Annual meeting of the Childhood TB Subgroup
Tuesday 29 October 2013

Hyatt Regency Paris Etoile, 3, Place du Général Kœnig, Paris, France, 75017

Meeting Report

Background

The agenda of the 2013 annual meeting of the Childhood TB subgroup was focused on scaling up childhood TB activities at country level. The meeting was attended by some 75-80 participants, representing pediatricians, NTP managers, partners, and WHO staff from regions and countries.

Summary of the meeting

1. Opening and welcome

The annual childhood TB subgroup meeting was opened by Steve Graham (Chair) and Mario Raviglione (Director, WHO Global TB Programme). In his opening address, Mario Raviglione welcomed the participants on behalf of the WHO Global TB Programme and recognized that the subgroup is very active and ever growing. He also congratulated Steve Graham for his leadership. In his openings remarks, Mario Raviglione referred to the launch of the Roadmap on 1 October 2013 outlining steps to end childhood TB related deaths. The Roadmap provides an opportunity to build linkages beyond the TB community, especially with partners working in the maternal and child health field (so important to reach children with TB).

2. Report from the Chair on 2013 activities

Steve Graham referred to the 10th anniversary of the Childhood TB subgroup founded in 2003 and added "When you hit your 10th birthday, adolescence starts" referring to the challenges ahead moving forward more independently with guidance of the Roadmap and the need to for greater inclusion of adolescents under the subgroup's umbrella.
Over the first ten years, the momentum has continued to build and there are increasing demands on the subgroup. In the last 12 months, members of the subgroup have actively engaged in:

- providing guidance to countries on child TB such as within NTP reviews and updating guidelines
- contributing to future policy development by serving on advisory and expert panels of WHO
- the development of the revised second edition of the Guidance to National TB Programmes on the Management of TB in children (currently with Guidelines Review Committee and hopefully available by end 2013) and the recent systematic review on the use of Xpert MTB/RIF in children to inform policy.
- advocacy for childhood TB e.g. the Childhood TB Roadmap 2013.
- contributed to efforts to improve estimates. The burden of TB disease among children was first highlighted in the Global TB Report in 2012 and will be included in 2013 report. We are also contributing to the UNITAID and USAID

funding STEP-TB project to quantify the pediatric drug market and encourage manufacturers to produce fixed-dose combinations with the right dosing.

- in their individual capacity, are actively involved in research: e.g. IMPAACT TB scientific committee of NIH – proposals on novel studies of diagnostics, therapeutics and preventive therapy ; along with implementation research, while noting huge scope for operational research by NTPs
- the Sentinel project to guide and advocate for better care for and estimates of children with MDR TB.

The subgroup should now give more emphasis on moving from policy to practice at the country level. There needs to be decentralization of activities and regional/national capacity building. In order to reach children with TB, we need to reach out to other health services including maternal and child health services and HIV services. We need to further offer training to the national TB programmes and pediatricians working with the NTP. With the growing number of requests for technical assistance (in light of the Global Fund New Funding Model), we now need to strengthen our capacity to facilitate and contribute to NTP reviews and identify additional individuals to ensure representation. The subgroup needs further regional representation and it is good to see that several regional initiatives are being established.

3. UNITAID funded STEP TB project on the development of new child-friendly FDCs

Cherise Scott of the TB Alliance gave an update on the UNITAID funded STEP-TB project on the development of new child-friendly Fixed Dose Combinations (FDCs). The TB Alliance has also received funding from USAID to start the project up.
Currently not enough children with TB are being treated or are not being treated appropriately.
The goal of the STEP-TB project is to increase access to optimal pediatric TB medicines which means correctly dosed, properly formulated, affordable, high quality pediatric TB medicines.
Providing proper treatment to end pediatric TB requires a multi-faceted approach: market understanding (how many patients are there and where); clinical (collect clinical data necessary for new formulations) and regulatory understanding (clarify and accelerate pathway); engaging manufacturers (to create competition in pediatric TB markets); engaging countries and donors (to encourage change in policy and uptake by countries); and, information exchange (created pediatric medicines information exchange platform). The TB Alliance and WHO are working on all the above approaches simultaneously.

