ORIGINAL ARTICLES

Longitudinal Incidence of Tuberculosis in a Cohort of Contacts: Factors Associated With the Disease

Carlos Salinas,[a] Alberto Capelastegui,[a] Lander Altube,[a] Pedro Pablo España,[a] Rosa Díez,[a] Mikel Oribe,[a] Isabel Urrutia,[a] and Urko Aguirre[b]

[a]Servicio de Neumología, Hospital de Galdakao, Galdakao, Bizkaia, Spain
[b]Unidad de Investigación, Hospital de Galdakao, Galdakao, Bizkaia, Spain

OBJECTIVE: To investigate the incidence of tuberculosis (TB) in a cohort of contacts and to analyze the variables associated with the disease.

METHODS: A prospective analysis was undertaken of all the contact investigations carried out in a health district in the Basque Country in northern Spain between January 1, 1995 and December 31, 2004. The dependent variable was the number of cases of TB detected among the contacts. Independent variables were age, sex, tuberculin skin test result, and the degree of contact. In index cases, additional variables were the site of the disease and smear test result.

RESULTS: Analysis of 5444 contacts of 596 patients with TB yielded 66 secondary cases of TB (40 at the time of the contact investigation and 26 at a later stage); the majority (73%) developed the disease within 12 months. Multivariate analysis revealed a significant relationship between the detection of secondary cases and the following variables: close contact (odds ratio [OR], 3.05; 95% confidence interval [CI], 1.75-5.31), positive smear test (OR, 8.54; 95% CI, 2.06-35.43), induration of 10 mm or larger (OR, 10.18; 95% CI, 4.27-24.26), and age under 30 years (OR, 3.35; 95% CI, 1.88-5.98). The final predictive model constructed on the basis of these 3 variables had a sensitivity of 77.4%, a specificity of 80.3%, and an area under the curve of 0.83 (95% CI, 0.78-0.88).

CONCLUSIONS: The contact investigation is a valid strategy for the detection of new cases of TB. Prophylactic treatment should be implemented at an early stage, and priority should be given to young contacts of smear-positive patients using an induration size of 10 mm or more as a reference.

Key words: *Tuberculosis. Contact investigation. Risk factors.*

Incidencia longitudinal de la tuberculosis en una cohorte de contactos: factores asociados a la enfermedad

OBJETIVO: Conocer la incidencia de tuberculosis (TB) en una cohorte de contactos y analizar las variables asociadas a la enfermedad.

MÉTODOS: Se ha efectuado un análisis prospectivo de los estudios de contactos (EC) realizados en un área sanitaria del País Vasco del 1 de enero de 1995 al 31 de diciembre de 2004. La variable dependiente fue el número de casos de TB detectados entre los contactos. Las variables independientes fueron la edad, el sexo, la prueba de la tuberculina (PT) y el grado de contacto, y en los casos índice, la localización de la TB y la baciloscopia del esputo.

RESULTADOS: De los 5.444 contactos de 596 pacientes con TB que se estudiaron, se encontraron 66 casos secundarios de TB (40 en el momento del EC y 26 en el período posterior), la mayoría de ellos (73%) durante el primer año. El análisis multivariante demostró una relación significativa entre la detección de casos secundarios y las siguientes variables: contacto íntimo (*odds ratio* [OR] = 3,05; intervalo de confianza [IC] del 95%, 1,75-5,31), baciloscopia positiva (OR = 8,54; IC del 95%, 2,06-35,43), PT de 10 mm o mayor (OR = 10,18; IC del 95%, 4,27-24,26) y edad inferior a 30 años (OR = 3,35; IC del 95%, 1,88-5,98). El modelo predictivo final que se obtuvo utilizando estas 3 variables alcanzó una sensibilidad del 77,4%, una especificidad del 80,3% y un área bajo la curva de 0,83 (IC del 95%, 0,78-0,88).

CONCLUSIONES: El EC es una estrategia válida para la detección de nuevos casos de TB. La intervención profiláctica debería realizarse de forma precoz y dirigirse prioritariamente a los contactos jóvenes de pacientes bacilíferos, utilizando como referencia una PT de 10 mm o mayor.

