Askeland Winje, S Sandbu (Norway), M Korzeniewska-Kosela (Poland), A Fonseca Antunes (Portugal), P Stoicescu (Romania), I Solovic (Slovakia), J Sorli (Slovenia), E Rodriguez Valin (Spain), V Romanus (Sweden), P Helbling (Switzerland), J Watson (United Kingdom).

Acknowledgements

Thanks to H Therre (Eurosurveillance), who supported the idea of the survey, and to D Che, D Lévy-Bruhl (InVS), and the members of the EuroTB Advisory Committee who provided useful comments and suggestions for designing the survey questionnaire and in drawing conclusions.

References

1. EuroTB (InVS/KNCV) and the national coordinators for tuberculosis surveillance in the WHO European Region. Surveillance of tuberculosis in Europe. Report on tuberculosis cases notified in 2003, Institut de Veille Sanitaire, Saint-Maurice, France. September 2005.
2. Trnka L, Dankova D, Zitova J, Cimprichova L, Migliori GB, Clancy L, Zellweger JP. Survey of BCG vaccination policy in Europe: 1994-96. Bull World Health Organ. 1998;76(1):85-91.
3. Trnka L, Dankova D, Svandova E. Six years' experience with the discontinuation of BCG vaccination. 1. Risk of TB infection and disease. Tuber Lung Dis. 1993;74(3):167-72.
4. Kelly P, McKeown D, Clancy L. Neonatal BCG vaccination in Ireland: evidence of its efficacy in the prevention of childhood tuberculosis. Eur Respir J. 1997;10(3):619-23.
5. Wasz-Hockert O, Genz H, Landmann H and Ocklitz HW. The effects of systematic BCG vaccination of newborns on the incidence of postprimary tuberculosis meningitis in childhood. Bull Int Union Tuberc Lung Dis. 1988 Dec;63(4):49-51.
6. Romanus V. Svennson A, Hallander O. The impact of changing BCG coverage on tuberculosis incidence in Swedish born children between 1969 and 1989. Tuber Lung Dis. 1992;73(3):150-61.
7. Romanus V, Hallander HO, Wahlen P, Olinder-Nielsen AM, Magnusson PH, Juhlin I. Atypical mycobacteria in extrapulmonary disease among children. Incidence in Sweden from 1969 to 1990, related to changing BCG-vaccination coverage. Tuber Lung Dis. 1995;76(4):300-10.
8. Villate JL, Cabriada V, Sanz A, Urcelay MI, Galarza A, Díez I et al. Infección por Mycobacterium avium en la población infantil de Bizkaia. Influencia de la BCG. Arch Bronconeumol. 1999; 35 (Supl.2): 52.
9. Romanus V. Selective BCG vaccination in a country with low incidence of tuberculosis. Euro Surveill. 2006;11(3): 14-7
10. Lamden K, Watson J M, Knerer G, Ryan M J, Jenkins P A. Opportunist mycobacteria in England and Wales: 1982 to 1994. Communicable Disease Review. 1996;11(6). http://www.hpa.org.uk/cdr/archives/CDRreview/1996/cdrr1196.pdf
11. Romanus V, Fasth A, Tordai P, Wiholm BE. Adverse reactions in healthy and immunocompromised children under six years of age vaccinated with the Danish BCG vaccine, strain Copenhagen 1331: implications for the vaccination policy in Sweden. Acta Paediatr. 1993;82(12):1043-52.
12. WHO. International Travel and Health, Geneva, 2005 (http://whqlibdoc.who.int/ publications/2005/9241580364_chap6.pdf) Last accessed 16/12/2005.
13. Department of Health. Immunisation against infectious diseases. HMSO, London. 1996. (http://www.dh.gov.uk/assetRoot/04/07/29/84/04072984.pdf). Last accessed 21/02/2006.
14. BCG-protocol. National centre for advice to travellers (LCR Amsterdam), 1999 (in Dutch).
15. Colditz GA, Berkey CS, Mosteller F, Brewer TF, Wilson M, Burdick E, Fineberg HV. The efficacy of bacillus Calmette-Guerin vaccination of newborns and infants in the prevention of tuberculosis: meta-analyses of the published literature. Pediatrics. 1995;96(1 Pt 1):29-35.
16. WHO Global Tuberculosis Programme and Global Programme on Vaccines. Statement on BCG revaccination for the prevention of tuberculosis. Wkly Epidemiol Rec. 1995;70(32):229-31.
17. Hersh AL, Tala-Heikkila M, Tala E, Tosteson AN, Fordham von Reyn C. A cost-effectiveness analysis of universal vs. selective immunisation with M. bovis bacilli Calmette – Guérin in Finland. Int J Tuberc Lung Dis. 2003;7(1):22-9.
18. Trnka L, Dankova D, Svandova E. Six years' experience with the discontinuation of BCG vaccination. 2. Cost and benefit of mass BCG vaccination. Tuber Lung Dis. 1993;74(4):288-92.

