

# TB in Internationally Displaced Children in Texas

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

[Sarah Gregory] Hi, I'm Sarah Gregory, and today I'm talking with Dr. Gabriella Lamb, an assistant in medicine at Boston Children's Hospital. We'll be discussing tuberculosis testing in internationally displaced children in Texas.

Welcome, Dr. Lamb.

[Gabriella Lamb] Hello, thank you for having me.

[Sarah Gregory] Tell us about internationally displaced children. Who are they in Texas and where do they come from?

[Gabriella Lamb] So, "internationally displaced children" is a term that we use to describe children with a variety of immigration statuses other than immigrant—it isn't the sole immigration status—and these children have resettled in another country, i.e., not their country of origin. And specifically in our study, we were looking at children with this variety of immigration statuses who wound up resettling in Harris County, Texas, which includes the city of Houston. So, specifically the immigration statuses that we looked at were refugee, asylee, parolee, which is a special immigration status for persons coming from Cuba or Haiti that have family members already in the United States, special immigrant visa holders, which is another unique immigration status for children in our study of parents who served as translators for the U.S. military in Iraq and Afghanistan, and victims of human trafficking. As far as where they came from, we had identified each country of origin that the children came from and then we grouped them by the World Health Organization region of origin. So, this included the Eastern Mediterranean region, which typically people might refer to as the Middle East, most of those kids came from Afghanistan and Iraq, Southeast Asia, sub-Saharan Africa, and the Americas, as well as a few children from the Western Pacific region and very few from Europe.

[Sarah Gregory] Okay. So, why are so many in Texas?

[Gabriella Lamb] So, that's a very good question. So, Texas, and Harris County actually, in particular, is a major destination for several reasons. One thing that is looked at when resettling internationally displaced persons is that there's a strong resettlement infrastructure. So, there's a total of nine national nonprofit refugee resettlement agencies that partner with the state department to help resettle refugees in the United States, and six of those nine national agencies operate in Houston. So, Harris County has a strong resettlement infrastructure. Other parameters that are looked at, they look at places that have a strong economy, which Texas and Harris County do, which helps with early employment. They also look at availability of affordable housing, again, Texas and Harris County tend to have affordable housing. And then lastly, family reunification. So, as there's been precedent of already having large...large persons...internationally displaced persons resettle in Harris County, wanting to keep families together.

Then as other family members come over, they want to have the family reunified and staying in one place together.

[Sarah Gregory] There are other places besides Texas though, right? Where do they tend to be?

[Gabriella Lamb] That's correct. So, in 2018, Texas was the largest refugee resettlement state, but other states that accepted a large number of refugees included Washington, Ohio, Virginia, New York, Arizona, Pennsylvania, and Georgia.

[Sarah Gregory] That's Washington state, right? Not D.C.?

[Gabriella Lamb] Oh, correct. Correct.

[Sarah Gregory] How many children are we talking about in Texas, and what ages do you define as children?

[Gabriella Lamb] So, I'll start with what age we defined as children. For our study, we elected to use less than 18 years old, typically used for pediatric studies in the U.S. I will say a lot of international TB studies will use 16 as a cutoff for child to adult, but we elected to use the age 18 in our study. I looked specifically for total numbers of refugee children in Texas, and I couldn't find that exact answer but I can tell you that over the past 10 years there's been about 57,000 refugees, adults and children, that have resettled in Texas. And then specifically in our study, which occurred over 6 years, there was 5,990 children that resettled in Harris County, Texas alone. And there's a nice quote from our local newspaper that I really liked, from the *Houston Chronicle*, that said, "Taken together, this data means that Harris County alone welcomes about 25 of every 1,000 refugees that the U.N. resettles anywhere in the world—more than any other American city, and more than most nations. If Greater Houston were a country, it would rank fourth in the world for refugee resettlement.

[Sarah Gregory] Wow. What percentage of the U.S. refugee population is in Texas?

[Gabriella Lamb] So, using data from the refugee services of Texas, it's reported that last year over 40% of all refugees relocating to the United States resettled in Texas.

[Sarah Gregory] What are the living conditions like for most of these children?

[Gabriella Lamb] So, in their country of origin, living conditions can vary. Some of our patients have reported that they were living in refugee camps. Others have reported living in large apartment complexes. If they resettled in Harris County, typically, families have tended to resettle in apartment complexes throughout the county. There does seem to be some geographic preferences, depending on the country of origin, where persons may resettle in Harris County, but it certainly is not uniform.

