Large measles epidemic in Switzerland from 2006 to 2009: consequences for the elimination of measles in Europe

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Switzerland adheres to the objective of eliminating measles within the European region of the World Health Organization (WHO) by 2010. After several years with a relatively low annual incidence rate (0.3 to 1 case per 100,000 inhabitants), there has been a large epidemic of measles from November 2006 to August 2009. By mid September 2009, 4,415 cases were notified by physicians and laboratories, corresponding to an incidence rate of 15 per 100,000 in 2007 and 29 per 100,000 in 2008; by far the highest rates in Europe. This exceptionally long nationwide epidemic comprised three successive waves, with peaks in August 2007 (171 cases), March 2008 (569 cases) and March 2009 (417 cases). It mainly affected children aged from five to 14 years (48% of cases). Most cases were not vaccinated (93%) or were incompletely vaccinated (5%). In total 656 patients (15%) suffered complications or were hospitalised. Insufficient, spatially heterogeneous immunisation coverage (87% for at least one dose at the age of two years at the national level) has allowed a sequence of numerous outbreaks to occur, despite the gradual strengthening of measures to control the disease. Several exportations to Europe (81 in 2007 and 2008) and to the rest of the world (10 for the whole of the epidemic) have in some instances caused large outbreaks. The epidemic was a threat to the goal of eliminating measles in Switzerland and in Europe. The Federal Office of Public Health (FOPH) and its partners are currently working on a national strategy to eliminate measles.

Introduction

Interruption of the endemic transmission of measles by 2010 is one of the objectives of the World Health Organization (WHO) for its European region [1]. The strategy proposed consists in particular of achieving and maintaining ≥95% vaccination coverage among young children (preferably before the age of two years), with two doses of MMR (measles, mumps and rubella) vaccine. Finland for example has achieved this objective, and many others are close to it [2,3]. Nevertheless, large-scale outbreaks have still been observed in Europe over the last ten years, for instance in the Netherlands, Italy, France, Germany and the United Kingdom, or in Israel [4-12].

In Switzerland, vaccination against measles has been recommended since 1976 (one dose at 12 months), with MMR vaccine being used since 1985. A catch-up vaccination has been recommended since 1985 for teenagers aged 12 to15 years. A second dose of MMR was introduced in 1996 for children aged four to seven years, and this age was lowered to 15 to 24 months in 2001 to increase immunity before entering kindergarten or school. In addition, catch-up vaccination, to reach a total of two doses is recommended since 1996 for anyone born after 1963, who has not been completely vaccinated, and has not had measles. Vaccination of young children and catch-up vaccination of children and adults are performed by pediatricians and general practitioners in private practice and reimbursed by mandatory health insurance. In some cantons, school medical services also ensure catch-up vaccination, usually during the first and the last year of compulsory school. For at least one dose at two years of age, vaccination coverage was stable at about 82% in Switzerland from the early 1990ies to the early 2000s, before increasing to 87% during the period from 2005 to 2007 [13,14]. At that stage it was 90% for children aged eight and 94% for adolescents aged 16 years. Coverage for a second dose only reached 71 to 76%, depending on age. Disparities in vaccination coverage are significant between the 26 Swiss cantons (range: 73–94% for at least one dose at two years). The coverage in the canton which recorded the highest amount of cases (Lucerne) was 78% in 2006 (86% at eight years and 94% at 16 years).

Despite over 30 years of vaccination against measles, this disease is still endemic in Switzerland with epidemic transmission occurring. From 1999 to 2006, an average of about 50 cases were notified per year (incidence rate 0.3 to 1 case/ 100,000) except in 2003, when there was an epidemic that affected the whole country (612 cases; 8.4/100,000) [15]. Whilst the circulation of the measles virus seemed very limited (three cases notified from July to October 2006), a new outbreak gradually spread across the country starting in November 2006 [16]. Since then, this epidemic has continued in three waves comprising numerous outbreaks [17,18]. The third wave began in the canton of Lucerne at the end of 2008 before spreading throughout the country. This report describes the measles epidemic that has been occurring in Switzerland over the past 34 months and the measures taken to control it. It also discusses causes and consequences of this particularly long nationwide outbreak.

Methods

Notification

The data analysed come from the mandatory notification system for measles (cases registered by the Federal Office of Public Health - FOPH, from 15 November 2006 to 17 September 2009). Since 1999, physicians have to notify the cantonal officers of health within 24 hours of any patient with a fever and a rash accompanied by at least one of the following three symptoms: cough, rhinitis or conjunctivitis. Laboratories must notify the cantonal officers of health and the FOPH within 24 hours of any confirmed measles case, whatever the test used. These initial rapid alerts allow the

cantonal physician to launch investigation and control measures. The physician later fills in a more detailed notification. The cantonal officers of health send the FOPH a copy of all notifications made by physicians.

Laboratory tests

The FOPH recommends laboratory confirmation of any suspect case of measles that has no epidemiological link to a confirmed case [19]. The analyses are carried out by numerous private laboratories or by public hospitals. Usually, Ig M and IgG are tested for in serum, using commercial tests. Two laboratories are able to test for the presence of measles virus RNA in clinical samples (throat smear or saliva) by RT-PCR. To trace the pathways of viral transmission, the WHO measles and rubella reference laboratory for Central Europe at the Robert-Koch Institute in Berlin, Germany, has genetically characterised 137 viruses and determined their genotype by sequence analysis of the variable part of the N-gene (456 nt) [20]. Since autumn 2008, genotyping of the measles virus has also been carried out at the Central Virology Laboratory of Geneva University Hospital.

