Towards elimination: measles susceptibility in Australia and 17 European countries

Nick Andrews,[a] Annedore Tischer,[b] Annette Siedler,[b] Richard G Pebody,[a] Christopher Barbara,[c] Suzanne Cotter,[d] Arnis Duks,[e] Nina Gacheva,[f] Kriz Bohumir,[g] Kari Johansen,[h] Joel Mossong,[i] Fernando de Ory,[j] Katarina Prosenc,[k] Margareta Sláčiková,[l] Heidi Theeten,[m] Marios Zarvou,[n] Adriana Pistol,[o] Kalman Bartha,[p] Dani Cohen,[q] Jo Backhouse,[r] Algirdas Griskevicius[s] & Anthony Nardone[a]

Objective To evaluate age-specific measles susceptibility in Australia and 17 European countries.

Methods As part of the European Sero-Epidemiology Network 2 (ESEN2), 18 countries collected large national serum banks between 1996 and 2004. These banks were tested for measles IgG and the results converted to a common unitage to enable valid intercountry comparisons. Historical vaccination and disease incidence data were also collected. Age-stratified population susceptibility levels were compared to WHO European Region targets for measles elimination of < 15% in those aged 2–4 years, < 10% in 5–9-year-olds and < 5% in older age groups.

Findings Seven countries (Czech Republic, Hungary, Luxembourg, Spain, Slovakia, Slovenia and Sweden) met or came very close to the elimination targets. Four countries (Australia, Israel, Lithuania and Malta) had susceptibility levels above WHO targets in some older age groups indicating possible gaps in protection. Seven countries (Belgium, Bulgaria, Cyprus, England and Wales, Ireland, Latvia and Romania) were deemed to be at risk of epidemics as a result of high susceptibility in children and also, in some cases, adults.

Conclusion Although all countries now implement a two-dose measles vaccination schedule, if the WHO European Region target of measles elimination by 2010 is to be achieved higher routine coverage as well as vaccination campaigns in some older age cohorts are needed in some countries. Without these improvements, continued measles transmission and outbreaks are expected in Europe.

Bulletin of the World Health Organization 2008;86:197–204.

Une traduction en français de ce résumé figure à la fin de l'article. Al final del artículo se facilita una traducción al español. **الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.**

Introduction

Live attenuated measles vaccines have been available since the early 1960s and are now in use worldwide. They have the potential to achieve highly effective measles control and elimination, as observed in the Americas.[1]

In 1998, the WHO European Region agreed to eliminate measles in Europe by 2007.[2] By 2002, the incidence of measles in Europe was estimated to be below 5 per 100 000 and a strategic plan was developed which outlined an approach for achieving elimination by the revised year of 2010.[3–5] The approach focused on each member state delivering two doses of measles vaccine through the routine programme at very high (> 95%) coverage, undertaking catch-up campaigns to address older susceptible cohorts, strengthening surveillance through case-based reporting and laboratory confirmation

[a] Centre for Infections, Health Protection Agency, 61 Colindale Avenue, London NW9 5EQ, England.
[b] Robert Koch Institute, Berlin, Germany.
[c] St Luke's Hospital, G'Mangia, Malta.
[d] Health Protection Surveillance Centre, Dublin, Ireland.
[e] Public Health Agency, Riga, Latvia.
[f] National Center of Infectious and Parasitic Diseases, Sofia, Bulgaria.
[g] National Institute for Public Health, Prague, Czech Republic.
[h] Swedish Institute for Infectious Disease Control, Sweden.
[i] Laboratoire National de Santé, Luxembourg.
[j] Centro Nacional de Microbiología, Madrid, Spain.
[k] National Public Health Institute of Slovenia, Ljubljana, Slovenia.
[l] Public Health Authority of the Slovak Republic, Bratislava, Slovak Republic.
[m] University of Antwerp, Antwerp, Belgium.
[n] Immunology Department, Nicosia General Hospital, Nicosia, Cyprus.
[o] National Centre for Communicable Diseases Prevention and Control, Bucharest, Romania.
[p] National Center for Epidemiology, Budapest, Hungary.
[q] Israel Centre for Disease Control, Tel Aviv University, Israel.
[r] Centre for Infectious Diseases and Microbiology, Westmead Hospital, Australia.
[s] Lithuanian AIDS Centre, Vilnius, Lithuania.
Correspondence to Nick Andrews (e-mail: nick.andrews@hpa.org.uk).
doi:10.2471/BLT.07.041129
(*Submitted: 9 March 2007 – Revised version received: 22 June 2007 – Accepted: 16 July 2007 – Published online: 20 December 2007*)

of suspect cases, and improving communication about the benefits and risks of vaccination.

