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Tuberculosis as an occupational hazard for health care workers in Estonia

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SUMMARY

SETTING: Tuberculosis incidence has been increasing in the Baltic states since the 1990s, accompanied by the emergence of drug resistance, including multidrug resistance (MDR). In this changing situation, the potential threat of nosocomial spread of tuberculosis to other patients and health care workers (HCW) has remained unrecognised.

OBJECTIVE: To investigate the risk of tuberculosis in health care workers in Estonia.

DESIGN: Cases of tuberculosis registered among HCWs from 1994 to 1998 were evaluated. The case records were analysed retrospectively and combined with bacteriological data including data on drug resistance.

RESULTS: Sixty-seven HCWs (23 physicians, 23 nurses and seven laboratory technicians, 12 assistant nurses and two cleaners), all of whom tested negative for human immunodeficiency virus, were diagnosed as having active tuberculosis. The incidence of tuberculosis among HCWs (mean 91/100 000/year) was 1.5 to three times higher than in the general population. In a chest hospital in charge of regional tuberculosis care, the incidence was 30 to 90 times higher, and was highest among physicians. In 49 HCWs tuberculosis was confirmed by culture. Among these, drug resistance was detected in 23 (49%), 18 (38%) of whom had MDR tuberculosis.

CONCLUSIONS: Health care workers, especially those working in a chest hospital where tuberculosis patients were treated, were found to be at an elevated risk of tuberculosis. MDR tuberculosis poses a particular threat which is difficult to combat.

KEY WORDS: tuberculosis; exposure; nosocomial transmission; drug resistance; MDR-TB

THE RISK OF nosocomial transmission of tuberculosis (TB) has traditionally had a considerable impact on infection control priorities in hospital settings. The routine procedures for prevention of spread of TB in hospitals seemed to lose their impetus in the years of steadily decreasing tuberculosis morbidity, while the availability of efficient drug treatment made the risk seem even more insignificant.[1] Consequently, many of the rules and practices were forgotten. Health service staff, including administrators of the tuberculosis control policy, regarded TB as a disease that had been overcome. With the disappearance of tuberculosis sanatoria, patients with suspected tuberculosis were integrated among those with other diseases. Many safety measures accepted in the past in sanatoria and hospitals, such as isolation of suspected TB cases and teaching the patients to minimise production of infective aerosols, are often regarded as unnecessary, if not intolerable. A false sense of security may render the health care system vulnerable, as experienced in the United States,[2,3] leading to nosocomial spread of infection among patients, from patients to employees, and vice versa. An increase in outbreaks of TB, particularly those caused by multidrug-resistant (MDR, i.e., resistant to at least isoniazid and rifampicin) strains of *Mycobacterium tuberculosis* were first recognised in health care institutions in the US.[4–7]

An increase in tuberculosis morbidity, accompanied by the appearance of MDR-TB, has been experienced in the Baltic countries since the early 1990s. In Estonia, after a steady decline in incidence from 417 per 100 000 population in 1953 to 25.8/100 000 in 1992, the incidence rate showed a steady increase, reaching 56/100 000 in 1998. This unexpected increase in morbidity was accompanied by an increase in mortality from 5 to 8/100 000/year in this period. In 1998, 70% of the new TB patients belonged to the age group 18–54 years, two-thirds of whom were men. Ninety-one per cent of the cases had pulmonary TB, and the diagnosis was verified by smear or culture in 73%.[8] Drug-resistant TB and particularly MDR-TB has become a serious problem in Estonia. In 1994 and 1998, MDR-TB comprised respectively 10% and 14% of the new cases detected.[9,10] So far there is little

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human immunodeficiency virus (HIV) infection in Estonia; by 1999 only two cases of dual infection with tuberculosis and HIV had been reported.

