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EDITORIAL

Lessons learnt in Europe on tuberculosis surveillance, outbreaks and BCG vaccination in 2011

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Only a few European scientific journals publish articles on respiratory infectious diseases and tuberculosis (TB). The *European Respiratory Journal* (*ERJ*) and *Eurosurveillance* are two examples with a different focus. *Eurosurveillance*, which is published by, but editorially independent from, the European Centre for Disease Prevention and Control (ECDC) is a European peer-reviewed scientific journal devoted to the epidemiology, surveillance, prevention and control of communicable diseases, with a focus on topics that are of relevance to Europe.

To inform the readers of the *ERJ* about what was published on TB epidemiology, surveillance, prevention and control this editorial will provide a summary of articles published in *Eurosurveillance* and in other journals in 2011 on TB in Europe.

We used *Eurosurveillance* as a model to get an overview of the TB areas covered by a European journal directed at public health. All articles published on TB in *Eurosurveillance* in 2011 were identified, and grouped into three categories: outbreak reports; surveillance reports; and BCG (bacille Calmette–Guérin) vaccination. We searched the bibliographic database MEDLINE for other studies from Europe on similar topics. The information provided in the articles was summarised in tables. The interpretation of the results and their relevance for TB control and elimination in Europe is discussed in the sections below.

OUTBREAK REPORTS

The articles published on TB outbreaks in Europe are summarised in table 1 [1–7].

Three papers published in *Eurosurveillance* described an outbreak of TB in a European country. A study from Rome, Italy showed that 118 (9%) neonates tested QuantiFERON-TB Gold In-Tube (QFT-GIT; Cellestis, Carnegie, Australia) positive after exposure to a sputum-culture positive nurse at a maternity ward [1]. Since there are no estimates of QFT-GIT sensitivity and specificity in newborns it is unknown what the risk of progression to active TB is for children with a positive QFT-GIT. Children identified with a positive QFT-GIT test were referred for isoniazid prophylaxis and will be followed up for 3 years. When the study by BORGIA *et al.* [1] was published, none of the QFT-GIT positive neonates had progressed to active TB.

Of 2284 students in the UK who were exposed to a sputum smear-positive fellow college student, 400 (17.5%) had evidence of TB infection [2]. Risk factors for a positive interferon-γ release assay (IGRA) result were being more exposed to the index case and having a history of travel to a high incidence country in the last 2 years. The association with foreign travel suggests that an assessment of the value of serial IGRA testing and treatment of positive persons as an intervention for travellers is needed. A BCG vaccination did not seem to protect against TB infection. Preventive therapy was offered to individuals aged <35 years with a positive IGRA result but no evidence of active TB, according to national guidelines. Another article about the same outbreak investigation reported on the 19 active TB cases diagnosed during the outbreak investigations [3]. Of the 19 active TB cases eight cases were culture confirmed and seven had a 24-locus MIRU-VNTR genotype indistinguishable from the index case.

Another study from the UK describing an outbreak of isoniazid-monoresistant TB in 293 cases showed that many faced complex social challenges including recreational drug use, being homeless and a history of prison detention [4]. Treatment completion was between 55% and 65%. An Incident Control Committee was established that recommended several control measures, including directly observed therapy (DOT). Given that the outbreak is still ongoing it can be concluded that it is difficult to control this largest outbreak of drug resistant TB in Europe.

Whole genome typing in Sweden of the first isolate (strain isolated in 1996) of a cluster of 115 cases with isoniazid-resistant TB and two isolates from 2005 showed a remarkable genomic stability [5]. This is in contrast to what has been observed for other outbreak lineages.

An assistant in a kindergarten with culture-positive TB was the source of an outbreak in Italy [6]. The assistant had a family history of TB and reported a positive tuberculin skin test (TST) but did not recall completing a chemoprophylaxis regimen. She reported persistent cough for 1 year. The major factor that contributed to this outbreak was the delay in diagnosis of the assistant. The study also highlights the importance of follow-up of contacts of TB cases.