Classification of cases

The definition of a clinical case corresponds to the notification criteria listed above. A case is considered confirmed if it i) is confirmed by a positive laboratory test and presents at least one of the typical signs of measles or ii) meets the clinical case definition and is epidemiologically linked to another laboratory confirmed case. A probable case is a clinical case that is not epidemiologically linked to a laboratory confirmed case. Possible cases include all reported cases without a positive laboratory result, which do not meet the clinical case criteria (clinical manifestations incomplete or unknown). In the current outbreak many possible cases had an epidemiological link with another probable or confirmed case, or belonged to space-time clusters of measles. Cases with a double negative laboratory result (two negative IgM tests or one negative IgM test with absence of RNA by RT-PCR) are discarded, as are those with a single positive IgM test without any clinical symptoms of measles, due to a high probability of false positive tests.

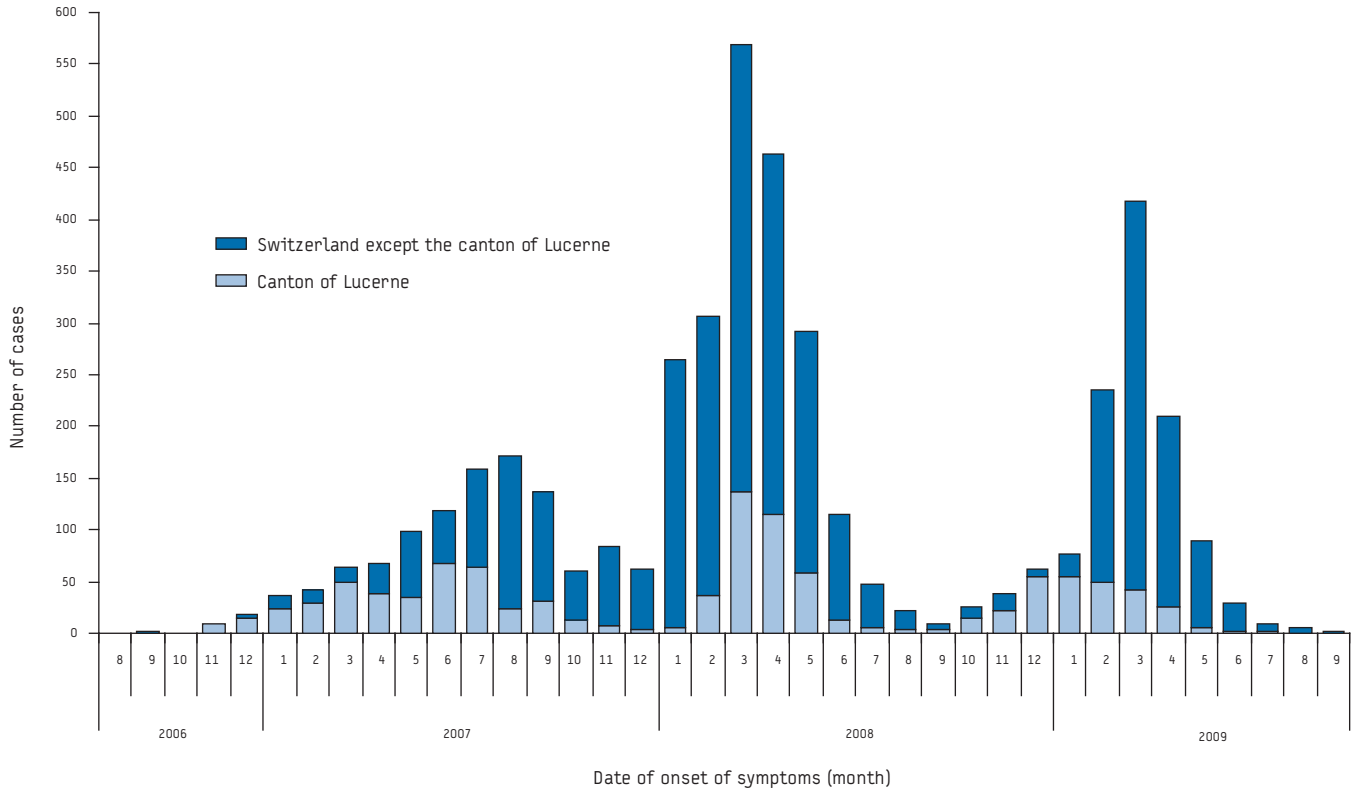
Description of the epidemic

The measles epidemic started in the canton of Lucerne in November 2006, probably following importation [16]. A first wave reached its peak in August 2007 (171 cases) (Figure 1). A second wave appeared in the Basel region around the end of 2007, with a surge from January 2008 and reinforced from February onwards by a strong return of measles in the canton of Lucerne (second peak in March 2008, with 569 cases). The number of cases then fell to a minimum of 10 in September, before constantly rising again, first in the canton of Lucerne, until March 2009 (417 cases). With only 29 cases in June, 10 in July, six in August and one case up to 17 September 2009, we consider that this epidemic has now come to an end. In total, 4,415 cases have been notified, 29 (1%) by the end of 2006, 1,098 (25%) in 2007, 2,214 (50%) in 2008 and already 1,074 (24%) by mid September 2009.

