

Active Tuberculosis Case Finding Among Immigrants in Barcelona

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OBJECTIVE: To assess the prevalence of tuberculous infection and disease in recent economic immigrants in Barcelona.

SUBJECTS AND METHOD: Examination and testing of immigrants. Tuberculin tests (TTs) were given and the presence of scars from tuberculosis vaccinations were noted. Thresholds of 5 and 15 mm were established for positivity in unvaccinated and vaccinated individuals, respectively.

RESULTS: A total of 3651 persons were examined, but only 3151 completed the study. Eighteen were diagnosed with tuberculosis (571.2 per 100 000) and 50.6% were classified as positive TT reactors, 34.4% because of infection and 16.3% possibly because of tuberculosis vaccination. The percentage of reactors was significantly higher in the sample of economic immigrants than in the local population. Age, male sex, place of origin, greater poverty, and higher prevalence of disease in the country of origin were associated with tuberculous infection in the sample.

DISCUSSION: Active case finding proved efficient. Interference from tuberculosis vaccination greatly affects TT findings, depending on the positivity threshold that is established. We recommend that chest radiographs be used in addition to TTs. Immigration will change the nature of endemic tuberculosis in Spain, and strategies should be specifically designed to deal with the new challenges that will appear.

Key words: *Tuberculosis and immigration. Epidemiology. Tuberculin test.*

Búsqueda activa de tuberculosis en inmigrantes en Barcelona

OBJETIVO: Conocer la prevalencia de la infección y de la enfermedad tuberculosa en inmigrantes económicos y recientes en Barcelona.

SUJETOS Y MÉTODO: Reconocimiento médico de inmigrantes. Se practicó la prueba de tuberculina (PT) y se indagó la presencia de cicatriz posvacunación antituberculosa. Se estableció el dintel de positividad de la PT en 5 mm para los no vacunados y en 15 mm para los vacunados.

RESULTADOS: Se examinó a 3.651 personas, pero sólo se incluyó en el análisis a las 3.151 que completaron el estudio. Se diagnosticó a 18 enfermos (tasa de 571,2 por 100.000) y el 50,6% se catalogó como reactores positivos a la PT, siendo el 34,4% reactores por infección y 16,3% por posible vacunación antituberculosa. El porcentaje de reactores es estadísticamente superior al encontrado en una población autóctona. La edad, ser varón, la región de procedencia, la mayor pobreza y la mayor tasa de enfermedad en el país de origen se mostraron asociados a la prevalencia de la infección tuberculosa de los inmigrantes.

DISCUSIÓN: La búsqueda activa se ha mostrado eficiente. La interferencia de la vacunación antituberculosa modifica mucho los resultados, según el dintel de positividad de la PT que se establezca. Se recomienda realizar la PT junto con la radiología del tórax. La inmigración modificará la endemia tuberculosa del país y se han de diseñar estrategias específicas para afrontar este nuevo reto de la tuberculosis.

Palabras clave: *Tuberculosis e inmigración. Epidemiología. Prueba de la tuberculina.*

Introduction

Tuberculosis (TB) has always been linked to poverty and social deprivation and has therefore been found mainly in poorer countries. There are currently more TB cases than ever¹ and many countries have come to

consider TB an emergent disease,² attributing its new status to a variety of factors such as population increase, its association with new diseases like acquired immune deficiency syndrome (AIDS), inadequate screening, and population migration.³

Migration has always taken place, as humans searched for food or a more favorable environment, or as a result of conflict between groups. Migration is currently a phenomenon that cannot be avoided as long as economic differences prevail between industrialized countries and the rest of the world.¹ Along with migrating humans come pathogens, particularly the

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airborne bacillus that causes TB—*Mycobacterium tuberculosis* (MTB). Such migrating pathogens can lead to disease and many complex problems of control for host countries.⁴