No standardised treatment of new cases of tuberculosis was universally applied before 1998, which often led to the use of unorthodox drug combinations. Since 1998, a standardised first-line treatment regimen ($2EHRZ/4H_3R_3$)* has been in use for all previously untreated cases, and a five-drug combination ($3EHRZS/4H_3R_3$) is used as initial treatment for all re-treatment cases. This regimen is modified, if necessary, according to drug susceptibility test (DST) results for first and second line anti-tuberculosis drugs. The laboratory turnaround time of identification and drug susceptibility testing of *Mycobacterium tuberculosis* is roughly 3 to 6 weeks.

Very little attention has generally been paid to tuberculosis among the employees in the health care system in Estonia. The present study was conducted to investigate the risk of occupational tuberculosis among health care workers (HCWs) in general, and in particular among the HCWs in a chest hospital in a region where an epidemic of MDR has been recognised. This hospital is responsible not only for TB, but also for other lung diseases in the southern areas of the country.

BACKGROUND DATA ON ESTONIA

Estonia, formerly a part of the Soviet Union, declared its independence in 1991. Estonia is the smallest of the three Baltic Republics, covering an area of 47 500 km^2. In January 2000, the total population was estimated at 1 439 197 (Statistical Office of Estonia), of whom 70% live in urban areas. Administratively, Estonia has been divided into 15 counties, the smallest of which has a population of approximately 12 000 and the largest one of 566 000. There are 71.9 hospital beds per 10 000 population,[8] of which 365 placed in six hospitals are reserved for tuberculosis patients.

Bacille Calmette Guérin (BCG) vaccine is universally administered to newborns at birth, with an annual coverage that has been around 95% for decades. BCG revaccination is performed at the age of 6–8 years; no re-vaccination is given to adult populations.

During the period 1994–1998, 4852 physicians and 8945 nurses and laboratory technicians were employed in health care settings. The Tartu University Lung Hospital (TULH), taken under a separate survey in the present study, had a 160-bed facility that employed on average 280 persons, including 30 physicians and 80 nurses and laboratory technicians. The numbers of patients with TB and those with MDR-TB hospitalised annually in TULH from 1994 to 1998 varied as follows: 284 in 1994, including 41 (14%) with MDR-TB; 328 in 1995, including 60 (18%) with MDR-TB; 341 in 1996, including 52 (15%) with MDR-TB; 283 in 1997, including 74 (26%) with MDR-TB; and 309 in 1998, including 78 (25%) with MDR-TB.

MATERIAL AND METHODS

Patients

HCWs eligible for the study were full-time employees registered in the databases of different health care institutions in Estonia. A case was defined as a HCW diagnosed with primary tuberculosis detected during the calendar years 1994–1998. The diagnosis was based on clinical and radiological evidence of active tuberculosis, and confirmed by either bacteriological or histopathological examinations, or by a relevant outcome of treatment with anti-tuberculosis drugs.

Characteristics of the study population, including profession, age, sex, ethnicity and site of disease, were obtained from the Central Tuberculosis Register. Information about bacteriological confirmation, including smear and culture positivity, and susceptibility patterns of the isolates, was obtained from the TB laboratories in Estonia. General data on HCWs in Estonia were obtained from the State Statistics Office and from the administration office at the TULH.

Bacteriological examinations

M. tuberculosis was isolated on Löwenstein-Jensen (LJ) medium and/or by the Bactec 460 system.[11] Mycobacterial strains were identified as *M. tuberculosis* complex using standard biochemical tests or by hybridisation with commercial molecular probes (AccuProbe, Gen-Probe Inc, San Diego, CA). Drug susceptibility was determined by the proportion method on LJ medium and/or the modified proportion method in BACTEC 460.

Statistical analysis

The case rates of active tuberculosis per 100 000 among HCWs were determined by the number of newly diagnosed cases during a calendar year. The case rates in the general population, used for comparison, were obtained from the Central Tuberculosis Register.

