SOUTHERN AFRICA MEDICAL UNIT (SAMU)
MEDICAL DEPARTMENT OPERATIONAL CENTRE BRUSSELS (OCB)

HIV-TB News for November 2013

The Child and Adolescent Edition

Photo credit: Saar Baert

MEDECINS SANS FRONTIERES
DOCTORS WITHOUT BORDERS

SAMU
SOUTHERN AFRICA MEDICAL UNIT

HIV-TB News for November 2013

Southern Africa Medical Unit (SAMU)
Medical Department
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Welcome to SAMU's HIV-TB News for November 2013. This edition is devoted to HIV and TB issues in children and adolescents, age groups that usually receive too little attention. The information presented here will hopefully help to strengthen prevention, diagnosis and management of HIV and TB not just in our 'vertical' programs where HIV and TB are the main focus, but also in 'non-vertical' programs that have primary health care, nutrition, and hospital activities, in which HIV and TB may go undiagnosed and unmanaged in children and adolescents.

Let's begin with new World Health Organization (WHO) recommendations from their recently released 'Consolidated ART Guidelines': www.who.int/hiv/pub/guidelines/arv2013/en/.

Expanded ART eligibility for children

There is increasing evidence that early antiretroviral therapy (ART) decreases mortality in HIV-infected children. The WHO now recommends expanded ART eligibility criteria for HIV-infected children as follows:

- all children <5 years of age, regardless of clinical stage or CD4 cell count, i.e. test and treat
- all children >5 years having a CD4 cell count ⩽500 cells/µl, regardless of WHO clinical stage
- all children with severe or advanced symptomatic disease (WHO clinical stage 3 or 4), regardless of age and CD4 cell count
- any child <18 months of age who has been given a *presumptive clinical diagnosis* of HIV infection (i.e. sick but without an HIV test result available)

Preferred first-line ART regimens

The WHO now recommends that **children <3 years** be prescribed a first-line ART regimen containing a **protease inhibitor (PI)**, for example lopinavir boosted by ritonavir (LPV/r). More specifically:

An LPV/r-based regimen should be used, regardless of NNRTI exposure. If LPV/r is not feasible, treatment should be initiated with a NVP-based regimen.

- Where viral load monitoring is available, consideration can be given to substituting LPV/rwith an NNRTI after virological suppression is sustained.
- One ongoing trial (named Neverest) is evaluating such a PI-sparing strategy, which can reduce exposure to LPV/r, offer an easier approach to maintaining treatment, and preserve PI-based therapy for 2nd line ART. Results are expected at the end of this year.

The NRTI backbone for ART regimens in children <3 years should be (ABC or AZT) + 3TC.

- In settings that still include d4T in the backbone, this would mean moving away from the 3-in-1 fixed dose combinations (FDCs) of Triomune

Junior and Baby, and more towards the use of non-FDCs.

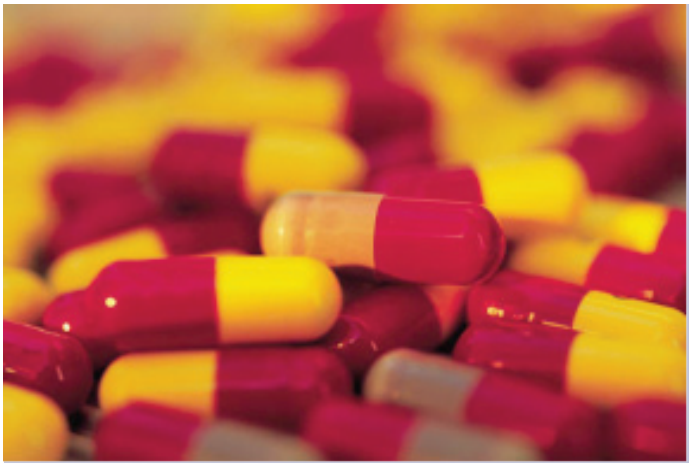
When active tuberculosis (TB) occurs in children <3 years or <10 kg (i.e. not yet able to be prescribed EFV) while on an ART regimen containing LPV/r or nevirapine (NVP), a triple NRTI regimen (ABC + 3TC + AZT) is recommended as an option by WHO. Once TB therapy has been completed, this regimen should be stopped and the initial regimen restarted.[1]

The rationale for use of a PI-based regimen in children <3 years (as opposed to NVP as previous) is to achieve **effective and rapid control of viral replication** in the context of a high HIV viral load (VL) and rapid infant growth. In addition, HIV-infected infants who were previously exposed to NNRTIs (e.g. NVP) used as part of regimens aiming to prevent mother-to-child transmission (PMTCT) have demonstrable viral resistance, which in turn compromises the 'response to therapy' of 1st-line ART containing NVP.

