

# CHILDREN AND TUBERCULOSIS

Exposing a Hidden Epidemic



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Tuberculosis (TB) remains among the top ten killers of children worldwide<sup>1</sup>, yet virtually no public or political attention is paid to TB as a children's health issue. Children have weak immune systems, making them prime targets for TB. Data show that in 2009, at least 1 million children became sick with TB. The World Health Organization (WHO) estimates that approximately 176,000 children died<sup>2</sup>, but the consensus among researchers says that actual figures are higher. TB preys on the most vulnerable children — the orphaned, the malnourished, those living with HIV — and it causes an almost unimaginable burden to children and their families. We must stop neglecting TB as a children's health issue and take immediate steps to stop TB from needlessly infecting and killing children.

### What is TB, and How is it Treated?



TB is an infectious disease caused by bacteria that often attack the lungs. It is spread through the air when an infected person coughs, sneezes, laughs, or even sings. When exposed to TB, most healthy people are able to fight the bacteria by sealing it off within a part of the body, usually the lungs. These people have a *latent TB infection*. They do not feel sick and they cannot spread the infection to others. Latent TB infection can be treated using only one drug, isoniazid, over the course of six to nine months.

In some cases, people are unable to fight the bacteria, and they become sick with *active TB disease*. If not treated properly, active TB is often fatal. Active TB is

treated using numerous drugs taken over a six-to-12-month period. It is crucial that patients take medication exactly as prescribed and complete the full course of treatment. If the medication is taken incorrectly or stopped prematurely, TB disease can easily reemerge and become resistant to medication. Drug-resistant strains of TB are much harder to cure and extremely expensive to treat.

## WHAT IS THE NATURE AND MAGNITUDE OF TB AMONG CHILDREN?

According to Dr. Jeffrey Starke, a leading TB specialist at Texas Children's Hospital, childhood TB "is a fundamentally different disease from adult tuberculosis. Its proper diagnosis, treatment, and prevention require specific planning and resources. We must consider the unique nature of childhood TB if we're to successfully eliminate TB anywhere in the world."

According to WHO, approximately 9 million people become sick with TB each year.<sup>2</sup> At least 10-15 percent of these cases are in children under 15 — but the percentage is probably much higher, because childhood TB is under-reported.<sup>1</sup> Most children have a type of TB classified as sputum smear-negative TB (see box on pg. 2: Types of TB), which makes them less likely to spread the disease to others — but it's still deadly if left untreated. Because on average children are less contagious than adults, they've been overlooked by national TB programs.

### CHILDREN ARE PRONE TO SEVERE TYPES OF TB ▶

While adults most often get TB in their lungs, in children the disease often spreads to other parts of the body. Children are therefore more likely than adults to develop severe forms of TB, including TB meningitis.<sup>1</sup> TB meningitis occurs when the bacteria spread to the central nervous system, including the brain. The bacteria inflame the tissue that protects the brain, causing it to swell. TB meningitis is most common in children under two years old, and the disease is almost always fatal without treatment. TB can attack virtually any part of a child's body in similar fashion.

### RATES OF TB IN CHILDREN ARE GROSSLY UNDER-REPORTED ▶

Most countries only report childhood TB cases that are considered "sputum smear-positive" (see box on pg. 2: Types of TB).<sup>2</sup> Because only 10-15 percent of children have this kind of TB, the vast majority of childhood TB cases go unreported — making it very difficult to deter-

mine the true burden of childhood TB that exists in the world. WHO estimates that 1 million children become sick with TB each year, but the real numbers are likely much higher. However, the true burden is unknown because nobody is collecting and merging enough data. According to Dr. Anneke Hesselning, a childhood TB expert at the Desmond Tutu TB Center at Stellenbosch University in South Africa, training health workers to diagnose TB in children leads to a significant jump in the proportion of cases detected — even using the inadequate tools currently available.<sup>3</sup>