The incidence of TB in poor countries from which migrants come ranges from 100 cases per 100 000 population to over 400, and the prevalence of infection among those under 50 years of age is very high. In wealthy countries the incidence rates range from 5 to around 30 per 100 000 population and the rates of exposure among the young are low,^{1,3,5} such that they are highly susceptible to MTB contagion. Because of cases occurring among immigrants, the tendency of TB to decrease in wealthy countries has come to a halt or has reversed.¹⁻⁷

According to official police figures (*Dirección General de Policía*) for Catalonia, Spain, 328 461 documented immigrants were resident in 2002, accounting for 5.05% of the population, while the incidence of TB among recent immigrants (with fewer than 5 years of residence) rose from 5% in 1996 to 22% in 2002.⁸ TB and immigration coincide mainly in large cities and particularly in the poorest neighborhoods,^{7,9,10} creating considerable additional load for the public health care services there.

It has been said that only young, strong, healthy individuals emigrate and that it is adverse conditions in the host countries that lead to tuberculous disease in those who are MTB infected.^{1,6,9-13} For this reason, knowledge of the prevalence of infection among immigrants is of interest. The aim of the present study was to screen for tuberculous infection and disease among immigrants coming to Barcelona for economic reasons and to investigate the relation between TB and a series of social, economic, and epidemiological factors related to immigrants' countries of origin.

Subjects and Method

A program to detect TB cases and infected individuals was started in 2001 with tuberculin tests (TTs) as the method for diagnosing infection followed by the usual methods for detecting cases.^{14,15} Inclusion criteria were a subject's consent to participate, status of being an immigrant for economic reasons, and having lived fewer than 2 years in a high-income country. Subjects were included from July 1, 2001 through March 31, 2003. Several nongovernmental organizations, meal programs, shelters, and other social service providers helped recruit subjects in addition to those enrolled at health care clinics.

For comparison with the local population, we took findings of a similar screening program carried out in educational institutions.¹⁶

TTs were administered using the Mantoux technique with 2 tuberculin units of purified protein derivative RT-23 tuberculin with Tween 80 following examination for scars from prior vaccination against TB. A subject's medical history was taken and a physical examination was carried out. Language difficulties made it impossible to use a questionnaire that had been designed for the study. The TT was administered and

assessed within 48 to 72 hours by expert personnel. Following guidelines,^{14,15} it was established that a TT was negative if it produced an induration measuring less than 5 mm. In an individual with scarring from vaccination against TB, an induration measuring between 5 and 14 mm was considered a possible reaction to that vaccination. Unvaccinated individuals with an induration greater than 4 mm and vaccinated individuals with indurations greater than 14 mm were considered infected. Regardless of induration size and vaccination status, individuals were classified as MTB infected if vesicles or necrosis were present or if there were radiographic lesions consistent with TB or signs and symptoms of nonpulmonary TB. If a vaccinated individual had been administered a TT within the past 2 years, an induration measuring less than 18 mm was considered an antigenic booster reaction. An induration 18 mm or larger was considered indicative of MTB infection.

Income per capita (IPC) was taken from world development indicators of the World Bank¹⁷ and TB incidence rates were taken from reports compiled by the World Health Organization.⁵

Statistical Analysis

Descriptive statistics were compiled: mean (SD) frequencies and ranges. Parametric (Student-Fisher *t* test and analysis of variance) and nonparametric (Kruskal-Wallis test) techniques were used to compare arithmetic means. A risk of approximately 5% was assumed. The odds ratio was calculated using the Mantel-Haenszel method and 95% confidence limits using the Cornfield test and the χ^2 test with Yates' correction. Multivariate statistical analysis was performed by unconditional logistic regression; included in the model were all variables showing statistically significant differences in the univariate analysis. The EpiInfo 2002 statistical program (Center for Disease Control, Atlanta, GA, USA) was used.