Palabras clave: *Tuberculosis. Estudio de contactos. Factores de riesgo.*

Introduction

After the identification and treatment of all cases of active tuberculosis (TB), contact tracing is the second priority of TB prevention and control programs in countries with sufficient resources.[1] The potential of the contact investigation lies in its proven capacity to facilitate early diagnosis of secondary cases among the contacts of patients

Correspondence: Dr. C. Salinas,
Servicio de Neumología. Hospital de Galdakao.
B.º Labeaga, s/n, 48960 Galdakao. Bizkaia. España.
E-mail: csalinas@hgda.osakidetza.net

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with active TB[2] and in the possibility it affords of preventing new cases through the treatment of latent tuberculosis infection.[3] Despite certain limitations,[4,5] an optimized contact investigation represents a cost-effective health intervention[6,7] that will play a key role in the future eradication of this disease.[8,9] However, different authors and institutions disagree on certain fundamental operational aspects related to the identification of high-risk populations among contacts, the threshold of positivity for the tuberculin skin test, the procedures used for contact tracing, and the indications for treatment of latent tuberculosis infection and their limits (which tend to be broader in scope in the United States of America and more restrictive in Europe).[10] Consequently, each community must adapt its strategy to the social, health care, and epidemiological situation of the country or region.[11,12]

In the Basque Country (a region in northern Spain), the contact tracing strategy used basically follows the model recommended in the USA by the Centers of Disease Control and the American Thoracic Society even though the epidemiology of TB is markedly different in Spain.[12,13] After several years in operation, a program was formalized in 1995 in both the Comarca Interior de Bizkaia (one of the health districts in the Basque Country) and in the entire province of Bizkaia for the control and prevention of TB with the contact investigation as one of its key strategies. Since this program started, the incidence of TB in the Comarca Interior de Bizkaia has dropped from 42 to 20 cases per 100 000 population.[14]

The objective of the present study was to investigate the incidence of active TB in a cohort of contacts over a 10-year period, to analyze the variables associated with the diagnosis of new cases of active disease among contacts, and to assess the effectiveness of the procedures currently in use for contact investigations.

Methods

In this prospective study, we analyzed the results of the contact investigations undertaken between January 1, 1995 and December 31, 2004 in the Comarca Interior de Bizkaia, 1 of the 3 health districts in the province of Bizkaia. The population of the health district studied is 300 000 inhabitants, and the TB contact-tracing program, which is integrated into the public health system, is managed by medical and health-care personnel—mainly specialists in respiratory medicine working in the referral hospital or the 5 outpatient clinics that provide health services to the entire population of the area covered by the study. Each health district in the province has a case manager responsible for finding all patients diagnosed with active TB (index cases) and identifying individuals who ought to be included in the contact investigation. Cases of TB were detected by consulting the registry of diseases subject to mandatory reporting and by weekly active case finding that involved screening information from various sources (reports from microbiology and pathology laboratories and pharmacies, and admission records for emergency departments and hospitals in the Bizkaia province). Contact selection and investigation procedures were in accordance with the criteria established by the TB prevention and control program of the health department of the government of the autonomous community of the Basque Country.[12]

We analyzed secondary cases (defined as cases of TB diagnosed among contact cohorts) detected during the initial contact investigation and a follow-up period between January 1995 and December 2004. Cases of active TB that developed during the follow-up period were identified by comparing contact databases with the registry of notified TB cases for the health district. When a smear-positive secondary case was detected from a smear-negative index case, the secondary case was then considered to be the true index case (this reclassification was made on 3 occasions). Annual incidence was calculated using the following formula: number of cases/number of contacts exposed by year and by 100 000 population.

On the basis of information provided by the index cases and individuals close to them, a list was drawn up of close and other-than-close contacts of smear-positive patients, close contacts of smear-negative patients, and contacts of secondary cases. Other contacts were also included, either at their own request or at the discretion of the medical professional, even though they did not fulfill the standard criteria. All these individuals were screened.

The definition of a close contact was modified during the course of the study. For the first 6-year period, a close contact was defined as any person living in the same household as the index case. From May 2001 onwards, the definition of a close contact was expanded to include persons who, although they did not live in the same household as an index case, were in close contact with one for over 6 hours a day. The criteria for an other-than-close contact remained unchanged throughout the study; an other-than-close contact was defined as a person in daily contact with the index case in an enclosed environment (such as an office, a classroom, or a room) for at least 6 hours a day.