### MULTIDRUG-RESISTANT TB IN CHILDREN ▶

Multidrug-resistant TB (MDR-TB) — defined as TB that is resistant to at least the two most powerful anti-TB drugs, isoniazid and rifampicin — afflicts approximately 440,000 people each year.<sup>4</sup> Despite studies that show children get MDR-TB, only adults are included in global MDR-TB surveys — meaning no one knows for sure how many children suffer from MDR-TB.<sup>1</sup> However, a few localized studies exist showing the burden is substantial. Studies in South Africa indicate nearly nine percent of childhood TB cases are drug resistant — a rate similar to adults.<sup>5,6</sup> Further research is needed to determine the true burden of childhood MDR-TB. While MDR-TB is curable in children, it takes expert medical care and extremely expensive treatment. It is far cheaper to prevent the development of MDR-TB in the first place, by ensuring that people are properly treated for drug-susceptible TB.

## WHAT FACTORS PLACE CHILDREN AT RISK FOR TB?

**POVERTY** ► Poverty is a major risk factor for TB. Poor children often lack access to care and live in overcrowded conditions that make them vulnerable to TB.

**YOUNG AGE** ► Infants and very young children have weak immune systems, which place them at higher risk of developing active TB. While the average adult with latent TB infection has a 5-10 percent lifetime risk of developing active disease, infants with a latent TB infection have a 40 percent chance of developing active TB during their first year of life.<sup>7</sup>

**MALNUTRITION** ► Malnourished children have weaker immune systems that make them more susceptible to developing active TB.<sup>8</sup>

**ORPHANS AND VULNERABLE CHILDREN** ► Orphans and vulnerable children are more likely to be malnourished, live in poverty, and lack access to medical care, which places them at higher risk of developing active TB.<sup>9,10,11</sup>

**HIV** ► HIV weakens the immune system, making a person vulnerable to TB. Children with HIV are up to 20 times more likely to develop TB than children with healthy immune systems.<sup>12</sup> TB remains the third leading killer of children with AIDS and nearly half of new childhood TB cases occur in children with HIV.<sup>13</sup>

**MATERNAL TB** ► Children whose mothers have TB are likely to both contract the disease and be born at a low birth weight. A child born to a mother with TB has an overall higher risk of death.<sup>14</sup>

### Types of TB

TB bacteria typically infect the lungs (called *pulmonary* TB) but may spread to virtually any other organ outside the lungs (called *extrapulmonary* TB), often the lymph nodes, brain, spine, or genital tract. Patients suspected to have pulmonary TB are asked to cough up phlegm — or *sputum* — which a laboratory technician then examines under a microscope. If a technician can see TB bacteria under the microscope, the patient is considered to have *smear-positive* TB, which is highly infectious. Many patients, especially children and people living with HIV/AIDS, have *smear-negative* TB — a form of the disease where the patient is sick but a technician does not detect TB bacteria under the microscope.

In December 2010, the World Health Organization endorsed a new tool to diagnose TB, Xpert MTB/RIF. Instead of using a microscope, this revolutionary tool uses DNA technology to rapidly identify TB bacteria in sputum samples in less than two hours.

## ANTHONY'S STORY

Gisele is the mother of twin boys, Anthony and Jordan. Both boys are very lively, so when Anthony stopped actively playing with Jordan, Gisele knew something was wrong. Anthony began to cry often and always appeared tired, so Gisele brought him to see the doctor. At first, the doctor thought Anthony had the flu and prescribed him flu medicine. Anthony didn't get better, so they returned to the doctor. Again, Gisele was told that Anthony had the flu. A few days later, Anthony's eyes started to glaze over and Gisele brought him to the emergency room. Anthony was then transferred to Texas Children's Hospital in Houston, TX, where doctors diagnosed Anthony with TB meningitis.

"It was terrifying to hear that he could die," says Gisele. Doctors traced Anthony's infection to a family friend who had been ill and provided Anthony life-saving surgery and medication for TB. Within weeks, he started to run around again with Jordan. Gisele is still troubled that it took so long to diagnose Anthony with TB. If detected earlier, chances are Anthony would not have needed surgery. "I was so angry. I did what I was supposed to do. I had been to the doctor so many times," exclaims Gisele. "It was heartbreaking to know how sick he was and how much pain he was in."

