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Active screening for pulmonary tuberculosis by chest x-ray among immigrants at the Swiss border

THESE

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par

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Le but de l'étude est d'évaluer le rendement du dépistage radiologique de la tuberculose pulmonaire chez les immigrés à l'entrée en Suisse.

Méthode: parmi les immigrés adultes entrés en Suisse en 2004, qui ont tous passé un contrôle radiologique, le nombre de porteurs de clichés thoraciques suspects de tuberculose et la proportion de cas chez lesquels un traitement antituberculeux a été prescrit ont été évalués rétrospectivement. La fréquence des symptômes chez les immigrés atteints de tuberculose a été comparée à celle d'un groupe contrôle sans tuberculose.

Résultats: parmi 8995 immigrés, 8240 avaient un cliché thoracique normal, 630 étaient porteurs d'une anomalie non suspecte de et 125 (1.4%) montraient des active tuberculose signes radiologiques suspects de tuberculose. Un diagnostic final de tuberculose nécessitant un traitement a été posé dans 50 cas (11 cas à frottis et culture positifs, 16 cas à culture positive, 23 cas à culture négative), 57 présentaient des lésions cicatricielles compatibles avec une ancienne tuberculose et 18 avaient une autre affection pulmonaire ou un cliché normal au contrôle. La prévalence des plaintes n'était pas différente entre les 27 immigrés porteurs d'une tuberculose documentée (frottis+/culture+: 82%, frottis-/culture+: 75%) et les 23 immigrés atteints d'une tuberculose non documentée (frottis-/culture-: 91%), mais elle était plus élevée que chez les 57 immigrés porteurs de lésions cicatricielles (59%). La toux était plus fréquente chez les 27 tuberculeux documentés (70%) que chez 198 fumeurs sans tuberculose (37%) et chez 229 non fumeurs sans tuberculose (15%).

Conclusions: seuls 22% (27/125) des immigrés dont le cliché thoracique est suspect de tuberculose sont porteurs d'une tuberculose documentée par examen direct ou culture et 40% (50/125) nécessitent un traitement antituberculeux. Deux immigrants sur les 11 cas frottis positifs n'auraient pas été dépistés par un questionnaire. Peer reviewed article

Active screening for pulmonary tuberculosis by chest x-ray among immigrants at the Swiss border

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Summary

Aim: To assess the number of immigrants with pulmonary tuberculosis detected by chest x-ray screening at the Swiss border.

Method: All adult immigrants entering Switzerland in 2004 were screened by chest x-ray (CXR). The number of radiological abnormalities suggestive of pulmonary tuberculosis, and the proportion requiring treatment for tuberculosis, were assessed retrospectively. The frequency of symptoms among immigrants with documented TB was compared with a sample of immigrants with a normal CXR.

Results: Among 8995 immigrants, 8240 had a normal CXR, 630 had some abnormality not suggestive of active TB and 125 (1.4%) had a CXR suggestive of pulmonary TB. A final diagnosis of tuberculosis requiring treatment was made in 50 (11 with positive smear and culture, 16 with positive culture and 23 with negative culture), 57 had fibrotic lesions and 18 had another disease or a

normal x-ray on control. The prevalence of symptoms did not differ between 27 immigrants with documented TB (smear+/culture+: 82%, smear-/ culture+: 75%), and 23 with smear-/culturetuberculosis (91%), but lower in 57 immigrants with fibrotic lesions (60%). Cough was more frequent among the 27 immigrants with documented TB (70%) than among 198 smokers without TB (37%) and among 229 non-smokers without TB (15%)

Conclusions: Only 22% (27/125) of immigrants with CXR abnormalities suggestive of pulmonary tuberculosis were documented by smear and/or culture and 40% (50/125) needed antituberculous treatment. 2/11 smear-positive immigrants would not have been detected by a questionnaire on symptoms.

