Epidemiol. Infect. (2006), **134**, 323–327. © 2005 Cambridge University Press
doi:10.1017/S0950268805005078 Printed in the United Kingdom

SHORT REPORT

A community outbreak of tuberculosis in Southern Austria: lessons learned for a targeted use of molecular epidemiological methods and tuberculin skin testing

D. SCHMID[1], A. INDRA[2], G. HÖGER[1], P. HASENBERGER[2], B. ROBL[2], M. SCHÖFFMANN[3], B. MAIERON[3], G. OLEXSINSKI[3], B. STONITSCH[3], W. M. PRODINGER[4] AND F. ALLERBERGER[1]*

[1] *Centre for Infectious Disease Epidemiology, Austrian Agency for Health and Food Safety, Vienna, Austria*
[2] *National Reference Laboratory for Mycobacteria, Austrian Agency for Health and Food Safety, Vienna, Austria*
[3] *Public Health Office, Klagenfurt, Carynthia, Austria*
[4] *Department for Hygiene, Microbiology and Social Medicine, Section Hygiene and Medical Microbiology, Innsbruck Medical University, Innsbruck, Austria*

(*Accepted 22 June 2005, first published online 5 September 2005*)

SUMMARY

A cluster of 10 cases of tuberculosis disease (one of them extrapulmonary) occurred from July 2001 until November 2003 in a health district in Southern Austria. Eight patients were culture confirmed and shared an identical strain. One of these eight cases was identified as outbreak-related by molecular strain typing only. Due to public pressure, a further 600 persons received chest X-ray and clinical examinations. Apart from one case which could be excluded from the outbreak because of a different strain pattern, no outbreak-related case of active tuberculosis was detected by this non-targeted procedure. Tuberculin skin testing, not part of the Austrian routine protocol of contact investigation in adults, was initiated after diagnosis of case 8. Forty-nine latently infected contacts were detected. Population-based genotyping of all isolates, prioritization of contact investigations and early use of targeted tuberculin skin testing are critical for effective tuberculosis control in low-incidence countries.

This paper is based on a retrospective review of the investigation of a time–space cluster of cases of tuberculosis (TB) disease in Austria. The aim of this report was to illuminate the measures taken by local health authorities for identifying the chain of infection and preventing further spread of TB. The 10-case outbreak was initially indicated by the occurrence of two TB cases, which were linked by the same worksite and occurred within 12 months. The median age of the 10 TB patients was 43·5 years (min 16, max 58) and eight cases were male (case details are given in the Table and Fig.). All patients recovered after a 6- to 10-month course of treatment. Contacts were identified by personal interview of the index case and of the successive generation cases focusing primarily on the period of time that the cases had had respiratory symptoms. Close contacts including household members and co-workers of the same working shift were screened for signs and symptoms of active TB. Adults were not offered tuberculin skin testing (TST) as a routine procedure in TB contact investigation by the health district. Since the outbreak was still ongoing 18 months after occurrence of the index case, TST was also performed in close adult contacts to the index case (household members, close worksite contacts). Molecular methods used were spoligotyping, mycobacterial interspersed repetitive units (MIRU)–variable number tandem repeats (VNTR) typing and

* Author for correspondence: Dr F. Allerberger, Centre for Infectious Disease Epidemiology, Austrian Agency for Health and Food Safety, Spargelfeldstr. 191, A-1220, Vienna, Austria.
(Email: Franz.Allerberger@ages.at)

Table. *Details of the 10 cases identified in the outbreak*

Date of diagnosis	Age at diagnosis (years)	Sex	TB site	Type of case	Sputum smears AFB positive	PCR result	Symptoms	Type of contact to case 1
Case 1 July 2001	52	M	Pulmonary cavitary	Definite	Yes	Positive for sputum	Yes	n.a.
Case 2 June 2002	39	M	Pleural	Definite	No	Positive for pleural exsudat	Yes	Close (work) contact
Case 3 Aug. 2002	16	F	Pulmonary cavitary	Definite	Yes	Positive for sputum	Yes	Close (family) contact
Case 4 Aug. 2002	50	M	Pulmonary	Definite	No	Positive for sputum	No	Close (work) contact
Case 5 Sep. 2002	46	M	Pulmonary	Definite	Yes	Positive for sputum	No	Casual (work) contact
Case 6 Oct. 2002	37	M	Pulmonary cavitary	Definite	Yes	Positive for sputum	Yes	Casual (leisure) contact
Case 7 Nov. 2002	18	F	Pulmonary	Other than definite*	n.a.	Negative for sputum	No	No contact†
Case 8 Jan. 2003	40	M	Pulmonary cavitary	Definite	Yes	Positive for sputum	Yes	Close (work) contact
Case 9 May 2003	50	M	Pulmonary	Other than definite	n.a.	Negative for sputum	No	Close (work) contact
Case 10 Nov. 2003	58	M	Pulmonary	Definite	No	Positive for sputum	Yes	Contact not recognized

