Medical Xpress

Girl's life saved by novel therapy for drug-resistant TB

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Belgian physicians report they have cured a young patient with extensively drug-resistant tuberculosis (XDR-TB) using a novel two-drug combination developed by researchers at Albert Einstein College of Medicine of Yeshiva University. The report, published in the Pediatric Infectious Disease Journal, marks the first known clinical use of this treatment for XDR-TB, the most deadly form of the disease.

"It was extremely rewarding to see that our in vitro biochemical studies would contribute to a successful clinical outcome for this seriously ill girl. I applaud the courage of the Belgian physicians," said John Blanchard, Ph.D., the Dan Danciger Professor of Biochemistry at Einstein, who led the development of the new therapy.

Dr. Blanchard and his colleagues reported in the February 27, 2009 issue of *Science* that a combination of clavulanate and meropenem inhibited the growth of drug-susceptible laboratory strains of TB as well as XDR-TB strains isolated from TB patients. The drugs work in tandem: clavulanate inhibits a bacterial enzyme (beta-lactamase) that normally shields TB bacteria from meropenem, a member of the beta-lactam class of antibiotics.

The U.S. Food and Drug Administration has approved Meropenem for adult and pediatric use, and clavulanate is used in combination with amoxicillin as an FDA-approved antibiotic. Clavulanate-meropenem therapy for XDR-TB has not yet been evaluated in clinical trials.

In 2010, physicians at Hôpital Universitaire Saint-Pierre in Brussels, Belgium, oversaw the care of a 14-year-old girl from Chechnya with XDR-TB. The acutely ill and malnourished patient failed to respond to standard first- and second-line TB medications. Tests showed that her TB strain was extensively drug resistant.

As a last resort, the Belgian physicians decided to try clavulanate and meropenem, the combination therapy they had read about in Dr. Blanchard's *Science* paper. "We had nothing to lose," wrote Marie-Christine Payen, M.D., leader of the Belgian team, in an e-mail to Einstein officials.

The girl showed clinical improvement after four weeks of therapy, the Belgian team reported in the *Pediatric Infectious Disease Journal*. After 11 weeks, her sputum tests were negative for TB.

"This is early and limited evidence that the therapy will be efficacious, but it's very encouraging," said Brian Currie, M.D., M.P.H., assistant dean for clinical research and professor of medicine and of clinical epidemiology & population health at Einstein and vice president and medical director for research at Montefiore Medical Center. "We look forward to beginning clinical trials with our colleagues in South Africa, where drug-resistant TB is a significant and growing problem." Dr. Currie expects that trials will start within a year.

Einstein has filed a patent application on the novel combination clavulanate-beta-lactam drug formulations to treat TB as an incentive for commercial drug manufacturers to support expanded clinical trials and to collaborate with Einstein on potentially developing these antibiotics for expanded use in TB therapy.

More information: Dr. Payen's paper, "Meropenem/clavulanate and linezolid treatment for extensively drug-resistant Tuberculosis," was

published March 3, 2011, in the online edition of the *Pediatric Infectious Disease Journal*. Dr. Payen of Université Libre de Bruxelles and Hôpital Universitaire Saint-Pierre, Brussels, Belgium, is the senior author.

Provided by Albert Einstein College of Medicine