Key words: tuberculosis; immigrants; screening; chest x-ray

Résumé

But de l'étude: évaluer le rendement du dépistage radiologique de la tuberculose pulmonaire chez les immigrés à l'entrée en Suisse

Méthode: parmi les immigrés adultes entrés en Suisse en 2004, qui ont tous passé un contrôle radiologique, le nombre de porteurs de clichés thoracique suspects de tuberculose et la proportion de cas chez lesquels un traitement antituberculeux a été prescrit ont été évalués rétrospectivement. La fréquence des symptômes chez les immigrés atteints de tuberculose a été comparée à celle d'un groupe contrôle sans tuberculose.

Financial support: none. Conflict of interest: none. *Résultats:* Parmi 8995 immigrés, 8240 avaient un cliché thoracique normal, 630 étaient porteurs d'une anomalie non suspecte de tuberculose active et 125 (1.4%) montraient des signes radiologiques suspects de tuberculose. Un diagnostic final de tuberculose nécessitant un traitement a été posé dans 50 cas (11 cas à frottis et culture positifs, 16 cas à culture positive, 23 cas à culture négative), 57 présentaient des lésions cicatricielles compatibles avec une ancienne tuberculose et 18 avaient une autre affection pulmonaire ou un cliché normal au contrôle. La prévalence des plaintes n'était pas différente entre les 27 immigrés porteurs d'une tuberculose documentée (frottis+/culture+: 82%, frottis-/culture+: 75%) et les 23 immigrés atteints d'une tuberculose non documentée (frottis-/culture-: 91%), mais elle était plus élevée que chez les 57 immigrés porteurs de lésions cicatricielles (59%). La toux était plus fréquente chez les 27 tuberculeux documentés (70%) que chez 198 fumeurs sans tuberculose (37%) et chez 229 non fumeurs sans tuberculose (15%).

Conclusions: Seuls 22% (27/125) des immigrés

dont le cliché thoracique est suspect de tuberculose sont porteurs d'une tuberculose documentée par examen direct ou culture et 40% (50/125) nécessitent un traitement antituberculeux. Deux immigrants sur les 11 cas frottis positifs n'auraient pas été dépistés par un questionnaire.

The incidence of tuberculosis in developing countries is higher than in industrialised countries. Migrants from developing countries have a higher risk of being carriers of active tuberculosis than the population of the regions they enter. In some countries this risk is considered serious enough to justify screening measures, which may be performed before entry, at the border, or after entry [1].

Screening systems differ between countries. Chest x-ray (CXR) allows an immediate check for the presence of lesions suggestive of tuberculosis. In spite of its seemingly objective character, the method is subject to the experience of the reader, and there is a risk of over- and underreporting. Several studies have reported intra-observer and inter-observer disagreement on the interpretation of x-rays [2, 3], but new studies show a higher degree of correlation than previously reported [4– 6]. Furthermore, CXR do not allow a distinction between active and healed forms of tuberculosis. Screening may also use questionnaires on respiratory or general symptoms [7]. Most (but not all) patients with an active form of tuberculosis have clinical symptoms, such as cough, sputum production, fever or weight loss [8], but these symptoms are not specific for tuberculosis and may be present in other diseases and among healthy smokers as well. The value of screening with questionnaires has not been demonstrated.

A screening system based on CXR examination was used from 1992 to 2005. We assessed retrospectively 1) the accuracy of the identification of tuberculosis on CXR by the readers and 2) the incidence of symptoms among immigrants with and without tuberculosis. Agreement in reading the CXR was assessed in a separate study [6].

Material and methods

In Switzerland, from 1992 to 2005, screening for tuberculosis was performed in 5 registration centres located close to the border, where immigrants applying for asylum are required to stay for a few days for administrative and medical workup. The examination included a tuberculin skin test and a chest x-ray (except for children <15 and pregnant women). The digitalised CXR from 4 of 5 centres were transmitted electronically to a reading centre located at the Department of Ambulatory Care and Community Medicine of the University of Lausanne, where they were read daily by a team of trained readers and coded according to the estimated likeliness of tuberculosis. One centre (not included in our study) used the traditional miniature X-ray technology and the images were interpreted locally by trained physicians. Immigrants with CXR suggestive of active tuberculosis were referred to a hospital for further examination and a decision on treatment. The referral was immediate or delayed according to the estimated likelihood of smear-positive tuberculosis on the CXR.