ORIGINAL ARTICLES

Surveillance report

PROSPECTS FOR THE BCG VACCINATION PROGRAMME IN FRANCE

D Lévy-Bruhl

Until recently, the French BCG vaccination programme consisted of a mandatory BCG vaccination before children started at daycare centres, and of re-vaccination of tuberculin-negative children. A re-assessment of this programme has been undertaken in recent years. It has led to the discontinuation of all revaccinations and post-vaccination tuberculin tests except those post-vaccination tuberculin tests performed as part of a diagnosis of tuberculosis infection or disease or of the follow-up of health or social workers for whom BCG vaccination remains mandatory. Based on an estimate of the epidemiological impact of either selective vaccination of high risk children or discontinuation of BCG vaccination, and taking into account the risk-benefit balance that can be made of the two options, the Conseil Supérieur d'Hygiène Publique de France (CSHPF, national high council of public hygiene) has recommended a change to selective vaccination. However, the committee has proposed the strengthening of other control measures aimed at decreasing the risk of infection for children, as a pre-requisite to the implementation of this strategy. This position is made more complex by the withdrawal of the multipuncture technique in early 2006, previously used in France in more than 90% of BCG primary vaccinations.

Département des maladies infectieuses - Institut de Veille Sanitaire, Saint-Maurice, France

Euro Surveill 2006;11(3): 11-4 Published online March 2006

Key words: BCG, vaccination, France, vaccination programme

Introduction

In France, primary BCG immunisation is mandatory for children before they can enter daycare centres or the care of childminders, and must be given by the age of six years at the latest, when school entry is compulsory. BCG is also recommended in the first month of life for high risk children. Until June 2004, a tuberculin test was required between 3 and 12 months after vaccination and at 11-13 years of age, followed in both cases by revaccination, if negative. Following an evaluation initiated by the publication of a report by the national institute for public health surveillance, the Institut de Veille Sanitaire (InVS), routine tuberculin testing in children and revaccination were discontinued in July 2004, as was revaccination for exposed professionals [1]. Tuberculin testing remains indicated as a diagnosis tool for tuberculosis infection or disease and for the follow up of health or social workers for whom BCG vaccination is still mandatory.

The InVS report also questioned the need for universal BCG immunisation of children. For the period 2000-2002, the incidence of positive sputum smear tuberculosis cases was 4.6 per 100 000 (5.7 when correcting for the lack of exhaustiveness of the notification). For the 1998-2002 period, the incidence of meningitis in children less than five years old was 0.4 per 10 millions. This epidemiological situation was thus very close to the threshold values proposed by the International Union Against Tuberculosis and Lung Diseases for possible discontinuation of BCG vaccination [2]. An overview of tuberculosis control strategies, and an epidemiological assessment of the consequences of reducing BCG vaccination activities was conducted in the context of a multi-disciplinary evaluation by the national institute for health and medical research (Inserm), at the request of the health authorities.