To measure progress towards elimination and to identify populations for vaccination campaigns, age-group specific susceptibility targets were established that corresponded to an effective reproduction number less than one, and hence elimination.[6,7] These age-specific susceptibility levels could be estimated from high-quality historical vaccine coverage data (but only in populations with no measles transmission) or from population serological surveillance data.[8] Progress towards elimination can also be assessed from age-specific incidence data, but this is less useful when close to elimination because it is possible for susceptible age cohorts to go unnoticed for many years. Outbreaks in older susceptible cohorts have occurred in Europe in recent years and are serious because of the greater morbidity caused by the disease in older individuals.[9,10] The size of outbreaks generated by imported measles cases can also be used to determine the effective reproductive number if cases are confirmed and extensive investigation to identify all cases in a cluster is performed.[7]

In many countries, high-quality historical vaccine coverage and disease incidence data are not available so serological surveillance is an essential part of assessing population immunity. Even in countries with good vaccine coverage and disease incidence, data serological surveillance can help identify older susceptible cohorts and also problems with vaccine effectiveness. Although serological surveillance has clear potential, in the past it has been difficult to compare countries because they have used different methods for testing serum antibody levels.

To obtain standardized serological data, countries participated in the measles work-package of the European Sero-Epidemiology Network 2 (ESEN2).[11] The ESEN2 project was a continuation of the original ESEN project with the same purpose of coordinating and harmonizing serological surveillance in Europe.[8,12,13] The measles component of the original project included seven countries, and identified four with a low risk of outbreaks (England and Wales, Finland, France and the Netherlands) and three with an intermediate/high risk of measles outbreaks (Denmark, Germany and Italy). Germany and Italy have since experienced outbreaks, highlighting the importance of seroepidemiological surveys and the need for targeted action based on the results.[14,15]

In this paper, the results from measles serological surveillance in participating countries, as well as data on measles vaccine coverage and disease incidence, are presented and compared to the WHO European Region elimination targets. The results are used to identify susceptible cohorts to help inform future vaccination strategies as well as to identify discordance with routine coverage estimates suggesting possible problems with vaccine effectiveness or coverage data.

Methods

Serum bank collection

Each participating country was required to test a serum bank representative of the general population in their country using their usual measles assay for measuring antimeasles IgG antibody. ESEN project guidelines recommended that approximately 100 sera be tested in each 1-year age band of those < 20 years of age and 200 in each 5-year age band in those aged ≥ 20 years. Although it was preferable that countries collected and tested the bank during the ESEN2 study (2001–2003), some countries had already collected and tested such banks between 1996 and 2000. Each country obtained ethical approval from the appropriate national authorities for the serum collections.

Vaccine programme, coverage and measles incidence

A questionnaire was distributed to each country and completed in 2001/2002 to obtain information on current and historical measles vaccine programme organization, vaccine coverage estimates by age since 1970 and measles incidence by age group (clinical notifications and laboratory confirmations) since 1970. This information was subsequently updated in 2006 using data from the WHO centralized information system for infectious diseases (CISID).[16]

Standardization and reference assay

A standardization panel of 151 sera was prepared by the measles, mumps and rubella (MMR) vaccine reference centre (Robert Koch Institute, Berlin, Germany) and tested by each participating country at the same time as the serum bank. Each country was required to use the same measles assay for testing the panel as used for testing the national serum bank. Standardization equations were obtained by regression of local results against the reference centre and were used to convert the titres of the national serum bank to the unitage of the reference centre (ESEN2 units). Further details of the standardization methodology, including the back-standardization method used for countries that had already tested their national serum bank, are given by Kafatos.[17] Details of the measles assays used by the participating countries and the selection of the standardization equations are given by Tischer.[18] The assay of the reference laboratory to which results were standardized was the enzyme immunoassay (EIA, Enzygnost, Dade Behring). The equivocal range for this assay was 0.15–0.35 IU/ml. After standardization, the results were classified as negative, equivocal or positive using these cut-offs. Comparisons of panel results obtained by this EIA and by the gold standard plaque neutralization test suggested that the equivocal titres could be regarded as positive.[18]

Data analysis

The proportion seropositive or equivocal (antimeasles antibody concentration > 0.15 IU/ml) was calculated in each age group along with 95% exact confidence interval and plotted to form a seroprofile. Reported first-dose vaccine coverage at 24 months for each age group was added along with an indication of the number of doses and type of measles vaccine scheduled for each age group. Second-dose vaccine coverage was not generally available and is therefore not shown.

The proportion seronegative in each country by age was compared to the WHO elimination targets of < 15% in those aged 2–4 years, < 10% in those aged 5–9 years and < 5% in those aged 10–19, 20–39 and 40+ years. Countries were grouped into those with low susceptibility to outbreaks (WHO elimination targets met for 2–4 year-old and 5–9 year-old age groups and at least two of the three older age groups), intermediate susceptibility (targets missed in two of the following age groups: 10–19, 20–39 or 40+) and higher susceptibility (targets missed in either

Table 1. **Year and number of samples collected in national serum banks of participating countries**