[Sarah Gregory] How are these children cared for medically?

[Gabriella Lamb] These children are seen initially at three medical visits with the Harris County Public Health Refugee Health Screening Program. During these visits, information on the patient's medical history and physical exams are performed and a variety of health screening labs

are obtained, including testing for tuberculosis and HIV. If a child is found to have a positive TB test, then they're referred to the Texas Children's Hospital TB clinic. Additionally, all of these children are set up with primary care providers in the clinics near their new home.

[Sarah Gregory] That's an enormous number of children. Are these health clinics staffed to be able to meet needs regularly?

[Gabriella Lamb] Yes. Actually, it's a really remarkable system that the Harris County Public Health Refugee Health Screening Program has put together. They do have very busy clinics, but they've been able to get every child seen and taken care of and established in a medical home. It's a really robust and impressive program they have.

[Sarah Gregory] Okay. So, how was TB discovered in these children? How did you go about that?

[Gabriella Lamb] Almost all of the children in this group, about 98%, were screened for TB, and there's two different testing modalities that can be used. You can either do the one that most people are familiar with, which is the tuberculin skin test, where they inject a small amount of protein under the skin on your forearm and make a bubble. That's more commonly used now in children under the age of 5 years old. Or they can be tested with a blood test, which is known as interferon-gamma release assay that we shorten to call IGRA, and that's typically used in older children. And the testing was either done prior to immigration from their country of origin or, if they hadn't been tested before they arrived or didn't have documentation of their test results, then the Harris County Public Health Refugee Health Screening Program would do the testing. We considered a skin test...we measure the bubble that's formed and if it's more than 10 millimeters, that's considered positive, unless a child was living with HIV, in which case we have a lower threshold to call it positive and that would be 5 millimeters. A positive blood test or a positive IGRA is based on a certain number, then it's based on the package inserts for that test.

[Sarah Gregory] Which children were most likely to have TB, age-wise and geographic origin?

[Gabriella Lamb] In our study, we found that children from southeast Asian countries and those from sub-Saharan Africa were more likely to have TB or positive TB testing compared to children from Eastern Mediterranean, or, the Middle East, or children from the Americas. And then additionally, age-wise, this was an interesting finding for us: younger children (under the age of two) as well as older children (over the age of fourteen) both have greater odds of having a positive TB test compared to children in between those ages.

[Sarah Gregory] Do you have any idea why this would be?

[Gabriella Lamb] So it's well-known that adolescents tend to be more likely to acquire TB because they're more likely to have greater social networks and greater contacts with a variety of people. So they're more likely, then, to be exposed to TB. In most prior studies, children under the age of two aren't necessarily at increased risk for developing or acquiring TB. Our hypothesis from this study was that these younger children are more likely to spend time in the

home as opposed to going out into school, and if they had a caregiver in the home that had TB, then they were more likely to have prolonged contact and exposure to tuberculosis.

[Sarah Gregory] You mentioned HIV, were there any other health conditions that correlated with having TB?

[Gabriella Lamb] Not that we identified in our study. Fortunately the majority of children that we evaluated and were ultimately seen in our TB clinic had no other underlying health conditions. Most children were otherwise healthy. We did look specifically at if there was an association with having intestinal parasites increasing your risk of having TB, because that's been studied before, but we didn't find that children with intestinal parasites had increased risk of having TB.

[Sarah Gregory] Why would parasites have a correlation? I mean it didn't in your study, I understand that, but you said in other studies.

[Gabriella Lamb] Yeah, so the thought process behind that is, when you have an infection with a parasite, it shifts the immune system's response to a very specific type of immune system response called Th2, which is really targeted at fighting allergies and parasitic infections, and is the opposite direction that you want your immune system to go as compared to when you're fighting TB, which is a Th1-type response. So the thought process is that the immune system's getting diverted so it's not able to protect you from TB as well.

[Sarah Gregory] I see, but you did not find this.

[Gabriella Lamb] That's correct.

[Sarah Gregory] How many children were tested and how many were found to have TB?

[Gabriella Lamb] In total, 5,870 children were tested. Among whom, 364, or 6 percent, had a positive TB test. However, we didn't actually count each of these children as having TB, and it's a little bit nuanced, because there are some children that had that positive skin test, but then were tested with the blood test and the blood test was negative. And we know that the skin test can interact and be falsely positive in children that have been vaccinated with the BCG or TB vaccine, whereas the blood test does not cross-react. So in those circumstances, we viewed the blood test as being correct whereas the skin test would be falsely positive. So after assessment by an expert in pediatric TB, a total of 325 children were considered to have TB infection or latent TB, and only 4 had TB disease, which is what people commonly think of as the infectious or contagious form of TB.