Of the total number of notified cases (4,565), 150 (3%) were discarded. Of the remaining 4,415 cases, 1,886 (43%) were confirmed, either by a positive laboratory result (35%), or by an epidemiological link with a laboratory confirmed case (7%). Of all cases, 48% were probable and 9% were possible.

Figure 1

Notified cases of measles by month, Switzerland, 1 August 2006 to 17 September 2009 (n=4,416)



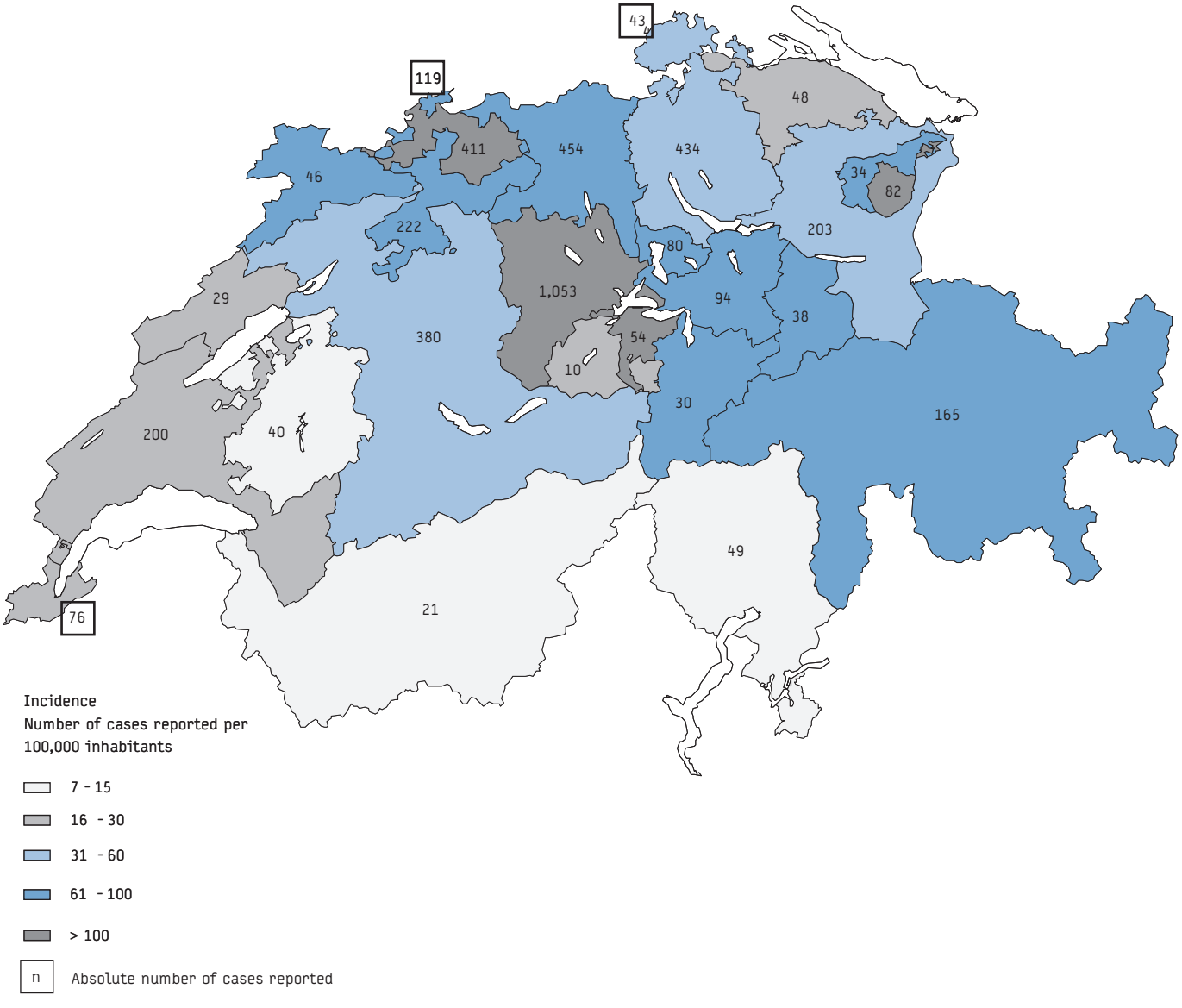
The epidemic has affected all 26 Swiss cantons. However, the total incidence rate for the whole of the epidemic has varied considerably from one canton to another, with a maximum of 530 per 100,000 in Appenzell Innerrhoden and a minimum of 7 per 100,000 in the canton of Valais, giving a national average of 58 per 100,000 (Figure 2). The cumulative incidence rate per canton has tended to be lower with increasing vaccination coverage (Figure 3). It reached 74 per 100,000 in the German-speaking part of Switzerland, compared with 21 per 100,000 in the French and Italian-speaking parts, with vaccination coverage of 84.7% and 92.3% respectively for at least one dose at two years of age. The first and third wave of the epidemic started in the canton of Lucerne and Lucerne contributed significantly to the second wave (Figure 1). Overall, that canton recorded 1,053 cases, 24% of the total (cumulative incidence rate 290/100,000).

