

# TB among Children and Teens at HIV Treatment Centers in Africa

*[Announcer] This program is presented by the Centers for Disease Control and Prevention.*

[Sarah Gregory] Hello, I'm Sarah Gregory, and today I'm talking with Dr. Anna Mandalakas, director of the Global Tuberculosis Program at Texas Children's Hospital and Baylor College of Medicine in Houston. We'll be discussing tuberculosis among children and teens with HIV in sub-Saharan Africa.

Welcome, Dr. Mandalakas.

[Anna Mandalakas] Thank you very much for having me here today, Sarah.

[Sarah Gregory] AIDS first came to national attention in the early mid-80s. At that time it was pretty much a death sentence. First, tell us what HIV and AIDS are. What's the difference and why is it now referred to as HIV-slash-AIDS together?

[Anna Mandalakas] Well, the terms have evolved quite a lot over the past several decades, and HIV specifically stands for Human Immunodeficiency Virus. And HIV belongs to a group of viruses called retroviruses. And these...this virus attacks the white blood cells in the immune system. And if untreated, HIV develops into AIDS, and AIDS actually stands for Acquired Immune Deficiency Syndrome. It's actually an umbrella term that encompasses all of the illnesses that occur in a person if they have untreated HIV infection. So after several years of untreated HIV infection, a person's immune system is severely damaged and they're unable to fight off infections. So, basically HIV is the virus that attacks the immune system and AIDS is the term that's used when the infection inside spreads, and the immune system falters and these people are at high risk of illness and death. However, HIV infection today is not a death sentence. And we know that if people living with HIV start medicine for the infection early, they actually can treat and contain the infection and actually have a long, healthy life.

[Sarah Gregory] What's the state of the infection now? I understand that in the last roughly 30 years things have improved dramatically for people who contract it.

[Anna Mandalakas] So actually, the US CDC published the first report about what would later be called AIDS in 1981—so it's actually 4 decades that we have been dealing with HIV. In 1992, HIV was actually the number one cause of death in the United States among men between the ages of 25 and 44. And then in the 90s (or actually the second half of the 90s) there were treatment guidelines put out that introduced the use of antiretroviral therapy which actually proved to be very, very effective and greatly reduced HIV mortality rates. So fast-forward now to 2020, and in the United States most people with HIV do not even develop AIDS because they're taking HIV medicine everyday as it's prescribed and it stops progression of the disease.

Globally, the organization...the WHO organization that deals with AIDS and works to control and eliminate AIDS is called UNAIDS. And they estimate that almost 38 million adults and children are living with HIV.

[Sarah Gregory] How many people still get AIDS and HIV annually?

[Anna Mandalakas] Well, Sarah, right, there are people with new infections each year. And in 2019, it was estimated that 1.7 million people became infected with HIV in just that year. And

this is actually a 23% decline since 2010. But of these people with new infections, about 1.5 million were adults and about 150,000 of the new infections occurred in children less than 15 years of age.

[Sarah Gregory] Is there a geographic location where HIV is most prevalent?

[Anna Mandalakas] Yes, absolutely. It varies based on geography, and the vast majority of people living with HIV live in low- and middle-income countries. And in 2019, they estimated that almost 21 million people living with HIV were in eastern and southern Africa and that's about 55% of the population overall living with HIV. After that, about 5 million (or 13%) are in west and central Africa, and another almost 6 million (which is another 15%) are in Asia and the Pacific. And actually only about 2 million (or 6%) in Western and Central Europe and North America.

[Sarah Gregory] Explain to us what tuberculosis is and how it differs from HIV.

[Anna Mandalakas] At the simplest level, tuberculosis is a disease caused by bacteria and HIV is a disease caused by a virus. The two diseases are very different and distinct but entwined. So, tuberculosis is often referred to as TB and the disease has existed in mankind for millions of years. And we know this because the DNA from the germ has been found in Egyptian and Caribbean mummies. We have amazing history from the industrial revolution, where TB was responsible for up to 25% of all deaths in major European and US cities. And the disease spreads very easily because the disease is spread through the air. So when an infectious person coughs, or sings or does anything that puts the germ into the air—into these little droplets—people around them can breathe the germ in and become infected. And actually about 25% of the world's population is infected with the germ that causes TB. But the vast majority of these people are not sick because their immune system contains the infection and prevents the germ from making them sick. And we'll come to this again, but HIV is caused by a virus. And HIV is spread through body fluids and blood. And so, the transmission of HIV is much different than that of TB.