4. The use of Xpert MTB/RIF in children

Anne Detjen presented the outcome of the systematic review on Xpert MTB/RIF for the diagnosis of tuberculosis in children which did inform the WHO policy update on the use of Xpert MTB/RIF launched in October 2013. The objectives of the review were to determine summary estimates of the diagnostic accuracy (sensitivity and specificity) of Xpert MTB/RIF for the detection of 1. Pulmonary TB; 2. RIF resistance (in respiratory specimens); 3. Peripheral lymph node TB (in LN aspirates/biopsies); 4. TB meningitis (in

cerebrospinal fluid specimens (CSF)) in children aged 0-15 years with presumed TB. 16 studies were included in the review. All were conducted in higher-level care facilities.

In summary, the analysis has shown that Xpert MTB/RIF shows similar performance in expectorated or induced sputum and gastric lavage. The results are associated with smear status. Smear status might be a proxy for severity/extent of disease. Xpert has an advantage over smear microscopy being about three times more sensitive when compared to culture. Overall, Xpert has sensitivity of 66% and specificity of 98% compared to culture. However, 40-80% of childhood TB cases (all diagnoses including clinical) will be Xpert negative (since only 20-60% of all children with TB are confirmed by culture). Increasing the number of Xpert MTB/RIF tests will increase the number of identified TB cases but has cost implications.

Regardless of the above finding, the results of the systematic review highlight the need for scale-up of Xpert MTB/RIF. Referral systems will need to be optimized. Scale-up may increase the motivation to get pediatric specimens and lead to an increased number of confirmed TB cases. But there is a clear need to emphasize that negative results must be interpreted with caution i.e. a negative Xpert does not rule out TB. Therefore, diagnosis will remain a composite in the context of contact history, signs and symptoms, or other diagnostic tools. There is a need for further research that applies clear criteria for inclusion of children with suspicion of TB as well as clinical case definitions. It is important to study the impact of disease severity on test accuracy; performance of Xpert in outpatients settings (uncomplicated disease); integration of Xpert in non-traditional TB settings such as malnutrition units; routine programme data; type of specimen and specimen collection techniques (including less invasive specimens); and, patient important outcomes for children: time to diagnosis, time to treatment initiation, and cost.

5. The Childhood TB Roadmap

On behalf of Heather Menzies (CDC Namibia), Anne Detjen gave a presentation on the Childhood TB Roadmap launched on 1 October 2013 in Washington DC through a press conference and workshop. The Roadmap outlines 10 steps to zero deaths:

1. include the needs of children and adolescents in research, policy development and clinical practices;
2. collect and report better data, including data on prevention;
3. develop training and reference materials for health care workers;
4. foster local expertise and leadership;
5. do not miss critical opportunities for interventions;
6. engage key stakeholders;
7. develop integrated family-centered and community-centered strategies;
8. address research gaps;
9. meeting fudning needs for childhood TB; and,
10. form coalitions and partnerships to improve tools for diagnosis and treatment.

The launch has been covered by at least 131 news stories. The associated press article ran in more than 70 media outlets worldwide. The US State Department Articles were sent to more than 300 US Embassies. The workshop gave examples of existing efforts to

integrate childhood tuberculosis into MNCH services. Participants discussed how to implement the Childhood TB Roadmap, defined next steps for different stakeholders and areas for operational research. Dr Obasanya, NTP manager Nigeria, presented Nigeria's roadmap for childhood TB. PATH presented field experience with integrating child TB in MNCH services. Reference was made to the WHO/UNICEF training modules for community health workers, which now are updated for TB and HIV. The CORE group outlined possible areas for TB intervenitons within community child health programmes. Round table discussions to identify challenges, opportunities, next steps and areas for operational research were organized for the following topics: childhood TB and common childhood illnesses; childhood TB and community health care; TB/HIV integration; contact screening, preventive therapy and treatment support; recording and reporting to improve data-driven decision making; and, advocacy. Common themes identified included the need: to "think TB"; for integration at all levels; to implement and make use of existing algorithms and approaches; to use new technologies (Xpert MTB/RIF and M-health); and, for training. Discussions took place on how we can accelerate the activities to country level (e.g. use existing contact lists; organize national childhood TB roadmap workshops); how we can best provide follow-up with MNCH groups (e.g. support through childhood TB subgroup); and, how we can ensure continued advocacy (beyond TB, with donors, and media coverage). World TB Day 2014 and the annual meeting of the subgroup in 2014 may be good opportunities to evaluate progress.