## ABHIJAT AND ABHISHAKT'S STORY

Abhijat and Abhishakt are playful twin boys, always giggling and running around. Their parents, Mamta and Jacob, are well educated and work as health advocates in India. One day Mamta and Jacob noticed their boys began coughing and wheezing, so they went to a private health facility. Since Jacob has a history of asthma, the doctor assumed asthma was causing Abhijat and Abhishakt to cough. He prescribed steroids and an antibiotic. Worried the humid weather was contributing to their coughing, Mamta and Jacob moved their family to a drier city in India.

Over the next six months, Mamta and Jacob brought their boys to see four different doctors at private health clinics, but their boys remained very ill. A friend suggested they see a public sector doctor, who was quickly able to diagnose Abhijat and Abhishakt with pulmonary TB. The boys were provided treatment and are happy and healthy today. For the first time in their life, Mamta and Jacob realized that TB is not "the other man's disease." It can happen to anyone.

If the private medical doctors realized TB was not a disease that only affects the poor and given attention to their symptoms, Abhijat and Abhishakt would have been cured much earlier. In many countries such as India, TB control efforts are focused around public health facilities. However, most people receive health care from private clinics. After their experience Mamta and Jacob believe the private health sector needs to be better integrated with national TB control efforts.

## HOW CAN TB IN CHILDREN BE PREVENTED?

It is more cost effective to prevent disease than it is to treat it. The most effective way to prevent childhood TB is to stop the disease from spreading in the wider community. According to Dr. Starke, “Even with the limited tools currently available, better organization of services and aggressively identifying recently exposed and infected children would prevent tens of thousands of tuberculosis cases in children every year.” This is achieved by what is commonly referred to as the *four I’s*<sup>15</sup> — intensified case finding, isoniazid preventive therapy, infection control, and integration.

### THE FOUR I’S ►

- **Intensified Case Finding** — When an adult is diagnosed with TB, all close contacts and family members — including children — should be identified and screened for TB, a method called intensified case finding. People with latent TB infection or active TB disease are then provided appropriate treatment, stopping the spread of the disease. Children who are considered high risk — especially those with HIV — should also be routinely screened for TB.<sup>16,17</sup>
- **Isoniazid Preventive Therapy (IPT)** — People with latent TB infection should be provided IPT, which prevents infection from developing into active disease.
- **Infection Control** — Homes, schools, health facilities, and other community settings need to be made safe from TB. Simple measures such as opening windows and doors in health facilities can establish natural ventilation and prevent the spread of disease.<sup>18</sup>
- **Integration** — TB services need to be integrated with primary health care, maternal and child health, and HIV services so that they’re widely available. Early initiation of antiretroviral therapy (ART) helps reduce the likelihood a child will become sick with TB.<sup>19</sup> Children with HIV should be placed on antiretroviral therapy (ART) immediately upon HIV diagnosis to reduce TB risk and death.

These methods are very effective at reducing childhood TB and are endorsed by WHO.<sup>20</sup> A program in Bangladesh is implementing active case finding by training community health workers to go door-to-door and screen children for symptoms of TB.<sup>21</sup> Unfortunately, many countries with constrained resources don’t follow the Four I’s. More supplies, training, and health care workers are needed to make TB prevention a reality.

**Tuberculosis is a disease of families.** When one family member gets TB, the disease can pass through the rest of the family. It happens easily, because TB germs spread from person to person through the air. Children typically get TB from parents or extended family, and oftentimes multiple family members are sick at the same time.<sup>3</sup> Even when parents aren’t sick, they take time off of work to care for their ill children, resulting in a loss of family income. The high cost of health care forces families to sell their belongings to pay for TB treatment, leading them into poverty. When parents are too sick to work, their children leave school to earn money for the family. Children with TB fall behind in their education and are heavily stigmatized, harming their ability to earn good wages in the future. In many countries, women with TB are abandoned by their families, who fear becoming infected themselves.