As part of the investigation, all contacts were administered a tuberculin skin test (2 U of RT-23 purified protein derivative tuberculin using the Mantoux intradermal method); a chest radiograph was obtained for close contacts irrespective of skin test reaction and for other-than-close contacts when the skin test reaction exceeded 4 mm. A chest radiograph was obtained directly (without prior skin test) for contacts reporting a history of TB and/or prior positive skin test result. The skin test was repeated after 2 months in the contacts of smear-positive patients whose initial reaction was under 5 mm. In contacts aged 44 years or older with an induration under 5 mm in diameter, the reaction was rechecked 7 to 10 days later to screen for a possible booster effect. The professionals who administered the skin tests and assessed the results were highly experienced nurses specialized in respiratory medicine who had received prior training and whose skills had been verified.

An epidemiological questionnaire that included the variables studied was answered by the patients with active TB detected among the cohort of contacts studied and their contacts. The detection of secondary cases was considered a dependent variable. The independent variables analyzed in the contact group were age, sex, and degree of contact with the index case. Independent variables analyzed in the group of index cases were age, sex, site of TB, and the result of cultures of the individual's sputum smear or other respiratory sample.

Statistical Analysis

Frequencies, percentages, means, and standard deviation were used in the descriptive statistical analysis. The χ^2 test and Fisher exact test were used to compare categorical variables.

The predictive model for patients with TB was constructed using univariate logistic regression models. The independent variables used were contact age, skin test result, degree of contact, smear test status, and a series of risk groups defined according to degree of contact and smear test result. Finally, a multivariate stepwise model was constructed, and the area under the receiver operating characteristic curve was also analyzed. The same

analysis was applied to the subgroup of contacts not treated for latent tuberculosis infection.

Poisson regression analysis was used to analyze differences between case incidence rates adjusted by year of diagnosis. The dependent variable was the cumulative TB incidence rate (per 100 000 population), and the independent variable was the year of diagnosis, with the second year as the reference.

Statistical significance was established at a *P* value of less than .05. Statistical analysis was carried out using the SPSS statistical package, version 8.02 for Windows and the Stata software package, version 8.

Results

During the study period, 835 index cases were notified in the Comarca Interior health district. Of these, 695 (83%) were confirmed by culture. A contact investigation was carried out for 596 index cases; that is 71% of all cases, 86% of the cases of pulmonary TB, and 92% of the smear-positive patients. Table 1 compares the characteristics of the group of index cases with those of the group of secondary cases. Secondary cases tended to be younger (*P*<.01), and there was a lower percentage of smear-positive patients in this group (*P*<.04).

Of the 4465 candidates for a contact investigation (this number included both the close and other-than-close contacts of smear-positive patients and the close contacts of smear-negative patients), 4356 (98%) individuals took part in the study and the other 109 refused to participate.

TABLE 1
Comparison of the Characteristics of Index and Secondary Cases of Tuberculosis*

	Index Cases	Secondary Cases	*P*
Number of cases	835	66	
Men	61%	53%	.20
Mean (SD) age, y	47.07 (21.07)	30.6 (15.17)	<.01
Pulmonary forms	68%	80.3%	.04
Smear positive	40.8%	28%	<.04
HIV infection	8%	8.7%	.75

*SD indicates standard deviation; HIV, human immunodeficiency virus.

However, the following available information concerning the nonparticipants was included in the analysis: age, sex, degree of contact with the index case, and smear test status of the index case. A further 1088 contacts who did not fulfill the criteria established by the guidelines[12] were also studied. Of this group, 43% were contacts of patients with extrapulmonary TB, 37% were other-than-close contacts of patients with TB who had a negative sputum smear and a positive culture, and 20% were contacts of patients with pulmonary TB not confirmed by culture. In total, 5444 contacts were studied, an average of 9.1 contacts per index case (Table 2).