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TABLE 1 Tuberculosis (TB) outbreak reports in Europe published in 2011

First author [ref.]	Location	Index case	Measures adopted	Latently infection contacts	TB disease affected contacts	Comments
Borgia [1]	Italy, Rome	Nurse in the maternity ward	Screening of all newborns with QuantiFERON-TB Gold In-Tube	118/1340 (8.8)	0	
Abubakar [2, 3]	UK	College student	Screening with interferon-γ release assay	400/2284 (17.5)	19	
Maguire [4]	London, UK	Index case not specified	Establishment of Incident Control Committee that recommended specific control measures		293	Outbreak of isoniazid-monoresistant TB
Sandegren [5]	Sweden	Index case not specified			115	Outbreak of isoniazid-monoresistant TB
Filia [6]	Italy	Female who worked as an assistant in the kindergarten	Mantoux tuberculin skin test of contacts	121/830 (14.6)	19	
Tagarro [7]	Spain, Madrid	School teacher	Mantoux tuberculin skin test of contacts	16/17 (94)[#] 1/81 (1.2)[¶] 10/64 (15)[+]	6 1 0	

Data are presented as n positive/n tested (%) or n. QuantiFERON-TB Gold In-Tube is manufactured by Cellestis, Carnegie, Australia. [#]: children exposed for >6 h per day; [¶]: children exposed for <6 h per day; [+]: school personnel.

Almost all primary school children (aged 3–5 years) exposed to a Spanish school teacher were TST positive, and one-third was diagnosed with TB [7]. This study shows that prolonged exposure may infect almost every child.

The literature review demonstrates that, in spite of the improvements achieved, micro-epidemics and epidemics still occur in the low TB incidence countries of Europe, with a burden of cases and cost. These public health episodes frequently originate from clinical mistakes in diagnosing and treating the disease [8, 9]. Although micro-epidemic management has been recognised as a core activity of the countries approaching the elimination phase [10], additional efforts are still necessary to limit the impact of these episodes.

To improve our understanding of how to manage outbreaks, outbreak reports should clearly describe the activities that were performed, the yield of the tests, the management of cases with a positive test, the compliance to treatment, and the results of follow-up of the individuals involved in the outbreak.

SURVEILLANCE REPORTS

The studies reporting surveillance data are summarised in table 2 [11–22].

Collection of standardised TB surveillance data at the European level had been ongoing for 15 years in 2011. Initially, it was a project implemented by the French surveillance institute Institut de Veille Sanitaire (Saint-Maurice, France). Since 2008, the coordination has been performed jointly by the ECDC and the World Health Organization Regional office for Europe. Every year a surveillance report is published, which is available on the ECDC website (www.ecdc.europa.eu). The analysis of surveillance data helped to identify areas where TB control can be improved, *e.g.* case confirmation and treatment [11].

The TB surveillance data of the European Union and European Economic Area countries were also analysed to describe and analyse the burden and trends of paediatric TB [12]. TB in children is an indication of ongoing transmission in the community. Especially in countries with a low notification rate of paediatric TB, outbreaks may influence the trends. Since only a small proportion of paediatric TB cases are confirmed by a positive culture (14.1% of pulmonary cases), over-diagnosis was identified as a potential problem.

Two studies focussed on TB in special groups, *i.e.* children in the UK [13] and the elderly in Germany [14]. Just as children, elderly patients may also be considered a vulnerable group.

The TB situation in the UK has been described as being out of control with 9040 cases of active TB notified in 2009. A study by Abubakar *et al.* [15] discussed what should be done to regain control. The main focus needs to be on migrants and hard to reach groups. Interventions to improve TB control in migrants can be screening, providing information, and providing quality care by local health authorities. Recommendations for improving TB control in hard to reach groups included active case finding and case management support and coordination of treatment of prisoners before their release to improve treatment completion. In addition, suggestions for adjusting the organisation of the services were provided.