RESULTS

The incidence of active tuberculosis among HCWs

Among the 14 730 HCWs in the registers, 67 were diagnosed as patients with primary tuberculosis during the study period, indicating a mean annual tuberculosis case rate of 91/100 000 HCWs. They were

* E = ethambutol; H = isoniazid; R = rifampicin; Z = pyrazinamide; S = streptomycin. Numbers before the letters indicate the number in months of the phase of treatment; numbers in subscript indicate the number of times the drugs are taken each week.

Table 1 Characteristics of health care workers (HCW) with tuberculosis in Estonia in 1994–1998 compared with the total population

Characteristic	HCW with TB 1994–1998 *n* (%)	Total patients with TB in Estonia* 1994 *n* (%)	Total patients with TB in Estonia* 1998 *n* (%)
Total number	67 (100)	518 (100)	820 (100)
Profession			
Physicians	23 (34)		
Nurses and laboratory technicians	30 (45)		
Assistant nurses and cleaners	14 (21)		
Sex			
Female	59 (88)	163 (31)	232 (28)
Male	8 (12)	355 (69)	588 (72)
Ethnicity			
Estonians	49 (73)	NA	540 (66)
Non-Estonians	18 (27)	NA	280 (34)
Site of tuberculosis			
Pulmonary	58 (87)	448 (87)	749 (91)
Extra-pulmonary	9 (13)	70 (14)	71 (9)
Bacteriological verification			
Smear positive	20 (30)	NA	372 (45)
Culture positive	49 (73)	329 (64)	545 (67)
Smear positive and culture positive	18 (27)	NA	NA
Smear positive and culture not done	2 (3)	NA	NA
Smear negative and culture positive	31 (46)	NA	NA
MDR-TB	18 (38)†	24 (10)‡	53 (14)§

* HCWs included.
† Susceptibility testing done in 47 cases.
‡ Susceptibility testing done in 266 cases.
§ Susceptibility testing done in 377 cases.
NA = no data available; MDR-TB = multidrug-resistant tuberculosis.

employed at 33 health care institutions, including 25 hospitals, seven out-patient clinics and one university institute; 23 were physicians, 23 nurses and seven laboratory technicians, 12 assistant nurses and two cleaners (Table 1). In 1994–1997, case rates among nurses and laboratory technicians varied between 66 to 82/100 000, which was over 1.5 times higher than among the general population, which increased during the same period from 41 to 56 cases/100 000 (Figure 1). During the same time period, case rates among physicians increased from 83 to 147/100 000, i.e., 1.5 to 2.9 times higher than among the general population. In TULH, the respective case rates among HCW were higher, reaching the highest level in 1996 among nurses and laboratory technicians (3450/100 000) and in 1998 among physicians (6900/100 000) (Fig-

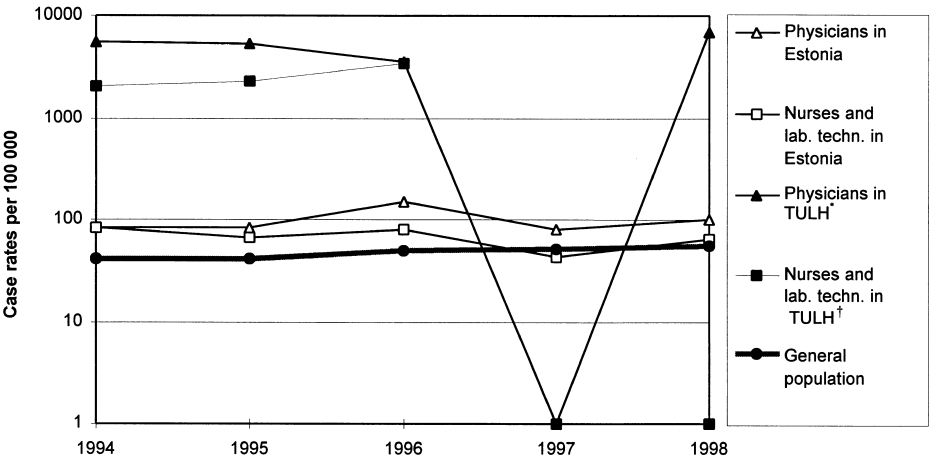

Figure 1 Annual case rates of tuberculosis among health care workers and the general population in Estonia. Case rates among employees of a chest hospital (TULH) with regional responsibility for tuberculosis are shown separately. * No new cases detected among physician at TULH in 1997. † No new cases detected among nurses and laboratory technicians at TULH in 1997 and 1998.