In addition, other evidence has become available suggesting the superiority of an LPV/r-based regimen regardless of PMTCT exposure. For example, the **IMPAACT p1060 study** looked at children <3 years having no prior exposure to single-dose NVP and found double the failure rate in those treated with an NVPcontaining regimen compared to a regimen with LPV/r.

ART regimens comprising a non-thymidine NRTI backbone (i.e. not AZT or d4T) and one NNRTI continue to be recommended by WHO as the preferred choice in **children >3 years:**

- ABC + 3TC + EFV for children between 3 – 9 years and adolescents <35 kg
- TDF + 3TC + EFV for adolescents (10 – 19 years) weighing >35 kg



[1] MSF recommends additional ARV options for co-infected children <3 yearson TB treatment, including 'super-boosting' of LPV with additional ritonavir; if LPV/r syrup is not tolerated or not possible (e.g. absence of a cold chain), then NVP can be given in a dose up to 200 mg/m2 (without the need for stepwise dosing).

Child-friendly ARV formulations

Despite WHO's current preference for PI-based regimens in children <3 years, HIV/ART programmes will find this a challenge to introduce, since the currently available formulation of LPV/r syrup does not taste good and is not heat-stable, the latter making it difficult to both transport and store.

Thus, we continue to wait for a better PI-containing formulation for children, especially one that can compete with the **convenience** of the FDCs currently available that contain NVP (e.g. Triomune Junior and Baby).

Meanwhile, the Drugs for Neglected Diseases initiative (DNDi) is partnering with Indian drug manufacturer Cipla to develop two different 4-in-1 ARV FDCs designed specifically for children <3 years of age (and those not yet able to swallow tablets): AZT+3TC+LPV/r and ABC+3TC+LPV/r. These new formulations will consist of granules that fit into a capsule that can be opened in order to spread the medicine onto soft food or be mixed with milk. These new formulations will be 'taste-masked', require no refrigeration, and be easy to dose according to the child's weight. The goal is to make these new FDCs available by 2015, following feasibility studies in the field (including possibly in the MSFOCB project in Kenya).
PI-containing mini-tabs (formerly called 'sprinkles') will be available in early 2014. These taste better than the syrup and are heat-stable. Projects should strongly consider ordering them next year while awaiting the granules...

Previous editions of this newsletter are available in the folder entitled 'SAMU HIV-TB Newsletters' in the Resources section of the SAMU website: http://samumsf.org/blog/portfolio-item/hivtb-briefing-documents/.

Other news related to paediatric drug formulations

- In addition to the new 4-in-1 FDCs described above, a formulation of ritonavir granules is being developed for babies and young children who require treatment simultaneously for HIV and tuberculosis (TB).
- We continue to wait for FDCs containing **Tenofovir (TDF)** to become available in paediatric formulations. Although the U.S. Food and Drug Administration (FDA) has already approved the use of TDF in children as young as 2 years (at a dose of 8 mg/kg once daily, up to a maximum of 300 mg), in practice only those children >35 kg are able to use the existing 300 mg tablets. A 2-in-1 FDC containing TDF 75 mg and 3TC 75 mg may be available as early as next year. Note however that some paediatricians and groups have expressed reservations about the use of TDF in young children due to potential renal toxicity and unknown effect on bone density.

- We also continue to wait for paediatric FDCs to become available that allow dosing of **first-line TB regimens** (i.e. Category I) according to the new WHO dosing recommendations for H, R, Z, and E. The new 'ideal' FDC proposed by WHO is HRZ 50/75/150; however, this is not expected to be available before 2015...
- The almost total lack of paediatric formulations of second-line TB drugs to treat **drug-resistant TB (DR-TB)** in children is shameful. The only child-friendly drug delivery system existing today related to DR-TB is a plastic spoon that allows for more accurate weight-based dosing of the adult granular formulation of **para-aminosalicylic acid (PAS)** in children. A case study related to this delivery system can be found at: www.thoracic.org/advocacy/stop-tb/FURIN_Case_Study.pdf.

Did I hear somebody use the 'C' word?

Have you heard about the 'Mississippi baby' that has been 'functionally cured' of HIV? Doctors treated the newborn with 3 ARV medications soon after being born to an HIV-infected woman. Despite confirmation of HIV infection at birth, the child remains in 'remission' 3 years later, despite being off medication.

Reducing the burden of HIV in children

The UNAIDS 2013 Global Report (www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2013/gr2013/UNAIDS_Global_Report_2013_en.pdf) reminds us that, in order to achieve the global goal of reducing the number of children newly infected by 2015, substantially greater efforts are needed to **link pregnant women and children to HIV treatment and care.** Not only are pregnant women living with HIV overall less likely than treatment-eligible adults to receive ART, treatment coverage among HIV-infected children in 2012 was less than half the coverage for adults.