The mean (SD) age of the contacts was 34.76 (18.7) years, and the predominant age group was the cohort under 45 years of age (72%). Overall, 54% of the contacts were men, 78% had been exposed to a smear-positive case, and 21% were close contacts. A tuberculin skin test was administered to 90% of the contacts, and was repeated 2 months later in 46.3% of the group of contacts of smear-positive patients. Treatment of latent TB infection was indicated in 901 and completed by 647 contacts (72%).

In total, 66 secondary cases of TB were detected: 40 during the initial contact investigation and a further 26 in the follow-up period. Most of these patients developed active TB during the first year (the incidence was 864 cases per 100 000 population), a rate significantly different to that found in later years (relative risk of 9.52 with reference to year 2; 95% confidence interval [CI], 3.79-23.90) (Table 3).

Table 4 shows the differences found between TB cases detected during the contact investigation and those detected at a later date. It was observed that the secondary cases detected among the contacts of smear-positive patients and those with a skin test reaction of 10 mm or more were mostly diagnosed at the time of the contact investigation (*P*=.03 and *P*=.02, respectively). Furthermore, 52.3% (19/36 cases detected) of the contacts aged between 15 and 29 years who developed active TB did so after the initial contact investigation, in contrast to the 23.3% (7/30 cases detected) of the contacts aged between 0 and 14 years or more than 29 years old.

Table 5 shows the univariate analysis of the factors associated with the diagnosis of active TB among the

TABLE 2
Descriptive Analysis of the Characteristics of the Contacts Identified During the Study: Patients in Whom Tuberculosis (TB) Was Detected, Disease Type in the Index Case, and Degree of Contact

Type of Tuberculosis	Index Cases	Degree of Contact	Contacts Studied				Contacts Not Studied	
			No.	Contacts/ Index Cases*	TB Cases Detected		No.	TB Cases Detected
					Contact Investigation	Later		
Pulmonary								
Smear positive	332	Close	1018	3.1	26	8	24	1
		Other-than-close	2973	9.0	14	11	65	3
Positive culture	132	Close	365	2.8	0	1	20	1
		Other-than-close	403	3.1	0	1	0	0
Negative culture	37	Close	73	2.0	0	0	0	0
		Other-than-close	194	5.2	0	0	0	0
Extrapulmonary	95	Close	263	2.8	0	0	0	0
		Other-than-close	155	1.6	0	0	0	0
Total	596		5444	9.1	40	21	109	5

*Figure obtained by dividing the number of contacts by the number of index cases.

TABLE 3
Annual Incidence of Tuberculosis During the 10 Years After the Initial Contact Investigation*

Year	Number of Cases	Rate†	RR (95% CI)
1	48	864.0	9.52 (3.79-23.90)
2	5	90.0	Reference
3	2	36.0	0.40 (0.08-2.06)
4	3	54.0	0.60 (0.14-2.51)
5	3	54.1	0.60 (0.14-2.51)
6	1	18.1	0.20 (0.02-1.71)
7	1	18.1	0.20 (0.02-1.71)
8	1	18.2	0.20 (0.02-1.71)
9	2	36.4	0.40 (0.08-2.06)
10	0	–	–
Total	66	118.8	

*RR indicates relative risk; CI, confidence interval.
†Per 10^5 population.

TABLE 4
Risk Factors for Developing Tuberculosis Among Contacts: A Comparison Between the Factors Associated With Cases Detected During the Contact Investigation and Those Detected Later*

Associated Factors	Cases Detected		*P*
	Contact Investigation (n=40)	Follow-Up (n=26)	
Sex			.45
Men	22 (55)	17 (65.38)	
Women	18 (45)	9 (34.62)	
Age, y			.15
0-14	4 (10)	1 (3.85)	
15-29	17 (42.50)	19 (73.08)	
30-44	11 (27.50)	4 (15.38)	
45-59	5 (12.50)	2 (7.69)	
>59	3 (7.50)	0 (0)	
Smear test			.03
Positive	40 (100)	23 (11.54)	
Negative	0 (0)	3 (88.46)	
Close contact			.08
Yes	26 (65)	11 (42.31)	
No	14 (35)	15 (57.69)	
Risk groups			.03
Smear positive and close contact	26 (65)	9 (34.62)	
Smear negative and close contact	0 (0)	2 (7.69)	
Smear-positive and other-than-close contact	14 (35)	14 (53.85)	
Smear negative and other-than-close contact	0 (0)	1 (3.85)	
Tuberculin skin test (mm diameter)†			.02
<10	1 (3.03)	5 (25)	
≥10	32 (96.97)	15 (75)	

