

**37<sup>th</sup> Union World Conference on Lung Health:  
Newsmaker Interviews:  
Dr. Kenneth Castro  
November 2, 2006**

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**JILL BRADEN BALDERAS:** Dr. Kenneth Castro, Director of the Division of Tuberculosis Elimination at the U.S. Centers for Disease Control and Prevention. Thanks for joining us today.

**KENNETH CASTRO, MD:** My pleasure.

**JILL BRADEN BALDERAS:** Could you start off by telling us exactly what is XDR TB?

**KENNETH CASTRO, MD:** Well, extensively drug-resistant tuberculosis, abbreviated XDR TB, is tuberculosis that is resistant to multiple drugs and it basically is resistant to the most powerful available drugs as well as to several of the second-line drugs available for the treatment of persons with tuberculosis. We have traditionally characterized persons who lose the two most powerful drugs as persons with multi-drug resistant tuberculosis, so this is a setting where not only have you lost these two drugs, but in addition to that you've lost at least three of the six available second-line types of drugs making it very difficult to treat these persons.

**JILL BRADEN BALDERAS:** So what are the major contributing factors to this XDR TB?

**KENNETH CASTRO, MD:** Well, what we have learned over the years is that drug resistance occurs as a result of persons not taking their treatment as they should be taking

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it for a period of six months to get cure or by doctors who prescribe treatment regimens that are not optimal.

And it's a shame when that happens, but we have a knowledge that as tuberculosis has become less common in many communities doctors lose proficiency in the treatment persons with tuberculosis. So those are the two most important contributors to that.

The third way how persons get multi-drug resistant tuberculosis is if they get initially infected by a strain that has already acquired resistance and share the air space with another person who has that type of tuberculosis.

**JILL BRADEN BALDERAS:** Now, where has XDR TB arisen, what countries?

**KENNETH CASTRO, MD:** Well, in the survey of about 25 supranational reference laboratories that form a network with the World Health Organization to provide these services to various countries, extensively resistant to tuberculosis was present in 17 of the countries that were surveyed. I must acknowledge that these are samples submitted that are biased and that very often these are persons who are not responding to treatment, and that's why at this moment in time I cannot talk about how frequently it occurs, but I can say with certainty that it occurs in these various settings, and that's what worrisome about it.

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**JILL BRADEN BALDERAS:** Now, many of the patients in South Africa that have been found to have EDR TB are also co-infected with HIV. What kind of role does HIV play in this spread of this XDR TB?

**KENNETH CASTRO, MD:** Well, the HIV, or the human immunodeficiency virus, renders an individual's immune system weak and they are very susceptible to progress from the stage of an infection to development of TB disease. In a person whose immune system is intact, you would expect no more than a 10% lifetime risk to progress from latent to active tuberculosis. In the case of HIV infection, the risk of progress is about 10% per year, so in five years 50% of risk exists, so you can see how this accelerates and amplifies the process of tuberculosis, as well as of transmission because often those around persons with HIV also happen to be HIV infected.

**JILL BRADEN BALDERAS:** And one of the important issues in all of this is protecting health care workers. Can you talk about efforts to educate health care workers about XDR TB and also to protect them?

**KENNETH CASTRO, MD:** Yes. What we have seen is that unfortunately the long kept secret throughout the world is that tuberculosis is much more commonly seen in health care workers. Not many people talk about it. And we have disregarded very necessary infection control precautions.

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The recent occurrence of extensively resistant tuberculosis is a rude awakening and wake up call to all of us to make sure that we implement the necessary infection control precautions. Infection control precautions are meant to prevent a transmission of tuberculosis to other persons whether it be other patients, as well as to health care workers. And in many settings where we've seen this occur, sadly not only patients developed TB, but health care workers and many of whom has also died in settings where the human resource capacity in health care is overly compromised.

**JILL BRADEN BALDERAS:** Now how would XDR TB actually be identified in countries? Is it when they actually treat people and people aren't responding or are there actual diagnostic tests to find out if there is XDR TB available?

**KENNETH CASTRO, MD:** Well, there are diagnostic tests to identify drug resistance. Unfortunately, they're not available in most parts of the world. We still rely on the staining of a sputum specimen and looking at the microbe under the microscope and stop there. We now need to overcome the complacency that has prevailed for too many years and make sure that we bring the lab capacity closer to the patients and make sure that persons who are at high risk of developing drug resistance get access to these tests and results back to the patient and to their provider in a timely fashion. In some of the scenarios that have been described,

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we have witnessed patients who have died while waiting for the test results.

**JILL BRADEN BALDERAS:** So, how do you actually make that available when you're working with people on the ground in these countries, how do you actually get those things implemented?

**KENNETH CASTRO, MD:** Well, clearly the absence of these diagnostic procedures are plagued with other prevailing deficiencies in the health care delivery system, so tuberculosis only helps unveil these other deficiencies. The way around it is that often the worry and fear will prompt individuals into action; unfortunately, in spite of very persuasive argument that has exists throughout the last many years and very often it moves people into action. Certainly, we're seeing effected communities and patients demanding access to these diagnostic services because they're seeing their friends and loved ones dying without the access to diagnostic services nor to treatment services. And there is some convincing that needs to take place of ministries of health decision makers about the importance of getting lab capacity implemented and closer to the patients rather than allow what has happened for the last multiple years to continue to occur.

**JILL BRADEN BALDERAS:** When you're working with these health ministers and local leaders on the ground, where do

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you advise them to start when they have so many problems to deal with in their health care systems besides tuberculosis and besides the excessively resistant tuberculosis?

**KENNETH CASTRO, MD:** Well, the advice that we provide is based on our own very painful lessons in the United States. After more than 30 years of studies downward trend, we had an unprecedented resurgence of tuberculosis of multi-drug resistance tuberculosis linked to HIV between 1985 and 1992. And that prompted congress to make resources available, health departments in the United States to change the way we did business, and rebuild the infrastructure that we had allowed to weaken to provide good TB services to stop the manufacture of drug resistance, as well as to provide the necessary treatment to those who have multi-drug resistant TB. So in many ways I can come to them with accredible and compelling argument because we've been there ahead of them and have been able to turn that around, so I can come also with the optimism associated with seeing how if you invest in the resources, have a plan in place, and make sure that you monitor the implementation of all the various elements of those plans you can change things around. And that then starts becoming a fairly persuasive argument.

We're also seeing that communities are starting to clammer for these services and are not accepting the status quo as a way to continue going.

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**JILL BRADEN BALDERAS:** And last question for you, where do we stand now in terms of drug development for drugs that can actually treat XDR TB?

**KENNETH CASTRO, MD:** Well, after many years of a dry spell, we are now looking at, at least four very promising compounds for tuberculosis. Now the problem that we are now confronted with is how do we accelerate their evaluation. Procedures that normally may take ten or 15 years from identification of the compound to testing in animals to then testing it in humans for both safety and efficacy to then licensure, purchasing, and availability. We need to truncate that process. It is unacceptable. We can learn from the HIV community who demand that that procedure be changed and successfully accelerated the evaluation and availability of antiretroviral agents in a setting that has now become to life saving for many of these individuals. We need to do the same and no less for tuberculosis.

**JILL BRADEN BALDERAS:** Dr. Kenneth Castro of the U.S. Centers for Disease Control and Prevention; thanks for joining us today. We appreciate your time.

**KENNETH CASTRO, MD:** My pleasure. Thank you.

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