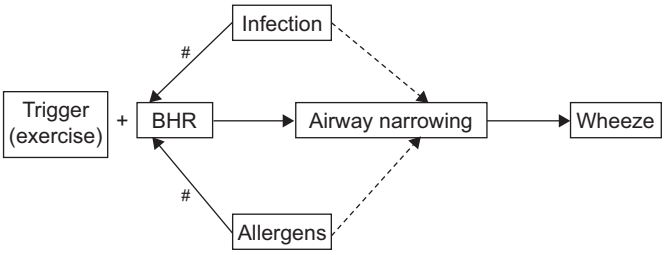

FIGURE 1. Triggers and inducers: model of possible mechanisms. BHR: bronchial hyperresponsiveness. #: in susceptible individuals.

called multiple-trigger) wheeze are indeed distinct disease entities [3–5, 10]. However, a clear limitation of the study is the fact that the results are based on parental report of triggers. Replication of the study or the analysis using alternative methods of documentation would be beneficial.

Our findings provide support for an old concept proposing that infection and allergy can cause airway narrowing in susceptible individuals, either by acting directly (as trigger factors) or by induction of bronchial hyperresponsiveness (as inducing factors). Exercise, in contrast, is merely a trigger, which leads to airway narrowing only in the presence of bronchial hyperresponsiveness caused by other factors (fig. 1). Finally and most importantly, our observation that there was no evidence of dependence between viral and allergic triggers suggests that the mechanisms underlying allergen- and infection-related wheeze might be independent. This supports the notion that exclusive viral wheeze and allergic wheeze are distinct phenotypes which differ in their aetiology [10]. This work should lead to further metabolomic and physiological studies in order to confirm the characteristics of different phenotypes of wheezing disease in young children.

M-P.F. Strippoli*, B.D. Spycher*, A.M. Pescatore*, C.S. Beardsmore#, M. Silverman# and C.E. Kuehni*

*Institute of Social and Preventive Medicine, University of Berne, Berne, Switzerland, and #Division of Child Health, Dept of Infection, Immunity and Inflammation, University of Leicester, Leicester, UK.

Correspondence: C.E. Kuehni, Institute of Social and Preventive Medicine (ISPM), University of Berne, Finkenhubelweg 11, CH-3012 Berne, Switzerland. E-mail: kuehni@ispm.unibe.ch

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Who misses the second step of evaluation in tuberculosis contact screening?

To the Editors:

Assessment of people likely to have been recently infected with *Mycobacterium tuberculosis* is important because of the risk to these people of progressing to active tuberculosis (TB) within 1–2 yrs [1]. In Portugal, contact investigation is an integral part of the TB control programme, enabling the identification and treatment of individuals with latent TB infection (LTBI), thus preventing active TB.

National guidelines require a two-step evaluation of pulmonary TB contacts, with the first step being performed at the

moment the index case is diagnosed and the second performed 10–12 weeks later if the first evaluation was negative. We have analysed the results of re-evaluating TB contacts and have identified risk factors associated with missing re-evaluation.

Our study was a retrospective cohort study of pulmonary TB contacts screened between January 1 and June 30, 2009, at the Chest Disease Centre of Vila Nova de Gaia, Porto, Portugal, an outpatient TB clinic. All individuals were administered a symptom questionnaire and underwent a tuberculin skin test (TST)/interferon-γ release assay (IGRA) and chest radiograph. The first TST was performed upon identification of the index case, with individuals testing negative being offered a second TST 12 weeks later. Individuals testing positive were offered an IGRA test (QuantiFERON®-TB Gold; Cellestis Ltd, Melbourne, Victoria, Australia). Individuals positive on both TST and IGRA were offered preventive treatment, after exclusion of risk factors for hepatotoxicity. Individuals with symptoms or chest radiograph abnormalities were assessed for active TB.

Active TB was defined as positivity for *M. tuberculosis* in biological samples, either by culture or nuclei-amplification tests. LTBI was defined, in patients not having active TB, as TST $\geqslant$10 mm with positive IGRA.