*Data are expressed as number (percentage).
†Of a total of 66 cases detected, only 53 had a tuberculin skin test.

contacts. Prevalence was significantly higher among contacts aged between 15 and 29 years (odds ratio [OR], 3.39; 95% CI, 1.04-11.07) and among those under 45 years of age (OR, 2.21; 95% CI, 1.12-4.32). The percentage of patients who developed disease was higher among contacts with a skin test reaction of 10 mm or more (OR, 9.73; 95% CI, 4.15-22.80) and among the close contacts of smear-positive index cases (OR, 26.76; 95% CI, 2.65-195.70). No secondary cases were found among contacts exposed to patients with nonpulmonary TB.

Multivariate analysis showed statistically significant associations between the following variables and diagnosis of TB in contacts (Table 6): close contact (OR, 3.05; 95% CI, 1.75-5.31); positive smear test (OR, 8.54; 95% CI, 2.06-35.43); skin test reaction of 10 mm or more (OR, 10.18, 95% CI, 4.27-24.26); and age under 30 years (OR, 3.35; 95% CI, 1.88-5.98). The final predictive model constructed on the basis of these 4 variables had a sensitivity of 77.4%, a specificity of 80.3%, and an area under the receiver operating characteristic curve 0.83 (95% CI, 0.78-0.88).

As shown in Table 7, when the contacts who completed treatment for latent TB infection were excluded from the multivariate analysis, the factors associated with the development of active TB remained very similar; however, in this case, the statistically significant association was found when the age of contact was under 45 years (OR, 4.12; 95% CI, 1.91-8.89).

Discussion

Our study identified the following risk factors associated with the development of active TB among contacts of patients diagnosed with the disease: close contact, smear-positive index case, induration diameter of 10 mm or greater, and age under 30 years. These factors were still associated with risk when contacts who completed treatment for latent TB infection were excluded from the analysis. However, in this latter analysis, the reference age changes to under 45 years. Our results also support the validity of the contact investigation and confirm that contacts have a greater risk of developing TB during the first 2 years after exposure.

The importance of this study lies in the originality of its design: it is a longitudinal and population-based study with a very long follow-up period analyzing a large cohort of contacts. The results found in this large cohort support practical conclusions that may lead to improvements in contact investigation methodology. We also consider that the method used to detect secondary cases—comparison of the registry of reported TB cases with contact records—could be a simple and valid method for evaluating TB control programs, and could be useful in research into the mechanisms of disease transmission.

We found a significant relationship between the age of the contact and the risk of contracting TB, with a higher risk among contacts under 45 years of age, and in particular in the age cohort between 15 and 29 years. In the latter age group, 52.3% of the contacts developed active TB during the follow-up period after the initial contact investigation as compared to 23.3% in the other age groups. This difference may be due to a failure to undertake or complete treatment for latent TB infection. We consider this finding particularly relevant given that 65% of patients in this age group rejected or abandoned treatment for latent TB and the remaining 35% refused to take part in the study or were not prescribed chemoprophylaxis because they were over 25 years of age (our own unpublished results).

TABLE 5
Univariate Analysis of the Factors Associated With Diagnosis of Tuberculosis Among Contacts*