Country or area	Type of sample	Year of collection	Age range collected (years)	No. samples aged < 20 years	No. samples aged ≥ 20 years
Australia	Residual	2002	1–34	2496	1278
Belgium	Residual	2002/2003	1–60+	1953	1421
Bulgaria	Residual	2001–2004	1–60+	969	697
Cyprus	Residual/Population	2003	1–50	1901	1000
Czech Republic	Population	2001	1–60+	1695	1318
England and Wales	Residual	2000	1–60+	1814	1756
Hungary	Residual	2003	1–60+	2014	1476
Ireland	Residual	2003	1–60+	1214	1376
Israel	Residual	1998	1–60+	1866	1484
Latvia	Population	2003	1–60+	1594	1432
Lithuania	Residual	2003	1–60+	1872	1480
Luxembourg	Population	2000/2001	4–60+	1381	1298
Malta	Residual	2003	1–60+	820	1047
Romania	Residual	2002	1–60+	2304	1535
Slovakia	Population	2002	1–60+	2080	1560
Slovenia	Residual	1999/2000	1–60+	2000	1399
Spain	Population	1996	2–39	1926	1679
Sweden	Population	1996/1997	[a]	994	398

[a] Sera collected from 2, 5, 8, 10, 14, 17, 20–34 and 65+ age groups.

2–4 or 5–9 year-old age groups). More emphasis is placed on the younger age groups because of increased spread of disease in the young and also because this is likely to reflect recent problems in vaccine coverage.

Results

Serum bank collection

Australia and seventeen countries in the WHO European Region undertook testing for measles IgG antibodies of serum banks collected between 1996 and 2004 (Table 1). Serum banks were obtained either through residual sera collected during routine laboratory testing (11 of 18 countries), by population-based random sampling (6 of 18), or a combination of these two methods (1 of 18). Sera were collected from all age groups, were evenly distributed between males and females, and were geographically representative of each country. Although using residual sera raises the possibility of bias it is unlikely that for measles immunity this would be large. Not all countries met the sample size targets with numbers too small for evaluation ($n < 75$) in under 2 year-olds in three countries (Bulgaria, the Czech Republic and Malta). In Spain, there was no sampling in under 2 year-olds, and in Luxembourg there was no sampling in under 4 year-olds and only 37 samples from 4 year-olds.

Vaccine programme, coverage and measles incidence

Routine measles vaccination has been in place for two or more decades in all the participating countries. All countries have now adopted a two-dose MMR vaccine schedule (Table 2). The first country to introduce a two-dose schedule was Slovenia in 1974 and the last was Spain in 1996. Most countries moved from one measles dose to a two-dose MMR vaccine schedule. In England and Wales and Romania large catch-up campaigns in older children were also performed when the MMR vaccine was introduced.[19,20]

Measles vaccine coverage data were usually obtained by routine administrative assessment (which may be subject to bias) or special surveys (which may be imprecise). Coverage data were only consistently available for the first dose as assessed at 24 months. The five-year mean reported first-dose coverage level (1997–2001) varied from 77% in Ireland to nearly 100% in Hungary (Table 2).

By 2001, reported measles incidence had declined to very low levels with clinical and laboratory notifications (< 2/100 000) in all countries except for Ireland where the incidence of notifications was 6/100 000 (Table 2). The last year before 2001 with significant measles incidence (> 20/100 000) varied from 1983 in Cyprus and Sweden, to 1997 in Belgium and 2000 in Ireland (Table 2).

Seroprofiles and comparisons to WHO age-specific targets for measles susceptibility

Measles seroprofiles, first-dose measles vaccine coverage and the vaccine(s) recommended for each age cohort for the 18 countries are available from the ESEN2 pages of the Health Protection Agency website: http://www.hpa.org.uk/esen2. These seroprofiles can be used to help identify susceptible age cohorts in each country that may have arisen through low vaccine coverage, poor effectiveness of the vaccine or a reduction in measles transmission in unvaccinated cohorts. The seroprofiles show that the proportion seropositive or equivocal increases from age 1–3 years in most countries, reflecting vaccine administration. In the older prevaccination cohorts (typically aged over 35 years), high seroprevalence is generated through natural exposure, whereas in the younger cohorts seroprevalence should reflect mostly vaccination. In the age cohorts not scheduled for more than one dose, reported vaccine coverage agrees approximately with measles seroprevalence in all countries, with the exceptions of Bulgaria, Latvia and Romania where reported official age-specific coverage is much higher than the proportion seropositive.

Table 2. **Measles vaccination policies, reported incidence in 2001and year of previous major outbreak**

Country or area	Year of introduction		Year two-dose MMR vaccine introduced	Age of vaccination in 2001		Mean first dose coverage 1997–2001 (%)	2001 reported measles incidence (per 100 000)	Year incidence last exceeded 20 per 100 000
	First routine dose	Second routine dose		First dose (months)	Second dose (years)			
Australia	1975	1993	1993	12	4	91	0.7[a]	1994
Belgium	1985	1994	1994	15	11/12	80	N/A	1997
Bulgaria	1969	1983	2001	13	12	93	0.1[a]	1992
Cyprus	1974	1989	1989	13–15	4–6	88	0[b]	1983
Czech Republic	1969	1975	1987	15	2	96	0.1[b]	1990
England and Wales	1968	1995	1995	12–15	4	88	0.1[a]	1994
Hungary	1974	1990	1991	15	11	100	0.2[a]	1989
Ireland	1985	1992	1992	15	4–5	77	6.3[a]	2000
Israel	1967	1994	1994	12	6	94	0.3[a]	1994
Latvia	1968	1987	2002	15	7	97	<0.1[b]	1987
Lithuania	1966	1992	1998	15	12 6–7[c]	97	0.2[a]	1987
Luxembourg	1986[d]	1994	1994	15–18	5–7	91	1.6[a]	1987
Malta	1983	1992	1995	15	7	90	0.5[a]	1986
Romania	1979	1994	2005	12–15	7	98	<0.1[a]	1998
Slovakia	1969	1977	1992	14	11	99	0[a]	1984
Slovenia	1968	1978	1990	12–18	5–7	92	0[b]	1995
Spain	1978	1996	1996	12–15	3–6	94	0.1[b]	1995
Sweden	1971	1982	1982	18	12	94	<0.1[a]	1983