The sex of 99.8% of the patients is known. The cumulative incidence rates were virtually identical for men and for women (59 and 57/100,000 respectively). Among the 99.5% of patients whose age is known, children aged five to nine years were most affected (25% of cases, cumulative incidence rate 285/100 000) (Table). They were followed by children aged 10 to 14 years and then adolescents from 15 to 19. Adults aged 20 or over made up 19% of cases, whereas cases in infants under one year were rare (< 3%). The median age of patients was 11 years.

The genotype of the measles virus is available for 105 of the 137 samples, with positive RT-PCR sent to the regional reference laboratory in Berlin, since the beginning of 2006. The genotype of further 20 virus samples was provided by a Swiss laboratory. In Switzerland in 2006, before the beginning of the epidemic

Figure 2

Incidence and number of notified cases of measles by canton, Switzerland, 15 November 2006 to 17 September 2009 (n=4,415)

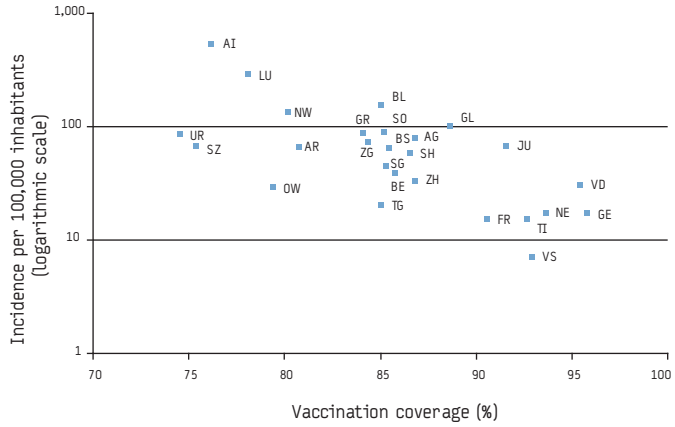


Souce: Swiss Federal Office of Public Health

in November, only the B3 genotype was identified (Figure 4). It was found in a sporadic measles case returning from London in late January and an outbreak lasting from March to May in the neighboring canton of Lucerne. Genotype D5, which was the source of the recent epidemic, was identified in a total of 91 samples from 14 cantons, between November 2006 and March 2009. Also, 13 measles cases caused by D4 virus were identified between October 2008 and March 2009, in four cantons of the German-speaking part of Switzerland. In addition, two D4 viruses were found in June in Geneva. In March 2009, there was an outbreak of genotype B3, mainly affecting the students from the Ecole polytechnique fédérale and from the University of Lausanne, following an importation of measles from Mali. B3 virus was identified in 13 patients, including the index case. In addition, two cases of B3 virus were detected in 2007 in isolated patients returning from abroad, as was a case of genotype A-related vaccine virus in a woman non-immune for rubella who developed a typical measles 12 days after a postpartum vaccination with MMR [16].

FIGURE 3

Cumulative incidence of measles by canton, Switzerland,15 November 2006 to 17 September 2009



AG: Aargau	GE: Geneva	OW: Obwalden	UR: Uri
AI: Appenzell Innerrhoden	GL: Glarus	SG: St. Gallen	VD: Vaud
AR: Appenzell Ausserrhoden	GR: Graubünden	SH: Schaffhausen	VS: Valais
BE: Bern	JU: Jura	SO: Solothurn	ZG: Zug
BL: Basel Land	LU: Lucerne	SZ: Schwyz	ZH: Zürich
BS: Basel-Stadt	NE: Neuchâtel	TG: Thurgau	
FR: Fribourg	NW: Nidwalden	TI: Ticino	

Note: Incidence displayed on logarithmic scale as function of vaccination coverage, ≥ 1 dose at two years of age according to the latest information available.

TABLE

Notified cases of measles and cumulative incidence per 100,000 inhabitants by age group, Switzerland, 15 November 2006 to 17 September 2009 (n=4,391)

Age (years)*	Number of cases	Proportion of all cases (%)	Incidence
< 1	114	2.6	153
1-4	531	12.1	180
5-9	1,095	24.9	285
10-14	1,033	23.5	244
15-19	775	17.6	170
20-29	399	9.1	43
≥ 30	444	10.1	9
Total	**4,391**	**100.0**	**58**

*information missing for 24 cases

Among the 3,916 (88.7%) patients for whom the vaccination status is known through a written document or by history, 92.9% had not been vaccinated, 4.5% had been incompletely vaccinated (one dose), 2.1% had been completely vaccinated (two doses) and 0.5% had been vaccinated with an unknown number of doses. There was a high preponderance of people who had not been vaccinated in each age group, although the proportion tended to decrease from adolescence, with more people who had been vaccinated and, in particular patients whose vaccination status was unknown (Figure 5).

A detailed notification is available for 4,278 cases (96.9%), of whom 339 (7,9%) were hospitalised. No complications were reported for 207 (61%) of hospitalised cases.The frequency of hospitalisation was significantly dependent on age (chi-squared test, $p < 0.0001$). It was 13% for infants, between 4 and 5% for each of the three five-year age categories covering children from one to 14 years old, 8% for adolescents from 15 to 19 years of age, 20% for adults from 20 to 29 years and 29% for adults aged 30 years or more. Among cases with detailed information available, 452 (10.6%) suffered from complications, of which 175 were pneumonia, 219 otitis and nine encephalitis. No follow-up information is available for the latter cases, however some were probably not severe because three of them were not hospitalised and a fourth was only a suspected case of encephalitis. Among cases with a complication only 135 (29%) were hospitalised. A 12-year-old girl living in the Haute-Savoie region of France, who had previously been in good health, died of measles encephalitis in late January 2009 at Geneva University Hospital.