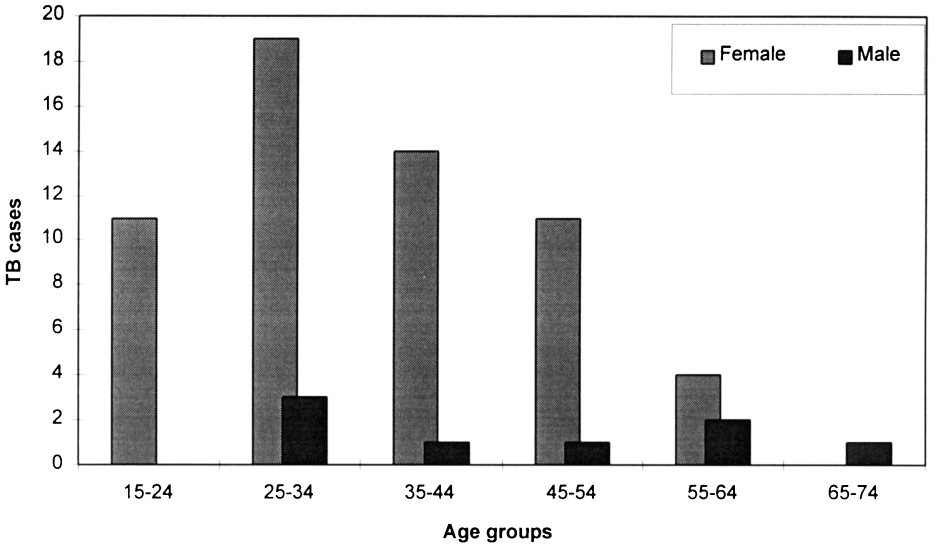

Figure 2 Tuberculosis in 67 health care workers diagnosed in 1994–1998, by age and sex.

ure 1). Thus, the incidence of tuberculosis was almost 30 to 90 times higher among physicians in TULH than in the general population.

Characteristics of HCWs with TB

The distribution of tuberculosis by age and sex is shown in Figure 2. The mean age at diagnosis of tuberculosis was 37 years (range 18–71) among HCWs, while in the general population in 1997–1998 it was 44 years. The majority of HCWs with TB were young women, with a female:male ratio of 11:1 (Table 1). Fifty-eight (87%) of diagnosed cases had pulmonary TB; extra-pulmonary TB, diagnosed in nine persons, included six cases with pleurisy, two with genitourinary TB and one with vertebral TB.

Bacteriological results

Twenty (30%) of the 67 cases were positive for acid-fast bacilli (AFB) by microscopy of sputum samples, bronchial washing or tissue samples. *M. tuberculosis* was isolated from the specimens of 49 (73%) patients, and in one patient it was confirmed by histopathology. In 15 (22%) cases, both smear and culture results were negative, and in two, the results were missing from the registers. Among the 47 *M. tuberculosis* isolates available for susceptibility testing, 23 (49%) were resistant to at least one of the first-line drugs, streptomycin, isoniazid, rifampicin or ethambutol. Eighteen (38.3%) isolates were MDR. The combinations of drug resistance are shown in Table 2.

