB cases- not stratified for children

TB deaths

Drug resistance

Treatment outcome
2 Key recommendations:

A. 2 age bands to be reported: 0-4, 5-14

“Enumerating children with TB is a key step in bringing their management into the mainstream of the Stop TB Strategy as part of routine NTP activities.”

B. Dosage adjustments for TB therapy

“revised recommended dose of Ethambutol is now 20 mg/kg (range 15–25 mg/kg) daily."
what else can we do?

to improve the care for children with TB in Europe

by creating a network of pediatric experts in TB in Europe

- to more accurately describe active and latent TB in children in Europe

- to identify differences in practice between European countries

- to improve clinical management and research in childhood TB in Europe

- to develop a European "expert panel" for consultation on paediatric TB and possibly a training course

- to conduct collaborative research
Aims

• enhance the understanding of the pediatric aspects of tuberculosis

• facilitate collaborative research studies for childhood TB in Europe

• provide expert opinion through excellence in science and teaching

• establish a better evidence base for diagnosis and treatment of TB in children
1. Presentations from each country:
   Theme 1: Data capture for TB in your country
   Theme 2: Practical Care for children in your country/at your hospital

2. Data collection:
   Discussion of shared database options

3. Discussion of multicentre studies:
   Defining research priorities and possible future studies

4. Conclusions and future plans:
   What do we want to be/do
   Possible funding streams- where to go
Summary of ptbnet-data: Epidemiology

National TB guidelines for children
Yes: 8/11 (72%)
No: 2/11 (18%)
Proposed: 1/11 (9%)
Summary of ptbnet-data:
MDR - TB

No data in children
• Routine use of BCG: 7/11
• Targeted use of BCG: 2/11
• No BCG: 4/11
• Chemoprophylaxis: 11/11, but ages vary, as do regimes
• Treatment: available free of charge
• Few data available on prevalence of HIV in children with active TB

• Only 2/11 countries routinely test TB cases for HIV

• HIV results generally not recorded in reporting systems
Summary of ptbnet-data:

Use of Interferon-gamma release Assays (IGRA)

- IGRA Recommended in 8/11 countries
- Widely used for diagnosis of active TB
- Used for LTBI screening in only 4 countries
- QFG-IT preferred test (7/11 vs 3/11)
- Data in different age groups could be combined to comment on age-related performance
1. Designated database

Consensus that a paediatric database is highly desirable

? Use existing platforms or start from scratch
? ECDC information- too limited, disease only
? Should be able to combine with adult data (contacts)

? What to include
Needs to not just focus on TB disease but include exposure/infection/disease

Designated funding needs to be identified to move this project forwards substantially

In the shorter term, we will investigate existing platforms and compile the data fields that we would like to include (potential data protection issues in our individual countries)
2. Defining research priorities

**Immunoo-assays in children**
Longitudinal studies, age related, MDR monitoring, site-specific, in immunocompromised

**Pharmacokinetics**
New and old TB drugs

**MDR TB**
Risk factors, management (exposed and cases)

Members with existing studies will liaise
to share data and compare experience and recommendations as well as
prepare shared data for joint publications

(f.ex.: Bamford et al, ptbnet (UK), Arch Dis Child 2009)

Protocol sharing in labs/training
Where from here

Database negotiations with TBNET- in process, needs to be intensified

Funding opportunities ? within EU- FP7 calls

Descriptive manuscript of childhood TB in Europe to be prepared

ptbnet members contributing to TBNET anti-TNF and IGRA consensus statement

Expansion of the group to include clinician, laboratory and epidemiologist in each place

Close collaborations with TBNET (www.tb-net.org)

Database
Website space
MDR study
Paediatric aspects of other studies
Consider TB as a family disease and set up your clinics in this way

Ensure that paediatric information is collected specifically/identifiable

Collect information on contact screening

Collect information on chemoprophylaxis and outcome

Join paediatric research studies
  - Diagnostics
  - TB/HIV coinfection- test the cases also in children
  - be aware of drug formulations for children

Join the
Muchas gracias por su atención

Hay preguntas???

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