

New look at XDR-TB in SA

Scientists awarded US\$3.9 million grant to study how XDR-TB transmitted in rural South Africa; new strategies in South Africa needed to combat fatal infections.

The National Institutes of Health (NIH) has awarded scientists at Albert Einstein College of Medicine of Yeshiva University a five-year, \$3.9 million grant to study how extensively drug-resistant tuberculosis (XDR-TB) is transmitted in rural South Africa. The findings could alter public health approaches for controlling the XDR-TB epidemic in the developing world.

"Most cases of XDR-TB are thought to arise when people infected with susceptible strains of TB don't take their medications correctly or are prescribed the wrong medications," explained principal investigator Sarit Shah, M.D., M.P.H., assistant professor of medicine and of epidemiology & public health. "These medication failures encourage the growth of drug-resistant strains of TB bacteria - a phenomenon known as amplified resistance."

XDR-TB can also arise when someone who never had TB, or who had TB that was cured, is directly infected with a drug-resistant strain of TB. "Person-to-person transmission of XDR-TB was believed to be rare," said Dr. Shah. "But increasing evidence suggests that it's much more common than previously thought. We estimate that two-thirds to three-quarters of XDR-TB cases arise this way."

Dr. Shah will prospectively interview and analyse the medical records of 400 patients with XDR-TB to determine how many new cases develop due to person-to-person transmission compared with new cases of amplified resistance. The study will take place in the area of Tugela Ferry in the KwaZulu-Natal district of South Africa which has exceedingly high rates of XDR-TB.

Co-infected with HIV

Adding to their woes, many TB patients in Tugela Ferry are co-infected with HIV, the virus that causes AIDS (South Africa has more people infected with HIV than any other country in the world.) Studies have found that TB patients co-infected with HIV face a higher risk of developing active TB disease than patients free of HIV. Thus, an HIV-infected person who contracts XDR-TB through person-to-person transmission - due to prolonged hospital stays for other medical conditions, for example - is more likely to develop active XDR-TB than a person without HIV.

Efforts to curb the growing XDR-TB epidemic currently focus primarily on preventing amplified resistance: healthcare workers directly observe patients to ensure they adhere to their medication regimen. But if person-to-person transmission turns out to be the major source of drug-resistant TB, public health agencies will have to adjust their XDR-TB control efforts by emphasising measures that prevent people from infecting others, including earlier diagnosis and treatment and more rigorous infection control measures. The findings would be applicable throughout sub-Saharan Africa, where the TB epidemic follows patterns similar to those in Tugela Ferry.

Finding out how the links work

To determine how person-to-person XDR-TB transmission is most likely to occur - within families, among

co-workers, or perhaps among people admitted to the hospital at the same time - Dr. Shah will combine classic contact investigation methods with advanced epidemiologic techniques (including molecular genotyping) and social network analysis. Molecular genotyping will allow the researchers to identify clusters of particular strains of XDR-TB.

"Then, using contact investigation and social network analysis, we'll investigate how the people in those clusters are linked," said Dr. Shah, noting that this is the first time such an approach will be used to study TB transmission in a population with a high prevalence of HIV.

"Working in Tugela Ferry - ground zero for the emerging XDR-TB epidemic - Dr. Shah has been at the forefront of understanding the deadly duet between TB and HIV," said Harris Goldstein, M.D., professor of paediatrics and of microbiology & immunology at Einstein and director of the Centre for AIDS Research (CFAR), which coordinates the diverse AIDS research efforts at Einstein and Montefiore Medical Centre, University Hospital and Academic Medical Centre for Einstein. "This study is critical for learning how co-infection with HIV increases mortality from TB and promotes the emergence of extensively drug-resistant strains."

Dr. Shah's initial work on transmission patterns of XDR-TB was funded by the Einstein-Montefiore CFAR. The current study, "Transmission of HIV-Associated XDR-TB in rural South Africa," is funded by the National Institute of Allergy and Infectious Diseases of the National Institutes of Health. Her Einstein co-investigators include William R. Jacobs, Jr., Ph.D., Michelle H. Larsen, Ph.D., Neel R. Gandhi, M.D., and Moonseong Hong, Ph.D.

Source: Albert Einstein College of Medicine

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