AFB, Acid-fast bacilli; PCR, polymerase chain reaction; n.a., not applicable.
* Other than definite case is a case meeting both of the following conditions: (i) a clinician's judgement that the patient's clinical and/or radiological signs and/or symptoms are compatible with TB, and (ii) a clinician's decision to treat the patient with a full course of anti-TB treatment. Cases 7 and 9 had radiological signs compatible with TB but no symptoms.
† Direct contact to the index patient's daughter (case 3).

restriction fragment length polymorphism (RFLP) typing [1–3].

A 52-year-old man, working in an iron alloy plant had been given a diagnosis of cavitary pulmonary TB in July 2001, following symptoms of cough, malaise, and weight loss of ~6 months' duration. Sputum smears were positive (>4+) for acid-fast bacilli (AFB), and sputum cultures grew *Mycobacterium tuberculosis*. The isolate was sensitive to all first-line chemotherapeutic agents. The source-case investigation revealed no memorable contact to the 20 cases of TB having occurred in that health district within 2 years prior to the clinical onset of the index case. The source of infection has remained unclear. The TB control team of the responsible local public health authority identified 150 persons who had contacts with the index case during the 6 months of symptoms before his TB was diagnosed including household members ($n=7$), co-workers specified as close contacts because of working the same shift as the index case ($n=130$), and local residents having visited local pubs with the index case – specified as causal leisure contacts ($n=13$). The medical evaluation of the contacts initially consisted of X-ray and clinical chest examinations. The second case was a close co-worker of the index case, who was one of the contacts examined within the contact investigations of the index case in September and December 2001. He was missed as an infected individual by that contact investigation strategy omitting TST. In June 2002 he presented himself to the local hospital with symptoms of ~6 weeks' duration and was given a diagnosis of pleural TB. Medical evaluations of his household members revealed no further case of active TB. Case 3 was the daughter of the index case and presented with cavitary pulmonary TB. The contact investigations for case 3 included household members other than those already covered by the contact investigations for the index case, and included co-workers of the restaurant, where case 3 worked as a waitress ($n=140$). Case 4 was a close co-worker of the index case. Cases 3 and 4 occurred in August 2002. Case 5 – a sporadic

https://doi.org/10.1017/S0950268805005078 Published online by Cambridge University Press

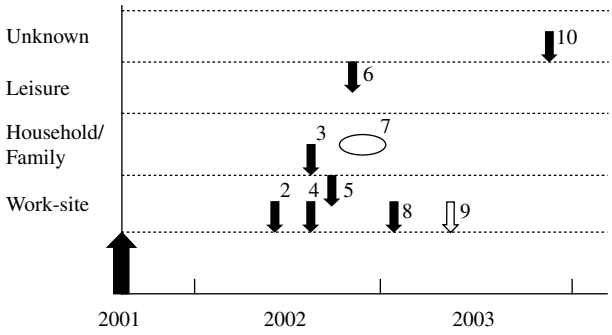

Fig. Epidemic curve of the TB outbreak including 10 cases by date of diagnosis and type of contact to the index case. Index case is represented by the large arrow; direct contacts are given by arrows placed on the line, and casual contacts by arrows hanging from the line. Ellipse indicates patient 7, a close contact to case 3. Black arrows, culture positive; white arrow and ellipse, culture negative.

co-worker of the index case – was identified in September 2002. Cases 4 and 5 had culture-confirmed pulmonary TB without symptoms. Contact investigations for cases 4 and 5 were confined to household members as their close co-workers were already covered by the contact investigations for the index case.