In this context, InVS assessed the epidemiological impact of discontinuing universal children BCG immunisation. Several arguments were in favour of also studying the impact of a strategy targeted on children at risk. The data from mandatory notification of tuberculosis cases in France show that the risk of tuberculosis is highly heterogenous, according to nationality or country of birth. In 2003, the incidence of the disease was 10.2 per 100 000 but was tenfold higher in non-French nationals than in nationals (respectively 72.1 versus 8.1 per 100 000, all ages together, and 18.7 versus 1.8 per 100 000, in children under 15 years old) [3]. In 2003, eight out of the then 15 European Union (EU) countries had chosen to target children at high risk of tuberculosis for immunisation [4]. By 2005, nine of the 25 member states of the EU had applied such targeted strategies [5].

Two scenarios for changes in BCG immunisation programme in France were therefore assessed: the total discontinuation of any vaccination and targeted vaccination for children living in a risk environment.

Methods

Assessment of the impact of total discontinuation of immunisation

The number of excess tuberculosis cases that would be observed if immunisation were completely discontinued is equivalent to the number of cases of tuberculosis avoided each year by the current immunisation programme. This figure was estimated from BCG effectiveness estimates, immunisation coverage and tuberculosis notification data [6]. Based on published data, we considered the hypothesis of a protection provided by BCG lasting until the age of 15 years, and concerning only vaccinated persons (no indirect protection for unvaccinated subjects due to the absence of reduction of the circulation of the tuberculosis bacillus, as childhood tuberculosis is rarely contagious). Two hypothesis on vaccine effectiveness were considered. In the basic hypothesis, BCG effectiveness was considered to be 75% for tuberculous meningitis and miliary, the most severe localisations of the disease, and 50% for other sites, mainly pulmonary. In the hypothesis most favourable to immunisation, considered in order to avoid underestimating the number of additional tuberculosis cases that would follow the reduction in BCG immunisation activities, the effectiveness of BCG was considered 85% on tuberculous meningitis and miliary and 75% on other sites.

The numbers of observed cases were estimated from mandatory notification data between 1997 and 2002, corrected for lack of exhaustiveness, on the basis of a notification rate of 75% for childhood tuberculosis [6]. The data on immunisation coverage are available through the analysis at national level of health certificates completed at 24 months of age for each child and from a national survey carried out in schools in 1997, in children 5 to 6 years old [7,8].

Assessment of the impact of immunisation targeted on children at risk

The definition used was based on the Swedish experience and matched the French epidemiology of tuberculosis. It included children meeting at least one of the following criteria:

- A child coming from a country with high tuberculosis prevalence;
- A child born into a family coming from a country with high tuberculosis prevalence;
- A child of any origin with a history of tuberculosis in his/her family.

Africa, Asia (except Japan), Central and South America, the Russian Federation and Baltic countries were considered as areas or countries with high tuberculosis prevalence.

Among total childhood TB cases, the proportion of those occurring in at-risk children was estimated at 75%, based on a study carried out in 1997 in the Parisian area [9].

Two levels of immunisation coverage of at-risk children were considered: 95% and 50%. Interrupting the universal immunisation of children could lead to a decrease in the current immunisation coverage among targeted populations, as such a decision would de facto imply the discontinuation of mandatory vaccination.

Based on data from a survey carried out by the National Institute for Demographic Studies (INED) [10], the number of children at risk was estimated at 14% of each yearly birth cohort (that is about 100 000 children out of a birth cohort of about 750 000).

Assessment of adverse effects of BCG immunisation

Frequency of clinically significant adverse effects was studied in the evaluation carried out by Inserm [4]. BCG immunisation was estimated to result each year in about 300 lymphadenitis (corresponding to a rate of about 40 per 100 000 vaccinated children) and about 12 disseminated BCG infections (corresponding to a rate of about 1.6 per 100 000 vaccinated children), the latter occurring in children with severe immunodeficiency. These data have been used to calculate the decrease of the expected number of side effects for the different options of reduction of immunisation activities.