The failure to expand access in many settings to **early infant diagnosis (EID)** is an important reason why HIV treatment coverage remains much lower in children than in adults. There are a number of ways that we can help to increase coverage of EID:

- Ensure that 'opt-out' HIV testing is routinely offered to all HIV-exposed infants at 6 weeks of age using dried blood spot (DBS) specimens taken by heel prick and sent for DNA PCR testing.
  - Note that some MSFOCB projects without access to in-country HIV DNA PCR testing currently send specimens to a laboratory in S.A. with a good turn-around-time (10 days) and price ($18/test).
  - In some settings, HIV testing immediately after birth may help to increase coverage of EID.
- Moreover, all HIV-exposed children should again be tested for HIV using a rapid diagnostic test (RDT) at 18 months of age and/or after completion of breastfeeding.
- Ensure that 'opt-out' HIV testing is routinely being offered in all 'non-vertical' projects having paediatric and nutrition activities, since the rate of HIV infection in children presenting for care in such projects will be much higher than the general HIV prevalence for that setting.
- Improved linkage of mother and child through the use of cards kept in facilities (as done in Malawi) or by patients themselves (as done in other sites).
- Looking into the future, new point-of-care (POC) HIV diagnostics will be available as early as the end of this year. These new technologies will help facilitate EID in settings that we support, including strategies that aim to test HIV-exposed neonates immediately after birth; such a strategy could improve retention and linkage to treatment, as well as ensure very early treatment initiation.

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Reducing the burden of TB in children

Wherever there are adults with active tuberculosis (TB) disease, there will be children at risk, as well as some likely to have undiagnosed active TB disease. Children at especially high risk of morbidity and mortality from TB include the very young, the malnourished, and those infected with HIV. Some ways to reduce the burden of TB in children in your projects include:

- Clinically based, setting-specific TB **diagnostic algorithm**s should be used to detect TB in children, replacing TB scoring systems (e.g. Keith Edwards scoring table), since the latter have shown to be not very effective, in particular at diagnosing pulmonary TB.

- Chapter 5 in the updated MSF TB Guide (2013) contains algorithms to assist with TB diagnosis in symptomatic children and management of child contacts of TB cases.

- Isoniazid preventive therapy **(IPT)**: Some MSFOCB non-HIV projects, e.g. the district-level hospital being supported by MSFOCB in Afghanistan, have started to implement IPT in child contacts under the age of 5, to help prevent active TB following exposure to a case of active TB --- setting a good example for other 'nonvertical' projects!
- Specific MSFOCB guidance is available for the management of **child contacts of DR-TB** cases. If you haven't already seen it, ask your Paediatric or HIV/TB Adviser for this MSFOCB guidance document.
- A **Roadmap for Childhood TB** was recently launched by WHO and others (available at apps.who.int/iris/bitstream/10665/89506/1/9789241506137_eng.pdf that outlines activities that need to be implemented in order to accelerate progress toward the elimination of childhood TB.

Sputum induction

Question: What if a child is coughing and suspected to have active TB, but it is not possible to obtain a quality sputum specimen?

Answer: Sputum induction (SI) --- a safe, affordable way to increase confirmation of paediatric TB!

A video describing how to perform SI can be found in the 'Recent Projects' section of the SAMU website: samumsf.org/blog/portfolio-item/sputum-induction-procedure/.

Some caveats to this video include:

- Salbutamol inhaler use prior to SI: Give 1-2 puffs (1 for children <3 years), wait 10 seconds, and repeat. The spacer device/mask should remain on for at least 10 seconds after the puff(s), in order to allow the child enough time to inhale the medication.
- If the child is not old enough to spontaneously produce a specimen, nasopharyngeal aspiration (NPA) should be performed with the child swaddled and in a ***supine position.***
- It is important to correctly measure the length of the tube prior to NPA, especially in young infants.
- As with any medical procedure, the HCW needs to be properly trained and supervised.
- Appropriate infection control measures are essential both during and following the SI procedure. The degree of sterilization that is required prior to reuse of nebulization materials is often debated, as this can be a challenge in resource-limited settings. Ask your SAMU focal point about which sterilization protocol is most suited to your setting. Remember that the benefit of SI must always outweigh any risk to a child suspected of having active TB disease.

Gastric lavage (GL) can be an alternative to sputum induction in certain settings. However, it should be noted that SI has a number of advantages over GL, as SI can be performed as an outpatient procedure, is relatively more easy to perform, and the yield is higher. ***More specifically, the yield from one induced sputum specimen has been shown to be equivalent to 3 GL specimens in a South African setting:*** www.ncbi.nlm.nih.gov/pubmed/15639294.