In 2007 and 2008, thirteen and 68 importations respectively from Switzerland were reported by European countries participating to the European surveillance network for vaccine-preventable diseases (EUVAC.NET), corresponding to 15% and 31% of the total of imported cases with a known origin [21,22]. Moreover, through the Swiss notification system and publications were are aware of at least 10 additional exportations outside of Europe during the epidemic: seven in North America; one in Asia, one in Africa and one in Australia. A number of these led to outbreaks, some of which were large, for instance in Germany, Austria, France and the United States [9,23-29]. Conversely, 54 possible or certain importations into Switzerland were reported during the epidemic, of which 33 were from Europe (in particular Italy, Germany and France), nine from Asia, seven from America (four from Latin America and three from the United States), four from Africa and one from an unknown Mediterranean country.

Public health measures

Control of outbreaks

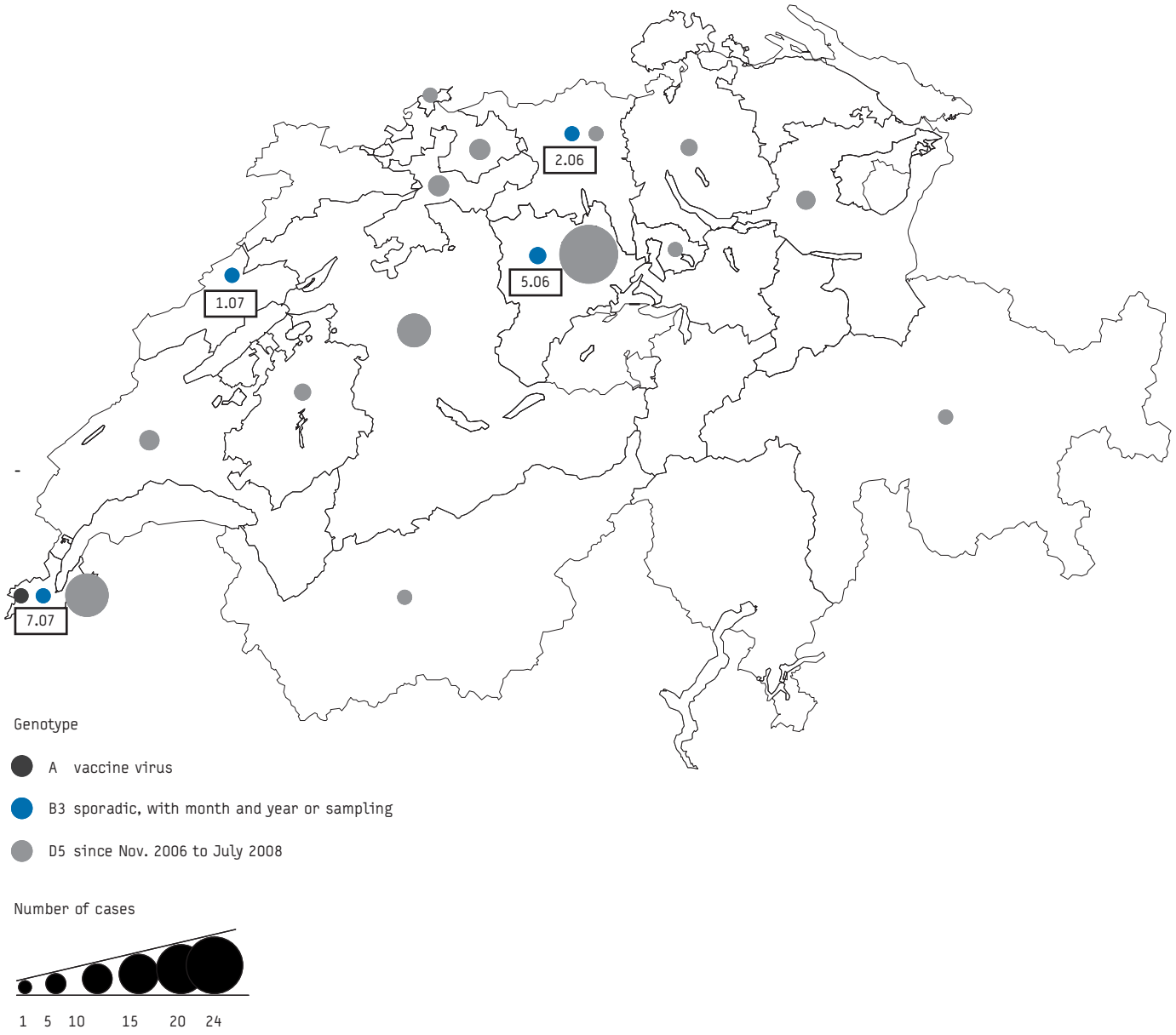
In Switzerland, public health measures to control outbreaks of infectious diseases are the responsibility of the cantons. The FOPH has no detailed overview on the measures taken by the cantonal health authorities and physicians, and their results. The FOPH has developed national guidelines to standardise the cantonal measures

intended to limit or stop transmission. Although they have not yet been finalised, they have already been widely applied in some cantons. These measures include, in particular, information for contacts of the case in settings such as schools, kindergartens, and universities, with recommendations on vaccination, active case finding and identification of susceptible contacts, post-exposure vaccination of contacts within 72 hours after exposure, exclusion of the sick from kindergartens and schools for four days after the appearance of the rash, exclusion of susceptible contacts (except if they had post-exposure vaccination) for 18 days after their last exposure and actions to vaccinate the extended circle of contacts. Post-exposure immunoglobulin is recommended for high risk groups. However, certain cantons, including some with a high incidence of measles, are not yet taking any measures or merely provide general information to the population or potential contacts.