Demographic, social and clinical data were collected and the results of the first and second screenings were reviewed.

Statistical analyses were performed using Epi Info (version 3.5.1; Centre for Diesease Control and Prevention (www.cdc.gov)). Chi-squared, Kruskal-Wallis, ANOVA and Fisher's exact tests were performed for univariate analysis, with logistic regression performed for multivariate analysis. A p-value <0.05 was considered statistically significant.

Screening of TB contacts was offered as part of the National Tuberculosis Program guidelines [2]. We evaluated 226 TB contacts, 150 females (66.4%) and 76 males (33.6%), of mean age 44.6$\pm$17.2 yrs.

The results of the first evaluation of the TB contacts are presented in figure 1. Of the 226 contacts, two (0.9%) were diagnosed with active TB, and 40 (17.7%) were diagnosed with LTBI. The remaining 161 TB contacts tested negative and were therefore eligible for the second evaluation. Of these 161 individuals, 56 (34.8%) missed the second evaluation.

Of the 105 re-evaluated individuals, none had active TB, whereas nine (8.6%) were diagnosed with LTBI. Thus re-evaluation led to the diagnosis of LTBI in 18.4% of all individuals diagnosed with LTBI.

Male sex and period of re-evaluation during the summer months (July, August and September) were associated with missing re-evaluation (table 1).

LTBI screening 10–12 weeks after exposure has been shown to be important, with 13.2–22.9% of all individuals with LTBI diagnosed at second evaluation. A negative result before this window period is considered unreliable for excluding infection [1]. We found that re-evaluation led to a diagnosis of LTBI in 8.6% of patients screened, suggesting that some individuals who were not re-evaluated were positive for LTBI.

This two-step evaluation can confound a booster phenomenon with a true conversion. Searching for boosting may not be useful because of the small number of patients identified in this way, and because this distinction is also difficult in two-step TST. Although a single evaluation performed $\geqslant$8 weeks after exposure may also be diagnostic, the first evaluation has been shown to be important in diagnosing active TB [1].

Compliance with re-evaluation was 65.2%, slightly higher than previously described (53–63%) [3]. Although no studies have determined factors associated with noncompliance with re-evaluation, male sex and seasonality have been associated with noncompliance in other clinical situations. For example, male sex has been associated with noncompliance during diagnosis in individuals suspected of TB [4] and in treatment for TB [5],

