Journal of Infection (2006) **53**, 5–11

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# Drug-resistant tuberculosis: A disease of target populations in Houston, Texas

**Hana M. El Sahly[a,b], Larry D. Teeter[c], Rebecca R. Pawlak[c], James M. Musser[c], Edward A. Graviss[b,c,*]**

[a]*Department of Molecular Virology and Microbiology, Center for Human Bacterial Pathogenesis Research, Baylor College of Medicine, Houston, TX, USA*
[b]*Department of Medicine, Center for Human Bacterial Pathogenesis Research, Baylor College of Medicine, Houston, TX, USA*
[c]*Department of Pathology, Center for Human Bacterial Pathogenesis Research, Baylor College of Medicine, Houston, TX, USA*

Accepted 3 October 2005
Available online 28 November 2005

**KEYWORDS**
Resistant tuberculosis;
Molecular epidemiology;
HIV;
Pleural effusion

**Summary** *Objectives*: To analyse the traditional and molecular epidemiology of drug-resistant tuberculosis (DRTB) in Houston and Harris County, Texas in the setting of decreasing disease incidence.
*Methods*: Case–control study of 193 patients with DRTB and 1977 patients with drug-susceptible TB (DSTB) identified from a population-based surveillance, 1995–2001.
*Results*: In a multivariate logistic regression, the following risk factors were found to be predictors of having DRTB ($P \leq 0.05$): human immunodeficiency virus (HIV) seropositivity, Hispanic ethnicity, Asian ethnicity, history of past TB; whereas being foreign born, having a history of past TB, and younger age were predictors of MDRTB. There were 15 patients who acquired drug resistance while on therapy, and they were significantly more likely than controls to be HIV-seropositive, be of Asian ethnicity, have smear-positive pulmonary disease and present with pleural effusion on chest radiograph. No difference in 6-month mortality between DRTB and DSTB cases was found. During the study period, the incidence of DRTB remained constant.
*Conclusions*: In Houston, there is a steady, low-level, incidence of DRTB which disproportionately affects specific subpopulations, with no evidence of increased mortality at 6 months.


## Introduction

*Mycobacterium tuberculosis*' (MTB) resistance to chemotherapeutic agents was recognized soon

* Corresponding author. Address: Department of Pathology (209E), Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030, USA.
*E-mail address:* egraviss@bcm.tmc.edu (E.A. Graviss).

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doi:10.1016/j.jinf.2005.10.002

after the discovery of streptomycin in 1944.[1] The dissemination of drug-resistant MTB (DRTB) especially multidrug-resistant MTB (MDRTB) has multiple implications. First, treatment cost is significantly higher.[2-4] Second, if DRTB exists in a certain population, most patients with TB are treated initially as if they had DRTB.[4,5] Third, MDRTB patients have lower cure rates and higher mortality rates than those with DSTB.[2,6-8]

The distribution of DRTB and MDRTB is worldwide. However, the World Health Organization (WHO) has identified 'hotspots' of relatively high prevalence of MDRTB among new TB cases.[9] In the US, the incidence of DRTB and MDRTB is relatively low. For example, in 1993 there were 410 cases (2.5% of all TB cases) of MDRTB reported in the US, and only 90 (0.9%) cases were reported in 2003.[10] However, the forces of migration threaten this discrepancy in the prevalence of MDRTB, especially in the US where a growing proportion of TB cases occur in foreign-born individuals.[11-13] For example, in 2003 and among new TB cases, 72% of MDRTB cases were identified in foreign-born individuals, while in patients with a history of previous TB, 83% of MDR cases were in foreign-born individuals.[10]

Predictors of DRTB and MDRTB have been analysed by the WHO in 11 countries: prior, but ineffective, treatment was found to be the strongest predictor of drug resistance.[14] Human immunodeficiency virus (HIV) infection was significantly associated with MDRTB in some studies, while no association was found in other studies.[15-17]

The reported number of TB cases in the US has declined steadily following a period of resurgence in 1985–1992. In New York City, a survey conducted in 1991 revealed that 19% of all isolates were multidrug-resistant.[18] Subsequently, the outbreak in New York City has been contained; and in 1994 a 52% decline in the number of MDRTB patients was observed.[19,20] Currently, MDRTB in the US has been mostly observed in institutional outbreaks.[21-24]

In the US, a population-based molecular epidemiology study of DRTB under the current trend of declining TB prevalence is lacking. In this analysis, we present the molecular epidemiology of DRTB in Harris County, including Houston, Texas, the 4$^{th}$ largest US city with a large foreign-born community. The TB incidence rate in Harris County was 25.8 cases per 100 000 persons in 1995 and steadily declined to reach 11.9 cases per 100 000 persons in 2003.

## Methods

### Study design

In this 6-year cohort study (10/01/1995–09/30/2001), patients were selected from the Houston Tuberculosis Initiative (HTI) database. The HTI is a population-based active surveillance and molecular epidemiology study of TB in Houston and Harris County. The participation of patients in the study is voluntary. Patient interviews and medical record review were used to gather pertinent sociodemographic and clinical data from TB patients. All available isolates of MTB were genotyped using three methods: major genetic group designation, spoligotyping, and restriction fragment length polymorphism (RFLP) of the IS6110 insertion element.[25-27] Strains with at least five IS6110 copies were considered to be clonally related (and part of the same 'print' or 'cluster') if they have exact matching of their IS6110 RFLP patterns. Strains with fewer than five IS6110 copies were considered clustered if they exactly matched IS6110 RFLP patterns, spoligotypes and major genetic group designations. Since 1995, the HTI has systematically enrolled $>85\%$ of reported TB cases in Houston. Moreover, basic sociodemographic and clinical data was available on non-enrolled patients for comparison. Common reasons for non-enrollment were: relocation, death and lack of a proxy to interview and refusal to participate in the study.

### Definitions

As part of the study, patients were identified as DRTB cases if they had a positive culture for an MTB strain that was resistant to any of the following: isoniazid, rifampin, ethambutol or streptomycin. MDRTB was defined as TB caused by strains that were resistant to at least isoniazid and rifampin. Rifampin-resistant tuberculosis (RRTB) was defined in this analysis as tuberculosis caused by strains that were resistant only to rifampin. If a patient had serial isolates and subsequent isolates showed drug resistance when initial ones did not, the susceptibility of the resistant isolate was used. However, this subgroup of patients was also analysed separately to identify risk factors of acquiring resistance on therapy.

### Statistical analysis

Cases with various forms of resistant TB were compared to the control group, which consisted of