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Brief communication

Social and clinical predictors of drug-resistant tuberculosis in a public hospital, Monterrey, Mexico

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ABSTRACT

Purpose: Drug-resistant tuberculosis (DRTB) is steadily increasing in Mexico, but little is known of patient risk factors in the Mexico–United States border region. This preliminary case-control study included 95 patients with active pulmonary TB with drug susceptibility results attending the José E. González University Hospital in the urban hub of Nuevo León—the Monterrey Metropolitan Area. We report potential social and clinical risk factors of DRTB among this hospital-based sample.
Methods: We collected data through face-to-face interviews and medical record reviews from 25 cases with DRTB and 70 drug-sensitive controls. DNA was collected to assess an effect of genetic ancestry on DRTB by using a panel of 291,917 genomic markers. We calculated crude and multivariate logistic regression.
Results: After adjusting for potential confounding factors, we found that prior TB treatment (odds ratio, 4.5; 95% confidence interval, 0.9–21.1) and use of crack cocaine (odds ratio, 4.6; 95% confidence interval, 1.1–18.7) were associated with DRTB. No other variables, including genetic ancestry and comorbidities, were predictive.
Conclusions: Health care providers may benefit from recognizing predictors of DRTB in regions where routine drug susceptibility testing is limited. Prior TB treatment and illicit drug use, specifically crack cocaine, may be important risk factors for DRTB in this region.

Introduction

Drug-resistant tuberculosis (DRTB) is increasing along the Mexico–United States border region, but little is known about patient risk factors [1,2]. Previous research has highlighted the concern of DRTB in this region and called for a better understanding of the predictors of drug resistance [1,3,4]. Nuevo León, one of six Mexican states bordering the United States, has the second highest prevalence of DRTB cases [5]. More than 90% of TB cases in Nuevo León occur in its urban center, the Monterrey Metropolitan Area (MMA), located 140 miles southwest of Laredo, Texas. The MMA is the third most populous metropolitan area in Mexico with approximately 4 million inhabitants. Recent studies have reported extensive drug resistance in the MMA [6], particularly among cases that have been previously treated with anti-TB drugs [3].

Because of the selective use of resources in Mexico, testing of suspect TB cases in the general population is limited to acid-fast bacilli smears. In most hospitals, routine cultures and drug susceptibility testing are not conducted, rather, they are often reserved for special case situations, such as if drug resistance is suspected from initial treatment failure [7]. Given financial constraints that prohibit routine cultures and drug susceptibility testing (DST) within most hospitals, health care providers may benefit from identifying patient risk factors for drug resistance. To this end, we explored the role of social factors and clinical measures on DRTB among a hospital-based sample of pulmonary TB patients in the MMA.

Conflicts of interest: None.

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Methods

Study population

We conducted a case-control study from January 2010 to February 2011 at the public José E. González University Hospital in Monterrey. This 500-bed teaching, research, and assistance facility treats approximately 25% of new TB cases in the MMA each year. As part of the Autonomous University of Nuevo León, the University Hospital receives University-based resources to conduct cultures on all suspect TB patients and the first-line DST for cases with positive cultures. The hospital's "open-door policy" treats all patients regardless of insurance status or income, and primarily serves a low socioeconomic status population [6].

The study sample was recruited from the hospital's TB clinic and included 95 adult individuals with culture-confirmed pulmonary TB disease who were being seen for diagnosis, treatment, or follow-up. Participants were recruited for the study by the TB-clinic nurse; individuals who declined enrollment did not differ from participants in terms of sex, age, or socioeconomic status.

Selection of cases and controls

DRTB cases ($n = 25$) were confirmed through mycobacteriology DST and included patients with a TB isolate that was resistant to the action of one or more first-line TB drugs: isoniazid (INH), rifampin (RIF), ethambutol (EMB), and pyrazinamide (PZA). Although streptomycin (SM) is used only in cases that did not respond to the other first-line drugs, it is still considered a first-line anti-TB drug in Mexico [2,8]. Twenty-three DRTB patients (92%) had been previously treated for 30 days or more, known as secondary or acquired resistance, and 2 (8%) had never been treated or had received less than 30 days of treatment, known as primary or initial resistance. A total of 17 DRTB cases (68%) were multidrug-resistant tuberculosis (MDR-TB), defined as drug resistance to at least INH and RIF.