[Sarah Gregory] Tell us about how you went about assessing the extent of the types of TB? How you found the children, that kind of thing.

[Gabriella Lamb] So, once a child was found to have a positive TB test, they were typically referred to the Texas Children's Hospital TB Clinic, where we would, again, get further information on the patient's medical history, do physical exams, especially listening to their lungs, and looking for any swollen lymph nodes, and chest x-rays were obtained to look for any

evidence of TB disease, or infectious or contagious TB. And that would help us distinguish: do they have TB infection or latent TB versus TB disease?

[Sarah Gregory] Give us a brief rundown of your study now.

[Gabiella Lamb] So, the study was done in collaboration with the Harris County Public Health Refugee Health Screening Program, and Jessica Montour, with the U.S. Committee for Refugees and Immigrants. The initial dataset actually came from the Texas Department of State Health Services, when the Texas Refugee Health Program resided there. And now it has shifted to the U.S. Committee for Refugees and Immigrants, so that's how we got connected with that group. And then, very kindly, we obtained some data from the U.S. Committee for Refugees and Immigrants, and then were able to link patients to extrapolate more data from the electronic medical records of both the Harris County Refugee Health Screening Program as well as the Texas Children's TB Clinic's electronic medical record.

We looked specifically at TB rates in children with these variety of immigration statuses that we talked about, we evaluated for factors that might correlate with having a positive TB test, such as age, immigration status, country of origin, HIV infection, and having infection with intestinal parasites. In total there were 5,990 children under the age of eighteen that were evaluated between 2010 and 2015. Of these, 98 percent were tested for TB, and 325 were found to have latent infection and 4 had TB disease. And really the two most notable correlates that we found for having a positive TB test were country of origin, as we talked about, children coming from Southeast Asia and Africa had the largest proportion of positive tests, and then age, both younger children and the adolescent age group. We did specifically look at immigration classification, and on initial statistical analysis it did appear to be an important variable, but then, as we did more sophisticated data analysis, it didn't wind up panning out, and I suspect really that the initial correlation was due to the fact that someone's immigration status pretty much correlates with their country of origin.

[Sarah Gregory] What were the challenges with this study? False negative and false positives, that sort of thing?

[Gabiella Lamb] There were several challenges in this study, and the first was not having documented BCG immunization status on every patient. Though most emigrated from countries that had universal immunization programs, we had to assume that they were BCG immunized if they didn't have documentation or didn't have a clear scar from their BCG immunization, which can make it tricky to determine the false positives from those TB skin tests. Also merging data from multiple sources was definitely a challenge. Dealing with discrepant test results, where one type of TB test was positive and the other was negative, and then really ensuring long-term follow-up of patients once they completed therapy. Fortunately, if they stayed within Harris County, then we're able to know long-term follow-up because they would reappear in the system if they were to develop TB disease or have future TB issues. But if they were to relocate to another health jurisdiction, then we wouldn't have long-term follow-up information on those patients.

[Sarah Gregory] And besides those things, were there any limitations to the study?

[Gabriella Lamb] So, I would say the biggest limitation for lack of follow-up data in any child that ultimately was not referred to the TCH TB clinic, though I will say the vast majority were; but earlier in the study some children were referred to other clinics, so we don't necessarily have long-term follow-up data for them. And then HIV infection was rare in our cohort, and though it was definitely correlated with positive TB testing, the numbers were so small that it does make it difficult to really draw meaningful conclusions about that. And then lastly, these data might not be generalizable to all immigrant children relocating to the United States because our dataset really included children that came from high TB burden countries.

[Sarah Gregory] And you did have somewhat surprising results. There were fewer children with TB than initially suspected, right?

[Gabriella Lamb] Yes, that's correct. We had lower rates of positive test results compared to prior studies. Looking at a variety of studies the range of refugee children with positive TB testing was 9 to 35 percent; our study found only about 6 percent had a positive TB test. This did correlate more closely with another more recent study that looked specifically at immigrant children, and not necessarily refugee children, that found about 5.6 percent positive rate. And one of the things that seemed to fit between those studies is that prior studies mainly used the skin testing to identify TB cases, whereas the studies that use more of the blood testing, we found fewer positive, total positive results. And we think that that might be a result of false positive skin tests causing an artificially high percentage of children testing positive.