GeneXpert testing in Children

Xpert MTB/RIF (also known as GeneXpert) has been shown to be a useful test for rapid diagnosis of paediatric TB from respiratory specimens in both primary care and hospital settings, plus lymph node aspirates. However, the impact of using Xpert MTB/RIF to test other extrapulmonary specimens from child TB suspects remains to be determined...

Interpreting Chest X-rays in Children

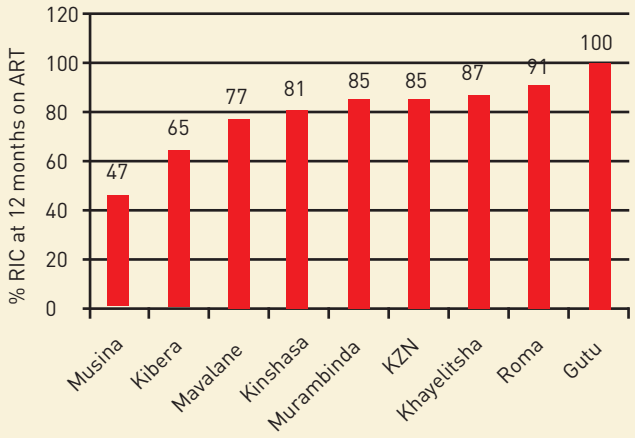
Since it won't always be possible to obtain a specimen for testing in children, it is important that clinicians in your program feel comfortable interpreting chest x-rays in children, including identification of enlarged lymph nodes inside the chest.

Two fabulous videos are now available on the SAMU website that can help diagnose TB in children, using frontal and lateral views, thanks to a collaborative effort between SAMU and radiologist Dr. Savvas Andronikou: samumsf.org/blog/2013/10/28/paediatric-tb-xrays-part-1-clues-from-the-frontal-films-by-savvas-andronikou/.

Paediatric ART outcomes

First, the good news: Retention rates for children on ART at 12 months (Figure 1) are higher than those for adults (not shown) in corresponding settings. In all of the decentralized HIV programmes supported by MSFOCB, paediatric ART has likewise been decentralized and is usually initiated by nurses. This means that children are able to access HIV care and treatment nearer to their homes, which should in turn further improve retention rates.

Figure 1: Retention in Care at 12 months of children initiated on ART during 2011 (in 9 MSFOCB-supported programs)



But now for the bad news: Following implementation and support for routine viral load (VL) monitoring in several high HIV prevalence contexts in sub-Saharan Africa (Figures 2 and 3), we are seeing higher rates of detectable VLs among children and adolescents as compared to adults. Not only does this suggest more adherence problems in adolescents and children (and their caregivers), but it also implies a higher risk of development of HIV resistance and eventual treatment failure.

Figure 2: Proportion of detectable VL results by age in 9769 people on ART in Shiselweni, Swaziland (2012-2013, MSFOCG)

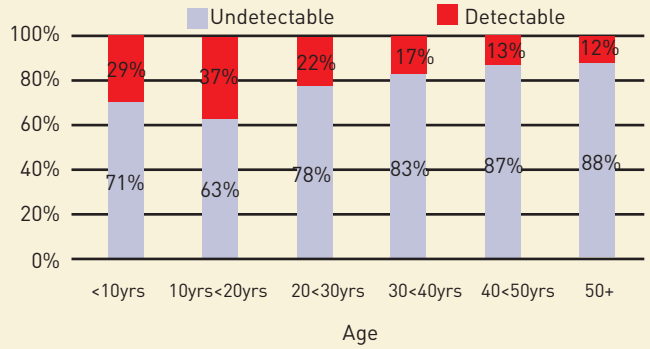
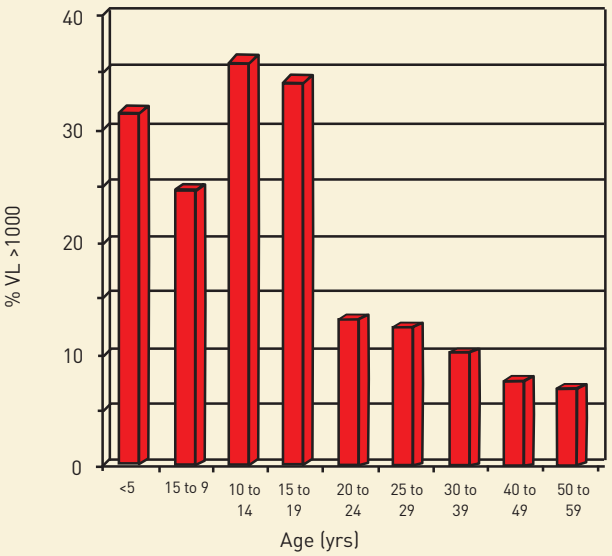