Associated Factors	Total Number of Contacts (n=5553)	Cases Detected (n=66)	OR (95% CI)	*P*
Sex				.45
Men	3028	39 (59.09)	1.21 (0.74-19.80)	
Women	2525	27 (40.91)	Reference	
Smear test				<.001
Positive	4075	63 (95.45)	Reference	
Negative	1478	3 (4.55)	0.13 (0.04-0.41)	
Close contact				<.001
Yes	1748	37 (56.06	Reference	
No	3805	29 (43.94)	0.36 (0.22-0.58)	
Risk groups				<.001
Smear positive and close contact	1038	35 (53.03)	26.76 (3.65-195.78)	
Smear negative close contact	710	2 (3.03)	2.17 (0.20-23.94)	
Smear positive and other-than-close contact	3037	28 (42.42)	7.14 (0.97-52.54)	
Smear negative and other-than-close contact	768	1 (1.52)	Reference	
Tuberculin skin test, mm diameter†				<.001
<5	2269	4 (7.55)	Reference	
5-9	473	2 (3.77)	2.4 (0.44-13.17)	
10-14	774	5 (9.43)	3.6 (0.99-13.75)	
≥15	1475	42 (79.25)	16.6 (5.94-46.38)	
Tuberculin skin test, mm diameter†				<.001
<10	2742	6 (11.32)	Reference	
≥10	2249	47 (88.68)	9.73 (4.15-22.80)	
Age of contact, y				.07
0-14	522	5 (7.58)	1.88 (0.44-7.91)	
15-29	2098	36 (54.55)	3.39 (1.04-11.07)	
30-44	1373	15 (22.73)	2.15 (0.62-7.45)	
45-59	973	7 (10.61)	1.41 (0.36-5.47)	
>60	587	3 (4.55)	Reference	
Age of contact, y				.02
0-29	2620	41 (62.12)	1.85 (1.12-3.05)	
≥30	2933	25 (37.88)	Reference	
Age of contact, y				.02
< 45	3993	56 (84.85)	2.21 (1.12-4.32)	
≥45	1560	10 (15.15)	Reference	

*Values are number (percentage) unless otherwise indicated. OR indicates odds ratio; CI, confidence interval.
†Out of the whole contact group (n=5553), the tuberculin skin test was not carried out in 562 cases (10.1%).

The unexpectedly low incidence of active TB among contacts under 15 years of age may be due to the impact of prophylactic treatment (because compliance was good in this age group) and to the protective effect of antituberculosis vaccination,[15,16] which protects a very high proportion of the population of the province (90% of newborn infants are vaccinated).

Another variable significantly associated with the appearance of secondary cases was an induration with a diameter of 10 mm or greater in reaction to the tuberculin

TABLE 6
Multivariate Analysis of the Factors Associated With the Diagnosis of Tuberculosis Among Contacts*

Associated Factors	OR (95% CI)	*P*
Close contact		<.001
Yes	3.05 (1.75-5.31)	
No	Reference	
Smear test		.003
Positive	8.54 (2.06-35.43)	
Negative	Reference	
Tuberculin skin test (mm in diameter)		<.001
<10	Reference	
≥10	10.18 (4.27-24.26)	
Age of contact, y		.001
0-29	3.35 (1.88-5.98)	
≥30	Reference	

*OR indicates odds ratio; CI, confidence interval.

TABLE 7
Multivariate Analysis of the Factors Associated With the Development of Tuberculosis Among Contacts Not Treated for Latent Tuberculosis Infection

Associated factors	OR (95% CI)	*P*
Close contact		<.001
Yes	3.93 (2.08-7.41)	
No	Reference	
Smear test		.005
Positive	17.39 (2.36-127.97)	
Negative	Reference	
Tuberculin skin test (mm in diameter)		<.001
<10	Reference	
≥10	15.46 (5.98-39.98)	
Age of contact, y		.001
0-45	4.12 (1.91-8.89)	
>45	Reference	

*OR indicates odds ratio; CI, confidence interval.

skin test. Moreover, the risk of developing TB increased progressively according to the diameter of the induration, a finding that supports the hypothesis that the greater the diameter of the tuberculin skin reaction, the more likely it is that the infection is caused by *Mycobacterium tuberculosis*.[17]

In our study, only 1 patient with an induration under 10 mm in diameter at the time of the initial contact investigation went on to develop active TB. This finding could call into question the need for chest radiography as a routine component of the contact investigation in such cases. Our findings differ from those of a study in which a considerable number of new asymptomatic cases among patients with an initial negative tuberculin skin reaction were diagnosed on the evidence of a chest radiograph alone.[18] We did identify 5 cases of patients with a skin test reaction under 10 mm who developed active TB during the period after the initial investigation. Four of these were other-than-close contacts of smear-positive index cases and they developed active TB after a mean interval of 47.6 months (range, 30-67 months). Given the length of the interval between the contact investigation and onset of active disease, we consider it highly unlikely that these 4 patients were in fact infected through contact with the initial index case. The fifth patient, a young person who lived with a smear-positive case, completed a 6-month course of prophylactic treatment and developed active TB 3 years later.