Results

TTs were administered to 3651 persons, 3151 (86%) of whom returned to have the results interpreted and who were included in the study; 91% had been in developed countries for less than 1 year. The mean age of the subjects was 29.49(9.79) years (mode, 27); 77.2% were men (mean age 29[9.86] years) and 22.8% were women (mean age 30.9[9.43] years). Immigrants coming from industrialized countries had a mean age of 39.05(10.73) years, whereas the mean age of Spaniards with whom their results were compared was 28.74(5.78) years. Scarring from prior vaccination against TB was observed in 2347 (74.3%) and not observed in 731 (22.7%) individuals (who were considered unvaccinated); scarring could not be ascertained in 73 (2.3%). Subjects came from 91 countries, distributed in 6 groups by geographic proximity or economic and social similarity.

Eighteen individuals were diagnosed with pulmonary TB. None of the diagnosed individuals had AIDS, and MTB was isolated in 6 subjects, 4 of whom had positive sputum tests. Three were harboring strains resistant to antituberculous drugs.

TABLE 1
Tuberculin Skin Test Reaction in Immigrants and in Subjects From the Local Population*

Induration Diameter, mm	Unvaccinated			Vaccinated Against TB		
	Immigrants	Local	P	Immigrants	Local	P
0-4	61.8	85.3	<.00001	44.8	54.2	<.00001
0-9	65.3	87.6	<.00001	50.3	13.4	<.00001
5-14	14.8	8.1	<.00001	22.0	31.5	<.00001
≥15	23.4	6.6	<.00001	30.2	14.3	<.00001

*Differences in reaction rates between vaccinated and unvaccinated individuals and between each population category were significant. TB indicates tuberculosis.

TABLE 2
Mean size of Induration in Immigrants and in Subjects From the Local Population*

Status	Negative Reactions	Positive Reactions	
		Possibly due to Vaccination	Possibly due to Infection
Immigrants	0.175(0.715)	10.922(2.541)	18.336(4.353)
Local	0.007(0.492)	9.815(2.789)	14.816(4.748)

*Results are shown as means (SD).

Positive tuberculin reactions were observed in 50.6% of the readings, of which 16.3% were probably due to prior vaccination and 34.4% were probably caused by MTB infection. Table 1 compares TT reactivity in immigrants to reactivity in the local population, according to vaccination status. The mean size of the induration (Table 2) was significantly greater in immigrants in all 3 categories established ($P<.0000001$).

Table 3 shows the prevalence of tuberculous infection among immigrants according to personal characteristics and sociodemographic features of

TABLE 3
Prevalence of TB Infection Among Immigrants by Economic and Personal Variables and Country of Origin*

Variable	No. of Individuals	Prevalence of Infection (95% CI)	Unadjusted OR (95% CI)	P
Total	3151	34.3 (32.6-35.9)		
Sex				
Female	719	26.4 (23.3-29.7)	1	
Male	2432	36.6 (34.7-38.5)	1.61 (1.33-1.94)	.0000006
Age groups, years				
15-19	509	19.8 (16.5-23.5)	1	
20-24	529	28.5 (24.8-32.5)	1.61 (1.20-2.18)	.0013
25-29	703	30.2 (26.8-33.6)	1.74 (1.32-2.31)	.000068
30-39	914	41.6 (38.4-44.8)	2.87 (2.21-3.74)	.0000001
40-49	376	46.8 (41.8-51.9)	3.55 (2.61-4.84)	.0000001
≥50	120	50.0 (41.1-58.9)	4.04 (2.60-6.28)	.0000001
			Unadjusted OR, all strata =2.38	
			Adjusted OR =2.43 (2.16-2.82)	.00000001
Origin				
Latin America	1245	25.4 (23.0-27.9)	1	
Wealthy Countries	56	42.9 (30.4-56.0)	2.20 (1.24-3.92)	.0058
Eastern Europe	325	42.8 (37.5-48.2)	2.20 (1.69-2.86)	.0000001
North Africa	831	31.8 (28.7-35.0)	1.37 (1.12-1.67)	.0017
Central and South Africa	293	47.1 (41.4-52.8)	2.62 (2.00-3.43)	.0000001
Asia and the Philippines	401	49.6 (44.7-54.5)	2.90 (2.28-3.68)	.0000001
			Unadjusted OR, all strata =1.97	
			Adjusted OR =2.04 (1.84-2.31)	.00000001
TB incidence, country of origin (rate per 10 ⁵)				
0-100	846	31.3 (28.3-34.5)	1	
101-200	1812	30.2 (30.2-34.5)	1.05 (0.87-1.25)	.6526
>200	493	46.6 (42.3-51.1)	1.92 (1.51-2.43)	.0000001
			Unadjusted OR, all strata =1.20	
			Adjusted OR =1.31 (1.14-1.52)	.00017
IPC, country of origin (US dollars, year 2000)				
≥3116	309	33.0 (27.9-51.9)	1	
785-3115	2129	29.8 (27.9-31.7)	0.86 (0.66-1.12)	.2758
<785	713	48.2 (44.6-51.9)	1.89 (1.42-2.53)	.0000089
			Unadjusted OR, all strata =1.06	
			Adjusted OR =1.24 (1.03-1.52)	.0242