Figure 3: Rates of VL >1000 copies/ml by age in 4 programs supported by MSFOCB (Kenya, Malawi, KZN, and Zimbabwe)



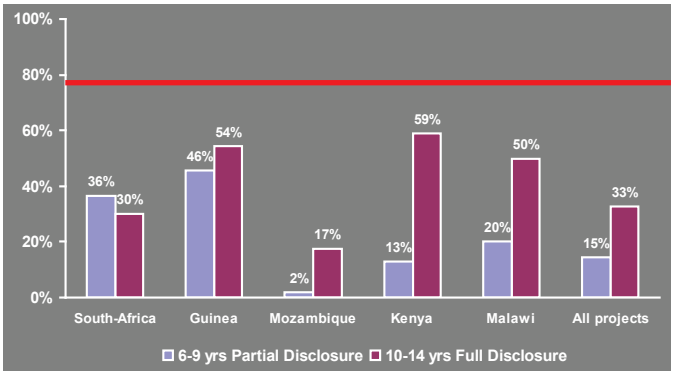
Disclosure of HIV status

WHO recommends disclosure of HIV status to children and adolescents of school-going age, as there is evidence of a health benefit by doing so. Such disclosure however can be a difficult task for caregivers due to lack of HIV/ART-related knowledge, fear of emotional consequences for the child, and fear that the child will disclose her/his status in the community.

But how to offer HIV disclosure support? MSFOCB projects currently offering disclosure support to caregivers use a model of progressive disclosure whereby children are gradually told about their disease. This involves two partial disclosure sessions in which, after agreement of the caregiver, children and adolescents are given information about what is happening in their body without naming the disease. The process is finalised with a full disclosure session before the age of 12, whereby the virus is named and more detailed information is given on treatment, transmission and family history. The way sessions are offered varies in different programs, as does the type of staff providing the disclosure support.

Table 4 below shows the disclosure status in 2013 of children and adolescents enrolled on ART in 5 MSFOCB programs. Analysis has shown that increased investment in disclosure support has led to better outcomes; but HIV status remains undisclosed to an unacceptably high number of young adolescents, which may contribute to poor adherence to ART.

Table 4: Disclosure Status in 2013 of Children and Adolescents enrolled on ART in 5 MSFOCB programs



Health centre-related barriers to disclosure include lack of task-shifting, training of counselors and delayed provision of disclosure support. **Caregiver-related barriers** include ongoing refusal to disclose and children having multiple caregivers. Future MSF interventions will need to find a balance between health care worker (HCW) and caregiver-driven models of disclosure. Routine and structured disclosure support should be offered earlier and counselors are to be further trained.

- A **presentation** on HIV disclosure from Brussels O.R. Day can be found here: samumsf.org/wp-content/uploads/2013/11/HIV_disclosure_to_infected_children_and_adolescents_how_well_is_MSF_doing.pdf.
- A number of different resources to help with disclosure can be found in the *'Guidelines and References > Patient and Community Support > Child Patient Support'* folders in the Resources section of the SAMU website: samumsf.org/blog/portfolio-item/hivtb-briefing-documents/. These include general and project-specific guidelines, child counselling cards, and other tools.
- An entire **DVD** on paediatric support can be requested from saar.baert@brussels.msf.org.

Progress since the Adolescent Workshop

Following a workshop on "Adolescents, Young Adults & HIV" in July 2012 (workshop report available at www.dropbox.com/s/l43fbiixb1utgbq/Adoworkshop_summary report_final.pdf, several MSFOCB projects have been working on improving care for this target group. The Khayelitsha project adapted their ART initiation counseling for youth, focusing on an individualized adherence plan around specific barriers that youth face.

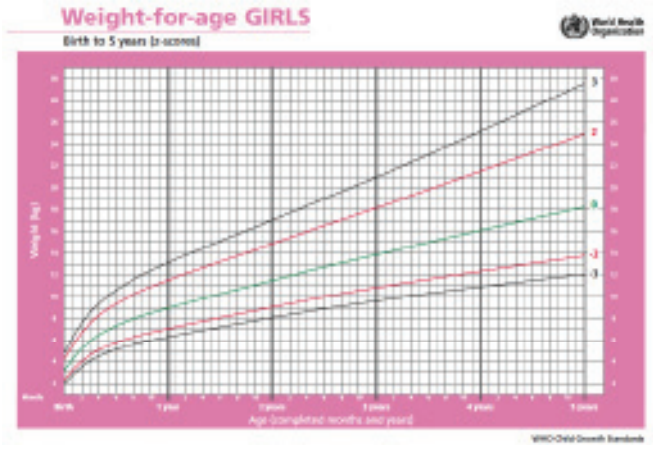
Projects in Mozambique started organizing group ART refills for adolescents in their Adolescent and Youth Friendly Services (also known by the acronym SAAJ), based on the Khayelitsha experience. The MSFOCB project in Buhera, Zimbabwe, identified several action points after counselors and health care workers received training on paediatric and adolescent care:

- improve facility-based HIV testing
  - ensure that all children of HIV-positive parents are tested
  - encourage better provider-initiated testing and counseling (PITC) for adolescents presenting with primary care conditions (albeit limited by the age of consent being 16 years)
- routine use of growth charts
- improve the attitudes of staff towards youth
- ensure that family planning is offered

If you have other examples of how to improve adherence in adolescents, or wish to send feedback to any of the stories in this newsletter, please e-mail samunews@joburg.msf.org. We would be happy to hear from you!

Measuring Growth

Children infected with HIV early in life are at risk of impaired growth and developmental delay. Thus, it is important that a number of parameters be monitored closely in all HIV-exposed/infected children in order to allow for early recognition of growth failure: weight, height, and head circumference (HC). Weight-for-age (W/A, a measure of nutritional status) and HC should then be plotted on individual growth charts (that should be kept in each child's folder).



A Virtual Support Group for Youth

MSF supports one of two youth clinics in Khayelitsha by organizing a virtual support group using a free instant messaging 'app' called **'Mxit'** that runs on cell phones. This **virtual support group**, open only to youth club members, is hosted in a private chat room on Mxit and allows for interaction between regular youth club meetings. A counselor facilitates the chat rooms for 30 minutes a day during the week.

Despite some positive responses related to the concept and the potential that virtual support groups have to provide support and information outside of regular youth club visits, it is not yet being widely used. Focus group discussions held in July 2013 identified the following barriers: cost (to access the internet, etc), a preference by youth for other platforms or other chat rooms, and logistical issues such as a loss of password or phone. Suggestions to improve the virtual support group included adding a feature to enable anonymity while chatting, provision of situation-specific information, ability to interact with peers other than just the counselor, having a critical mass of peers on the platform to chat with at all times, having the availability to see past chats from others, and being able to leave questions for the counselors to answer if they are not online at the same time.

Photo credit: Samantha Reinders

Other HIV/TB Resources you should know about

- As mentioned earlier, an updated version of the MSF TB guide was released this year (available at refbooks.msf.org/msf_docs/en/tuberculosis/tuberculosis_en.pdf and contains useful information related to diagnosis and treatment of TB in children, including weight-based tables that follow the new WHO dosing recommendations for paediatric TB patients using currently available 3-in-1 and 2-in-1 FDCs (see Appendix 8).
- SAMU is in the process of updating 'Management of HIV-related conditions and ART in Adults and Children', the **field guide for HIV clinicians (including nurses) working at the primary health care level.** MSF projects in all contexts will find it useful for its practical information on HIV, TB, other opportunistic infections, and ART.
- These and other HIV/TB resources can be found in the 'Guidelines and References' folder in the Resources section of the SAMU website: samumsf.org/blog/portfolio-item/hivtb-briefing-documents/.

Thank you for ensuring that the information in this newsletter makes it all the way through the MSF chain to those important and hard-working people in our field projects and their clinics...

From the entire SAMU team

P.S. If you think that your setting would be a good place to pilot any of the innovations mentioned in this newsletter, please let us know...

Annex: A selection of recent articles from the Journals

i. Contact Investigation for Active Tuberculosis among Child Contacts in Uganda

How useful is tracing of child contacts of known TB cases? Jaganath et al (CID, Sept 2013) assessed the yield of contact tracing on childhood TB and indicators for disease progression in Uganda. They evaluated 761 child TB contacts using clinical, radiographic, and laboratory methods for up to 2 years, and found a TB prevalence of 10%, of which 71% were culture confirmed positive. There were no cases of disseminated disease, and **483 (99%) of 490 children started on isoniazid preventive therapy (IPT) did not develop disease.** Multivariable testing suggested HIV status and baseline positive TB skin test (TST) as risk factors; BCG vaccination was particularly protective, especially among children 0-5 years.
They conclude that *"contact tracing for children in high burden settings is able to identify a large percentage of culture confirmed positive TB cases before dissemination of disease, while suggesting factors for disease progression to identify who may benefit from targeted screening."*
www.ncbi.nlm.nih.gov/pubmed/24077055

ii. It's hard work, but it's worth it: the task of keeping children adherent to isoniazid preventive therapy