For all immigrants with digital CXR suggestive of active tuberculosis detected at the border in 4 centres between January 1 and December 31 2004, the final diagnosis, including the results of bacteriological tests, was assessed retrospectively from the medical records of the hospitals to which the immigrants had been referred. The proportion of documented pulmonary tuberculosis with positive smears (S+) and/or cultures (C+), with no bacteriological documentation (S-/C-) but a clinical decision on treatment and with other diagnoses, was calculated. The results from the only centre using miniature X-rays, representing 6.7% of the total, were not considered for this analysis.

Before referral to the hospital for tests, each immi-

grant with an abnormal CXR was asked by a nurse about symptoms possibly related to tuberculosis (cough, sputum production, fever, sweating during the night, weight loss). We compared this information with a set of similar questions put prospectively to all adult immigrants with normal CXR, in January and February 2005, after completion of the main study. This group of 427 immigrants comprised 198 smokers and 229 non-smokers. The answers given by immigrants with normal CXR were compared with the symptoms mentioned by immigrants with suspected tuberculosis. Immigrants were also asked if they had ever had tuberculosis or antituberculous treatment.

The proportion of affirmative answers to each of the questions was calculated for all patients with CXR suggestive of tuberculosis, for patients with smear- or culture-positive tuberculosis only, and for immigrants with-out tuberculosis.

Code of CXR reading

The code of interpretation used for the CXR taken at the border was aimed at assessing 1) whether the image was normal or abnormal, 2) if abnormal, whether it was compatible with tuberculosis or not and 3) if compatible with tuberculosis, whether the immigrant needs to be assessed urgently due to a risk of active pulmonary tuberculosis, or if the assessment can be postponed. CXR with extensive lesions, cavities or bilateral lesions were considered highly suggestive of active tuberculosis requiring immediate investigation. Immigrants with fibrotic or calcified lesions were considered not to need urgent assessment. Details on the code of reading and agreement between readers have recently been published [6].

Results

Between January 1 and December 31 2004, 8995 digital CXR were taken at the border in 4 centres and read in our clinic. CXR was considered normal in 8240, and in 630 demonstrable abnormalities were not considered suggestive of active TB. In 125 immigrants (1.4%) the CXR was considered suggestive of active tuberculosis. The demographic data of these persons are reported in table 1. The final diagnosis after examination is reported in figure 1. 107 CXR (86%) corresponded to tuberculosis, 50 of them requiring treatment (11 smear and culture positive, 16

		n (%)	
Age group	16–24 years	45 (36)	
	25–44 years	69 (55)	
	45 and more	11 (9)	
Gender	Male	76 (61)	
	Female	49 (39)	
Origin	Africa	64 (51)	
	Asia	2 (2)	
	Eastern Europe	50 (40)	
	Latin America	0	
	Other regions	9 (7)	

smear negative/culture positive and 23 smear and culture negative). 57 had fibrotic lesions compatible with prior tuberculosis (13 mentioned past treatment for tuberculosis) and did not receive full antituberculous treatment. Some received preventive treatment. A diagnosis other than tuberculosis was established in 10 cases (sarcoidosis, pneumonia, lymphoma) and in 8 cases the CXR were considered at control to show abnormalities without clinical relevance.

The prevalence of symptoms among immigrants with documented tuberculosis (positive culture), undocumented tuberculosis (negative culture) requiring treatment based on a clinical decision and immigrants with fibrotic lesions is reported in table 2. Cough was counted separately from symptoms possibly related to tuberculosis (cough, sputum production, fever, night sweating, weight loss)

Table 3 reports the prevalence of symptoms among 27 immigrants with documented tuberculosis compared with a group of 427 immigrants with normal CXR, by smoking status. Cough and sputum production are more prevalent among immigrants with documented tuberculosis than among smokers without tuberculosis, who had more symptoms than non-smokers.