[Sarah Gregory] Once a child is diagnosed with TB and they start their treatment, how do they get it? Who makes sure they get it, and how is it administered?

[Gabriella Lamb] The providers at the Texas Children's Hospital TB Clinic write orders for medication for treatment of TB, which are then sent to either the Harris County TB Program or the City of Houston TB Program, depending on where the family lives. And these health departments actually deliver the medication to the patients at no cost to the patient or family. And then medication administration, actually both for latent and TB disease, which is pretty unique, from my understanding, for the Harris County Health Department, is that it's done via either in-person or via video, what we call directly observed therapy, which means that someone watches them take the medication. And we found that these patients tend to have really excellent completion rates for their TB treatment, which is actually another study that we're working on.

[Sarah Gregory] Okay, that's very interesting, because I was going to ask that. I know that a lot of times with TB the problem is people don't complete their medicine.

[Gabriella Lamb] Yeah, yeah. We have something in the upper nineties percent completion rate for our clinic, it's really remarkable.

[Sarah Gregory] That is remarkable and wonderful. What are the public health implications from your findings? What should other health departments be looking for and doing? And do you have any recommendations?

[Gabriella Lamb] So, the first thing I really wanted to highlight is that both TB infection and disease were rare, so the vast majority of children did not have TB, and if they did have TB they were not contagious or infectious from their TB. The second thing that I think is really important from a public health perspective, is that the lower prevalence of positive TB tests likely is from the predominant use of the blood testing, and as a result of these data and from our experience, they actually agitate for other health jurisdictions to implement the routine use of blood testing rather than skin testing for children, really regardless of their immigration classification or region of origin. And with time we're actually lowering the age cutoff for being able to reliably use the blood testing.

[Sarah Gregory] Lowering the age cutoff to what?

[Gabriella Lamb] So right now, according to the American Academy of Pediatrics' Red Book, the lower end...age end of being able to use the test is two years of age. But there are definitely TB experts across the country that have used it in children down to one year of age, and there are other health departments that are using these blood tests in children of all ages. So as we get more data on the reliability of the blood tests in children of these ages, I suspect that blood testing will likely replace routine use of skin testing entirely.

[Sarah Gregory] I realize it wasn't part of this study but can you tell us what the ramifications of COVID-19 might be on these populations?

[Gabriella Lamb] Sure. I do worry that these children might be at increased risk for acquiring COVID-19 and it very much depends on their living situation. So if they're living with several other people in more crowded living circumstances, it's definitely concerning that there's possible increased risk for acquiring infection and developing COVID-19. Additionally, there's certainly been data that have been published, that show that minorities in the U.S. are becoming ill with COVID at disproportionate rates. Additionally, actually, there was just an article posted, in *PLOS Neglected Tropical Diseases* that talks specifically about the increased risk of COVID-19 in immigrant children and really nicely outlined the different reasons that immigrant children might be at more risk. And then the last thing I think that's really important, among the TB community there are concerns we will actually lose gains we've made towards the goal of eliminating TB, due to strains on resources as a result of the pandemic.

[Sarah Gregory] Well, that would be most unfortunate, since they're having such success with it. Tell us about your job, what you do and what you enjoy most about it?

[Gabriella Lamb] I am currently working as an attending physician in pediatric infectious diseases at Boston Children's Hospital. My main role as...is as a clinician on the inpatient service, but I also do outpatient clinic, and I'm the director of quality improvement in the

division. I most enjoy spending time caring for patients as well as teaching the learners on our service, so our fellows, as well as residents and medical students.

[Sarah Gregory] What about your free time? Can you tell us about any hobbies or activities that you enjoy?

[Gabriella Lamb] Sure. During my free time I actually most enjoy traveling, which has been really difficult during this time. And I really like getting to know new places, learning about new cultures, trying new foods. I'm also very much a big fan of the arts, and the ballet in particular. And then lastly really getting to do anything outdoors is one of my favorite things to do.

[Sarah Gregory] And thank you so much for taking the time with me today, Dr. Lamb.

[Gabriella Lamb] Thank you again for having me.

[Sarah Gregory] And thanks for joining me out there. You can read the August 2020 article, Tuberculosis in Internationally Displaced Children Resettling in Harris County, Texas, USA, 2010–2015, online at [cdc.gov/eid](https://www.cdc.gov/eid).

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

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