Isoniazid preventive therapy (IPT) is effective, as long as it is taken. Skinner et al (Public Health Action, Sept 2013) performed in-depth interviews with parents of children and health care workers in 3 clinics in South Africa to understand what encourages or inhibits children from adhering to IPT. They found that adherence was affected by social problems, stigma about TB and its link to HIV, and the extended treatment period. Clinic nurses acknowledged problems of staff shortages, lengthy waiting times and conflict between staff and community members. The authors concluded that "parents who maintained adherence to the IPT regimen showed that it was possible even in very difficult circumstances and that further effort is required to improve some of the clinic services, correct misinformation, reduce stigma and provide support to parents."
www.ingentaconnect.com/content/iuatld/pha/2013/00000003/00000003/art00003

Are you still uncertain about which children, adolescents and adults should be offered IPT? Then take a look at MSF's intersectional 'Guidance Paper on Intensive Case-Finding, TB Skin Testing, and IPT'. If your setting has not yet implemented IPT, then it is more manageable to do so in stages, e.g. children first, followed by HCWs, pregnant women, other adults, etc...

iii. Preventive therapy for child contacts of multidrug-resistant tuberculosis: a prospective cohort study

Have you ever wondered if drugs could be used to prevent active TB disease in child contacts of adults with MDR-TB? Seddon et al (CID, Sept 2013) gave 3-drug prophylaxis --- ofloxacin, ethambutol and high-dose isoniazid --- for 6 months to 186 child contacts of ofloxacin-susceptible MDR-TB index cases in Western Cape province, South Africa. Six (3.2%) developed incident TB during 219 patient years of observation time; one child (0.5%) died, and 7 (3.7%) developed Grade 3 adverse events. Factors associated with poor outcome were: age <1 year, HIV-positive status, exposure to multiple source cases and poor adherence. The authors conclude that *"this 3-drug preventive therapy regimen was well tolerated and few children developed TB or died if adherent to therapy.*
The provision of preventive therapy to vulnerable children following exposure to MDR-TB should be considered."
www.ncbi.nlm.nih.gov/pubmed/24065321

iv. High treatment success in children treated for MDR-TB: an observational cohort study

Despite the challenges related to lack of evidence-based guidelines, no paediatric formulations, and few pharmacokinetic data in children, good outcomes can be achieved. Seddon et al (Thorax, Sept 2013) reported on the treatment and outcomes in 149 children with MDR-TB in Cape Town, South Africa. Their median age was young (36 months), 32/146 tested (22%) had HIV infection and 59 (40%) had a confirmed diagnosis. Ninety-four (66%) children were treated with an injectable drug and the median total duration of treatment was 13 months. Thirty-six (24%) children were cured, 101 (68%) probably cured, 1 (1%) was transferred out, 8 (5%) were lost to follow-up and 3 (2%) died. They concluded that, "a confirmed diagnosis of MDR-TB is not possible in all cases but this should not impede the treatment of MDR-TB in children. More than 90% of children with MDR-TB can be successfully treated."
www.ncbi.nlm.nih.gov/pubmed/24064441

v. Poor Outcomes in a Cohort of HIV-Infected Adolescents Undergoing Treatment for MDR-TB in Mumbai

The excellent treatment success in children with MDR-TB mentioned above does not translate to HIV-positive adolescents! Isaakidis et al (PLoS ONE, July 2013) found that early mortality and 'mortality after default' were the most common reasons for poor outcomes in a group of 11 adolescents with MDR-TB co-infected with HIV receiving care and treatment in the OCB project in Mumbai. Early mortality suggests the need for rapid diagnosis and prompt treatment initiation, and adolescents might benefit from active contact-tracing and immediate referral. Default occurred at different times, suggesting the need for continuous, intensified and individualized psychosocial support for co-infected adolescents. Operational research among coinfected adolescents will be especially important in designing effective interventions for this vulnerable group.
www.plosone.org/article/info:doi/10.1371/journal.pone.0068869

Contact tracing allows for earlier diagnosis of active TB. If a contact tracing strategy does not yet exist in your setting, your SAMU focal point can help with this. A number of documents and tools already exist, including a MSFOCB Guidance Paper on 'Follow-up of child contacts of drug-resistant TB cases' (May 2012).

vi. Evaluation of Point-of-Care Nucleic Acid Testing for HIV Viral Load and Early Infant Diagnosis in Primary Health Clinics