A description of the TB epidemiological situation in the general population was provided for Croatia [16], North Jutland,

TABLE 2 Studies using tuberculosis (TB) surveillance data in Europe published in 2011

First author [ref.]	Location	Focus	Core findings
Hollo [11]	EU and EEA countries	Overall notifications	Decline of TB notifications to 79 665 TB cases in 2009 Seven countries had notification rates >20 per 100 000
Sandgren [12]	EU and EEA countries	Children	Paediatric TB rates dropped between 2000 and 2009 Notification rates varied considerably between countries, ranging from 0.3 to 29.6 per 100 000 in 2009
Ruwende [13]	London, UK	Children	Between 1999 and 2006, 1379 TB cases in children <15 years of age were notified About half of the TB cases in children were in Black-Africans, and 52% of the children were born in the UK Most (59%) children were diagnosed with pulmonary disease
Hauer [14]	Germany	Elderly	TB patients >59 years of age had a higher proportion of genitourinary TB, low drug resistance rates, lower treatment success rates, and high mortality rates compared to younger patients
Abubakar [15]	UK	Overall notifications	In 2009 the number of reported TB cases was at its highest since the 1970s and rates of TB exceeded those in all other Western countries Most cases occurred in people born outside the country
Jurcev-Savicevic [16]	Croatia	Overall notifications	TB notification rates decreased significantly from 45 per 100 000 in 1996 to 26 per 100 000 in 2006 Paediatric cases represented 4.5% of all TB cases and only 16% were foreign born 90% of all TB cases had pulmonary TB and 0.7% MDR
Andersen [17]	North Jutland, Denmark	Overall notifications	Between 2000 and 2008, 251 TB patients were identified (notification rate 5.4 per 100 000) Of these, 71% had pulmonary TB and 29% extra-pulmonary, with lymph node TB in 84% of the extra-pulmonary cases MDR-TB was infrequent with only one case observed 55% of the TB patients were tested for HIV and five were HIV-infected A successful treatment outcome was reported for 83%
Odone [18]	Emilia Romagna, Italy	Overall notifications	Increase in the proportion of migrants with TB from 19% in 1996 to 53% in 2006 The cases not born in Italy were younger compared to those born in Italy and more frequently had risk factors for TB such as homelessness and prisoner status
Mandal [19]	UK	Overall notifications: *M. bovis*	Between 2005 and 2008, 129 *M. bovis* were cases diagnosed, only nine were individuals born in the UK after 1960 when widespread pasteurisation of milk was introduced and, thus, could be due to transmission between humans Four cases did not have specific risk factors Of the other five, one had a history of immunosuppression and the remaining four reported occupational contact with animals The annual incidence of *M. bovis* disease was low and decreased during the investigation period
Majoor [20]	The Netherlands	Overall notifications: *M. bovis*	Between 1993 and 2007, 231 patients were registered with *M. bovis* infection, 138 (60%) in native Dutch Most (n=54) foreign born patients came from Morocco *M. bovis* appeared as an extrapulmonary disease in 136 (59%) of the patients 17% of the patients received a treatment not compliant with international guidelines Treatment was completed by 65% of the cases
Winqvist [21]	Sweden	Overall notifications	Approximately 10% of persons with latent TB infection will develop TB When indigenous transmission was assumed to have disappeared (after 1967) the reactivation rate of latent TB infection was only 2%
Blondal [22]	Estonia	Overall notifications	Analysis of surveillance data and data from the Estonian Reference Laboratory of TB and Microbacteriosis showed that country wide management of TB can reverse increasing notification rates

EU: European Union; EEA: European Economic Area; *M. bovis*: *Mycobacterium bovis*; MDR: multidrug resistance.

Denmark [17], and Emilia Romagna in Italy [18]. Detailed analysis of surveillance data will help in identifying areas for improvement of TB control.

Both at the European [23] and at the global level [24] information about cases with *Mycobacterium bovis* are not reported separately but are included in the notification reports of *Mycobacterium*

tuberculosis complex. Two studies reported on *M. bovis* [19, 20]. In the UK and the Netherlands the number of *M. bovis* cases is low compared to the number of *M. tuberculosis* cases.

Two studies used surveillance data to answer research questions [21, 22]. The database of TB in the Sweden-born population from 1920–2009 and estimations of the number of infected individuals were analysed to assess the long-term risk and time pattern of reactivated TB. The analysis indicated that most cases occurred shortly after TB infection and the long-term follow up data indicate extensive spontaneous clearance of latent TB infection.

BLONDAL *et al.* [22] showed how surveillance data and data from the Estonian Reference Laboratory of TB and Mycobacteriosis can be used to assess the impact of a TB control programme with country-wide management of TB and availability of second-line drugs.

