

Report on meeting of childhood TB subgroup, Monday 17 October 2005, Versailles.

Background

Urgent and effective action is necessary to decrease the burden of childhood TB. The management of children with TB often falls outside the routine operations of National TB Programmes (NTPs). There is broad consensus on current international guidelines for case finding and treatment of children with TB, contact tracing of children at high risk of TB for preventive TB treatment, and including all childhood TB cases in routine NTP recording and reporting activities. However, many NTPs do not routinely include the management of children with TB as part of their routine operations.

In support of the subgroup's objectives to promote a) implementation of guidelines, b) mobilisation of human resources, c) ongoing policy development, and d) research, the subgroup held its second meeting under the auspices of the DOTS Expansion Working Group on 17 October 2005 in Versailles, France. The agenda appears in Annex 1 and the list of participants in Annex 2.

Main issues

1. Doses of anti-TB drugs for children

Anti-TB drugs have rarely been evaluated specifically to establish recommended doses in children. The literature is sparse on pharmacokinetic and pharmacodynamic studies on anti-TB drugs in children, including in those with HIV infection. The results of some pharmacokinetic studies are awaiting publication and several pharmacokinetic studies on isoniazid and rifampicin in children with and without HIV infection are under way.

a) Ethambutol

Peter Donald presented the preliminary results of a literature review of ethambutol efficacy and toxicity, commissioned by the WHO Stop TB Department in view of the need for a consistent recommended daily dose. Pharmacokinetic studies have indicated that daily doses of ethambutol up to the maximum 15 mg/kg currently recommended by the WHO Stop TB Department often result in substantially sub-therapeutic serum concentrations. Since reported toxicity in children is very rare using 20 mg/kg daily, a recommended dose of 20 (15-25) mg/kg would represent a satisfactory compromise between efficacy and toxicity. This is in line with the revised recommendation to be published shortly by the WHO Department of Child and Adolescent Health.

Action point:

WHO secretariat to finalise (with Peter Donald) the review of the daily dose of ethambutol and promote a standard recommendation of 20 (15-25) mg/kg.

b) Other anti-TB drugs

The subgroup discussed how members could contribute to review of the existing evidence concerning pharmacokinetic and efficacy studies of other anti-TB drugs, to promote the development of improved recommendations.

Action point:

Subgroup members to let the secretariat know if they propose to undertake a review of pharmacokinetic and efficacy studies of other anti-TB drugs.

2. Making best use of routine NTP data regarding TB in children, including TB/HIV

Pierre-Yves Norval and Mark Cotton made a presentation on making best use of routine NTP data regarding TB in children, including TB/HIV. Pierre-Yves Norval indicated the proposed changes to the standard NTP Form 1 "Quarterly report on TB case management in basic management unit". The consensus among the group was to ensure that the form enables the enumeration of children in at least two age categories (0-4 and 5-14 years) instead of the current single category (<15 years) for new pulmonary and new extrapulmonary TB cases (block 1). This distinction is crucial in ordering drugs (since child-friendly formulations are particularly important in children aged 0-4 years) and in enabling monitoring of trends in these two distinct age groups. At the same time, since very few children aged 0-4 years have sputum smear-positive pulmonary TB, the single category 0-14 years is adequate instead of the two age categories (0-4 and 5-14 years) for new sputum smear-positive pulmonary TB cases (block 2).

Action point:

Pierre-Yves Norval to revise the standard NTP Form 1 so that it has the two age categories (0-4 and 5-14 years) for new pulmonary and new extrapulmonary TB cases (block 1), and one age category (0-14 years) for new sputum smear-positive pulmonary TB cases (block 2).

3. Developing an operational research agenda on childhood TB

Peter Donald gave an update on development of the prioritised research agenda commissioned by the WHO Stop TB Department for improved management of childhood TB as part of NTP activities. The main discussion points concerned the need to ensure the agenda covered the full range of aspects of the management of childhood TB, and to highlight the research implications of the impact of HIV on childhood TB.

Action point:

Peter Donald to further develop the research agenda in the light of the discussion and then circulate it around the subgroup members for final comments.

4. Child-friendly use and formulation of anti-TB drugs

Hugo Vrakking provided an update on the proposals by the Global Drug Facility (GDF) to respond to demand from countries by making available the following fixed-dose combinations (FDCs) for treating children with TB:

Category 3, initial phase (daily): Rifampicin 60 mg / Isoniazid 30mg / Pyrazinamide 150 mg (R60/H30/Z150)

Categories 1 and 3, continuation phase (daily): Rifampicin 60 mg / Isoniazid 30mg (R60/H30)

Categories 1 and 3, continuation phase (three times weekly): Rifampicin 60 mg / Isoniazid 60 mg (R60/H60)

Action point:

Regarding the treatment of children in Category 1, Hugo Vrakking to explore with the GDF a) the provision of four-drug FDCs for children, and b) the possibility of modifying the GDF Patient Kits, e.g. by scoring tablets.

5. Brief reports on other issues

a) The International Standards for TB Care

Rob Gie reported that these standards satisfactorily covered the management of children with TB and children who were TB contacts.

b) The Stop TB Strategy

Dermot Maher reported that the new WHO Stop TB Strategy (that builds on and goes beyond the DOTS strategy) incorporates the management of children with TB and children who were TB contacts.

c) Guidance for NTPs on mainstreaming the care of children with TB into routine NTP activities - next steps in dissemination

Lisa Nelson reported that she will finalise this guidance shortly so that the document "Guidance for National TB Programmes on the practical management of children with TB" can be published for all subgroup members to help disseminate. The document will ensure consistency as far as possible with current international policies, e.g. IUATLD policies on child lung health, WHO policies on the Integrated Management of Childhood Illness (IMCI), and WHO policies on TB control, in order to promote the uptake and usefulness of the final document.

d) Sharing information, e.g. use of website

Lisa Nelson suggested that the subgroup members can make use of the Stop TB Partnership website for disseminating information.

e) Establishing a technical committee to review TB/HIV issues

Lisa Nelson volunteered to be the focal person for this activity.

The next subgroup meeting will as usual be held just before the annual IUATLD World Conference on Lung Health in Paris (scheduled from 31 October to 4 November 2006 in Paris, France).

Annex 1: Agenda

	Topic	Presenter
13.30 - 13.45	Welcome and introduction	Rob Gie (chairperson)
13.45 - 14.30	Topic 1. Doses of anti-TB drugs for children a) ethambutol - need to agree on recommendation based on literature review b) other drugs - how can the subgroup promote the development of improved recommendations based on review of the existing evidence and better pharmacokinetic and efficacy studies?	Peter Donald
14.30 - 15.15	Topic 2. Making best use of routine NTP data regarding TB in children, including TB/HIV	Pierre-Yves Norval and Mark Cotton
15.15 - 16.00	Topic 3. Developing an operational research agenda on childhood TB	Peter Donald
16.00 - 16.15	Coffee break	
16.15 - 16.45	Topic 4. Child-friendly use and formulation of anti-TB drugs	Hugo Vrakking and Shamim Qazi
16.45 - 17.30	Topic 5. Brief reports on other issues	
	a) The International Standards for TB Care	Rob Gie
	b) The Stop TB Strategy	Dermot Maher and Rob Gie
	c) Guidance for NTPs on mainstreaming the care of children with TB into routine NTP activities - next steps in dissemination	Lisa Nelson
	d) Sharing information, e.g. use of website	Lisa Nelson
	e) Establishing a technical committee to review TB/HIV issues	Lisa Nelson

Annex 2: List of participants

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