*CI indicates confidence interval; OR, odds ratio; TB, tuberculosis; IPC, income per capita.

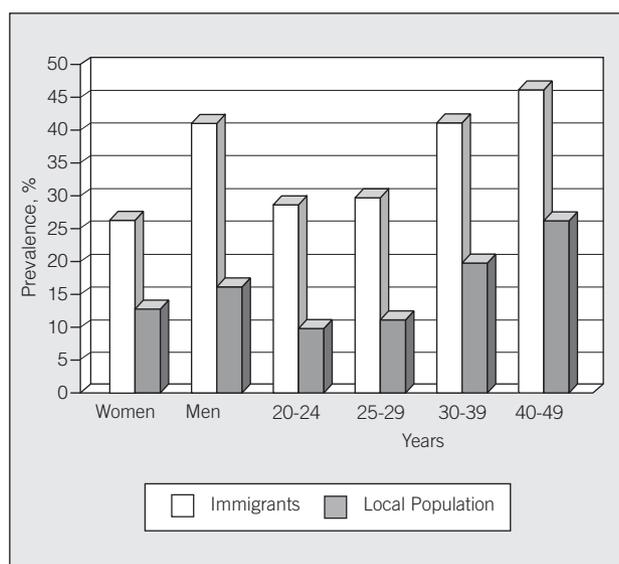


Figure. Prevalence of MTB infection among immigrants and the local population by sexes and age groups.

TABLE 4
Unconditional Logistic Regression of Variables Related to Tuberculous Infection Among Immigrants*

Variable	Adjusted OR (95% CI)	P
Sex, male	1.20 (0.97-1.48)	.0854
Age	1.05 (1.04-1.06)	.00001 [†]
Origin		
Latin America	1	
Other geographic areas	1.95 (1.59-2.38)	.00001 [†]
TB incidence in country of origin (rate per 105)		
0-100	1	
101-200	1.14 (0.93-1.39)	.1816
>200	1.60 (1.18-2.17)	.0025 [†]
Income per capita (US dollars, year 2000)		
<785	1.30 (1.02-1.66)	.0305 [†]

*CI indicates confidence interval; OR, odds ratio; TB, tuberculosis.

[†]Statistically significant differences.

country of origin. Table 4 shows variables independently associated with MTB infection in this group of immigrants: age, origin other than a Latin American country, coming from a country with a TB rate exceeding 200 per 100 000 population, and coming from a country with an IPC less than US \$785 in the year 2000. Without taking any other factors into consideration, recent economic emigration from countries outside Latin America increased the risk of tuberculous infection 95% over the risk for emigration from Latin America. Emigration from countries whose IPC was less than US \$785, on the other hand, increased the risk of being infected by 30% over emigration from wealthier countries.