Controls ($n = 70$) represented individuals with culture-confirmed pulmonary TB disease that responded to first-line medications, also known as pan-susceptible. Controls were not matched to cases with respect to clinical or demographic characteristics. Exclusion criteria were extrapulmonary TB and human immunodeficiency virus (HIV) because patients with these characteristics represented too small a subset for stratified analysis. HIV among this study population is considered to be low, as seen with a previous study of pulmonary TB patients sampled from January 31, 1996 to March 31, 1998 from the University Hospital's TB clinic that showed HIV seropositivity in only three of 103 patients aged younger than 40 years, and no clinically suspect cases or risk factors for HIV among 83 TB patients aged older than 40 years [6].

Mycobacteriology

The University Hospital's laboratory performed all mycobacteriology testing for the study. Cultures were conducted with specimens on Löwenstein–Jensen slants and identified as positive for *Mycobacterium tuberculosis* based on a positive niacin test. DST was conducted on initial isolates using the proportion method [9]. Drug concentrations (microgram per milliliter) were used to test the susceptibility for INH (0.2), RIF (40), SM (4), and EMB (2), and resistance was defined by 1% or more of growth on the drug-containing medium compared with the control medium.

Data collection and analysis

To investigate patient risk factors for DRTB, we conducted face-to-face interviews, reviewed medical records, and assayed Native American, European, and African genetic ancestry from 291,917 single nucleotide polymorphisms [10]. The interview questions were derived from established Mexican and other Latin American questionnaires and hospital risk assessments [11,12]. Interviews were conducted based on patient availability at random points during the treatment process. Comorbidities, such as diabetes, were queried in the interview and confirmed by reviewing medical records.

Crude associations between DRTB and the social, clinical, and genetic ancestry variables were assessed using Pearson's chi-square tests, Fisher's exact tests, and *t*-tests. Potential risk factors of DRTB were introduced into multivariate logistic regression models and retained based on a significance level of 0.1 [13]. Multicollinearity of variables was assessed using a variance inflation factor cutoff of 2.5. We reported crude and adjusted odds ratios (OR) and 95% confidence intervals (CI) for the full and final models. Statistical analyses were performed in SAS 9.3 (SAS Institute Inc., Cary, NC, 2008).

This project was approved by the Institutional Review Boards of the University of New Mexico (No. 09-318) and the Autonomous University of Nuevo León (No.IN09-001). Participation was voluntary and participants gave informed, written consent.

Results

Sample characteristics

The mean age of the sample was 44.9 years (SD, 17.1), 54% were male, 72% had an education level of secondary or less, and 74% were unemployed or had nonprofessional employment for most of their life. Most participants reported nonindigenous ethnicity and did not speak an indigenous language (82%). Genetic ancestry proportions estimated from the polymorphisms ranged from 1.5% to 57.8% European, 39.6% to 98.5% Native American, and 0% to 8.1% African. Mean sample ancestry estimates were 37.2% (SD, 11.7), 58.2% (SD, 12.7), and 4.3% (SD, 2.0) for European, Native American, and African, respectively. Participants represented all MMA municipalities, with the highest proportion from Monterrey (39%).

The drug resistance patterns for the 25 DRTB cases are displayed in Table 1. Five patients (20%) had monoresistance to INH or SM, and three (12%) had polyresistance to INH + SM, and INH + SM + PZA. There were 17 cases (68%) with multidrug resistance, three of which were resistant to all five drugs (Table 1). DST results for PZA were

Table 1
Drug resistance patterns to the first-line anti-TB drugs among the 25 DRTB cases recruited at the José E. González University Hospital, Monterrey, Mexico, 2010–2011

Drug resistance patterns	*N*	%
Monoresistant		
RIF	0	0
INH	2	8
EMB	0	0
PZA*	0	0
SM	3	12
Subtotal	5	20
Polyresistant		
INH + SM	2	8
INH + SM + PZA	1	4
Subtotal	3	12
Multidrug resistant		
INH + RIF	2	8
INH + RIF + EMB	7	28
INH + RIF + SM	1	4
INH + RIF + SM + EMB	3	12
INH + RIF + SM + PZA	1	4
INH + RIF + EMB + PZA + SM	3	12
Subtotal	17	68
Total	25	100

EMB = ethambutol.
* PZA susceptibility results were unavailable for 20 cases.