MMR, measles, mumps and rubella; N/A, not available.
[a] Notifications.
[b] Laboratory confirmations.
[c] Age in 2002.
[d] First year of routine MMR vaccine, measles vaccine used previously.

Table 3 shows the percentage seronegative in five age groups for each country and the classification of countries into low, medium and high risk of measles outbreaks. Three countries (the Czech Republic, Luxembourg and Spain) met the WHO targets for elimination in all age groups and a further four (Hungary, Slovakia, Slovenia and Sweden) only missed the target in the 20–39 year-old age group by < 3.5%. In these countries the risk of measles outbreaks is low. Four countries (Australia, Israel, Lithuania and Malta) had met the recommended WHO susceptibility targets in the under 10 year-old age groups but not for older children/adults and were classified as having intermediate susceptibility. The remaining seven countries (Belgium, Bulgaria, Cyprus, England and Wales, Ireland, Latvia and Romania) had not met the WHO targets for susceptibility in the 2–4 or 5–9 year-old age groups or, with the exception of Romania, in some older age groups either and were therefore classified as having high susceptibility.

Discussion

This paper provides an overview of measles seroepidemiology in Australia and a large number of countries throughout Europe for the period 1996–2004. The results of the ESEN2 project and those of the earlier ESEN project, provide invaluable information about progress towards the WHO measles elimination target for 2010 in the WHO European Region.[4]

The results of the serological surveys illustrate the heterogeneity of measles control in the region. This reflects the wide range in current and historical measles vaccine policy and vaccine coverage. Three groups of countries can be distinguished. Seven countries (the Czech Republic, Hungary, Luxembourg, Slovakia, Slovenia, Spain and Sweden) have age-specific susceptibility levels congruent with having achieved or approaching measles elimination. All these countries have had two-dose measles vaccine programmes from the 1970s onwards with very high reported first-dose measles vaccine coverage (mostly > 95%) for at least the previous five years. The notable exception is Spain, which only implemented a second dose in 1996 at the time the serosurvey was undertaken. Reflecting this high population immunity, all these countries except Spain had very low reported measles incidence with an average incidence from notifications of less than 4/100 000/year and incidence from confirmed cases (where available) of < 0.5/100 000/year in the decade before the serosurveys. In Spain, the population immunity comes from both vaccination and disease. To ensure measles elimination is achieved in 2010, it will be critical that these countries maintain very high routine coverage (> 95%) with two doses of measles vaccine.

In four countries (Australia, Israel, Lithuania and Malta), the proportion susceptible had reached the WHO susceptibility targets in children under 10 years of age, but was above the target for adolescents and young adults. These countries have employed routine two-dose measles programmes since the early

1990s, with high reported routine vaccine coverage for the previous five years (> 90%). The susceptible cohorts in young persons in these countries either reflect those who were scheduled only for a single dose or for two doses, but presumably delivered at a lower coverage than the target of > 95%. The levels of coverage were high enough to interrupt measles circulation leading to the accumulation of a pool of susceptible older persons. These countries need to ensure routine two-dose coverage is at least 95% and also consider implementing catch-up campaigns. Such strategies have been successfully undertaken in other countries, such as the Republic of Korea.[21]

It is of concern that in seven (Belgium, Bulgaria, Cyprus, England and Wales, Ireland, Latvia and Romania) of the 18 countries, there is high susceptibility in several age groups, including young children. In Belgium, Cyprus, Ireland and England and Wales, first-dose measles vaccine coverage in the five years up to 2001 was below 90%. This has led to the proportion of children susceptible to measles exceeding the WHO susceptibility targets. This lower coverage has only been a recent phenomenon in England and Wales, and to some extent in Ireland (which also has high susceptibility in adults), reflecting the impact of parental concern on the safety of MMR vaccine on uptake.[22] The decreased coverage in England and Wales can also be seen in the reduced seropositivity in children compared to the ESEN 1996 survey.[8] Since these ESEN2 surveys, outbreaks in Ireland and England and Wales have been reported in young children.[23] In Belgium and Cyprus, in addition to high susceptibility in young children, a significant proportion of adolescents remain susceptible to measles reflecting lower historical measles vaccine uptake.