[Sarah Gregory] Why are people with HIV more susceptible to TB?

[Anna Mandalakas] So, people living with HIV are more prone to develop TB disease after becoming infected with the germ because of their weakened immune system. HIV actually attacks the immune system and specifically wipes out the cells which fight the TB germ. So people living with HIV are not able to contain the HIV infection and prevent the infection from developing into disease like healthy individuals without HIV infection.

[Sarah Gregory] Your study is about TB among children and teens with HIV in sub-Saharan Africa. Where's sub-Saharan Africa?

[Anna Mandalakas] Sub-Saharan Africa is the area of the continent of Africa that lies south of the Sahara desert. And this region includes about 40 countries. Our study actually included clinics from 6 of these 40 countries, and the countries that we included in our study were Eswatini (which used to be called Swaziland), Lesotho, Botswana, Malawi, Uganda, and the United Republic of Tanzania.

[Sarah Gregory] How do children and teens get HIV?

[Anna Mandalakas] Children and teens can become infected with HIV two different ways. So if an infant is born to a mom living with HIV, they can become infected at the time of birth. And this is referred to as vertical transmission, and this type of transmission can be prevented if the child receives medicine to prevent the infection around the time of birth and thereafter. And similar to adults, children and teens can also become infected with HIV from exposure to blood or body fluids that contain HIV. And this exposure most commonly happens sexually, but exposure can also occur from using dirty needles or receiving infected blood if proper screening is not completed.

[Sarah Gregory] What's the age span of these kids in your study?

[Anna Mandalakas] So, our study included children from birth all the way up to 19 years of age.

[Sarah Gregory] And is TB a big problem there also?

[Anna Mandalakas] So in 2016, 2.5 million people fell ill with TB in the African region. And that accounts for a quarter of the new TB cases worldwide. In total, an estimated 417,000 people died from the disease in the African region in 2016 alone. Over—again— over 25% of deaths from TB that year occurred in the African region.

[Sarah Gregory] Approximately how many kids are there with TB and HIV in that region?

[Anna Mandalakas] So the UN Joint Program on HIV/AIDS (which I mentioned previously is called UNAIDS) estimates that 85% of the 2.6 million children with HIV infection are living in sub-Saharan Africa. And about 650,000 children living with HIV and approximately 1,000 infected infants are born every day in Africa. Of the 10 million people who fought TB in 2019, about 2.5 million of these lived in Africa. And of these people, about 600,000 are living with HIV. So basically about 30% of the people with TB in Africa actually are also living with HIV.

[Sarah Gregory] What kinds of treatment is available for both TB and HIV? What did you find works best? Do the treatments work in conjunction or do you treat them separately?

[Anna Mandalakas] So there are specific drugs that you use to treat TB and specific drugs that you use to treat HIV. Some TB-specific drugs that's routinely given to people with TB infection to prevent the germ from replicating and prevent the person from becoming ill—from developing active disease and being symptomatic. Some TB drugs can also be given to a person once they have TB disease. And depending on the type of disease that the person has and how severe their disease is, the drugs are taken anywhere from 6 months to 2 years. So, a longer period of 2 years is when people have drug-resistant TB. But in the vast majority of cases, TB drugs can cure TB disease.

So, the specific drugs used to treat HIV are referred to as antiretroviral therapy... and they are called ART for short. And if ART is taken regularly, people with...people living with HIV can have a long, happy life. And for these medications—unlike the TB medications—the HIV medications don't cure HIV but they actually control the infection and prevent people from getting severe complications of the disease. And in adults, research has clearly shown that the risk of developing TB is much lower in people who are living with HIV and taking their ART regularly everyday, the way they're prescribed, compared to people who are not taking ART.

[Sarah Gregory] Why did you do this study?

[Anna Mandalakas] So in contrast to what I've just shared with adults, research in children has not consistently shown that taking ART prevents TB. And our team completed this study to help identify factors that increase the risk of TB in children and adolescents living with HIV and to better understand if ART prevents TB in these children.

[Sarah Gregory] And how did you go about doing this study? What kind of data did you use?

[Anna Mandalakas] Well, over the past 20 years, pediatricians from Texas Children's Hospital and Baylor College of Medicine (which are both in Houston, Texas) have partnered with clinicians in Africa to provide care and treatment for children and their families who are living with HIV. And then since TB is the leading cause of death in people living with HIV, our network of HIV clinics have integrated TB care and treatment within these clinical programs. So to answer our study questions, we were actually able to use data extracted from the medical records of children and adolescents living with HIV who had been receiving care at our clinics.