Table 2
Social and clinical characteristics of drug-resistant and drug-sensitive tuberculosis patients

Patient characteristic	Drug-resistant cases ($n = 25$)	Drug-sensitive controls ($n = 70$)	*P* value
	Mean ± SD	Mean ± SD	
Age	39.2 ± 13.9	48.9 ± 17.7	**.05**
European genetic ancestry (%)*	40.3 ± 9.9	36.6 ± 10.5	.14
Native American genetic ancestry (%)*	52.5 ± 10.9	56.3 ± 12.1	.17
African genetic ancestry (%)*	7.3 ± 2.3	7.1 ± 2.2	.77
Smoking score in pack years†	5.4 ± 10.2	7.2 ± 17.6	.63
Travel time to UANL hospital (min)	61.2 ± 41.4	65.4 ± 68.6	.77
	N (%)	*N* (%)	
Sex			
Female	9 (36.0)	35 (50.0)	.23
Male	16 (64.0)	35 (50.0)	—
Self-reported indigenous ethnicity			
Indigenous heritage	23 (92.0)	55 (78.6)	.13
Nonindigenous	2 (8.0)	15 (21.4)	—
Educational attainment			
<Primary through secondary	16 (64.0)	52 (74.3)	.33
Commercial, high school, or higher	9 (36.0)	18 (25.7)	—
Principal lifetime employment			
Professional, semiprofessional, student	8 (32.0)	17 (24.3)	.45
Nonprofessional or unemployed	17 (68.0)	53 (75.7)	—
Diabetes			
No	17 (68.0)	49 (70.0)	.85
Yes	8 (32.0)	21 (30.0)	—
History of alcohol problems			
No	23 (92.0)	60 (85.7)	.51
Yes	2 (8.0)	10 (14.3)	—
Asthma			
No	24 (96.0)	69 (98.6)	.46
Yes	1 (4.0)	1 (1.4)	—
Hypertension			
No	24 (96.0)	62 (88.6)	.43
Yes	1 (4.0)	8 (11.4)	—
Marijuana use			
No	20 (80.0)	65 (92.9)	**.07**
Yes	5 (20.0)	5 (7.1)	—
Crack cocaine use			
No	19 (76.0)	66 (94.3)	**.02**
Yes	6 (24.0)	4 (5.7)	—
Methamphetamine use			
No	23 (92.0)	69 (98.6)	.17
Yes	2 (8.0)	1 (1.4)	—
Injection drug use			
No	23 (92.0)	68 (97.1)	.28
Yes	2 (8.0)	2 (2.9)	—
Inhalant use			
No	22 (88.0)	69 (98.6)	**.05**
Yes	3 (12.0)	1 (1.4)	—
Previously treated for TB			
No (<1 mo of treatment, "new case")	2 (8.0)	21 (30.0)	**.03**
Yes (≥1 mo of treatment, "previously treated")	23 (92.0)	49 (70.0)	—
Knowledge of TB airborne transmission			
No	5 (20.0)	14 (20.0)	1.0
Yes	20 (80.0)	56 (80.0)	—
Knowledge that TB is curable			
No	0	5 (7.3)	.32
Yes	25 (100.0)	64 (92.8)	—
Social stigma by preference to treat a family member with TB in secrecy			
No	18 (72.0)	61 (87.1)	**.08**
Yes	7 (28.0)	9 (12.9)	—
Ever saw or felt discrimination against TB			
No	12 (48.0)	44 (65.7)	.12
Yes	13 (52.0)	23 (34.3)	—
Ever felt fear related to TB			
No	9 (36.0)	34 (48.6)	.27
Yes	16 (64.0)	36 (51.4)	—
History of family TB			
No	19 (76.0)	41 (58.6)	.12
Yes	6 (24.0)	29 (41.4)	—
Close contact with a TB patient			
No	13 (52.0)	38 (54.3)	.84
Yes	12 (48.0)	32 (45.7)	—
Place first learned about TB			
Health clinic, doctors, hospital	18 (72.0)	52 (77.1)	.61
Other (family, public media, school, and books)	7 (28.0)	16 (22.9)	—
Use of alternative remedies/ therapies to treat TB			
No	22 (91.7)	53 (94.6)	.63
Yes	2 (8.3)	3 (5.4)	—
Marital status			
Single, divorced, separated, widow	12 (48.0)	37 (52.9)	.68
Married, free union	13 (52.0)	33 (47.1)	—
Household income per 15 d (pesos)			
<2000	8 (33.3)	22 (38.9)	.99
2001–5999	12 (50.0)	33 (50.8)	—
≥6000	4 (16.7)	10 (15.4)	—
Current socioeconomic status‡			
Highest, upper middle	8 (32.0)	17 (24.3)	.26
Middle	10 (40.0)	41 (58.6)	—
Lowest, low middle	7 (28.0)	12 (17.1)	—
Running water inside home			
No	4 (16.0)	8 (11.4)	.55
Yes	21 (84.0)	62 (88.6)	—
Normal mode of transportation			
Personal car	8 (32.0)	15 (21.4)	.29
Other (public bus, metro, taxi, and bike)	17 (68.0)	55 (78.6)	—
Residence in MMA municipalities (socioeconomic status groupings based on geospatial analysis)			
San Pedro, San Nicolás (high)	1 (4.0)	7 (10.0)	.59
Monterrey, Guadalupe, García, Santa Catarina (medium, medium low)	14 (56.0)	42 (60.0)	—
Apodaca, Escobedo, Juarez (very low)	7 (28.0)	12 (17.1)	—
Other	3 (12.0)	9 (12.9)	—
Ever been a resident in prison			
No	23 (92.0)	62 (88.6)	.63
Yes	2 (8.0)	8 (11.4)	—