## KOFI'S STORY



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It started when Kofi's mother couldn't stop coughing, even after several weeks of taking medicines her husband had purchased from their local market in Kangemi, Kenya. Kofi, only four months old, was also sick and getting worse despite the treatment. After becoming too sick to work and care for her children, Kofi's mother found a ride to the clinic where she was diagnosed with pulmonary tuberculosis. Because Kofi was so young and had received the BCG vaccine which protects children against some forms of TB (see page 7 to learn more about BCG

vaccine), Kofi's mother never imagined his sickness might also be pulmonary TB, she never imagined his sickness might also be TB.

Kofi's health continued to deteriorate. He became listless, had difficulty breathing, and lost a lot of weight. His mother took him to the hospital, where he was diagnosed with pneumonia and admitted. After two weeks in the hospital, further tests were run and Kofi's mother was interviewed. She described her own illness, and only then was Kofi diagnosed with TB.

At first, Kofi's father did not understand what it meant for Kofi to have TB. He blamed Kofi's mother, believing TB to be a hereditary illness passed from mother to son. After all, his wife's father and sister died of TB three years earlier. To Kofi's father, his son had been given *ugonjwa ya familia ya bibi* — a disease from the wife's side of the family.

A community health worker educated both Kofi's mother and father about TB — how it spreads, how to look for signs and symptoms, and how it was important to take an entire course of treatment to cure the disease. They were assured about the importance of seeking proper health services, rather than self-medicating, when their children became very sick. After nine months of receiving treatment and care, Kofi and his mother were both cured and returned to normal health.

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## HOW ARE CHILDREN WITH TB DIAGNOSED AND TREATED?

There's no gold standard for diagnosing TB in children. Children have difficulty coughing up sputum to test for TB. Health workers therefore have to rely on other tests, including screening children for the symptoms of TB, seeing if the child has been in contact with an infected adult, and giving a tuberculin skin test (TST).<sup>22</sup> A TST — where a needle is placed under the skin, a solution is injected, and the injection site swells if the body is infected with TB — can merely tell if a child has been infected, not if he or she has active disease. Chest x-rays and other scans are helpful to diagnose active TB, but they're rarely accessible in developing countries where they're needed. Oftentimes, children suspected to have TB are treated with a broad spectrum of antibiotics. Those who fail to respond to treatment are given a speculative TB diagnosis.<sup>1</sup>

### DIAGNOSING AND TREATING CHILDREN WITH MDR-TB ►

If diagnosed early and given proper treatment, children with MDR-TB can often be cured. However, there are many challenges to diagnosing and treating children with drug-resistant TB. Diagnosis is often done by trial and error. Children are diagnosed with MDR-TB when they do not respond to regular treatment, get recurring TB, or live in close contact with someone confirmed to have MDR-TB.<sup>23</sup> MDR-TB is particularly dangerous to children with HIV, who are at greater risk of severe illness and death. Early diagnosis and treatment, combined with the use of ART, greatly improves outcomes. It is critical that these children are diagnosed early and receive proper treatment for both MDR-TB and HIV.<sup>24</sup>





## WHAT ARE THE CHALLENGES SURROUNDING CHILDREN AND TB?

### THERE'S A VACCINE TO PREVENT TB — BUT IT'S OLD AND DOESN'T WORK WELL ▶

The only TB vaccine that exists, called the Bacille Calmette-Guérin (or BCG) vaccine, was invented before World War II. In most developing countries, BCG vaccine is given at birth to help protect young children against the most severe forms of TB, including TB meningitis. However, it fails to protect children and adults against most other forms of TB. WHO recommends that all children who live in countries with high TB rates receive the immunization, saving even a small percentage of children is a big success. Unfortunately, as children grow older the effect of the vaccine wears off. Furthermore, children with HIV are unable to receive BCG vaccine because it can make them sick.<sup>25</sup> Scientists are working on developing a new vaccine that addresses these shortcomings, but further funding is needed to develop and deliver it worldwide.

### WE NEED NEW TB DIAGNOSTICS THAT WORK FOR CHILDREN ▶

Further resources are needed to certify a rapid, point-of-care test that accurately diagnoses TB in children. The most widely used diagnostic dates to the turn of the 20th century — predating the automobile. Although WHO has yet to approve Xpert MTB/RIF for use in children, preliminary studies indicate the new DNA-based, rapid diagnostic test is effective in children under 15.<sup>26</sup> Studies are now being conducted to see if Xpert can be used to diagnose TB in children.