In mid-October 2002, the sixth case, an unemployed man living in the hometown of the index case, was detected with cavitary pulmonary TB. He was linked to the outbreak by molecular strain subtyping. It is very likely that he had experienced unrecognized contacts with the index case or with the other outbreak cases outside the company in one of the local public houses around the iron alloy plant. Case 7, an adolescent girl, was detected in November 2002 within the investigations of close contacts to case 3. Sputum was smear-negative for AFB, culture was negative for *M. tuberculosis* and no clinical symptoms were reported, but based on radiological signs compatible with TB, a positive TST and the epidemiological linkage to the outbreak, the case was clinically diagnosed. Due to public pressure contact investigations were extended at the end of 2002. There was no systematic method of deciding the extent of further contact tracing. A total of 600 persons such as workers of the iron alloy plant (casual co-workers of cases 1, 4, 5), casual worksite contacts of case 3 and casual leisure contacts to cases 3, 4, 5 and 6, were medically evaluated as described. One case of cavitary pulmonary TB – a 49-year-old male day-worker – was detected in November 2002. This case was outbreak-unrelated as the molecular subtyping of the isolate revealed a different strain pattern. In January 2003 outbreak case 8 was detected within the X-ray follow-up examinations of worksite contacts of the index case. Case 8 was a close co-worker of the index case and of cases 2 and 4 – all were employed on the same working shift. No active TB case was identified among the household members of case 8. After occurrence of the eighth case, a baseline TST and a follow-up TST $\sim$8 weeks later were offered to adult household members and close worksite contacts of the index case ($n=117$), in addition to the ongoing X-ray and clinical examinations. Of these 117, 48 persons had a positive TST (44 persons at the baseline test and four at the follow-up test). One of the 44 persons with a positive reaction at the baseline test had radiological pulmonary signs compatible with TB. This 50-year-old close co-worker of the index case and also of cases 2, 4 and 8 was given the diagnosis 'other than definite case of TB disease' in May 2003 and was considered as the ninth outbreak case. In November 2003, case 10, a retired man living in close proximity to the hometown of the nine outbreak cases, was self-presenting with symptoms compatible with TB and was given a diagnosis of pulmonary TB. He was identified as an outbreak-related case only upon molecular epidemiological linkage to the other culture-proven outbreak cases. No further outbreak-related case of active TB was detected since 20 November 2003.

This outbreak comprised a total of 10 cases of TB disease and 49 cases of latent TB infection having occurred over a period of 28 months, restricted to two neighbouring towns of altogether $\sim$10 000 inhabitants. Taking into account the long period of infectiousness (6 months), the high degree of infectiousness (cavernous pulmonary TB) and the congregate working situation of the index case, it is likely that eight out of the nine cases of TB (all except case 7) and 47 out of the 49 cases of latent tuberculosis infection (LTBI) were generated by this single patient. The remaining two cases of LTBI and case 7 were probably generated by case 3. Although TB is only moderately infectious in most circumstances, it is well known, that individual persons can be highly infectious, while other persons can excrete bacilli without any proven transmission [4–6]. Prodinger et al. described an outbreak in Western Austria in which nine related cases were attributable to the highly infectious index patient [7, 8].

In order to utilize resources of the public health authorities wisely, it is critical to appropriately focus contact tracing and investigations [9–13]. Contact investigations are not indicated for extrapulmonary TB for which pulmonary TB has been ruled out. Case 2 of

the Austrian TB outbreak had an extrapulmonary TB. Respiratory secretions were negative for AFB and also culture negative. However, the local public health authorities also investigated the household contacts of case 2. None of the household members turned out to be infected. The results of these unnecessarily performed contact examinations underline the recommendation not to test contacts of cases of extrapulmonary TB. In view of the limited resources of public health authorities, testing individuals who are at low risk of infection has no priority. In the described outbreak, contact investigations were extended to contacts at low risk of infection mainly because of public demand for testing. No further outbreak-related case of active TB was detected by this widespread contact investigation. The fact that one outbreak-unrelated case of TB was found, should not be misinterpreted as a justification for such a resource-consuming approach. A systematic approach for deciding the extent of contact tracing is indispensable. No data on the HIV status of the contacts are available. Austria is a country with a relatively low HIV prevalence (~0·01%) [14]. Nevertheless, it might be prudent to offer HIV testing to close contacts of cases of infectious TB as a routine procedure for TB control also in Austria. The TST is the only proven method for identifying infection with *M. tuberculosis* in persons who do not have TB disease [9–13]. In the recent Austrian outbreak TST was not applied in the early phase of the contact investigation of the index case. As a large proportion of the adult population in Austrian has a positive history of BCG vaccination, the responsible health authorities feared a high number of false-positive TST results [15, 16]. After the occurrence of seven related cases within 17 months after identification of the index case, high infectiousness of the index patient was presumed. Therefore, the local health authorities decided to perform a second round of contact investigation of the close contacts to the primary case (including close co-workers and family members) by using TST based on the aforementioned recommended cut-off values. In hindsight, one might argue that if the targeted TST had already been applied in the early phase of the contact investigation of the index case, cases 2, 3, 4, 8 and 9 could have been detected and treated earlier. Thereby, the progression to TB disease and the infection of case 7 and the 2 LTBI cases attributable to case 3 might even have been prevented.