Bold values represent potential DRTB risk factors that met the cutoff for significance level of 0.1.

* Individual genetic ancestry estimated from 246,240 single nucleotide polymorphisms.

† Total pack years calculation to estimate lifetime smoking exposure: (number of cigarettes per day × years of smoking)/20 [25].

‡ Calculated from the AMAI Mexican 10-item survey [11].

not available for 20 patients, and all five with available PZA results showed resistant strains.

Predictors of DRTB

Crude association tests showed that drug-resistant patients were more likely than drug-sensitive patients to be younger, use

Table 3
Crude and multivariate logistic regression to assess predictors of DRTB ($n = 95$)

Patient characteristic	Drug-resistant cases ($n = 25$, %)	Drug-sensitive controls ($n = 70$, %)	Crude odds ratio (95% CI)*	*P* value	Adjusted odds ratio† (95% CI)*	Adjusted *P* value
Age, y (mean ± standard deviation)	39.2 ± 13.9	46.9 ± 17.7	0.97 (0.94–1.00)	.054	—	—
Prior TB treatment						
New, <1 mo of treatment	2 (8.0)	21 (30.0)	Reference	.03	Reference	.059
Prior, ≥1 mo of treatment	23 (92.0)	49 (70.0)	4.93 (1.1–22.8)		4.46 (0.94–21.1)	
Stigma measure: preference to treat a family member with TB in secret						
No	18 (72.0)	61 (87.1)	Reference	.082	—	—
Yes	7 (28.0)	9 (12.9)	2.64 (0.86–8.07)	—	—	—
Marijuana use						
No	20 (80.0)	65 (92.9)	Reference	.072	—	—
Yes	5 (20.0)	5 (7.1)	3.25 (0.85—12.38)	—	—	—
Crack cocaine use						
No	19 (76.0)	66 (94.3)	Reference	.019	Reference	.032
Yes	6 (24.0)	4 (5.7)	5.21 (1.33–20.39)		4.61 (1.1–18.7)	
Inhalant use						
No	22 (88.0)	69 (98.6)	Reference	.055	—	—
Yes	3 (12.0)	1 (1.4)	9.40 (0.93–95.05)	—	—	—

* 95% CI.
† Odds ratios are adjusted for all variables in the table; no other variables were significant in crude or adjusted analyses.

marijuana, crack cocaine, and inhalants, report social stigma, and have prior TB treatment ($P \leq .1$) (Tables 2 and 3). Other variables, including genetic ancestry, comorbidities, and socioeconomic measures, showed no significant differences between drug-sensitive and drug-resistant patients (Table 2). Multivariate logistic regression analyses revealed that independent predictors of DRTB were prior TB treatment ($P \leq .1$, OR 4.5; 95% CI, 0.9–21.1) and use of crack cocaine (OR, 4.6; 95% CI, 1.1–18.7) (Table 3).