6. Experiences in scaling up childhood TB activities:

Tanzania

Richard Christopher presented Tanzania's experiences in scaling up childhood TB. The Ministry of Health and Social Welfare and International Centre for AIDS Care and Treatment Programs (ICAP) have established a pediatric TB centre of excellence in Dar es Salaam, a learning centre with new advanced technology. The NTLP, in collaboration with WHO, USAID, ICAP and other partners have developed pediatric guidelines including a training manual for facilitators and health care workers. Job aids have also been developed. So far 1800 health care workers in 17 regions have been trained. Programmatic challenges include: insufficient funds to build capacity among health care workers, to print and distribute guidelines and to procure effective tools; insufficient human resources for health; TB notifications are not disaggregated by pediatric age groups; there are no ACSM materials and activities focusing on TB in children; and there is a lack of research targeting children. Clinical challenges include: lack of adequate capacity among health care workers to manage TB in children; difficult to obtain sputum samples sometimes requiring invasive procedures (IS, GA); bacillary burden is lower and yield from sputum, gastric aspirates and culture is low. Opportunities include: political commitment; presence of guidelines and training materials; presence of a centre of excellence on childhood TB; availability of pediatric TB formulations; partners supporting implementation of pediatric TB; and, community linkage with former TB patients for active case finding. Tanzania is planning to scale up its activities to 5 regions with a high TB burden with a focus on capacity building among health care workers (training and mentorship), strengthening of laboratory services, advocacy and community engagement.

Vietnam

Steve Graham presented review experiences from south east Asia. In 2011, Vietnam NTP established a Child TB working group, updated the national TB guidelines and included recommendations for contact screening and Isoniazid Preventive Therapy (IPT). With technical support provided by KNCV through TB Care, NTP also initiated training of trainers for community-based contact screening and strengthening child TB diagnosis in 4 pilot provinces. The desk guide was adapted and training materials and updated reporting and recording forms were developed. At the end of 2012, the activities were reviewed. 1480 health workers had been trained so far. Although there's political will, there is a wide policy-practice gap. There is a variable updake of IPT and low numbers of TB cases are referred or diagnosed. Vietnam NTP intends to roll out activities to an additional 21 provinces in 2013/14 with funding from the Global Fund. The next review of this project is planned for September 2014.

Lao PDR

There is also political will in Lao PDR to improve child TB diagnosis and management and to reduce infant and child mortality. National guidelines are available. But also in Lao PDR, we see a wide policy-practice gap. Child TB is under-diagnosed and under-recognized. Almost no child contact screening and management is happening. There is a lack of confidence in making a clinical diagnosis of TB in children at all levels. Appropriate formulations are available but there are difficulties to provide treatment if the TB in child is not confirmed. There is limited linkage between child health workers including pediatricians and the NTP. During the programme review, it was recommended that Lao PDR identifies child TB champions and forms a national child TB working group that improves the linkage and supports NTP in training and operational research. Lao PDR should strengthen diagnosis including at the district level through training and development of a child TB management manual for health workers in the local language. Finally, it was recommended that Lao PDR implements symptom-based screening and management of contacts including children.

