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RESEARCH NEWS

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Inexpensive Treatment Stops Multi-Drug Resistant TB in its Tracks

A standard and inexpensive tuberculosis treatment regimen cut the overall TB rate in half and lowered the rate of drug-resistant cases even more dramatically in a remote Mexican health district with a high prevalence of the disease. “This shows what basic TB control can accomplish,” said Maria de Lourdes García García, a Howard Hughes Medical Institute international research scholar who led the Mexican study.

To learn more about TB transmission in less developed countries, García García and colleagues from the National Institutes of Mexico and Stanford University launched a five-year study in the Orizaba Health Jurisdiction, four hours by bus southeast of Mexico City. The district, which has a higher rate of TB than Mexico as a whole, encompasses five mostly urban communities in an industrialized valley and surrounding rural mountains.

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> **— Ma. de Lourdes García García**

Supported by HHMI, the U.S. National Institutes of Health, and the Wellcome Trust, the study used modern molecular epidemiologic approaches, in addition to screenings, clinical assessment of people reporting symptoms, supervised treatment, and follow-up, to explore a global health problem.

At the outset, 22 percent of previously untreated patients with pulmonary TB were carrying drug-resistant strains, and 6.7 percent had multiple-drug resistance. By the study's final year, only 7.8 percent of new TB patients carried drug-resistant strains, and there were no cases of multiple-drug resistant TB.

The researchers report their findings in the April 2, 2005 issue of the British medical journal *The Lancet* . A commentary by Marcos Espinal, executive secretary of the World Health Organization's Stop TB Partnership, appears in the same issue.

People with TB must take four standard drugs daily for six months. They may begin to feel better after a month, which tends to lead them to skip doses, but if they stop taking the drugs for any reason, the drugs may become ineffective

and multi-drug resistant TB may result. Multi-drug resistance refers to resistance to two of the most powerful anti-TB drugs, rifampicin and isoniazid. Overcoming this drug resistance is a major goal of public health programs fighting TB.

When García García's study began in 1995, regional health officials in Mexico had begun to upgrade their TB treatment program to a World Health Organization model called directly observed therapy (DOTS). The five-pronged strategy of DOTS includes political commitment to the eradication of TB, case detection by sputum microscopy, supervised administration of drugs for at least the first two months of treatment, an uninterrupted supply of all essential drugs, and a rigorous assessment of treatment and outcomes.

The results of the Mexican study "strongly suggest that DOTS reduces transmission of resistant strains by curing cases of TB that otherwise could become multi-drug resistant if they are not properly treated," said Marcos Espinal, executive secretary of the Stop TB Partnership at the World Health Organization. "This study shows that DOTS is needed to control multi-drug resistance. Without DOTS, measures directed to multi-drug-resistant TB will not work."

The unexpected effectiveness of DOTS in reducing the transmission of multi-drug-resistant TB in the Orizaba region of Mexico underscores the importance of a global strategy for tackling the TB pandemic, said García García, director of the tuberculosis unit of Mexico's National Institute of Public Health and corresponding author of *The Lancet* paper.

"The fact that DOTS can control drug-resistant tuberculosis is some of the best news in recent years for the field of TB control," she added. "It is also an urgent call for the world to do more with the cost-effective interventions already at our disposal."

Fewer people may catch the drug-resistant form of the deadly infectious disease, but those who do are more likely to die without second-line drugs, which tend to be more expensive, García García and her colleagues noted. The study demonstrates the need for a new supplemental public health strategy to provide additional drugs for people with resistant strains, said García García.

"We need both—DOTS to cure the majority of cases, so the transmission of some drug resistant strains is stopped, and DOTS-Plus to manage patients with multiple-drug resistance, which requires special drugs " said Espinal, who wrote an accompanying editorial in the same issue of *The Lancet* .

The Orizaba study complied with the ethical guidelines for research in less developed countries by providing the standard of care recommended for 98 percent of the world's TB patients. Since then, a study in Peru reported better outcomes when patients with multi-drug resistant TB were given individualized, supervised therapy. "The international research community still needs to come to an agreement about what extra care should be provided

to study participants with multi-drug resistant TB," García García and colleagues wrote in *The Lancet* paper.