In Bulgaria and Latvia, there is evidence of susceptible age groups in both young children and young adults, and only in young children in Romania. This disagrees with the officially reported measles coverage data, which in each case is > 90% in the last five years. In Latvia, MMR vaccine coverage estimates agree with the observed rubella seroprofiles,[24] suggesting that the reported vaccine coverage is accurate and that there may either be a problem with the vaccine, the samples or the standardization process. If there was a problem with the standardization then this would need to be age specific because the oldest age cohorts showed high levels of antibody; also, samples were tested immediately upon collection and the testing of the standardization panel was satisfactory. The affected cohorts received the Leningrad strain of measles vaccine during the 1980s and 1990s. If the problem is the vaccine and true seroprevalence is as low as reported then it is surprising that large outbreaks have not already occurred. However, large outbreaks in older populations that had been highly vaccinated with the Leningrad strain have been reported from neighbouring countries, such as Ukraine.[25] The discrepancy requires further study.

In Bulgaria, the discrepancy between vaccine coverage and seroprevalence is smaller and more consistent across age groups, including vaccinated adults. This could represent a possible problem with sample storage or with the assay, but this seems unlikely because seroprevalence is high in the oldest age groups and the standardization panel results were good. A large outbreak in 1992 in children and young adults suggests that routine vaccine coverage could be overestimated[26] and that significant pools of susceptibles may exist, but recent incidence has been very low with no cases reported in 2002–2004 and no indigenous spread following an imported case from China in 2005.[27]

In Romania, the low susceptibility in the adolescent and adult age groups presumably reflects the impact of the 1998 catch-up campaign that targeted 7–18 year-olds and after which the reported incidence of measles was very low. However, levels of susceptibility are particularly high in the younger (< 8 years) age groups, and the discrepancy with reported routine vaccine coverage suggests that it is lower than reported. Indeed Romania recently reported a large, national outbreak, which particularly affected younger age groups from marginalized populations.[16,28]

To achieve elimination, all these higher susceptibility countries will need to strengthen their routine measles programmes to achieve > 95% with both

Table 3. **Percentage measles seronegative (antibody titre < 0.15 IU/ml) by age group compared to WHO targets**

Country or area	Measles seronegative (%)				
	2–4 years	5–9 years	10–19 years	20–39 years	40+ years
WHO target	< 15	< 10	< 5	< 5	< 5
Low susceptibility					
Czech Republic	1.0	0.8	1.5	3.2	0.2
Hungary	2.9	3.8	3.5	8.5	0.3
Luxembourg	5.4[a]	4.7	5.0	2.6	0.2
Slovakia	3.8	4.8	3.3	6.1	0.3
Slovenia	4.0	3.2	4.2	6.1	1.5
Spain	5.0	7.2	4.0	0.8	–
Sweden	1.0	5.8	4.7	5.9	0.5
Intermediate susceptibility					
Australia	10.8	8.0	7.9	9.4	–
Israel	9.1	6.9	5.2	7.0	1.4
Lithuania	4.7	9.8	9.6	12.4	0.3
Malta	9.6	4.3	6.9	5.3	3.1
Higher susceptibility					
Belgium	12.4	14.1	13.3	4.6	2.0
Bulgaria	30.4	25.9	20.7	10.1	9.0
Cyprus	21.8	21.8	13.2	5.9	1.0
England and Wales	18.9	10.2	6.9	2.8	0.2
Ireland	14.2	11.8	8.6	7.8	7.6
Latvia	19.0	42.9	39.8	30.8	3.5
Romania	24.3	11.4	4.2	1.4	0.3

[a] Based on only 37 sera.

doses and address older susceptible age groups through catch-up campaigns. These activities will need to be supported by information campaigns highlighting the importance and safety of MMR vaccine.

In this paper, we have employed a fixed cut-off of 0.15 IU/ml. There is only limited observational data to support this arbitrary cut-off.[18] In several countries with long-standing high coverage two-dose measles programmes (Hungary, Slovakia, Slovenia and Sweden), the proportion classified as "seronegative" is marginally > 5% in young adults (20–39 year-olds). These "seronegatives" may reflect waning antibody over time in highly vaccinated (and protected) cohorts, who have not had an opportunity to be exposed to natural measles infection.[29] This has been observed previously and there is no evidence to date to suggest secondary vaccine failure occurs in these cohorts despite follow-up for up to three decades.[30,31] Further analysis of the quantitative antibody titres using mixture modelling may be used to examine waning immunity and also estimate the proportion of the population falling into groups such as vaccinated, past infection, recent infection and negative.[32]

In conclusion, the ESEN2 project has demonstrated which countries have met or are approaching measles elimination and what other countries need to do to reach this target. It is critical that all countries in Europe achieve and maintain very high vaccine coverage with two doses of measles vaccine and address older susceptible groups, if the target of measles elimination by 2010 in the WHO European Region is to be reached. ■

Acknowledgements

This work was funded by a grant from DG X11 of the European Union under contract QLK2-CT-2000–00542 (concerted action). The Luxembourg serological study was partially funded by the Centre de Recherché Public – Santé. The Spanish serological study was partially funded by ISCIII MPY 1075/01. The Hungarian serological study was partially funded by the Office of the Chief Medical Officer. We would also like to thank the following individuals for input into the project: L Hesketh, E Miller, MP Balfagón and T Minguito.