Myanmar

All forms of TB are being registered and recorded since 2007. A high proportion of children is treated for TB. Before 2007, Myanmar reported only smear-positive cases. Since 2008, the proportion of child TB among all cases increased 22% to 29% (from 28,000 to 42,000 cases). In 2012, 96% of child TB cases were pulmonary TB ("primary complex disease" diagnosed on CXR), and only small numbers are EPTB. In 2012, 43% of childhood TB cases were in the age group 0-4 and 57% were in the age group 5-14. National data can however hide patterns by averaging out variations amongst the regions. It is therefore important to look at various states and regions in more detail. The national guidelines have a very good algorithm for diagnosis of child TB. The problem is in application i.e. if the child has prolonged symptoms of presumed TB. Only the CXR highly suggestive of TB should be treated. For those with an uncertain diagnosis and without a contact history, should be followed up after 1 month. Only if cough, lethargy or weight loss is worsening, then TB should be suspected. The role of CXR needs to be clarified in the guidelines, only considered with clinical picture and contact history. It

must be unequivocal, not just minor changes. Steve Graham finished with a word of caution: increased attention to child TB can lead to overdiagnosis.

Pakistan

Farhana Amanullah gave an overview of childhood TB activities in Pakistan. The TB prevalence rate is estimated at 350 per 100,000 population (child and adult cases). WHO estimated in 2012 that children comprise about 10% of the TB case load (25,733 out of 255,094). There are no data available on the incidence of childhood TB in Pakistan. However, about 34.7% of the population is younger than 15 years. This means that the incidence could be about 42 cases of childhood TB per 100,000 population. Provincial TB data are disaggregated in categories: 0-4 and 5-14 years. BCG coverage is reported as 95%. The NTP has developed child TB guidance and a desk guide in 2007. Childhood TB was also included in the JMM 2010. Recommendations included: update child TB guidelines, train NTP and non-NTP sectors, introduce DOTS in children's hospitals and achieve high BCG coverage. Current activities include: A training of trainers on childhood TB for Pakistan and Afghanistan in May 2013. There were 26 participants including GPs, pediatricians, chest physicians and NTP workers. The training and course materials were based on the Cape Town 2012 training but the modules were adapted to Pakistan and Afghanistan's context. Following the training, a large public sector children's hospital in Karachi has started reporting on child TB and is now the largest TB reporting center in the city. The NRL Islamabad is now using Xpert MTB/RIF for child TB diagnosis with increasing numbers of gastric aspirates and sputum samples. In August-September, the TB Alliance and WHO conducted a rapid assessment of pediatric TB to understand under (or over) diagnosis and treatment in non-NTP facilities. The assessment was supported and facilitated by the NTP. Challenges identified included: poor facility recording systems; lack of awareness that accurate recording and reporting will inform and enable child TB drug procurement from the NTP; recording and reporting tools are not always available; PPM partnerships are weak or lacking in the private/academic hospitals that were targeted. Next steps in scaling up child TB activities will therefore include: raising the profile of childhood TB in the National Strategic Plan to control TB; identification of the child TB champion who can work closely with the NTP and liaise with pediatricians, private hospitals and academia; mandatory recording and reporting of child TB cases; steady supply of quality assured pediatric FDCs; dissemination of the updated national child TB guidance; dissemination of and training in the use of recording and reporting tools for child TB; development of a clear referral system from private diagnostic centres seeing child TB suspects; and, inventory studies for child TB.

India

Vijay Edward presented on the work on childhood TB of World Vision India. WVI has received funds through GF Round 9 and supports the Revised National Tuberculosis Control Programme (RNTCP) in eight districts of Andhra Pradesh at district and sub-district levels by mobilizing the community. TB CARE groups (8-15 members were trained, linked to a network of existing registered community based organizations and linked to microfinance and women's development projects). Over 9,000 community based DOTS workers have been trained. WVI has reached out to remote areas and

marginalized populations and provided logistical support to the RNTCP. WVI is also active in schools to sensitize children about tuberculosis. Through this programme, WVI contributed to the cure of over 30,000 TB patients including approximately 3000-3600 children. Critical elements to success are: political will; multisectoral involvement (building links with MCH and other child health services); public-private initiatives (e.g. academic schools); school health screening and involvement of children; training of pediatricians in diagnosis, treatment and on contact investigation and uptake of IPT; increase diagnostic and treatment capacity and establish clear referral systems; develop training modules for different health care workers; sensitization of communities; ensure availability of child friendly FDCs ; recording and reporting and notification to national TB programme; and, operational research.