Results for the group of immigrants are compared with those for the local population in the Figure. In all categories, the prevalence of infection was much lower in local individuals than in immigrants ($P<.001$ for the 40-50 year age group and $P<.0000001$ for the remaining age groups and for both sexes).

Discussion

Active case finding proved efficient and was useful for estimating the epidemiological impact for Spain of receiving immigrants from countries with high prevalences of TB.

The 18 TB cases diagnosed represent a rate of 571.2 per 100 000 individuals examined, similar to estimated rates for Barcelona (555.9/100 000)¹⁰ and Madrid (560/100 000),¹⁸ although higher than estimates for Australia in a group of immigrants from southeast Asia (363/100 000 in their first year after immigration)¹⁹ and considerably lower than rates reported for Italy (650/100 000²⁰ and 1180/100 000²¹). Radiographic lesions in 3 patients indicated that they had been ill while traveling, although symptoms were denied; TB may be well tolerated by a patient, but there is indication that a growing number of immigrants travel to a developed country in order to obtain treatment there.²² Such high rates of disease must be attributed to extremely adverse conditions faced by immigrants upon their arrival in Spain. If conditions improved or morbidity could be reduced in their countries of origin, immigration would have less impact on endemic TB in host countries.

The results of this study demonstrate that significantly more positive TT reactions are found among immigrants and the prevalence of MTB infection is higher than in the local populations of the same age and sex. The rates for immigrants are not different from those among incarcerated local individuals, however,²³ probably because the local reference population that is incarcerated also comes from underprivileged social strata that have high rates of tuberculous disease and infection.²⁴ We also saw that the probability of immigrants being infected by MTB increases 5% with each year of increased age; moreover, men are 61% more likely to be infected than women, although the difference between the sexes disappears in multivariate analysis, probably because female immigrants are older than male immigrants. These results are consistent with those that have been widely reported elsewhere.^{3,16,25,26}

The rates of infection in a country depend on the incidence of disease there, which in turn is related to economic level.^{3,5,24} Immigrants in our study coming from Central and South America had lower rates of infection. Africa had the next higher rate, with 37% greater risk of infection, followed by immigrants from the remaining geographic areas studied, whose risk of infection was between 120 and 190 times higher. The higher rate of infection found among immigrants coming from higher-income countries is probably due to the fact that that group was small and older.

The prevalence of infection in our study was independently associated with coming from countries whose incidence of TB is 200 or more cases per 100 000 population or from countries with an IPC less than US \$785. However, immigrants whose countries of origin have TB incidence rates between 101 and 199 per 100 000 population—which would classify such immigrants as belonging to a group at risk—did not in fact have a prevalence of infection that was statistically different from that of countries with rates less than 100 per 100 000. A similar pattern was seen when rates for individuals emigrating from the lowest-income countries were compared with those for individuals emigrating from countries with higher IPCs. Our results indicate that immigrants from a country with an IPC less than \$785 have a 30% higher risk of infection than those from higher-income countries, considering that countries with an IPC between \$785 and \$3115 also have scarce resources. The low-income countries were mainly those from sub-Saharan Africa and southeast Asia and those in Latin America, where the mean IPC was less than \$3580. In many of these countries, the AIDS pandemic, wars, and famines complete the circle aggravating economic and health deficits. The fact that the infection rates of countries with mid-level prevalences of TB but with IPCs that are mid-level-to-low (often coincident) do not have statistically significantly lower infection rates than countries that are wealthier and enjoy low TB prevalence rates can be explained by the efficacy of anti-TB campaigns underway in those countries for several years, under the supervision of the International Union Against Tuberculosis and Lung Diseases of the World Health Organization.

Immigration has increased the incidence of disease or halted its decline in many countries, but epidemiological indicators of rising MTB infection rates have not been ascertained, and therefore the impact that immigration has or will have on endemic TB in host countries is still disputed.^{4,9,13,18,21,22} In Holland, it was estimated that a fifth of cases could be attributed to recent infection from a non-Dutch source.³ However, among immigrants with TB in San Francisco and in New York, it was found that 21% and 19%, respectively, had been recently infected in the aforementioned cities,^{27,28} demonstrating that contagion can occur in both directions.