[Sarah Gregory] Tell us briefly all about it.

[Anna Mandalakas] Ok. So, we were actually able to analyze data on almost 1,200 children and adolescents living with HIV in whom TB was diagnosed during a 4-year period. And as the clinical network that I just described provides care for so many children, the data actually encompassed over 57,000 patient-years' worth of data. And that's a huge, huge amount of patient-years' worth of data. And so first we determined how much TB disease these children and adolescents have actually been battling. And next, we looked at the amount of TB disease that occurred in this group of children over time, and we compared this to the amount of HIV treatment that these children were receiving over time. And then finally....finally, we looked at a long list of characteristics in the children who developed TB disease to see if any of these characteristics were associated with an increased chance of the children recovering from TB disease versus dying from TB disease.

[Sarah Gregory] What did you find?

[Anna Mandalakas] We were actually able to answer our questions, and one of the most impressive things we found was there are extremely high rates of TB in children and adolescents living with HIV that came to our clinics for care. So each year, about 2 out of every 100 of these children and adolescents developed TB. So for comparison, this is about 2,000 times higher than the amount of TB we find in children in the United States.

Next we observed that during the four-year study period, the number of children who were receiving ART for treatment for their HIV infection increased and the number of children developing TB decreased. So among the children receiving care at our clinics, a 10% increase in the number of children taking ART was associated with about a 2% reduction in the number of children developing TB disease. And that's a pretty impressive association to show how the HIV medicine can prevent TB in children just like they do in adults.

And then finally, we were actually able to identify some factors that were associated with recovering from TB. And the really impressive thing we were able to show that children and adolescents living with HIV were less likely to die from TB if they had been receiving ART and participating in routine HIV care for a longer period of time—so taking their medicines, seeing their doctors regularly—they were much, much more likely to do well after developing TB disease in children who had just entered care but were not getting their HIV medicine.

[Sarah Gregory] Is there a way to stop or slow the increase of cases of children and teens with both these infections?

[Anna Mandalakas] So at this broad level, HIV is found in really vulnerable groups and marginalized populations. So, improving the lives of millions of children and adolescents in these settings and improving access to care and access to testing will actually really improve outcomes for children and teens. Once we actually get down at the individual patient level, we know that earlier and more comprehensive detection of cases is one of the most important things we can do to help control both TB and HIV epidemics. And if we can detect cases early, we can decrease the risk of secondary cases—so, decrease the spread of both HIV and TB to other people. For TB, once we know people have been exposed to TB or infected with the germ, we can get them preventive treatment to prevent them from going on to develop disease. And for HIV, if we know moms are living with HIV, we can treat their exposed newborn babies and minimize the chance almost to zero that the babies are infected with HIV. And similarly, if we know that a teen is living with HIV, we can empower these teens to use safe sexual practices and limit the spread of HIV infection to their sexual partners.

[Sarah Gregory] How about individually? I mean, either HIV or TB?

[Anna Mandalakas] Yes, at the individual level, we can help to curb both the TB and HIV epidemics by eliminating social stigma associated with these infections. And actually fear of stigma is one of the major barriers that holds people back from getting testing for both TB and HIV. And in addition, fear of stigma is a barrier for people to complete or give preventive treatment to their children actually. And as a result of these parents being afraid that someone is going to think that their family has TB or HIV if they give their children this medicine, we miss opportunities to prevent disease in children. Yes, so one really easy first step to actually minimize stigma is to be careful about the language we use when talking about these diseases. And every single one of us can do this. So for example, rather than referring to a person being infected with HIV, we can say, a person that's living with HIV, because having an infection in general sounds negative and judgmental, and also disempowering. Because, you know, the language we use is very powerful and something that every one of us can do every time we're involved in a conversation about this.

[Sarah Gregory] Were there any challenges to this research?

[Anna Mandalakas] A specific challenge in this analysis was our ability to measure the amount of TB preventive treatment that children received to prevent TB disease. And that's actually probably a good problem to have in a way because during the study period, there was a lot of energy and...and commitment from the World Health Organization to push forward the use of TB preventive therapy. And because of this, the guidelines in all these countries were rapidly changing as more and more children were starting to get TB preventive therapies. But because of these rapid changes in the guidelines, we weren't able to accurately measure the amount of TB preventive therapies that the children received. So it made it difficult to understand how much of the improvement or how much of the decline in TB disease was a result of TB preventive therapy rather than HIV treatment.