Results

The epidemiological consequences of the different immunisation options that were considered, for children under 15 years old, are summarised in the table. If immunisation is restricted to children at risk, there might be 80 to 200 additional cases per year in the non vaccinated low risk population, corresponding to an incidence rate between 0.9 and 2.3 per 100 000 non vaccinated children. In case of a decreased coverage in the targeted population, additional cases would also occur in children at risk. For a vaccination coverage of 50%, annual additional cases could range from around 200 to almost 500,

corresponding to an incidence rate in non vaccinated children between 2,1 and 5,2 per 100 000. If vaccination were discontinued, 320 to 800 additional cases might occur every year, depending on the hypothesis for vaccine effectiveness, corresponding to an estimated incidence of additional tuberculosis cases between 3,2 and 8,0 per 100 000.

The projected increase to the current incidence in children 0-14 years, and the number of additional cases and incidence in non-vaccinated children, broken down for pre-school (0-5 years) and school-age children (6 to 14 years) are also presented in the table.

As about 15% of the children can be considered to be at risk, at least 85% of side effects due to BCG would be avoided through targeting immunisation to those children.

Discussion

The first option analysed the total discontinuation of BCG vaccination. Our study shows that such a choice could lead to several hundreds of additional tuberculosis cases in children each year. These results are in accordance with observations from other European countries, particularly Sweden, when immunisation was first completely discontinued [11], and are in favour of maintaining the current programme. In another hand, such an option would induce several disseminated BCGitis cases each year.

The alternative option analysed was the targeting of BCG vaccination on children living in a risk environment. Based on our assessment, this programme would avoid approximately three quarters of tuberculosis cases that are currently avoided by the universal vaccination, while requiring the vaccination of only about 15% of children. The real impact of this option will depend on the ability in maintaining a high vaccine coverage among children at risk. Such an option would also facilitate the interpretation of tuberculin tests performed in non-vaccinated children exposed to tuberculosis cases.

To analyse the epidemiological impact of immunisation, we relied on hypotheses or point estimates, particularly those concerning the exhaustiveness of tuberculosis notifications in France, the vaccine effectiveness, the proportion of tuberculosis cases occurring among children with a risk factor, and the size of this latter population. The resulting estimates should be considered as orders of magnitude of the current or future impact of different immunisation options. Nevertheless, the conclusions on the relevance of the different options can be considered as fairly reliable. It is worth mentioning that in this analysis, we did not consider the increase of incidence of non-tuberculosis mycobacterial diseases that would follow the decrease in BCG immunisation coverage, and that only mainland France was considered.

These results were presented in 2005 to the Comité Technique des Vaccinations (CTV, national advisory board on vaccination) and to the Conseil Supérieur d'Hygiène Publique de France (CSHPF, national high council of public hygiene). Both recommended that the Ministry should adopt the BCG vaccination strategy targeted at children at high risk of tuberculosis. They also recommend, as a prerequisite before actually switching to such a strategy, the strengthening of other tuberculosis control measures aimed at reducing the risk of infection for children (such as early identification of cases, tracing of secondary cases and of the source of contamination, and supervision of treatment of cases), in the context of a national tuberculosis control plan. Following this recommendation, the Ministry of Health has, in early 2006, set up an ad hoc national committee that has began to formulate such a document.

