Improving Tuberculosis Care for Children in High-Burden Settings

Why are we still struggling to control the devastating effects of childhood tuberculosis? This disease has been with us since ancient times and yet, even with known effective prevention and treatment strategies, much of the world has unacceptable levels of childhood morbidity and mortality due to tuberculosis.

As expected, progress in identification and treatment has occurred primarily in high-income countries. Dr Starke’s column captures the current state of affairs and highlights the needed actions that would make a difference for millions of children’s lives.

Jay E. Berkelhammer
Column editor

Despite the availability of inexpensive diagnostic tests, curative and preventive therapies, and the widespread use of the BCG vaccines, tuberculosis (TB) remains an important cause of morbidity and mortality, and its lack of control is one of our biggest public health failures. Childhood TB has been a troublesome and largely neglected subject for organizations dedicated to TB or child health. A clinical diagnosis usually can be established by using epidemiology (especially recent contact with a case subject) and clinical findings such as symptoms, radiography, and a test for TB infection. However, because of its paucibacillary nature, TB is difficult to confirm microbiologically with sputum smear or culture specimens.

Given the reliance on sputum microscopy for diagnosis and reporting cases in most high-burden countries, the majority of childhood TB cases are not diagnosed; for most of those cases that are diagnosed clinically, the World Health Organization (WHO) is not notified. Over the last 20 years, there has been a veritable explosion of research on childhood TB. Although microbiologic confirmation of childhood TB remains elusive, we have effective and safe regimens for treating TB disease and infection, and we know that early intervention via contact tracing and treatment can prevent many cases of childhood TB. The goal is for no child to die of TB. We know what to do; what we are lacking mostly is the motivation, means, and coordination of services to do it.

**Epidemiology of Childhood TB**

In most high-income countries, childhood TB has decreased remarkably over the past 30 years, but decreases have not occurred in many low- and middle-income countries. In 2012, total notifications of childhood TB cases to WHO were as follows: smear-positive pulmonary, 46 448; smear-negative pulmonary, 163 477; and extrapulmonary, 91 308. Based on the number of reported childhood TB cases and techniques used to estimate adult TB case numbers, WHO estimated that in 2012 there were 530 000 TB cases among children <15 years of age and 74 000 TB-related deaths among HIV-negative children (no estimates of mortality in HIV-positive children were given). However, 2 recent articles report much higher estimates. Jenkins et al reviewed 97 articles on multidrug-resistant TB in children and used setting-specific estimates and TB incidence to estimate that there were 999 792 cases of childhood TB in 2010. Dodd et al used sophisticated mathematical modeling techniques on reported TB data and local household structure. Their estimates, using the 22 WHO-classified high-burden TB countries in 2010, were as follows: 15 319 701 children cohabitating with a TB case; 7 591 759 children who became infected with *Mycobacterium tuberculosis*; and 650 977 children who developed TB disease. However, the case detection rate was estimated to be only 35%. The same study showed that cumulative exposure in these 22 countries meant that 53 234 854 children were infected and at risk for developing TB disease in the near or distant future. Clearly, the burden of childhood TB infection and disease is enormous, and few cases are being prevented.
WHY HAS CHILDHOOD TB BEEN NEGLICTED?

There are many reasons why childhood TB has not received adequate attention from child health and TB programs (Table 1). The child survival movement has not embraced TB as an important issue because of the lack of accurate estimates of TB morbidity and mortality in this age group. TB services in most low- and middle-income countries, including access to drugs and diagnostic tests, are restricted to national TB programs; understandably, therefore, little activity in the diagnosis, treatment, and prevention of TB has been undertaken by child health programs. As a result, there has been little advocacy for child TB services on the part of pediatricians and child health experts. Because childhood TB is difficult to confirm with a sputum smear specimen and because children with TB are rarely contagious, many national TB programs have paid little attention to children, and case notifications have been woefully inadequate. A common but misguided perception has been that giving infants a BCG vaccine and controlling adult TB in a population would be adequate to prevent childhood TB. As a result, effective prevention measures that are standard in low-burden countries, such as treatment of TB exposure and infection, have not been implemented in most high-burden countries. For several decades, WHO has recommended evaluating children who live in a household with a TB case subject; children with symptoms should be evaluated for TB disease, and those without symptoms should receive 6 months of isoniazid treatment. However, this simple, safe, and effective approach is rarely used in high-burden countries. Finally, there have been missed opportunities to correctly diagnose and treat children with TB in programs focused on other health problems of children who also are at risk for TB.4,5

CHILDHOOD TB AND HIV INFECTION

Children with untreated HIV infection are at high risk of developing TB disease if they become infected with *Mycobacterium tuberculosis*. Unfortunately, a recently published survey of pediatric antiretroviral treatment programs in Africa, Asia, the Caribbean, and Central and South America documented a low utilization of TB diagnostic and screening services in these programs.4 Although sputum microscopy and chest radiography were available in all programs, among the 146 children diagnosed with TB during the study period, chest radiography was used in 86%, sputum microscopy in 52%, induced sputum microscopy in 26%, culture in 17%, and Xpert MTB/RIF in 8% of children. Only 86% of the sites provided treatment of TB disease, and 30% never provided isoniazid preventive therapy to HIV-infected children. Recent studies have found that HIV-infected pregnant women are at increased risk of transmitting both HIV and TB to their infants.5 Although WHo guidelines6 recommend integration of TB/HIV activities into prevention of mother-to-child HIV transmission programs, this integration is inadequate or totally lacking in most programs in countries with a high TB burden.7