Xpert represents the very latest in TB diagnostics, but it relies on the patient's ability to cough up sputum — something many children, particularly young children, have difficulty doing. While Xpert is a vital tool, pediatricians believe new tests should also be designed for children that use easy-to-get samples like urine or feces. A few innovative approaches are showing promise. In Peru, physicians are using the 'string test' to diagnose TB in children as young as four.<sup>27</sup> Children swallow a gel capsule with a nylon string that unravels once inside. When the string is retrieved four hours later, it is tested for TB bacteria. Recent studies of the string test show promise, however further research is needed to determine its effectiveness.

### THERE ARE NO TB TREATMENT OPTIONS SPECIFICALLY FOR CHILDREN ▶

No child-specific TB drugs exist, and children are routinely excluded from drug treatment clinical trials. Currently, children with TB are treated using many different medicines, up to 15 tablets a day, over six to nine months. Although some companies started manufacturing smaller, crushable tablets that are easier for children to take, these are not widely available. Often, doctors crush adult tablets and estimate appropriate doses, which runs the risk of over- or under-dosing a child.<sup>28</sup>

WHO has proposed a better way to treat children with TB using one tablet containing all medicines — a Fixed Dose Combination (FDC).<sup>29</sup> An FDC would make TB treatment easier, more effective, and ensure more children are cured of TB. Currently there is no FDC to treat TB in children. Development of a WHO-approved FDC is a top research priority requiring urgent funding.

### CHILDREN ARE EXCLUDED FROM TB DRUG CLINICAL RESEARCH TRIALS ▶

The exclusion of children from clinical trials is the main reason no child-friendly TB treatment options exist. Children are left out of clinical trials for a number of reasons, including the difficulty of confirming diagnosis, concerns about pediatric-specific adverse effects, and complex regulatory requirements.<sup>30</sup> Nearly forty years after modern anti-TB drugs were developed, questions still exist regarding the appropriate dosages to give children. Barriers from including children in clinical trials ostensibly exist to protect children from the potential harm of participating in scientific studies. However, many pediatricians are worried that this attempt to protect children has done the opposite — instead denying children new lifesaving treatment.

## CHILDREN AND TB: A CALL TO ACTION

A lack of political will, inadequate funding, and children's exclusion from research remain barriers to eliminating childhood TB. To date, little has been done to prioritize childhood TB in national health programs and to eliminate the disease as a major killer of children. "For too long, childhood tuberculosis has been neglected throughout the world," says Dr. Starke. "Pro-actively finding and treating children with TB will not only improve child health, it will prevent millions of new infections in people of all ages."

- Fighting childhood TB must become a global health priority among both donors and national TB programs. New resources are needed to eliminate TB as a killer of children.
- Children need universal access to the current tools available to diagnose and treat TB. National TB programs must implement the Four I's and ensure that all children who are in contact with an adult who has TB are actively traced, treated, and given isoniazid preventive therapy.
- TB diagnostics, treatment, and care services should be integrated with child health primary care, maternal and child health programs, and HIV services.
- The scientific community needs to include children of all ages in clinical trials. Children have the same right as adults to receive treatment and benefit from research.
- Innovative research is needed to develop child-friendly TB diagnostics, drugs, and vaccines.
- Through advocacy, civil society must demand equitable prevention, diagnostics, treatment, and care services for childhood TB and monitor the scale-up of these services worldwide.
- Children with HIV should be placed on ART immediately upon diagnosis to reduce risk of TB disease and death.



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## THE “WHO” OF ACTION

ACTION (Advocacy to Control TB Internationally) is an international partnership of civil society advocates working to mobilize resources to treat and prevent the spread of tuberculosis (TB), a global disease that kills one person every 20 seconds.

ACTION’s mission is to build support for increased resources for effective TB control, especially among key policymakers and other opinion leaders in both high TB burden countries and donor countries. With effective policy advocacy and greater political will, rapid progress can be made against the global TB epidemic.

To learn more about ACTION’s advocacy strategies and tactics, go to: <http://www.action.org/>

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