Testing for HIV viral load (to monitor response to ART) and early infant diagnosis (EID) of HIV is sophisticated and takes place in central laboratories, which means a long turn-around-time for a clinician in a rural setting to receive a result. In an 8 abstract presented at CROI (March 2013, Paper #607), Jani et al presented findings related to the evaluation of a new point-ofcare (POC) nucleic acid test (NAT) platform for conducting on-site viral load and EID in primary health clinics in Mozambique. They found that, *"when conducted in a primary health care setting, the Alere HIV POC NAT device demonstrated high sensitivity for detecting virological failure and both high sensitivity and specificity for EID. The lower specificity for viral load indicates that confirmatory testing may be required for patients diagnosed with virological failure with this test. While further assessment is needed to determine the impact and cost-effectiveness of POC NAT in low resource settings, these results demonstrate the technical feasibility of POC testing for decentralized viral load and EID."*

vii. Adherence and Viral Suppression Among Infants and Young Children Initiating Protease Inhibitor-based ART

How best to measure adherence (apart from monitoring with HIV viral load testing) with the move towards PI-based ART? Teasdale et al (Pediatr Infect Dis J, May 2013) found that caregiver reports of missed doses did not predict virologic response to treatment in South Africa. Instead, pharmacist medication reconciliation correlated strongly with virologic response for children taking a LPV/r-based regimen and appears to be a valid method for measuring pediatric adherence.
http://journals.lww.com/pidj/Abstract/2013/05000/Adherence_and_Viral_Suppression_Among_Infants_and.12.aspx

viii. Effectiveness of First-line ART and Acquired Drug Resistance Among HIV-1–infected Children in India

We already know that HIV viral load testing is more accurate than CD4 count testing to monitor 'response to therapy' in adults on ART. What about in children? Shet et al (Pediatr Infect Dis J, May 2013), in an analysis of treatment response among HIVinfected children in India on first-line antiretroviral treatment for >2 years, found that 85% were virologically suppressed. Of those with virologic failure, only 17% manifested immunologic failure, whereas the majority had resistance-associated mutations.
The presence of resistance highlights the need for virologic monitoring of children receiving antiretroviral treatment to optimize treatment success and preserve future treatment options. http://journals.lww.com/pidj/Abstract/2013/05000/Effectiveness_of_First_line_Antiretroviral_Therapy.47.aspx

ix. Safety of Perinatal Exposure to Antiretroviral Medications: Development Outcomes in Infants

Sirois et al (Pediatr Infect Dis J, June 2013) evaluated effects of perinatal exposure to ARV medications on neurodevelopment of 374 HIV-exposed infants in the U.S. who were ultimately found to be uninfected, assessing cognition, language, motor skills, social-emotional development and adaptive behaviour. Overall 83% of the 374 infants were exposed to combination ART (given to the mother); 79% were exposed to regimens containing protease inhibitors. For individual ARVs, following sensitivity analyses, the adjusted group mean on the Language domain was within age expectations but significantly lower for infants with perinatal exposure to atazanavir ($p = 0.01$). They concluded that their results support the safety of perinatal ARV use. Continued monitoring for adverse neurodevelopmental outcomes in older children is warranted, and the safety

of atazanavir merits further study.
www.ncbi.nlm.nih.gov/pubmed/23340561

x. Resistance in Paediatric Patients Experiencing Virologic Failure with first-line and second-line ART

Orrell et al (Pediatr Infect Dis J, June 2013) examined HIV-1 resistance in children failing first-line and second-line ART in South Africa, all with clade C virus. Those exposed to full-dose ritonavir had multiple protease resistance mutations. Nineteen percent had wild-type virus. They concluded that currently recommended treatment regimens (i.e. NNRTI-based ART followed by LPV/r-based ART) have the most favorable resistance profile at second-line failure, and that use of genotype resistance testing for children failing second-line ART is an essential tool to allow for rational and efficient use of limited ART resources.
www.ncbi.nlm.nih.gov/pubmed/23303240

xi. Integration of TB and PMTCT of HIV programmes in South Africa

TB prevention activities should be integrated with other health programmes, including mother and child health. Uwimana and Jackson (Int J Tuberc Lung Dis, Oct 2013) assessed the integration of TB services into a PMTCT programme in KZN province in S.A. by performing exit interviews with pregnant women attending 10 antenatal care (ANC) clinics. Of 150 women interviewed, 112 (75%) reported being educated on TB symptoms on the day of their visit; 56% were screened for TB symptoms and 27% were suspected to have TB; 26 (17%) women were HIV-positive and 2 (8%) were co-infected with TB. There was no record of provision of isoniazid prophylaxis for PMTCT clients with latent tuberculous infection. The predominant barriers to the integration of TB-PMTCT services included lack of skilled providers and their supervision, the physical layout of the TB-PMTCT services and the service delivery mechanisms. They concluded that, *"the integration of TB prevention and care into the PMTCT programme was inadequate. Integration of TB services into the ANC PMTCT programme will require strong leadership to address barriers such as training gaps, lack of supervision and service delivery mechanisms."*
www.ncbi.nlm.nih.gov/pubmed/24025379