Competing interests: None declared.

Résumé

Sensibilité à la rougeole en Australie et dans 17 pays européens : vers une élimination de cette maladie

Objectif Evaluer la sensibilité par âge à la rougeole en Australie et dans 17 pays européens.

Méthodes Dans le cadre du Réseau européen d'épidémiologie sérologique 2 (ESEN2), 18 pays ont constitué entre 1996 et 2004 de grandes banques nationales de sérum. On a soumis ces banques à des tests pour détecter les IgG antirougeoleuses et on a converti les résultats de ces tests en unités communes pour permettre des comparaisons valides entre pays. On a également recueilli des données sur l'historique des vaccinations antirougeoleuses et sur l'incidence de la rougeole. On a comparé les niveaux de sensibilité de la population stratifiée par âges aux objectifs pour la Région européenne de l'OMS concernant l'élimination de la rougeole, à savoir moins de 15 % dans la tranche d'âges 2-4 ans, moins de 10 % dans la tranche d'âges 5-9 ans et moins de 5 % dans les tranches d'âges supérieures.

Résultats Sept pays (Espagne, Hongrie, Luxembourg, République tchèque, Slovaquie, Slovénie et Suède) remplissaient les objectifs ou en étaient très proches. Quatre pays (Australie, Israël, Lituanie et Malte) présentaient des niveaux de sensibilité dans certaines tranches d'âges indiquant d'éventuelles brèches dans la protection. Sept autres pays (Belgique, Bulgarie, Chypre, Angleterre et Pays-de-Galles, Irlande, Lettonie et Roumanie) ont été jugés à risque d'épidémie en raison de la grande sensibilité des enfants et dans certains cas des adultes.

Conclusion Bien que tous ces pays appliquent actuellement un calendrier de vaccination antirougeoleuse en deux doses, certains d'entre eux devront étendre la couverture vaccinale systématique et procéder à des campagnes de vaccination dans certaines cohortes plus âgées si l'on veut que la Région européenne de l'OMS atteigne les objectifs d'élimination d'ici 2010. Si ces améliorations ne sont pas apportées, on peut s'attendre à ce que la transmission se poursuive et à ce que des flambées de rougeole apparaissent en Europe.

Resumen

Hacia la eliminación: vulnerabilidad al sarampión en Australia y en 17 países europeos

Objetivo Evaluar la vulnerabilidad específica de la edad al sarampión en Australia y 17 países europeos.

Métodos Como parte de la Red Europea de Seroepidemiología 2 (ESEN2), 18 países crearon grandes serotecas nacionales entre 1996 y 2004. Tras analizar dichas serotecas para determinar los anticuerpos IgG contra el sarampión, los resultados obtenidos se expresaron en las mismas unidades para poder realizar comparaciones válidas interpaíses. Se recogieron también datos temporales sobre la vacunación y la incidencia de la enfermedad. Los niveles de vulnerabilidad de la población estratificados por edades se compararon con las metas de la Región de Europa de la OMS para la eliminación del sarampión: menos del 15% en los niños de 2-4 años, menos del 10% en los de 5-9 años, y menos del 5% en los grupos de más edad.

Resultados Siete países (República Checa, Hungría, Luxemburgo, España, Eslovaquia, Eslovenia y Suecia) habían alcanzado las metas de eliminación o se aproximaban mucho a ellas. Cuatro países (Australia, Israel, Lituania y Malta) presentaban unos niveles de vulnerabilidad superiores a las metas de la OMS en algunos grupos de más edad, lo que parece indicar que presentan lagunas en sus sistemas de protección. En cuanto a los otros siete países (Bélgica, Bulgaria, Chipre, Inglaterra y Gales, Irlanda, Letonia y Rumania), se consideró que corrían el riesgo de sufrir epidemias como resultado de la alta vulnerabilidad de los niños, y también en algunos casos de los adultos.

Conclusión Aunque todos los países aplican hoy día una pauta de vacunación antisarampionosa de dos dosis, para alcanzar la meta de la Región de Europa de la OMS de eliminar el sarampión

para 2010 algunos países deberán garantizar una mayor cobertura sistemática, y llevar a cabo además campañas de vacunación centradas en algunas cohortes de más edad. Sin esas mejoras, cabe prever que continuarán en Europa la transmisión y los brotes de sarampión.

ملخص

نحو التخلُّص من الحصبة: الاستعداد للإصابة بالحصبة في استراليا و17 بلداً أوروبياً

الغرض: تقييم الاستعداد للإصابة بالحصبة الخاص بكل مجموعة عمرية على حدة في استراليا وفي 17 بلداً أوروبياً.