DISCUSSION

The risk of nosocomial tuberculosis among HCWs can be evaluated either by the occurrence of clinical disease or by the rate of tuberculin conversions, often regarded as an indicator of tuberculous infection among asymptomatic persons. According to Connolly, the former criterion is preferable.[12] Published data indicate that tuberculous infection is more common among health care staff working in high-risk work places[13–15] than among the general health care staff.[16–18] Our findings confirm that this also applies to clinical tuberculosis: the incidence of clinical tuberculosis was 1.5 to three times higher among HCWs than in the general population. In a chest hospital in charge of the tuberculosis patients of a whole region, the incidence was 30 to 90 times higher, and was highest among physicians.

Table 2 Susceptibility to anti-tuberculosis drugs of 47 *Mycobacterium tuberculosis* strains isolated from HCWs with tuberculosis in 1994–1998, compared with the general resistance situation in Estonia in 1994 and 1998

	Strains of HCW tested *n* (%)	Total in Estonia in 1994* *n* (%)	Total in Estonia in 1998* *n* (%)
Total	47 (100)	266 (100)	376 (100)
Fully susceptible	24 (51)	191 (72)	237 (63)
Mono-resistant	1 (2)	30 (11)	51 (14)
Isoniazid (H)	0	11 (41)	10 (3)
Rifampicin (R)	1 (2)	0	1 (<1)
Ethambutol (E)	0	2 (1)	1 (<1)
Streptomycin (S)	0	17 (6)	39 (10)
MDR	18 (38)	27 (10)	53 (14)
H + R	1 (2)	6 (2)	1 (<1)
H + R + E	0	0	2 (<1)
H + R + S	4 (9)	9 (3)	18 (5)
H + R + S + E	13 (28)	12 (5)	32 (9)
Other resistance	4 (9)	18 (7)	35 (9)
H + S	2 (4)	13 (5)	28 (7)
H + E + S	1 (2)	5 (2)	5 (1)
R + S	1 (2)	0	0

* Only new cases of tuberculosis included.
HCW = health care workers; MDR = multidrug-resistant.

The risk of TB among HCWs was substantial in the era before antibiotics, but declined rapidly after 1950 due to decreasing TB incidence in the population and the advent of effective therapy.[1] According to a US study based on data from 1920–1953, medical students and physicians accounted for 9% of all tuberculosis patients, and were therefore to be regarded as a specific risk group.[19] Although an epidemiological treatise in the 1980s did not indicate physicians as a risk for TB,[20] later surveys have reported substantial rates of both tuberculous infection and disease among pulmonary physicians as well as among internal medicine specialities.[12,21] Occupational TB particularly involves young age groups between 20 to 35 years.[21,22] Physicians seem to take too few precautions to prevent infection; their failure to implement prevention measures is probably related to both lack of perceived vulnerability and the press of other priorities.[23]

Over the past decade, two factors, both also identifiable in Estonia, have profoundly altered views about the risk of TB in HCWs: the resurgence of TB and the emergence of MDR strains of TB.[1] From 1970 to 1989, only two cases of tuberculosis were registered among hospital employees in the chest hospital where 18 cases of pulmonary tuberculosis were diagnosed in 1994–1998. Thirteen (72%) of the employees with tuberculosis in TULH were infected with MDR strains. No known risk factors for tuberculosis other than increase in occupational exposure could be identified. All of the HCWs with TB tested negative for HIV.

Our data illustrate how TB in HCWs is often MDR after MDR-TB becomes more common in the general population. The prevention of nosocomial spread of tuberculosis is particularly important when MDR-TB is being exposed in the hospital environment. Degree of patient infectivity, intimacy and duration of contact and lack of effective anti-tuberculosis therapy are factors thought to be essential to the risk of spreading tuberculosis.[13] During the first weeks of chemotherapy for pulmonary tuberculosis, a patient's sputum may contain large quantities of tubercle bacilli.[23] It has been shown in numerous studies how smear-positive tuberculosis presents the most significant risk to contacts.[24] However, extended exposure even to smear-negative tuberculosis, i.e., 400 hours of contact, may also significantly increase risk of infection.[25] The implications of hospital dissemination are consequently even more serious.[24,26–28] Poor response to initial chemotherapy in MDR-TB causes excretion of high bacillary loads, extended infectivity, and subsequently also extended hospital stay. Compared with TB with no drug resistance, each case of MDR-TB treated in a hospital exposes HCWs to a particular risk of TB caused simply by extended exposure to highly infectious doses. As the results indicate, this exposure also leads to MDR-TB in HCWs.