The schedule for implementation of a targeted strategy will have to take into account a new situation that could influence the BCG vaccination coverage and the acceptability of maintaining the current programme. Since early 2006, the multipuncture device used in France for more than 90% of BCG primary vaccinations, is no more available. Administrating the vaccine intradermally in young infants is a difficult technique for untrained vaccinators. Currently, more than 80% of children are vaccinated in their first year of life. A survey of over 800 general practitioners carried out in 2005 found that fewer than 30% felt ready to routinely immunise very young infants intradermally [12]. To avoid the problems that would arise from mandatory vaccination before entering school or daycare centre, when only intradermal inoculation would be possible, a strategy targeting the most exposed children, who are mainly those from families of foreign origin, should perhaps be considered rapidly. The feasibility and social acceptability of this option would have to be ascertained beforehand.

Acknowledgements

We wish to thank the members of the Inserm collective expertise for their contribution in this analysis, as well as Didier Che and Bénédicte Decludt† from InVS, for supplying epidemiological data on tuberculosis.

Table

Estimates of the epidemiological impact of various BCG vaccination strategies or level of coverage according to BCG effectiveness assumptions, France

		Estimated additional tuberculosis cases (incidence rate per 100 000 in non vaccinated)			Estimated avoided BCG side effects
		0-5 years old	6-14 years old	Total 0-14 years old % increase/universal vaccination	
Targeted BCG – Vaccine coverage 95%	Low BCG effectiveness scenario	31 (1.0)	49 (0.9)	80 (0.9) 20%	10 disseminated BCG infections 260 lymphadenitis
	High BCG effectiveness scenario	68 (2.3)	132 (2.4)	200 (2.3) 51%	
Targeted BCG – Vaccine coverage 50%	Low BCG effectiveness scenario	75 (2.3)	117 (1.9)	193 (2.1) 49%	11 disseminated BCG infections 280 lymphadenitis
	High BCG effectiveness scenario	166 (5.1)	320 (5.3)	486 (5.2) 124%	
Discontinuation of BCG	Low BCG effectiveness scenario	124 (3.5)	194 (3.0)	318 (3.2) 81%	12 disseminated BCG infections 300 lymphadenitis
	High BCG effectiveness scenario	274 (7.8)	528 (8.1)	800 (8.0) 204%	

→→→

References

1. Lévy-Bruhl D, Barrault Y, Decludt B, Schwoebel V. Impact épidémiologique d'une modification de la politique de vaccination par le BCG en France, Editions InVS 2001, available at http://www.invs.sante.fr/publications/rap_bcg_1101/index.html
2. Criteria for discontinuation of vaccination programmes using Bacille Calmette-Guerin (BCG) in countries with a low prevalence of tuberculosis. A statement of the International Union Against Tuberculosis and Lung Disease. Tuber Lung Dis. 1994 Jun;75(3):179-80.
3. Che D, Decludt B. Peut-on parler d'émergence de la tuberculose en France en 2003. Antibiotiques. 2005; 7:165-70
4. Expertise Collective. Tuberculose : Place de la vaccination dans la maîtrise de la maladie. Editions INSERM 2004.
5. A Infuso, D Falzon on behalf of the EuroTB network. European survey of BCG vaccination policies and surveillance in children, 2005. Euro Surveill. 2006;11(3): 6-11
6. Lévy-Bruhl D. Estimation de l'impact épidémiologique de différentes options de vaccination BCG en France. Rev Epidemiol Santé Publique. 2005 ;53:501-8
7. Badeyan G, Guignon N. Vaccination contre la tuberculose. DREES. Études et Résultats 1999, available at http://www.sante.gouv.fr/drees/etude-resultat/er-pdf/er008.pdf
8. Antona D, Bussière E, Guignon N, Badeyan G, Lévy-Bruhl D. La couverture vaccinale en France en 2001. Bulletin Epidémiologique Hebdomadaire. 2003.36:169-172
9. Decludt B. Infection et maladie tuberculeuse de l'enfant en Ile-de-France en 1997. Institut de Veille Sanitaire, Décembre 2000, available at http://www.invs.sante.fr/publications/tuberculose2000/index.html
10. Tribalat M. Une estimation des populations d'origine étrangère en France en 1999. Population-F 2004, 58(1)
11. Romanus V. Experiences from selective BCG vaccination in Sweden during the period from 1975 to 2004. Euro Surveill. 2006;11(3): 14-7.
12. De La Rocque F, Cohen R, Vie Le Sage F, Bocquet A, Boucherat D, Lévy Bruhl D. Enquête sur les pratiques actuelles et futures du vaccin contre la tuberculose auprès des pédiatres et généralistes en France. Archives de Pediatrie. 2005;12:1665-9