There were no epidemiologic links among the DRTB cases that used crack cocaine. Of these six cases, including five males and one female, none had known contact with another drug-resistant case. All six cases lived in different colonias (neighborhoods), and their residences were dispersed throughout the MMA. None had the same occupation or had common residential exposures through prison or homeless shelters. Additionally, their anti-TB drug resistance profiles differed; four had MDR-TB, one had monoresistance (INH), and one had polyresistance (INH + SM).

Discussion

The increasing rates of DRTB in Mexico, especially along the Mexico–United States border, presents substantial challenges to TB control. Multidrug resistance is of particular concern throughout the country and especially in the MMA [3,6]. An improved understanding of the risk factors for DRTB in this region is crucial for prevention and intervention strategies [2].

Illicit drug use has been previously linked to DRTB in urban areas and along the Mexico–United States border region [14]. Crack cocaine has been described as a "dangerous synergy" because of addiction-related obstacles that pose treatment barriers, often correlated with race, low income neighborhoods, and comorbidities [15]. Previous reports describe distrustful patient-provider relationships and nonadherence to treatment among crack cocaine users [16]. These treatment barriers increase the risk for DRTB [15,17]. Although our study did not reveal any epidemiologic links between the DRTB cases that used crack cocaine, it is possible that transmission of drug-resistant strains occurs at crack houses [16]. Future studies may consider including locations of drug use to explore potential links.

Inhalation of crack cocaine can also biologically impair pulmonary immune response [18], notably limiting the ability of alveolar macrophages to kill bacteria [19,20]. The concerning increase in crack cocaine addiction in Mexico is part of a trend of increasing drug consumption throughout the country [21,22]. Recently, the link with DRTB has been called on for investigation in light of the increase in cocaine trafficking in Mexico [21].

A history of prior TB treatment is an established risk factor for DRTB [23], but not always measured and reported in DRTB studies. A Mexican National Survey on DRTB (ENTB-2008) conducted in nine states found previous treatment to be associated with multidrug-resistant TB (OR, 3.3; 95% CI, 1.1–9.4) [7]. Inadequate treatment can select for the emergence of drug-resistant mutations of TB bacilli, resulting from improper combinations of anti-TB drugs, interrupted availability of drugs, or treatment for too short a period [24]. This is considered a major complication to TB control in the country and highlights adequate treatment as a keystone for preventing DRTB.

This study has several limitations. First, the small sample size limited statistical power to identify other potentially significant DRTB predictors and to assess interactions among these predictors. Second, patients in this study were treated at a public hospital in the MMA, so results might not be generalizable to patients that are unable or choose not to seek hospital care. Third, we may have failed to collect social variables that influence DRTB, and we excluded patients with HIV, which might increase risk.

The findings of this preliminary study may be useful to DRTB research and control efforts in Mexico and beyond. The findings highlight the importance of DST and suggest that, given limited financial resources, health care providers in Mexico should consider screening patients with a history of illicit drug use and prior TB treatment. Patients with these risk factors may benefit from rapid tests to detect mutations associated with TB drug resistance. Risk factors for DRTB warrant greater attention to address the threat to TB control in Mexico and in adjoining regions of the United States.

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References

[1] Taylor JP, Suarez L. Prevalence and risk factors of drug-resistant tuberculosis along the Mexico-Texas border. Am J Public Health 2000;90(2):271–3.

[2] Zazueta-Beltran J, Leon-Sicairos C, Canizalez-Roman A. Drug resistant Mycobacterium tuberculosis in Mexico. J Infect Dev Ctries 2009;3(3):162–8.

[3] Becerril-Montes P, Said-Fernandez S, Luna-Herrera J, Caballero-Olin G, Enciso-Moreno JA, Martinez-Rodriguez HG, et al. A population-based study of first and second-line drug-resistant tuberculosis in a high-burden area of the Mexico/United States border. Mem Inst Oswaldo Cruz 2013;108(2):160–6.

[4] Quitugua TN, Seaworth BJ, Weis SE, Taylor JP, Gillette JS, Rosas II, et al. Transmission of drug-resistant tuberculosis in Texas and Mexico. J Clin Microbiol 2002;40(8):2716–24.

[5] CENAVECE. Centro Nacional de Programas Preventivos y Control de Enfermedades: Situación actual de la tuberculosis en México. In: Mexican Secretary of Health; 2012. Available at: http://web.ssaver.gob.mx/saludpublica/files/2012/03/01-SIMPOSIO-VERACRUZ.pdf.