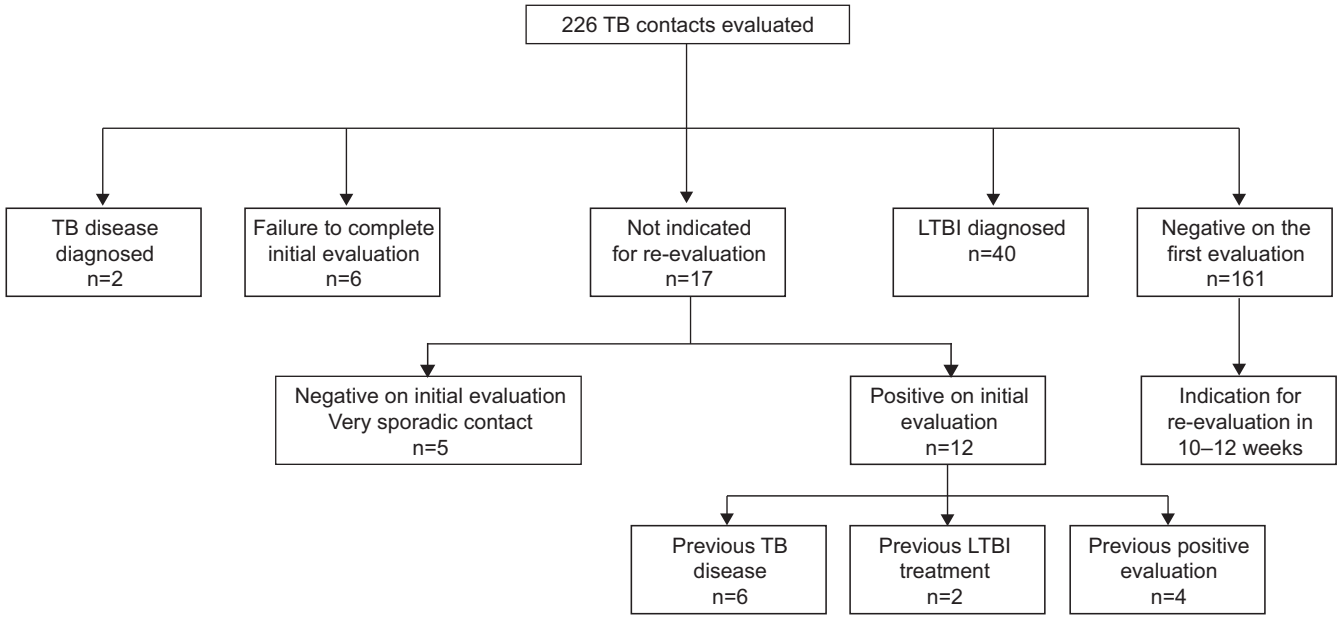

FIGURE 1. Results of the first evaluation of 226 tuberculosis (TB) contacts. LTBI: latent TB infection.

TABLE 1 Factors associated with missing the second evaluation, as shown by univariate and multivariate analyses

Factors evaluated	Individuals n	Factors re-evaluated	Factors not re-evaluated	Univariate analysis	Multivariate analysis	
					p-value	OR
Total n		105	56			
Male	161	20/105 (19.0)	25/56 (44.6)	0.0006*	0.0076	3.2
Mean age yrs	161	43.3	46.4	0.76	NS	
Mean body weight kg	145	68.3	68.2	0.98	NS	
Active smoking	47	14/31 (45.2)	13/16 (81.3)	0.019*	0.2761#	
Period of re-evaluation during summer months	161	25/105 (23.8)	26/56 (46.4)	0.003*	0.0088	2.9
Professional contact	155	46/103 (44.7)	15/52 (28.8)	0.058	NS	
Familiar contact	155	48/103 (46.6)	22/52 (42.3)	0.61	NS	
First degree relatives among family contacts	70	31/48 (64.6)	9/22 (40.9)	0.07	NS	
Co-residence	155	30/104 (28.8)	14/51 (27.5)	0.86	NS	
Presence of symptoms	161	16/105 (15.2)	6/56 (10.7)	0.43	NS	
Radiological abnormalities	161	5/105 (4.8)	5/56 (8.9)	0.24	NS	
Tuberculin anergy¶	161	64/105 (61.0)	30/56 (53.6)	0.37	NS	
Comorbidities	156	36/105 (34.3)	9/51 (17.6)	0.03*	0.2005	1.8

Data are presented as n/N (%), unless otherwise stated. NS: not significant. #: active smoking was analysed by bivariate analysis with male sex, but was not included in the multivariate analysis because smoking data on many individuals was missing; ¶: defined as 0 mm on tuberculin skin test. *: $p<0.05$.

and seasonality has been found to be associated with non-compliance for appointments at outpatient clinics [6].

The main limitation of our study was its retrospective design, which did not allow us to test the effectiveness of strategies to improve adherence. Future prospective studies should test different strategies, including oral and written information about the importance of TB screening and particularly of the second evaluation, using reminder telephone calls and other reminder strategies to encourage attendance.

F. Soares Pires*, C. Pinto# and R. Duarte¶+§ƒ
Pulmonology Depts of *Hospital de São João, #Centro Hospitalar de Trás-os-Montes e Alto Douro, and ¶Centro Hospitalar de Vila Nova de Gaia/Espinho, +CDP Vila Nova de Gaia, §Reference Center for Multidrug Resistant Tuberculosis of North Region, CDP Vila Nova de Gaia, and ƒEpidemiology Dept, Faculdade de Medicina, Universidade do Porto, Porto, Portugal.

Correspondence: F. Soares Pires, Pulmonology Dept, Hospital de São João, Alameda Prof. Hernâni Monteiro, Porto, 4200-319 Portugal. E-mail: filipasp@gmail.com

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