ORIGINAL ARTICLES

Surveillance report

SELECTIVE BCG VACCINATION IN A COUNTRY WITH LOW INCIDENCE OF TUBERCULOSIS

V Romanus*

In 1975 the BCG vaccination policy in Sweden changed from routine vaccination of all newborn infants to selective vaccination of groups at higher risk. This report aims to evaluate the present BCG policy, with focus on the tuberculosis situation in Sweden during the period from 1989 to 2005. The population structure in Sweden has changed, with increasing numbers and proportions of people who were born outside Sweden, especially in countries with high prevalence of tuberculosis. BCG vaccination coverage fell from more than 95% before 1975 to less than 2% in 1976 to 1980, and then again increased to around 16 % (corresponding to about 88% of the risk group recommended for vaccination). The increasing proportion of foreign born tuberculosis patients among all tuberculosis cases of illness in Sweden, and the high age-specific incidence of tuberculosis in the childbearing age groups in the foreign-born population, indicate the need to continue selective vaccination of children in families originating from countries with high tuberculosis incidence. The cumulative incidence of tuberculosis in the 30 cohorts born in Sweden after 1974 and observed to the end of 2004 was estimated at 0.5 cases per 100 000 person-years.

Sweden still has one of the lowest incidences of tuberculosis in the world, which means a minimal average risk of infection for the majority of children born to Swedish parents. The observed increase of tuberculosis in 2005, partly attributed to an outbreak at a day nursery, is a reminder of the serious consequences of delayed diagnosis.

Intensified active case finding is the most important action to prevent childhood tuberculosis, by means of eliminating the sources of infection to prevent transmission to the child population. Early detection and treatment of infected children is necessary to prevent development of serious disseminated tuberculosis.

Swedish Institute for Infectious Disease Control, Solna, Sweden

Euro Surveill 2006;11(3): 14-7 Published online March 2006

Key words: selective BCG vaccination, tuberculosis in children, tuberculosis in Sweden

Introduction

In 1975 the BCG vaccination policy in Sweden changed from routine vaccination of all newborns to selective vaccination. The impact of the changed BCG policy on tuberculosis among children born in Sweden has previously been analysed and reported [1].

This report aims to evaluate the selective vaccination program in relation to the epidemiological tuberculosis situation in Sweden, with focus on the period from 1989 to 2005. It is based on impact studies conducted following the change towards selective BCG vaccination. The analysis is based mainly on routine surveillance of BCG vaccination coverage, as reported once a year for two year old children, and on information from the statutory notifications of tuberculosis [2].

BCG vaccination policy in Sweden

Starting in the 1940s, vaccination against tuberculosis was offered to almost all newborns and also to school children who were nonreactive to the tuberculin skin test at seven and 15 years of age. General neonatal vaccination was ended in 1975. Tuberculin skin testing and revaccination of nonreactive schoolchildren was ended in 1965 for seven year olds and in 1986 for 15 year olds [3].

The main reason for the changed BCG policy in 1975 was an increased frequency of BCG vaccine induced osteomylitis (BCG osteitis), with 29 cases per 100 000 vaccinated infants during the period from 1972 to 1974 [1,4]. In view of the declining incidence of tuberculosis in Sweden, the risk of infection and disease was estimated to be much lower in the Swedish child population than the risk of serious vaccine adverse reactions. However, it was still recommended that vaccination be offered to children who had higher risk of exposure to tuberculosis than the general population [5].