These patterns are of great interest for Spain, because immigrants here often care for persons susceptible to TB (children, patients, the elderly, etc) and because 49% of immigrants who have negative TTs are exposed to contagion from their companions in living conditions that propitiate tuberculous infection and the development of disease, suggesting that incidence rates will continue to rise in the short- and medium-term. Although it has been shown that immigrants are among those who have the shortest delays in diagnosis²⁹ and that by shortening diagnostic delay transmission of infection is reduced by 33%,³⁰ it is nevertheless also true

that immigrants experience difficulties in gaining access to health care and in being retained by health care service providers.^{3,9,31} That situation favors transmission.

Another factor affecting endemic TB is the number of infected immigrants who stay in Spain, given that the rates of infection among them seem to be maintained for 2 generations after settlement.¹ The percentage of reactions attributed to tuberculous infection in our study was 34.3%; extrapolating from the results of Marks et al³² for the cohort we studied, we can expect to see 40 cases, 18 of which have already been diagnosed, but that the number of cases can be expected to rise as new individuals arrive.

One of the difficulties we faced in carrying out this research was in establishing the threshold of TT positivity appropriate for screening the study population. Opinions differ about the threshold of positivity to use because specificity is low,³ mainly owing to the high rates of vaccination against TB and the possibility of infection by one of the non-MTB pathogens prevalent in tropical or subtropical countries (cross reactions). We applied a threshold of positivity of 15 mm in the present study, following the guidelines of the Consensus Conference for the Control of TB¹⁴ and the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR),¹⁵ because 74% of the population had been vaccinated. Other authors have fixed the positivity threshold²³ at 5 mm or at 10 mm without distinguishing vaccinated and unvaccinated individuals.^{25,26,33,35-37} Were we to apply a TT positivity threshold of 5 mm to data from our study, the rate of MTB infection would rise to 50.6% and it would decrease again to 42.7% if the positivity threshold applied to all subjects were 10 mm, giving rates similar to figures reported in the literature. In a study of a North African population,³⁸ on the other hand, the prevalence of infection found was higher than that of our sample (76.3%, 72.5%, or 66.3% depending on whether a cut point of 5, 10, or 15 mm is applied) and no significant difference was observed between the TT reaction rates of individuals with or without scarring from vaccination. The differences in infection rates for scarred and unscarred individuals in our study, however, were highly significant, as were the differences between the infection rates for both vaccinated and unvaccinated immigrants with rates for the local population.

The mean size of TT induration in immigrants was significantly greater than that of the indurations in tested Spanish subjects. This observation could be attributed to the influence of vaccination or infection by non-MTB bacteria that can produce an undetected booster effect or to reinfections by MTB,³ but the most likely explanation is that all the immigrants who reacted to the TT were in fact MTB infected. Language difficulties may have been a reason why positive reactions caused by a booster effect were not detected, and this is a limitation and possible source of bias in the present study.

An additional difficulty that is often cited is that of

poor cooperation of immigrants with the health care services in this type of screening,^{12,20,31,34} owing to their mobility and the precariousness of their employment—specifically that they do not earn unless they work—and to the fact that health is not always their main worry. These factors have come into play even when interpreters were available and uncooperative patients were contacted to improve cooperation.³⁹ In the present study, 24% of subjects did not return to have the results of their TT read, possibly leading to underestimation of the rates of positive reaction.

Given the present situation, we conclude that a chest radiograph is the most sensitive TB screening tool for immigrant populations. An initial TT is not an appropriate screening technique for patients who are not living in a family or who do not have stable jobs, for example,^{31,39} or in those who are unlikely to adhere to treatment of infection. In other cases a TT should not be carried out in order to avoid repeated skin testing and antigenic booster effects that are difficult to detect.

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