In some instances, large-scale actions were carried out, in particular in the canton of Vaud. Following the notification of a case at the beginning of February 2009, an investigation of the contacts showed that there were already about ten non-notified cases in an anthroposophic school near Lausanne. As it was not possible to distinguish between people who had and had not been

Figure 4a

Circulating genotype of measles virus by canton, Switzerland, January 2006 to July 2008 (just before and during the first two waves of the epidemic, n=85)



NB the number of samples per canton is not proportional to the number of cases per canton

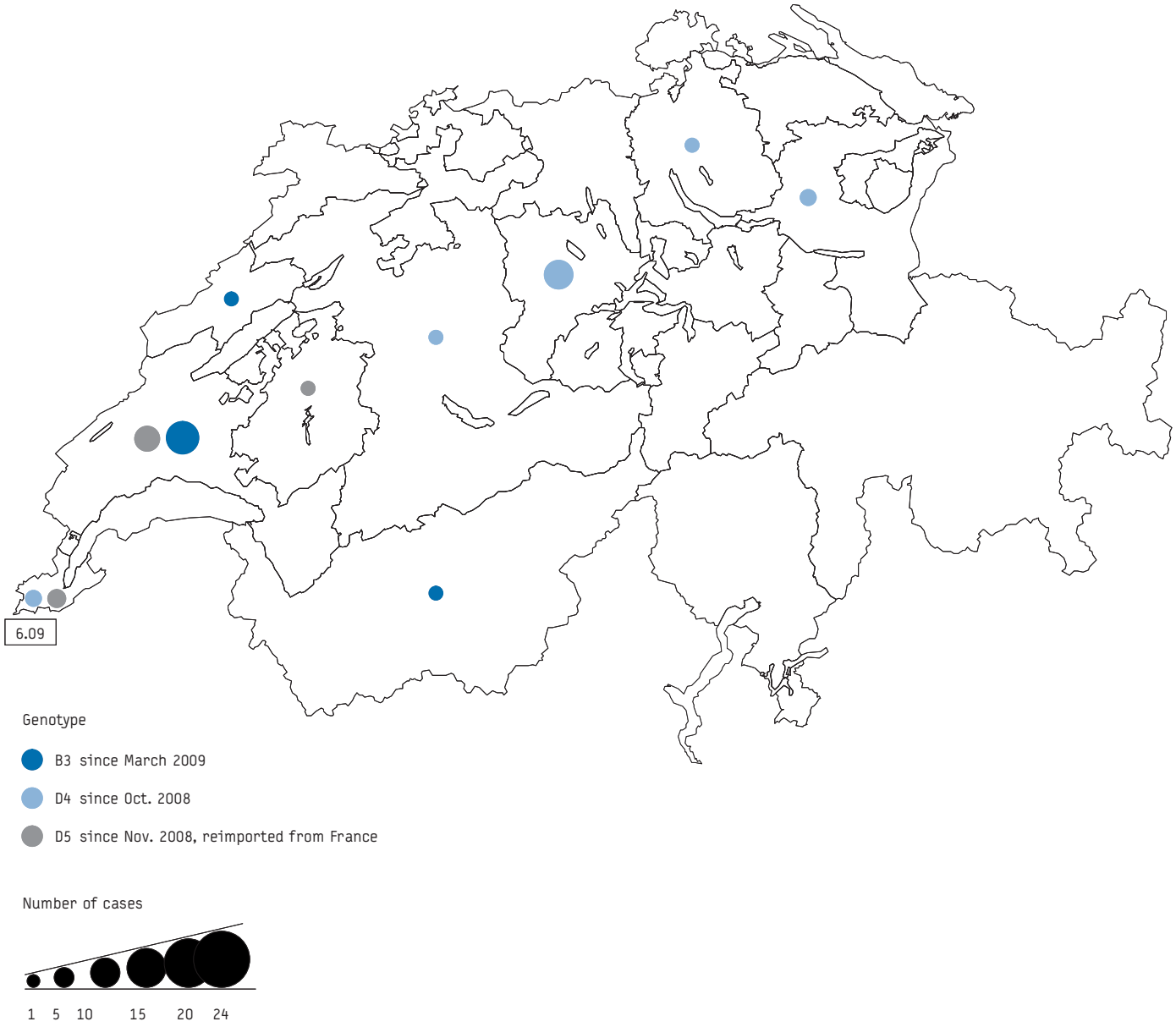
Source: Swiss Federal Office of Public Health

exposed, the cantonal officer of health immediately ordered that any pupil or teacher who had not been vaccinated at all and had not already had measles be excluded from the school and remain at home for 21 days which affected around 200 people. In March 2009, the campus of Lausanne was the centre of an outbreak of measles comprising about fifty cases. A large catch-up vaccination campaign was organised, to stop the transmission of the virus. All students and teachers were informed by email. More than 3,800 doses of MMR were administered within two and a half weeks, bringing vaccination coverage up to 97% for at least one dose of MMR vaccine from an estimated 90%.