7. Panel discussion on participation in recent programme reviews

In the afternoon session, the experts who had recently joined a programme review were asked to share their experiences and to give their opinion on how to strengthen our capacity to participate in programme reviews and to develop a cohort of people who can do this in different part of the worlds. Farhana Amanullah went to Indonesia and Thailand; Gloria Oramasionwu (CDC) and Lisa Obimbo went to Nigeria; Anthony Enimil went to Ethiopia and Chishala Chabala went to Uganda; Steve Graham to Lao PDR and Myanmar. Although each programme review is unique, there were many common experiences. The following was considered to be important: availability of political will; having a national childhood TB working group; guidance and desk guides; linking public and private sectors; reaching out to other child health programmes including MCH and HIV services; strengthening of recording, reporting and notification; childhood TB to be part of routine training; appropriate referral mechanisms; and, local pediatricians to be part of the review. The panel members all considered it a very useful exercise and agreed that the experiences need to be written up and published. A template (check list) should be shared with experts who will participate in future programme reviews. There was also a call to all subgroup members to actively respond to future requests for participation in programme reviews. With the growing demand for technical assistance in this area, the subgroup will need to further strengthen and create regional expertise.

8. Regional initiatives on childhood TB

Currently, three WHO regions are setting up regional initiatives on childhood TB. EURO has set up a European Task Force on childhood TB and has mapped who is currently engaged in childhood TB in the region. EURO is finding recurring issues related to diagnosis, treatment, contact investigation and IPT. A survey was designed and 15 countries in EUR participated in that study. Findings were presented in May during the NTP managers meeting in The Hague. Although there is high political commitment, there is a huge diversity throughout the European region e.g. TST cut-off points, BCG vaccination schemes, few guidelines follow the 2010 WHO Rapid Advice, etc. EURO is trying to keep the discussions ongoing through regular webinars. Indicators to measure progress are needed. EURO is planning to prepare and organize a first regional Childhood TB conference in a Central Asian country around World TB Day 2014.

AFRO recently organized a regional meeting (July 2013). A regional framework for childhood TB has been developed. Tanzania, DRC and Mozambique have started pilot projects which will be evaluated next year.
In 2013, WPRO circulated a questionnaire to capture what is already happening in the various countries of the region. Most countries have a chapter on children in the national TB guidelines or a separate guideline. But the big issue is implementation. Other issues include: overdiagnosis and underdiagnosis, underreporting; lack of collaboration with the private sector. The initiative has lead to some funding from Japan and a regional task force on childhood TB has been set up. The task force will meet in March 2014 in Ha Noi. In addition to NTPs, MCH and HIV programmes will be invited as well as many partners active in this field.

9. Challenges of adolescents living with HIV

At the end of the meeting, Anthony Enimil presented the challenges of adolescents living with HIV in Kumasi, Ghana. An adolescent HIV clinic was set up in March 2010. Currently, over 100 adolescents are being registered. About 60% of them are orphaned. 98% of adolescents living with HIV in this area were infected through mother-to-child transmission (MTCT). The median age is 14.5 years. There are many adherence issues. About 70-80% miss their follow-up date. Camps are being organized for these adolescents. There is always a TB/HIV advisor present. Medical students are rotating through the clinic. Challenges include: rampant drug shortages; inappropriate pediatric dosages; shortage of reagents for CD4 count/viral load; disclosure issues; poor adherence; and, the health information system. Urgent attention to adolescents living with HIV is needed at the national level; appropriate and regular pediatric and adolescent drug formulations should be made available as well as CD4/viral load reagents/machines and drug resistance tests. During a lively discussion, it was mentioned that peer pressure and the way health care workers manage adolescents have an impact on adherence.

10. Way forward for 2014:

- Bring childhood TB to STAG-TB 2014 and invite colleagues working on maternal and child health as well as HIV/AIDS to facilitate integration.
- Document and publish scaling up activities.
- Assist countries to include Childhood TB in all steps of the Global Fund New Funding Model (e.g. NTP review, National TB strategic plan, gap analysis, concept note).
- Encourage countries to identify national champions on pediatric TB.
- Build and expand regional capacity to address growing requests for technical assistance.
- Consider to add a module on participation in programme reviews to the South Africa training course (annual workshop in Cape Town).
- Consider to include adolescents in the scope of work of the Childhood TB subgroup.