The problems underlined by the studies mentioned above show the importance of surveillance to understand where we are and indicate where to go. In the perspective of elimination, surveillance needs to be enhanced to ensure that each single case diagnosed either in the private or in the public sector (sometime only at the laboratory level) is promptly notified. Diagnosis is typically a clinical activity. Only if a diagnosed case is notified can a public health activity pivotal to initiate several interventions, including contact tracing and monitoring and evaluation, be initiated. Improved information on the magnitude of the TB epidemic and associated risk factors is a pre-requisite to plan for better control and possible elimination.

Besides using surveillance data to regularly monitor and evaluate TB programmes, surveillance data should also be used to conduct more in depth analysis to guide further improvement of TB control.

BCG VACCINATION

In the 53 countries of the World Health Organization region of Europe, 34 have a universal BCG vaccination programme, 14 countries used to recommend BCG vaccination for everyone but currently do not, three countries never had a universal BCG vaccination programmes, and for three countries data are not available [25]. In 2006, the method of BCG vaccination in France was changed to an intradermal BCG device. In July 2007, the French policy of mandatory BCG immunisation was changed to vaccination of children considered at high risk of TB. An assessment of the effects of these two changes on vaccination coverage showed that the sales of BCG to private pharmacies decreased considerably after the device for vaccination was changed [26]. Studies among children in whom BCG was recommended according to the 2007 policy showed that 40–51% of children in private practices had been vaccinated and 73% of children in the public sector had been vaccinated. It is important to assess whether a new policy is satisfactorily implemented. The authors of the paper recommended that in France, training of doctors in intra-dermal vaccination and communication on the new vaccination policy should be strengthened [25].

ROSSIGNOL *et al.* [27] studied what factors influenced whether a child would receive a BCG vaccination in France after the policy for BCG vaccination had changed. Vaccination had been administered more often to children aged >6 months, living in a region with a high TB incidence, planning to travel to TB endemic regions, or being at higher risk of TB according to their general practitioner's opinion. If their general practitioners had good knowledge of vaccination guidelines and perceived TB as a common disease children were also more frequently vaccinated. Thus, education of general practitioners might improve BCG vaccination coverage.

Despite the fact that BCG vaccination is an old intervention in TB control, and Europe represents a relatively homogeneous setting, discrepancies on how to implement it at the public health level exist. Further research is necessary to better define the role that BCG today and new vaccines under development tomorrow play or will play under the perspective of eliminating TB from the continent.

LESSONS LEARNED

1) TB outbreaks frequently originate from clinical mistakes in diagnosing and treating TB. In many of the reviewed studies extensive efforts were performed to manage the outbreak. 2) The problems identified by the reviewed studies shows the importance of surveillance information to plan for better control and possible elimination. 3) Even though BCG vaccination has been used for many decades in Europe, differences in implementation of BCG vaccination exist.

IMPLICATIONS FOR TB CONTROL AND ELIMINATION IN EUROPE

The publications on TB in 2011 in *Eurosurveillance* and other journals (six from the UK, three from Italy, two from Sweden and France, two covered the whole EU and six were from a single European country each) provided information on topics (TB outbreaks, TB surveillance and BCG vaccination) which are relevant to control and eliminate TB in the countries of Europe.

How do we define control and elimination? TB control is the strategy aimed at reducing the incidence of TB infection and, consequently, of TB disease, being based on early diagnosis and treatment of infectious cases of TB. Less and less new people in the community will be exposed to a contact with the bacilli and will develop the disease [28].

After having controlled TB, the following step is decreasing the prevalence of TB infection. TB elimination is, in practice, a strategy aimed at reducing the prevalence of TB infection, based on preventive treatment of latently TB infected individuals. By reducing the large pool of infected individuals, future cases of TB will be prevented. The definition of TB elimination is the point at which less than one infectious (sputum-smear positive) case per 1 000 000 inhabitants emerges annually in the general population [29].

To reach TB elimination we need to ensure that latently infected individuals and individuals with TB disease are correctly diagnosed, notified and treated, and that monitoring and evaluation is performed. This is the challenge for the years to come. A good collaboration between the European Respiratory Society (a respiratory society of clinicians) and ECDC (an infectious disease public health organisation) will be important to guide this effort. An excellent example of this collaboration is the development and publication of the European Union Standards for TB Care, which are now available [8, 9].

STATEMENT OF INTEREST

None declared.

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