For the first time following a risk linked to measles, in February 2009 the FOPH launched an international warning for passengers on two flights (Tel Aviv – Geneva via Zurich), with a direct search for some of the passengers. A girl, who had been infected in Switzerland before leaving for Israel, developed a rash soon after returning to Switzerland. She was thus infectious during the flights. At least one of the potentially exposed passengers sitting three rows in front and behind the girl obtained vaccination.

Figure 4b

Circulating genotype of measles virus by canton, Switzerland, October 2008 to June 2009 (third wave of the epidemic, n=40)



NB the number of samples per canton is not proportional to the number of cases per canton

Source: Swiss Federal Office of Public Health

Intensification of primary prevention

Primary prevention of measles has been intensified through information and vaccination in kindergartens, schools, universities etc. In 2008, a MMR catch-up action enabled 4,500 pupils in compulsory education in the canton of Vaud to be vaccinated. Following an outbreak in an army barracks at the beginning of 2009, which led to post-exposure vaccination of about forty soldiers, the army health directorate introduced free, voluntary catch-up MMR vaccination for all conscripts. In order to improve coverage for vaccines recommended by the FOPH, in particular the MMR vaccine, Switzerland took part in the European vaccination week for the first time in 2009. On that occasion, the FOPH revised its Internet site dedicated to the promotion of vaccination [30] and distributed two new brochures to the population via physicians and pharmacists, one brochure being specifically about measles.

Media coverage of the third wave of measles reached an unprecedented level for measles. The messages of the federal and cantonal health authorities, in particular calls for vaccination, were transmitted on a large scale.

Political dimension of the elimination of measles

This epidemic has also become a political topic. The conference of cantonal health ministers has publicly committed to fight against measles in February 2009, with a view to its elimination, and to make further efforts to achieve ≥95% vaccination coverage [31]. It will consider introducing compulsory vaccination against measles before children go to kindergarten or to school, if this objective cannot be achieved by other means. Parliamentary interventions originating in both federal chambers have also successfully requested that the federal government launch a national plan to eliminate measles. This political impetus speeds up the preparation of such a plan, which was already underway at the FOPH. The main strategic focuses are to obtain the commitment of political and public health stakeholders, to reinforce the promotion of MMR vaccination through communication campaigns, to facilitate access and encourage vaccination through organisational measures, to control outbreaks of measles and to strengthen the surveillance of measles.

Discussion

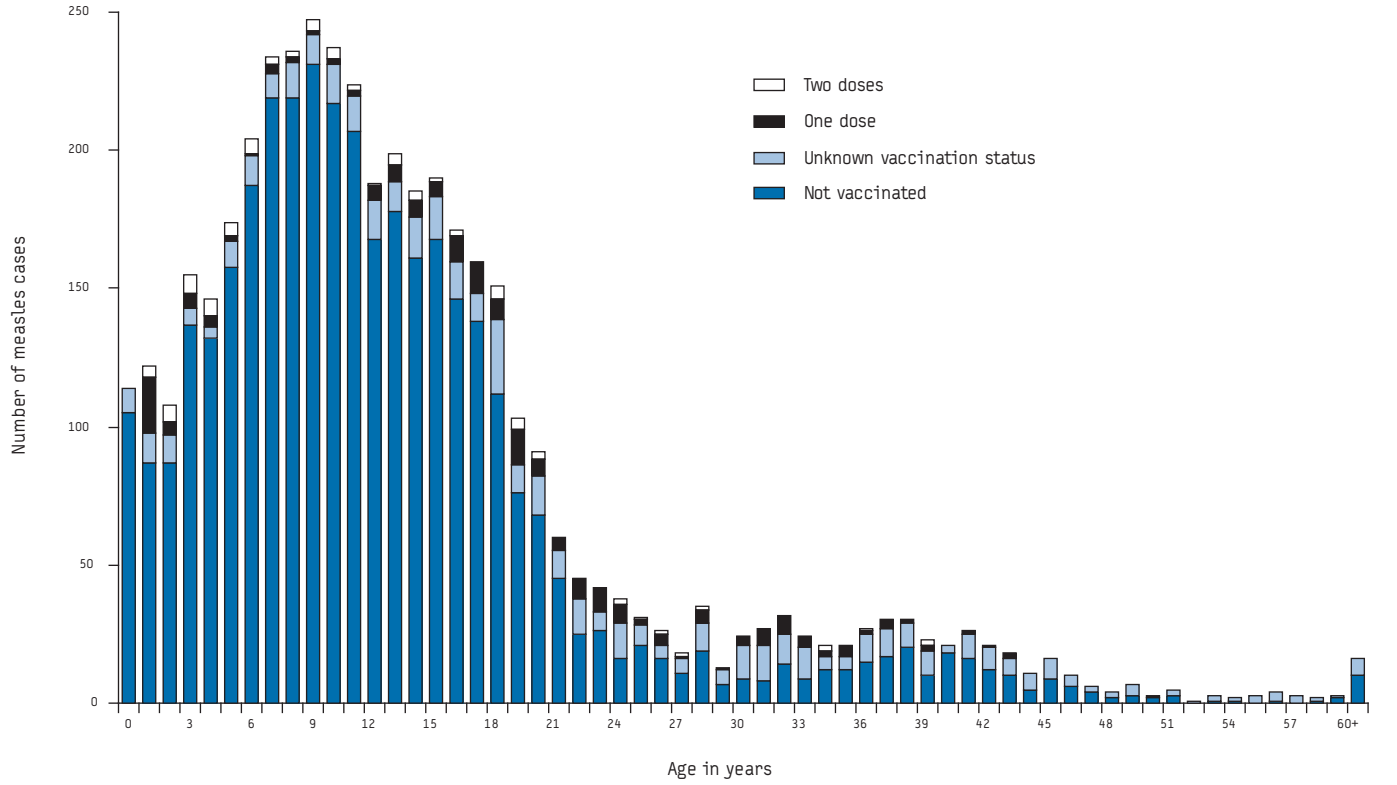
With 4,387 reported cases, since the end of 2006, Switzerland has recorded the largest and longest lasting measles epidemic since compulsory notification of this disease was introduced ten years ago (82% of all cases notified). However, the actual number of cases is certainly higher: an intensive survey of contacts suggests that only about one out of two cases were diagnosed by a physician and notified [personal communication Dr. E. Masserey]. The epidemic mainly affected younger school children and to a lesser extent adolescents and adults who had not been vaccinated. Ninety eight percent of patients had not been vaccinated or had been incompletely vaccinated.