Annex 1. Agenda

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Agenda Childhood TB subgroup meeting - 29 October 2013		
08:30 - 09:00	*Registration*	
09:00 - 09:15	Opening and welcoming words	Steve Graham, Chair Childhood TB subgroup, Mario Raviglione, Director WHO GTB Lucica Ditiu, Executive Secretary, Stop TB Partnership Secretariat
09:15 – 9:40	Report from Chair on the 2013 activities of the Childhood TB subgroup	Chair
9:40 – 10:00	Update on the UNITAID-funded project on development of new fixed-dose combinations	Cherise Scott, TB Alliance
10:00 - 10:20	Update on the use of Xpert MTB/Rif in children	Anne Detjen, The Union
10:20 - 10:40	Coffee/Tea break	
Experiences in scaling up childhood TB activities		
10:40 – 11:10	Childhood TB Roadmap – update & next steps	Anne Detjen
11:10 – 11:25	Tanzania	Richard Christopher
11:25 – 11:40	Myanmar, Lao DPR and Vietnam	Steve Graham
11:40 – 11:55	Pakistan	Farhana Amanullah
11:55 – 12:10	India	Vijay Edward
12:10 – 12:50	Discussion	
12:50 – 14:00	Lunch break	
14:00 – 15:00	Experience from recent NTP reviews by Childhood TB experts – panel discussion Laos, Indonesia, Nigeria, Thailand, Ethiopia and Uganda	Steve Graham Farhana Amanullah Gloria Oramasionwu Lisa Obimbo Anthony Enimil Chishala Chabala
15:00 – 15:30	Regional initiatives: panel discussion (10 minutes per region) AFRO, EURO and WPRO	Daniel Kibuga Martin van den Boom Rep from WPRO
15:30 – 16:00	Tea/Coffee break	
16:00 – 16:20	Challenges of adolescents living with HIV	Anthony Enimil
16:20 – 17:20	Discussion on how to scale up Childhood TB activities using the country and regional experiences	All
17:20 – 17:40	Wrap up, next steps and closure	

Annex 2. List of participants (based on sign-up sheets)

Core team members:
Steve Graham (Chair)
Farhana Amanullah
Anneke Hesseling
Cleotilde (Telly) Hidalgo How
Elizabeth (Lisa) Obimbo
Gloria Oramasionwu
Clydette Powell
James Seddon

Subgroup members, presenters and other participants:
Lisa Adams
Irfan Akhtar
Valentina Anisimova
O. Batbayar
Leoopold Blanc
David Bryden
Chishala Chabala
Richard Christopher
Charlotte Colvin
Clemax Couto Sant Anna
Luis Cuevas
Maria Fatima Pombo March
Anne Detjen
Triya Novita Dinihari
Vijaykumar Edward
Penny Enarson
Kayt Erdahl
Anthony Enimil
Nicolas Enrich
Anne Fanning
Sharmin Ferdous
Jacqueline F.
Lena Fiebig
Kari Franu
Deliana Garcia
Elizabeth Gardiner
Anna Marie celina Garfin
Agnes Gebhard
Jeffrey Hafkin
Morley Hanson-Nortey
Nuruzzaman Haque
Meghan Holohan
Mar Mar Htay
Faustin Kitetele
Michelle Lafay
Keri Lijinski
Thandar Lwin
Vishnu Mahamba
Rifat Mahfuza
Shelly Malhotra
Anna Mandalakas
Mariquitz Mantala
Ya Diul Mukadi
Gigado Mustapha
Dyah Erti Mustikawati
Dorcas Muteteke
Katerine Ngo
Betty Nsangi
Temtayo Ofusofe
Colleen Pero
Ejaz Qadeer
Abdul Hamid Salim
Simon Schaaf
Cherise Scott
Alena Skrahina
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