الطريقة: جمع 18 بلداً بنوكاً مصلية وطنية ضخمة في الفترة بين 1996 و2004، كجزء من الشبكة الثانية الأوروبية للوبائيات السيرولوجية. وأجريت اختبارات على هذه البنوك لتحرِّي الغلوبولين المناعي الخاص بالحصبة، ثم تم توحيد النتائج ليصبح بالإمكان إجراء مقارنات صحيحة بين البلدان، كما جمعت معطيات تاريخية حول التلقيح (التطعيم) ومعدلات حدوث الأمراض. وأجريت مقارنات بين استعداد السكان وفق طبقات المجموعات العمرية وما يقابلها من الأهداف التي حددها الإقليم الأوروبي لمنظمة الصحة العالمية للتخلص من الحصبة، وهي أقل من 15% لدى من تتراوح أعمارهم بين 2 و4 سنوات، وأقل من 10% لدى من تتراوح أعمارهم بين 5 – 9 سنوات، وأقل من 5% لدى المجموعات الأكبر سناً من ذلك.

الموجودات: لقد حقَّقت سبعة بلدان الأهداف المتوخَّاة لاستئصال الحصبة أو شارفت على تحقيقها (جمهورية التشيك، وهنغاريا، ولوكسمبورغ، وإسبانيا، وسلوفاكيا، وسلوفينيا، والسويد) وفي أربعة بلدان أخرى (استراليا، وإسرائيل، وليتوانيا، ومالطا)، كانت مستويات الاستعداد للإصابة بالحصبة أعلى من أهداف منظمة الصحة العالمية في بعض المجموعات العمرية الأعلى سناً، مما يشير إلى وجود ثغرات في الوقاية. ويخشى أن يكون سبعة من البلدان (بلجيكا، وبلغاريا، وقبرص، وإنكلترا وويلز، وإيرلندا، ولاتفيا، ورومانيا) معرضين لخطر الأوبئة نتيجة المستوى المرتفع من الاستعداد للإصابة بالحصبة لدى الأطفال، وفي بعض الحالات، لدى البالغين.

الاستنتاج: رغم أن جميع البلدان تنفذ في الوقت الحاضر جدول التلقيح (التطعيم) بجرعتين للحصبة، فإن الإقليم الأوروبي لمنظمة الصحة العالمية إذا أراد أن يحقق هدفه بالقضاء على الحصبة عام 2010، فعليه أن يحقِّق معدلاً أعلى للتغطية الروتينية وبحملات التلقيح (التطعيم) في مجموعات عمرية أعلى في بعض البلدان. وبدون إدخال هذه التحسينات، فإن سراية الحصبة ستتواصل، وسيتوقع حدوث فاشياتها في أوروبا.

References

1. Centers for Disease Control and prevention (CDC) Progress towards measles elimination – region of the Americas, 2002-2003. *MMWR Morb Mortal Wkly Rep* 2004;53:304-6. PMID:15085074
2. *Health21: the health for all policy for the WHO European Region* (European Health for All Series, No.6). Copenhagen: WHO Regional Office for Europe; 1999.
3. Centers for Disease Control and Prevention (CDC). Progress toward elimination of measles and prevention of congenital rubella infection – European Region, 1990-2004. *MMWR Morb Mortal Wkly Rep* 2005;54:175-8.
4. *Strategic plan for measles and congenital rubella infection in the WHO European Region*. Copenhagen: WHO Regional Office for Europe; 2003. Available from: http://www.euro.who.int/document/e81567.pdf
5. *Surveillance guidelines for measles and congenital rubella infection in the WHO European Region*. Copenhagen: WHO Regional Office for Europe; 2003. Available from: http://www.euro.who.int/document/e82183.pdf
6. Ramsay M. *A strategic framework for the elimination of measles in the European Region. The Expanded Programme on Immunization in the European Region of WHO* (EUR/ICP/CMDS 01 01 05). 1999. pp. 1-26.
7. Gay NJ. The theory of measles elimination: implications for the design of elimination strategies. *J Infect Dis* 2004;189 Suppl 1;S27-35. PMID:15106086 doi:10.1086/381592
8. De Melker H, Pebody RG, Edmunds WJ, Levy-Bruhl D, Valle M, Rota MC, et al. The seroepidemiology of measles in Western Europe. *Epidemiol Infect* 2001; 126:249-59. PMID:11349976 doi:10.1017/S0950268801005234
9. Six C, Franke F, Mantey K, Zandotti C, Freymuth F, Wild F, et al. Measles outbreak in the Provence-Alpes-Cote d'Azur region, France, January-July 2003. *Euro Surveill* 2005;10:46-8. PMID:15701935
10. Dayan GH, Zimmerman L, Shteinke L, Kasymbekova K, Uzicanin A, Strebel P, et al. Investigation of a rubella outbreak in Kyrgyzstan in 2001: implications for an integrated approach to measles elimination and prevention of congenital rubella syndrome. *J Infect Dis* 2003;187 Suppl 1;S235-40. PMID:12721919 doi:10.1086/368037
11. ESEN2 website. Available from: http://www.hpa.org.uk/esen2
12. Osborne K, Weinburg J, Miller E. The European Seroepidemiology Network. *Euro Surveill* 1997;2:29-31. PMID:12631820
13. Andrews N, Pebody RG, Berbers G, Blondeau C, Crovari P, Davidkin I, et al. The European Sero-Epidemiology Network: standardizing the enzyme immunoassay results for measles, mumps and rubella. *Epidemiol Infect* 2000;125:127-41. PMID:11057968 doi:10.1017/S0950268899004173
14. Ciofi Degli Atti ML, Filia A, Massari M, Pizzuti R, Nicoletti L, D'Argenzio A, et al. SPES Study Group. Assessment of measles incidence, measles-related complications and hospitalisations during an outbreak in a southern Italian region. *Vaccine* 2006;24:1332-8. PMID:16219394 doi:10.1016/j.vaccine.2005.09.031
15. Siedler A, Tischer A, Mankertz A, Santibanez S. Two outbreaks of measles in Germany 2005. *Euro Surveill* 2006;11:131-4. PMID:16645244
16. Centralized Information System for Infectious Diseases (CISID). Available from: http://data.euro.who.int/cisid
17. Kafatos G, Andrews N, Nardone A. Model selection methodology for inter-laboratory standardisation of antibody titres. *Vaccine* 2005;23:5022-7. PMID:16002191 doi:10.1016/j.vaccine.2005.05.030
18. Tischer A, Andrews N, Kafatos G, Nardone A, Berbers G, Davidkin I, et al. Standardisation of measles, mumps and rubella assays to enable comparisons of seroprevalence data across 21 European countries and Australia. *Epidemiol Infect* 2007;135:787-97. PMID:17394675 doi:10.1017/S0950268807008266
19. Pistol A, Hennessey K, Pitigoi D, Ion-Nedelcu N, Lupulescu E, Walls L, et al. Progress toward measles elimination in Romania after a mass vaccination campaign and implementation of enhanced measles surveillance. *J Infect Dis* 2003;187 Suppl 1;S217-22. PMID:12721916 doi:10.1086/368228
20. Ramsay ME, Jin L, White J, Liiton P, Cohen B, Brown D. The elimination of indigenous measles transmission in England and Wales. *J Infect Dis* 2003; 187 Suppl 1;S198-207. PMID:12721914 doi:10.1086/368024
21. Kim SS, Han HW, Go U, Chung HW. Sero-epidemiology of measles and mumps in Korea: impact of the catch-up campaign on measles immunity. *Vaccine* 2004;23:290-7. PMID:15530670 doi:10.1016/j.vaccine.2004.07.030
22. Burgess DC, Burgess MA, Leask J. The MMR vaccination and autism controversy in United Kingdom 1998-2005: inevitable community outrage or a failure of risk communication? *Vaccine* 2006;24:3921-8. PMID:16564116 doi:10.1016/j.vaccine.2006.02.033