Cases detected among hospital employees represent only part of a greater problem. The risk of nosocomial tuberculosis also includes fellow patients, with or without TB, who are similarly exposed during hospitalisation if isolation measures are not taken fully into account. Nosocomial TB can remain undetected unless genotyping of *M. tuberculosis* strains accompanied by exposure surveys are used in routine practice.

In this study, the risk of tuberculosis infection was not evaluated. Tuberculin skin testing programmes are poorly implemented, and the data available are not systematically registered. On the other hand, BCG vaccination is in widespread use in Estonia. Particularly in adult populations, BCG-induced tuberculin conversion may limit the value of skin testing as an epidemiological and diagnostic tool.[22]

Tuberculosis is a historic public health problem that was considered for some time as being successfully controlled by basic public health approaches. Today, it has returned at alarming rates, and its resurgence is complicated by MDR strains spreading epidemically in the community, simultaneously increasing occupational exposure.[29]

So far a general infection control policy regarding TB transmission and an infrastructure that would empower the implementation of such a policy have not yet been developed in Estonia. After independence was regained in the 1990s, many rapid political and economic changes were initiated, including a reform of the health sector. This included integration of patients with suspected tuberculosis among patients with other diseases. A national tuberculosis programme started to function actively only in 1998. Before that, community-based directly observed therapy (DOT), with a focus on completion of a full treatment course, was not implemented. In ambulatory treatment, self-administration of TB drugs was a rule, and non-standard regimens of anti-tuberculosis drugs were prescribed. Due to the many changes in the health care systems, the incidence of new cases of tuberculosis, mortality and MDR have steadily increased since 1993. For several years, the health service staff, including health care institution administrators, regarded TB as a disease that had been overcome, which led to disregard of the routine procedures necessary to prevent nosocomial spread of TB.

To stop the TB epidemic, early identification, diagnosis and effective treatment of potentially infectious TB patients are the basic means. To interrupt the transmission of nosocomial tuberculosis, a strict policy of isolation of potentially infectious TB patients must be made a basic rule. Precautions must be taken in procedures leading to production of infective aerosols in both the clinical setting and laboratories. HCWs must be trained to understand the epidemiology of tuberculosis: the potentials for occupational exposure and the principles of infection control measures. Attention needs to be paid to the principles of

preventive health care and particularly the importance of early medical care if symptoms of tuberculosis emerge.

In hospitals that care for TB patients, all possible attempts need to be made to limit the areas in health care facilities where exposure to potentially infectious TB patients may occur. Separate areas must be assigned for different patient categories, such as 1) patients without symptoms or signs of tuberculosis; 2) potentially infectious patients with TB but with unconfirmed diagnosis; 3) patients with TB under anti-tuberculosis therapy and clinically improving; 4) patients known to be infectious but without suspicion of MDR-TB; and 5) patients with known or suspected MDR-TB. The categories must be physically isolated from each other, e.g., in separate wards or isolation rooms, and efforts should be made to improve ventilation in high-risk areas to diminish potential exposure of HCWs. Separation policies should be enforced to minimise the activities of infectious TB patients in the hospital premises outside their own wards. From their arrival patients need to be educated to reduce infectious hazards by simple measures such as cough etiquette, and to understand the importance of completing treatment.