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**TABLE 1** Ten Reasons Why Childhood TB Has Been Neglected

<table>
<thead>
<tr>
<th>Reason</th>
<th>Description</th>
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<tbody>
<tr>
<td>1.</td>
<td>Inadequate data on cases and contacts</td>
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<tr>
<td>2.</td>
<td>Difficulty with microbiologic confirmation of disease</td>
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<td>3.</td>
<td>Children are rarely contagious (public health “dead end”)</td>
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<tr>
<td>4.</td>
<td>Perception from TB policy makers that treating adults is enough</td>
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<tr>
<td>5.</td>
<td>National TB programs fail to address children</td>
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<tr>
<td>6.</td>
<td>Lack of family-centered contact tracing</td>
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<tr>
<td>7.</td>
<td>Perceived lack of scientific study and scrutiny</td>
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<tr>
<td>8.</td>
<td>Misplaced faith in the BCG vaccine</td>
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<td>9.</td>
<td>Lack of industry support for drug formulations and new diagnostic tests</td>
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<tr>
<td>10.</td>
<td>Inadequate attention and advocacy by pediatricians and child health experts</td>
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</tbody>
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**TABLE 2** Roadmap for Childhood Tuberculosis: 10 Steps Toward Zero Deaths

1. Include the needs of children and adolescents in research, policy development, and clinical practice
2. Collect and report better pediatric data, including data on prevention
3. Develop child-specific training and reference materials for health care workers
4. Foster local expertise and leadership in childhood TB
5. Do not miss critical opportunities for intervention
6. Engage all key stakeholders
7. Develop integrated family-centered and community-centered strategies for children
8. Address research gaps in childhood TB
9. Meet funding needs for childhood TB
10. Form coalitions and partnerships to improve tools for diagnosis and treatment


**TABLE 3** Some Programs Into Which Childhood TB Services Can Be Integrated

- Integrated Management of Pregnancy and Childbirth
- Integrated Management of Childhood Illness
- Integrated Community Case Management
- Child HIV Care Programs
- Prevention of Mother-To-Child Transmission of HIV
- Nutrition programs for children
- Family planning and fertility services


**MALNUTRITION AND PNEUMONIA**

In countries with a high TB burden, malnutrition in children is a predictor of TB disease and worse outcomes.8 Pulmonary TB in young children often presents as pneumonia, but the diagnosis is usually not considered even in high-burden countries until the disease is far advanced. Chisti et al9 prospectively investigated causes of pneumonia in severely malnourished children aged <5 years in a hospital in Bangladesh. Of 1482 children with severe malnutrition, 405 had respiratory symptoms and an abnormal chest radiograph; TB was confirmed microbiologically in...
7% and clinically in 16%. Most of the confirmed cases did not have a known contact or a positive tuberculin skin test result. Unfortunately, TB screening at nutritional rehabilitation centers is often lacking. Bhat et al10 reviewed TB screening at nutritional rehabilitation centers in Karnataka, India, and found that a standardized TB diagnostic algorithm was followed for only 37% of the children. They also found operational challenges at the centers, including nonavailability of a pediatrician, nonfunctioning radiograph equipment, use of an inferior tuberculin solution, and poor training of the staff.

THE ROADMAP FOR CHILDHOOD TUBERCULOSIS

In recognition of the severity of the childhood TB problem and the many missed opportunities for diagnosis and prevention, WHO, UNICEF, and several other organizations released the Roadmap for Childhood Tuberculosis in October 2013.11 Reaching the goal of zero TB deaths among children will require “sustained advocacy, greater commitment, mobilization of increased resources, and a joint effort by all stakeholders involved in providing health care for children and in TB control.” Ten basic steps are described (Table 2). The most crucial steps include: better training of TB program personnel and child health workers in TB-related skills and techniques; engaging key stakeholders and fostering local expertise and leadership through coalitions and partnerships; integrating child TB services into existing health programs, especially those dealing with HIV infection and malnutrition (Table 3); developing family- and community-centered strategies, especially for prevention; and increasing funding for childhood TB programs and research. Improvement will depend on child health workers and policy makers determining the best ways to integrate TB content into existing programs that serve high-risk children, especially those who have HIV infection, malnutrition, and clinical pneumonia. In many cases, simply asking if anyone in the household is being treated for TB will alert the clinician that the child needs evaluation and treatment.

Although the roadmap discusses the 10 general steps to improve TB services for children, the actual implementation of these steps will need to be designed and conducted at the country and local level. It is crucial that pediatric societies and pediatricians working in high-burden countries become engaged in these efforts, to determine how the diagnosis, treatment, reporting, and prevention of childhood TB can be improved within the national TB program and addressed within existing child health programs at the local level. One key is simply to ask if the child has been exposed recently to an adult with TB; by intervening in this situation, millions of childhood TB cases and deaths can be averted.

REFERENCES


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### Improving Tuberculosis Care for Children in High-Burden Settings

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