Category	n	Cough	Any symptom	Past TB	Prior TB treatment	
S+/C+	11	9 (82)	9 (82)	1 (9)	1 (9)	
S-/C+	16	10 (64)	12 (75)	1 (6)	1 (6)	
S-/C-	23	15 (65)	21 (91)	7 (30)	7 (30)	
Fibrotic lesions	57	22 (39)	34 (60)	14 (25)	13 (23)	

Discussion

The radiological screening of 8995 immigrants at the Swiss border correctly identified 107 cases of pulmonary tuberculosis among 125 persons with abnormal CXR. One half of them needed treatment and were notified, the other half had fibrotic lesions (after treatment or spontaneous healing), and did not need full treatment. This confirms that CXR is appropriate for the detection of pulmonary tuberculosis in a high-risk population, but provides no information about the activity of the disease. On the other hand, considering that only 1.4% (125/8995) of CXR were suggestive of tuberculosis, and only one quarter of these were confirmed by bacteriological examination, the global yield from screening may seem very low. From our data, tuberculosis needing treatment was notified in 1/180 immigrants screened at the border, documented TB in 1/333 and smear-positive pulmonary TB in 1/817.

Screening with CXR will miss cases of ex-

trathoracic tuberculosis and cannot rule out the possibility that pulmonary tuberculosis may develop after the border screening in immigrants presenting with normal CXR at entry and be diagnosed at a later stage of the disease. The probability that CXR read by experienced readers missed active pulmonary tuberculosis (with positive smear), or that an immigrant has active tuberculosis with a normal CXR, seems highly remote. In a Danish study, among 519 cases of tuberculosis documented by positive culture, only 3 were observed in patients with a normal CXR [9]. In the same study, 93% of patients with documented tuberculosis had a CXR considered typical by the readers and 7% were atypical but abnormal.

The quality of the information given by CXR depends on reading accuracy. Other studies have demonstrated that following a predefined reading code improves the findings [4], but that even experienced readers may diverge in their interpreta-

Table 1

Demographic data of 125 immigrants with chest x-ray suggestive of TB.

Table 2

Symptoms and history of TB among 1 immigrants with ab normal CXR, by fina diagnosis (S+/C+: smear-positive TB, S-/C+: culture-positive TB, S-/C-: culturenegative TB, and fibrotic lesions). Any symptom is a positive answer to at least one of the questions about cough. sputum production, fever, night sweating or weight loss. Absolute numbers with % in brackets.

Table 3

Symptoms among 27 immigrants with documentedTB (S+/C+ and S-/C+), 198 smokers with normal CXR and 229 non-smokers with normal CXR. Any symptom is a positive answer to at least one of the questions about cough, sputum production, fever, night sweating or weight loss. Absolute numbers with % in brackets.

Category	n	Cough	Any symptom	
S+/C+ and S-/aC+	27	19 (70)	21 (78)	
Smokers without TB	198	74 (37)	109 (55)	
Non-smokers without TB	229	35 (15)	80 (35)	

tion of CXR if there is no preliminary agreement on the definitions [3]. A study performed in our department has demonstrated a satisfactory concordance of interpretation between observers [6]. One of the reasons may be that we used a simple reading procedure with predefined categories.

The cost-effectiveness of screening immigrants for tuberculosis has been addressed in a Canadian study showing that screening by CXR is of value for young immigrants from countries with a high prevalence of tuberculosis [10]. The final value of the screening procedure must consider not only the fact that it allows a start to immediate treatment in active cases, but also that it probably prevents the transmission of mycobacteria to other immigrants and staff members in the centres. According to the Swiss Federal Office of Public Health, some 4500 x-rays need to be performed to avoid the occurrence of one extra case in the local population [11]. Considering this, several authors have cast doubt on the cost-effectiveness of screening at the border [12] and the Swiss health authorities have decided to change the system.

The incidence of symptoms, as assessed from the questionnaire, appears to be high in all groups of immigrants with abnormal CXR, irrespective of the final diagnosis. The prevalence does not differ significantly between patients with documented tuberculosis with positive smears and/or culture, and immigrants with fibrotic lesions. Some immigrants with documented tuberculosis had no symptoms (18% among S+/C+ and 25% among S-/C+). Obviously, active screening at the border detects cases of tuberculosis at an earlier stage of disease than passive screening in the general resident population, a fact which may explain the absence of symptoms in some immigrants [13, 14]. Immigrants with tuberculosis who did not mention symptoms would not have been detected without CXR, at any rate on entry into Switzerland. Considering that most immigrants stay for several days or weeks in the registration centres, those with active tuberculosis may have been detected at a later stage if the disease had progressed. The prevalence of symptoms was higher among immigrants with documented tuberculosis than among smokers with normal CXR, who in turn had a higher prevalence than non-smokers with normal CXR.