The risk of nosocomial tuberculosis will continue as long as health care is provided to patients with active TB. The complete elimination of risk among health care workers is an unrealistic goal.[1] The objective of the infection control plan is to reduce this risk to as low a level as possible. A combination of administrative, engineering and personal respiratory control measures needs to be employed to further reduce the risk of TB transmission in individual health care facilities.[6,7]

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RÉSUMÉ

CADRE : Au cours des années 1990, l'incidence de la tuberculose a augmenté dans les Etats Baltes et a été accompagnée par l'apparition d'une résistance aux médicaments incluant la multirésistance. Dans cette situation mouvante, l'on ne s'est pas rendu compte de la menace potentielle de dispersion nosocomiale de la tuberculose vers d'autres patients et vers le personnel de santé.

OBJECTIF : Investiguer le risque de tuberculose chez les travailleurs de la santé en Estonie.

SCHÉMA : Les cas de tuberculose enregistrés parmi les travailleurs de la santé pendant les années 1994 à 1998 ont été enrôlés. On a étudié rétrospectivement les dossiers des cas en combinaison avec les données bactériologiques incluant celles concernant la résistance aux médicaments.

RÉSULTATS : Le diagnostic de tuberculose active a été porté chez 67 travailleurs de la santé (23 médecins, 23 infirmières et sept techniciens de laboratoire, 12 infirmières sociales et deux nettoyeurs) ; chez tous, les tests sérologiques pour le virus de l'immunodéficience humaine étaient négatifs. L'incidence de tuberculose parmi les travailleurs de la santé (moyenne 91/100 000/année) fut de 1,5 à 3 fois plus élevée que celui de la population générale. Dans un hôpital pulmonaire ayant en charge les soins de la tuberculose dans la région, l'incidence fut de 30 à 90 fois plus élevée, étant la plus élevée encore parmi les médecins. La tuberculose a été confirmée par culture chez 49 travailleurs de la santé. On a détecté une résistance aux médicaments chez 23 (49%) d'entre eux et une multirésistance chez 18 (38%).

CONCLUSION : Les travailleurs de la santé, particulièrement ceux occupés dans un hôpital pulmonaire qui traite également les patients tuberculeux, s'avèrent avoir un risque accru de tuberculose. La tuberculose multirésistante représente une menace particulière, difficile à maîtriser.

RESUMEN

MARCO DE REFERENCIA : La incidencia de la tuberculosis ha aumentado en los países bálticos en la década del 90, acompañada por la emergencia de resistencia a las drogas y a la multirresistencia (MR). En esta situación cambiante, el riesgo potencial de la diseminación de la tuberculosis a otros pacientes y al personal sanitario ha permanecido ignorado.

OBJETIVO : Investigar el riesgo de la tuberculosis en los trabajadores de la salud en Estonia.

MÉTODO : Se incluyeron los casos de tuberculosis registrados entre los trabajadores de la salud entre los años 1994 y 1998. Se analizaron las historias clínicas retrospectivamente y se combinaron con los datos bacteriológicos, incluyendo los datos de drogo-resistencia.

RESULTADOS : Sesenta y siete trabajadores de la salud (23 médicos, 23 enfermeras y siete técnicos de laboratorio, 12 ayudantes de enfermería y dos encargados de limpieza) todos con test del virus de la inmunodeficiencia humana negativo, fueron diagnosticados con tuberculosis. La incidencia de tuberculosis entre los trabajadores de la salud (media 91/100.000/año) fue 1,5 a 3 veces mayor que en la población general. En un hospital a cargo de la atención de la tuberculosis regional, la incidencia fue 30 a 90 veces más alta, siendo la más alta el de los médicos. En 49 trabajadores de la salud la tuberculosis se confirmó por cultivo. Se detectó la drogoresistencia en 23 (49%) de ellos, con una tuberculosis MR en 18 (38%).

CONCLUSIONES : Los trabajadores de la salud, en especial los que trabajan en un hospital de enfermos pulmonares y tuberculosos, presentaron un riesgo elevado de tuberculosis. La tuberculosis MR plantea una situación particular, difícil de combatir.