The proposal—made on the basis of the results of our study—of establishing a new threshold of positivity (≥10 mm diameter) for the tuberculin skin test is particularly relevant in areas such as our own province where high levels of environmental mycobacteria may interfere with the interpretation of skin test results.[19-21] Moreover, this proposal is supported by the results we obtained in a prior study[22] and by those of an epidemiological study of tuberculosis infection in the province of Bizkaia analyzing a sample of 7500 schoolchildren of 7 years of age.[23]

We were also able to demonstrate a significant association between a positive smear test result in an index case and the appearance of secondary cases. In fact, only 3 (4.5%) cases of active TB were found among the contacts of smear-negative patients, and these were diagnosed between 3 and 10 years after the contact investigation. Given the time elapsed, it would appear reasonable to assume that the real source of infection in these cases was not the index case initially investigated but rather some other untraced exposure or an independent reactivation of the initial contact. This assumption is supported by other studies, such as that of Behr and colleagues,[24] who analyzed 11 200 contacts (in San Francisco, California) and, using molecular techniques, showed that the strains isolated in 30% of secondary cases were different from those found in the index case to which they had been linked using conventional contact investigation methods.

According to some studies, even smear-negative patients can infect a high percentage of contacts,[18,25] but our results, in line with those of other authors,[16,26] call into question the risk of infection from smear-negative patients. In practice, this finding suggests that contacts of smear-negative patients should be excluded from screening. The differing results of the studies cited may be due to methodological differences, such as the criteria defining an index case or the definition of a case as smear negative on the basis of a single sputum sample.

Our findings agree with those of earlier studies[27,28] in that they confirm that the risk for untreated contacts of developing TB is higher during the first 2 years. The percentage of contacts who developed the disease was higher during the first and second year, with incidence rates of 864 per 100 000 population and 90 per 100 000 population, respectively. The incidence declined significantly after the end of the second year, and by the sixth year the rate was similar to that of the general population.

Finally, we were able to substantiate the usefulness of the contact investigation, not only because of the high number of secondary cases detected, but also because of the early diagnosis achieved in these cases. Although the overall prevalence of cases of TB detected among contacts was 1.1% (n=66), the percentage of TB cases diagnosed during the initial study (0.8%, n=40)—the annual incidence of TB in the population of the Bizkaia region ranges from 0.02% to 0.04%—was lower that that observed by other Spanish authors, who found percentages of up to 6% of new cases in contact investigations.[18,29-31] A possible explanation for the lower yield of our investigations may be the large number of contacts studied (9.1 for each index case) and the fact that many of the participants did not fulfill the predefined criteria. In any case, given the scant yield of screening in low risk populations, our study supports the validity of the criteria currently being used for contact investigations.

This study has certain limitations. First, since we did not use genetic techniques to identify the strains isolated in the index and secondary cases, we were unable to verify whether they were in fact linked. However, if we were to exclude cases with a greater probability of not being linked to the index case the analysis, the results would be reinforced. Second, since we used lists of contacts and a registry of TB cases for the Comarca Interior de Bizkaia health district alone, patients with active TB who moved to another health district were not included. However, in light of the low rate of population movement in the Basque Country—10 per 1000 population left the province of Bizkaia in 2004[31,32]—we consider it unlikely that this factor could have influenced our results.

In conclusion, we find that the contact investigation continues to be an effective strategy for identifying new cases of active TB and facilitating early diagnosis, thereby preventing evolution to more serious and infectious forms of the disease. The contacts are at greatest risk for developing disease during the months following initial contact. For this reason, prophylactic treatment should be initiated as early as possible, and priority should be given to the contacts of smear-positive patients and those under 45 years of age. Our results also indicate that the use of an induration diameter of 10 mm or larger as a threshold for positivity for the tuberculin skin test has a greater discriminatory power than diameters of under 5 mm. Furthermore, a chest radiograph would not be routinely necessary in the initial study given the high sensitivity of the 10 mm threshold.

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