[Sarah Gregory] There are some programs I know that are funded by the U.S. and other countries to help with HIV/AIDS. Is this true for TB also?

[Anna Mandalakas] Yes, yes. That is absolutely true for TB also. So in 2019, actually, 87% of the world's TB cases interestingly were found in 30 countries that are primarily low- and middle-income countries. And actually two-thirds of the world's TB cases occurred in only eight countries, and India leads this, followed by Indonesia, China, the Philippines, Pakistan, Nigeria, Bangladesh, and South Africa. And through many, many mechanisms, high-income countries help to support these countries to combat TB. And one of the primary routes is through support of the World Health Organization. And in addition, the U.S. provides substantial support through funding that flows through USAID, PEPFAR, CDC, the NIH, and the Department of Defense. But in addition to these governmental organizations, a substantial amount of funding comes from nongovernmental organizations. And within the TB arena, the two organizations that provide the most funding for TB is the Bill and Melinda Gates Foundation and also CHAI, which is the Clinton Health Access Initiative.

[Sarah Gregory] Are there any actions or further studies that you'd like to see?

[Anna Mandalakas] So although we've made major progress over the past decade, there remains a lot of opportunity to improve our ability to accurately detect TB disease. So in 2019, about 30% of the people battling TB were not diagnosed and they never received any treatment. In children, this...this case detection gap is over 50%. That's just incredibly unacceptable. And there's actually recent evidence that demonstrates that over 96% of the children who die from TB were never diagnosed and never received treatment, and they never even had the chance to fight the infection. So, I would actually like to see a lot more studies completed to improve not only testing to help better diagnose TB disease in these children, but also studies to identify better ways to screen children at risk for TB disease and infection. And by improving screening methods, we can then more accurately identify what children and teens should then go on to complete additional diagnostic testing. Thereby we can diagnose disease earlier and more completely and increase the number of children who recover from disease. To put this into a little bit of a context for you, the United Nations target, actually (with respect to TB) are to achieve 90% diagnosis, and that's high.

[Sarah Gregory] What are the recommendations to help people not get TB or HIV?

[Anna Mandalakas] Consistently practicing safe sex and safe use of needles is indisputably the most effective way to prevent becoming infected with HIV.

Similarly, without a doubt, completing TB preventive therapy after becoming infected with the TB germ reduces the risk of developing TB to negligible levels. And TB preventive therapy is safe and is effective. And, most recently, shorter and equally effective treatment options have become available. And TB control programs in many places have developed great capacity to support patients to complete TB preventive therapy, and in the United States we actually do this with video messaging apps. And it's actually never been easier to prevent yourself from developing TB.

[Sarah Gregory] Tell us about your work and what you enjoy most about it.

[Anna Mandalakas] I'm actually based in Houston, Texas at Baylor College of Medicine and Texas Children's Hospital, and I'm actually really fortunate to work with an amazing group of clinicians and researchers working in different settings around the world who are really, truly committed to serving vulnerable children and families that are battling both TB and HIV. And

then, the work that we do on the frontlines really makes a difference in people's lives every day. And so my job is outrageously rewarding and I...I really...I'm really privileged to work with committed and passionate group of people. And I am actually excited when I wake up for a 6 AM conference call with colleagues in half a dozen countries in time zones spanning from Papua New Guinea to Eswatini to Houston. And I just...I really love my work.

[Sarah Gregory] And what do you enjoy doing in your personal time?

[Anna Mandalakas] So, I have three wonderful daughters and four very spoiled puppies which keep me pretty busy and feeling pretty blessed. And I'm pretty good about carving out time for gardening and yoga, and a few long runs every week.

[Sarah Gregory] Thank you for taking time to talk with me today, Dr. Mandalakas.

[Anna Mandalakas] Yes, thank you so much for having me. It was really a pleasure to be here with you. And thanks to all your listeners for having an interest in TB and HIV.

[Sarah Gregory] And thanks for joining me out there. You can read the December 2020 article, Tuberculosis among Children and Adolescents at HIV Treatment Centers in Sub-Saharan Africa, online at [cdc.gov/eid](https://www.cdc.gov/eid).

I'm Sarah Gregory for *Emerging Infectious Diseases*.

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