23. Cronin M, Fitzgerald M. Measles outbreak in the Republic of Ireland: update. *Eurosurveillance Weekly* 2000; 9. Available from: http://www.eurosurveillance.org/ew/2000/000914.asp#2
24. Nardone A, Tischer A, Andrews N, Backhouse J, Theeten H, Gatcheva N, et al. Comparison of rubella seroepidemiology in 17 countries: progress towards international disease control targets. *Bull World Health Organ* 2008;2:118-25.
25. Spika J, Aidyralieva C, Mukharskaya L, Kostyuchenko N, Mulders M, Lipskaya G, et al. Measles outbreak in the Ukraine, 2005-2006. *Eurosurveillance Weekly* 2006; 11, E060309.1.
26. Anon. Measles outbreak in Bulgaria. *Wkly Epidemiol Rec* 1992;67:84-5. PMID:1571234
27. Gatcheva N, Mihneva Z, Mehandjieva V, Petkova V. The fever-rash surveillance revealed no indigenous transmission following the importations in 2005 and 2006. *Problems of Infectious and Parasitic Diseases* 2007;35. In press.
28. Lyons S. Investigation of risk factors for developing measles and for non-vaccination in children, Romania, June 2006. Presentation at: *11th EPIET Scientific seminar, Menorca, Spain, Oct 2006*. Available from: http://www.epiet.org/seminar/2006/index.html
29. Pebody RG, Gay NJ, Hesketh LM, Vyse A, Morgan-Capner P, Brown DW, et al. Immunogenicity of second dose measles-mumps-rubella (MMR) vaccine and implications for serosurveillance. *Vaccine* 2002;20:1134-40. PMID:11803074 doi:10.1016/S0264-410X(01)00435-2
30. Davidkin I, Valle M. Vaccine-induced measles virus antibodies after two doses of combined measles, mumps and rubella vaccine: a 12-year follow-up in two cohorts. *Vaccine* 1998;16:2052-7. PMID:9796064 doi:10.1016/S0264-410X(98)00081-4
31. Dine MS, Hutchins SS, Thomas A, Williams I, Bellini WJ, Redd SC. Persistence of vaccine-induced antibody to measles 26-33 years after vaccination. *J Infect Dis* 2004;189 Suppl 1;S123-30. PMID:15106101 doi:10.1086/380308
32. Vyse AJ, Gay NJ, Hesketh LM, Pebody R, Morgan-Capner P, Miller E. Interpreting serological surveys using mixture models: the seroepidemiology of measles mumps and rubella in England and Wales at the beginning of the 21st century. *Epidemiol Infect* 2006;134:1303-13. PMID:16650326 doi:10.1017/S0950268806006340