[6] Yang ZH, Rendon A, Flores A, Medina R, Ijaz K, Llaca J, et al. A clinic-based molecular epidemiologic study of tuberculosis in Monterrey, Mexico. Int J Tuberc Lung Dis 2001;5(4):313–20.

[7] Bojorquez-Chapela I, Backer CE, Orejel I, Lopez A, Diaz-Quinonez A, Hernandez-Serrato MI, et al. Drug resistance in Mexico: results from the National Survey on Drug-Resistant Tuberculosis. Int J Tuberc Lung Dis 2013;17(4):514–9.

[8] Sd Salud. [Official Mexican Standards NOM-006-SSA2-1993, for the prevention and control of tuberculosis in primary health care]. Official Journal of the Federation 2005.

[9] WHO/IUATLD. Guidelines for surveillance of drug resistance in tuberculosis. WHO Geneva/IUATLD Paris. International Union Against Tuberculosis and Lung Disease. Int J Tuberc Lung Dis 1998;2(1):72–89.

[10] Illumina. HumanCytoSNP-12 DNA Analysis BeadChip Kit. In: Illimina, Inc.; 2012. Available at: http://www.illumina.com/products/humancytosnp_12_dna_analysis_beadchip_kits.ilmn.

[11] AMAI. Asociación Mexicana de Agencias de Investigación y Opinión Publica: Indice de niveles socioeconómicos. In: Asociación Mexicana de Agencias de Inteligencia de Mercado y Opinión; 2009. Available at: http://www.amai.org.

[12] ENDSA. Encuesta nacional de demografia y salud. Instituto Nacional de Estadistica. Bolivia: Ministerio de Salud y Deportes; 2008.

[13] Hosmer DW, Lemeshow S. Applied logistic regression. 2nd ed. New York City, NY: John Wiley & Sons, Inc; 2000.

[14] Escobedo M, de Cosio FG. Tuberculosis and the United States-Mexico border. J Border Health 1997;2(1):40–7.

[15] Story A, Bothamley G, Hayward A. Crack cocaine and infectious tuberculosis. Emerg Infect Dis 2008;14(9):1466–9.

[16] Asghar RJ, Patlan DE, Miner MC, Rhodes HD, Solages A, Katz DJ, et al. Limited utility of name-based tuberculosis contact investigations among persons using illicit drugs: results of an outbreak investigation. J Urban Health 2009;86(5):776–80.

[17] CDC. MMWR weekly: epidemiologic notes and reports crack cocaine use among persons with tuberculosis-Contra Costa County, California, 1987-1990. Atlanta, GA: Centers for Disease Control and Prevention; 1991.

[18] Laposata EA, Mayo GL. A review of pulmonary pathology and mechanisms associated with inhalation of freebase cocaine ("crack"). Am J Forensic Med Pathol 1993;14(1):1–9.

[19] Baldwin GC, Tashkin DP, Buckley DM, Park AN, Dubinett SM, Roth MD. Marijuana and cocaine impair alveolar macrophage function and cytokine production. Am J Respir Crit Care Med 1997;156(5):1606–13.

[20] Roth MD, Whittaker K, Salehi K, Tashkin DP, Baldwin GC. Mechanisms for impaired effector function in alveolar macrophages from marijuana and cocaine smokers. J Neuroimmunol 2004;147(1-2):82–6.

[21] Brouwer KC, Case P, Ramos R, Magis-Rodriguez C, Bucardo J, Patterson TL, et al. Trends in production, trafficking, and consumption of methamphetamine and cocaine in Mexico. Subst Use Misuse 2006;41(5):707–27.

[22] Salud Sd. Encuesta Nacional de Adicciones 2008 [National Survey of Addictions 2008]. In. Instituto Nacional de Salud Publica 2009. Available at: http://www.conadic.salud.gob.mx/pdfs/ena08/ENA08_NACIONAL.pdf.

[23] Iseman MD. A clinician's guide to tuberculosis. Philadelphia, PA: Lippincott Williams & Wilkins; 2000.

[24] WHO. Multidrug and extensively drug-resistant TB (M/XDR-TB): 2010 global report on surveillance and response. Geneva, Switzerland: World Health Organization; 2010.

[25] Prignot J. Quantification and chemical markers of tobacco-exposure. Eur J Respir Dis 1987;70(1):1–7.