The prevalence of symptoms in tuberculosis patients varies with the population considered. Cough is reported to be present in the majority of patients with tuberculosis in some studies, particularly if the patients are coinfected with HIV [15, 16]. In Thai prisons, cough >2 weeks was present in 78% of prisoners with smear-positive tuberculosis, but also in 16% of prisoners without tuberculosis [17]. In a study of 542 patients in Brazilian hospitals the presence of respiratory symptoms and young age correlated with the probability of tuberculosis [18]. In Sudan, cough was reported by 72% of patients diagnosed with tuberculosis, followed by weight loss (13%) and fever (2%). A combination of several chest symptoms was associated with a greater likelihood of smear positivity [18]. On the other hand, it has been shown that a large proportion of patients with tuberculosis have no symptoms even with positive smears. In the Sudanese study, 28% of patients with pul-

Figure 1

Flow chart of the study. CXR: Chest x-ray, S+ Smear positive, C+ culture positive.



monary tuberculosis did not cough and 9% coughed for less than 3 weeks. In a Swiss study, 22% smear-positive patients did not mention pulmonary symptoms [13]. In a survey of 313 tuberculosis patients in California, 73% complained of cough but only 48% for more than 2 weeks. Even in patients with pulmonary tuberculosis, the prevalence of cough for more than 2 weeks was only 52% [19]. Cough for more than 2 weeks was also prominent among patients with extrapulmonary tuberculosis (27%). In a study of 101 patients with radiological abnormalities suggestive of tuberculosis, cough was more prevalent among those with tuberculosis as the final diagnosis (69% vs 47%) [20]. This difference was not significant, but the prevalence of symptoms was significantly higher among patients with smear-positive tuberculosis (79%) than among smear-negative patients (46%). In some studies, symptoms were reliable predictors of the presence of tuberculosis [21], but not in all cases. A study among prisoners in Brazil demonstrated that screening based only on symptoms could not reliably discriminate between inmates with and without tuberculosis [7]. In a study conducted in South Africa, the sensitivity of CXR for the detection of bacteriologically positive tuberculosis was higher than symptoms alone (0.97 vs 0.54 for cough >2 weeks) [22].

The main weakness of this study is that it assessed the frequency of symptoms retrospectively from the records of patients with abnormal CXR. We cannot exclude communication problems with immigrants unable to use one of the local languages. Furthermore, we did not assess the intensity and duration of individual symptoms. As a control, we used the indications given by a group of immigrants with normal CXR, questioned in winter. We cannot rule out that the prevalence of cough may have been higher than average during that period, even among non-smokers and healthy immigrants. Furthermore, some of the symptoms may appear normal for smokers, such as cough and sputum, and are not interpreted as possible signs of disease.

Another potential weakness is that we used data from only 4 of the 5 centres where immigrants were screened. As the centre we could not

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Finally, it is not impossible that some cases of tuberculosis may have been missed by the CXR, particularly extrapulmonary TB or pulmonary TB at an early stage of development. We could not assess the number of cases discovered after entry into the country, as the immigrants who enter Switzerland are not followed prospectively and many leave the country shortly after arrival.

In conclusion, CXR performed at the border among immigrants entering Switzerland detected abnormalities suggestive of tuberculosis in 1.4% of the group, but less than half of them needed treatment. Some cases would probably have been missed by a questionnaire.

From 1 January 2006, the screening system for immigrants at the Swiss border was modified and includes a scoring system based on the presence and duration of symptoms associated with tuberculosis, general health status and the origin of the immigrant, in order to predict the likelihood of tuberculosis and select individuals needing a chest x-ray and further tests [23]. A prospective assessment of the new screening system is ongoing.

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