The full extent of an outbreak regarding manifest TB cases can often be more precisely assessed using DNA fingerprinting techniques [4, 9]. In the TB outbreak in Southern Austria, the suspected link between case 6 – a homeless problem-drinker – and the index case and the other culture-proven outbreak cases was confirmed by the identical molecular subtype of the *M. tuberculosis* isolates. Case 10 was identified as outbreak-related only by strain genotyping. The epidemiological link to the cluster was not recognized by mere conventional outbreak investigation. On the other hand, a case of pulmonary TB detected in a temporary worker of the afflicted factory in the course of extended contact investigations could be classified as outbreak-unrelated by that approach. Since 1994, more than 1000 *M. tuberculosis* isolates have been DNA fingerprinted in Austria [8]. Approximately 61% of all *M. tuberculosis* isolates having undergone DNA fingerprinting in Austria are unique isolates which is in good keeping with data from neighbouring Western European countries. Within that database, no other isolate showed the DNA fingerprinting pattern as described for the outbreak strain, a fact that should help to detect further outbreak-related TB cases in the coming years.

DECLARATION OF INTEREST

None.

REFERENCES

1. **Kamerbeek J, Schouls L, Kolk A, et al.** Simultaneous detection and strain differentiation of Mycobacterium tuberculosis for diagnosis and epidemiology. J Clin Microbiol 1997; **35**: 907–914.
2. **van Embden JD, Cave MD, Crawford JT, et al.** Strain identification of Mycobacterium tuberculosis by DNA fingerprinting: recommendations for a standardized methodology. J Clin Microbiol 1993; **31**: 406–409.
3. **Supply P, Lesjean S, Savine E, et al.** Automated high-throughput genotyping for study of global epidemiology of Mycobacterium tuberculosis based on mycobacterial interspersed repetitive units. J Clin Microbiol 2001; **39**: 3563–3571.
4. **Broekmans JF, Migliori GB, Rieder HL, et al.** European framework for tuberculosis control and elimination in countries with a low incidence. Recommendations of the World Health Organization (WHO), International Union against Tuberculosis and Lung Disease (IUATLD) and Royal Netherlands Tuberculosis Association (KNCV) Working Group. Eur Respir J 2002; **19**: 765–775.
5. **Fitzgerald D, Haas DW.** *Mycobacterium tuberculosis*. In: Mandell G, Bennett J, Dolin R, eds. Principles and

practices of infectious diseases. Philadelphia: Elsevier Churchill Livingstone, 2005: 2852–2896.
6. **Anon.** Tubeculosis. In: Chin J, ed. Control of communicable diseases manual. Washington: American Public Health Association, 2000: 521–532.
7. **Prodinger W, Pavlic M, Allerberger F.** Molecular epidemiology of tuberculosis: five years of DNA fingerprinting in Western Austria. In: Janata O, Reisinger E, eds. Infektiologie: Aktuelle Aspekte. Wien: Österreichische Verlagsgesellschaft, 2000: 193–203.
8. **Pavlic M, Allerberger F, Dierich MP, Prodinger WM.** Simultaneous infection with two drug-susceptible *Mycobacterium tuberculosis* strains in an immunocompetent host. J Clin Microbiol 1999; **37**: 4156–4157.
9. **Joint Tuberculosis Committee of the British Thoracic Society.** Control and prevention of tuberculosis in the United Kingdom 2000. Thorax **55**: 887–901.
10. **Anonymous.** Guidelines for Prevention and Treatment of tuberculosis, 2003. Maryland Department of Health and Mental Hygiene (http://edcp.org/tb/pdf/final2003TBbook.pdf). Accessed 13 May 2005.
11. **American Thoracic Society and Centers for Disease Control.** Targeted tuberculin testing and treatment of latent tuberculosis infection. Am J Respir Crit Care Med 2000; **161**: 5221–5248.
12. **Ferlinz R, Bussmann H, Forßbohm M.** Guidelines for contact investigations of tuberculosis. In: Gesundheitswesen 58. Stuttgart: Georg Thieme Verlag, 1996: 657–665.
13. **Arbeitsgruppe 'Tuberkulosis' der Lungenliga Schweiz.** Manual of tuberculosis. Schweiz Med Forum 2003; **3**: 485.
14. **Anon.** AIDS Epidemic Update 2004. UNAIDS (www.unaids.org/wad2004/report_pdf.html). Accessed 13 May 2005.
15. **Wang L, MO Turner, RK Elwood, M Schulzer, JM FitzGerald.** A meta-analysis of the effect of Bacille Calmette Guerin vaccination on tuberculin skin test measurements. Thorax 2002; **57**: 804–809.
16. **Allerberger F.** An outbreak of suppurative lymphadenitis connected with BCG vaccination in Austria. Am Rev Respir Dis 1990; **144**: 469.