In 2007 and 2008, Switzerland reported more cases, over a quarter of the total, with a 20-times greater incidence rate than the average, than any of the other 31 countries taking part in EUVAC.NET network [21,22].

The current epidemic is unusually long for Switzerland: 34 months with three distinct waves. In comparison, the 2003

Figure 5

Vaccination status by age for notified cases of measles, Switzerland, 15 November 2006 to 17 September 2009 (n=4,391)



epidemic only lasted six months, with six times less cases. Epidemics with several thousand or tens of thousands of cases, lasting for two to three years have been recorded recently in Europe, in particular in Romania, Georgia and Ukraine [32]. The proportion of people susceptible to measles in the Swiss population, their spatial distribution and the intensity of their contacts with parts of the world where measles are endemic are factors that allowed this prolonged though fluctuating circulation of the measles virus at the national level. During the last three years it led to numerous local and regional outbreaks, occurring successively or simultaneously, sometimes reaffecting regions that had already been affected.

Despite many importations of measles, only the D5 virus was circulating widely throughout Switzerland from the start of the epidemic until summer 2008. The beginning of the third wave, in autumn 2008, seems to coincide with the appearance of a new virus, D4, MVs/Enfield.GBR/14.07, that is endemic in the United Kingdom since April 2007 [33]. It was found in Eastern and Central Switzerland, from where the previous D5 virus was no longer reported. However, the same variant of the D5 virus reappeared in the French-speaking part of Switzerland at the beginning of 2009, following reintroduction from France, where it had been imported from the German-speaking part of Switzerland in spring 2008 [27]. Before this epidemic in Switzerland and the secondary outbreaks in neighbouring countries, the D5 virus had recently only been reported in Europe as rare, with sporadic cases or limited outbreaks, generally related to importations [34].

Inadequate vaccination coverage for many years and relatively low incidence of measles since 2004 has allowed the number of non-immune individuals to build up, feeding the current outbreaks. As expected, the incidence of measles per canton tends to increase with lower vaccination coverage. In addition, the high proportion of unvaccinated patients among cases confirms that this large epidemic was mainly due to inadequate vaccination coverage. The number of people in Switzerland who are under 20 years of age and are not immune to measles is currently estimated to be 214,000 (13% of this age group) from data on vaccination coverage and on notified cases. No seroepidemiological survey has been performed recently. The proportion varies from 9% to 18% depending on the canton, but is always above 5%, the threshold below which herd immunity establishes itself [35]. In addition, an unknown but likely small proportion of adults, in particular those under 45 years of age, is not immune.

This unsatisfactory situation can be explained by the deliberate choice not to vaccinate, made by certain parents, rather than by limited access to vaccination. Indeed, vaccination is widely available through paediatricians and family doctors. Up to 90% of the cost is covered by the compulsory health insurance scheme and several cantons offer free catch-up MMR vaccination in schools. The low amount payable by parents is probably just a minor barrier to access to vaccination. Indeed, vaccination coverage with at least three doses of a vaccine against diphtheria, tetanus, pertussis and poliomyelitis reaches approximately 95% compared with 87% for measles, while the recipient must also pay at least 10% of the invoice. In addition, vaccination coverage for measles decreases with the increasing level of education of the mother, and children of foreign nationality have a higher rate of vaccination than Swiss children [36]. As a result, vaccination coverage for measles is most probably higher in families with a lower income than in affluent families. Children of families using alternative medicine are in particular less often vaccinated than others. The canton of Lucerne where there are relatively high numbers of homoeopathic medical practitioners, has recorded about a quarter of all cases, often notified by such physicians. Some of these families who chose not to vaccinate their children also favour alternative education, in particular in private anthroposophic schools, which are often major foci as soon as measles are introduced. This was recently observed in Switzerland in the area of Basel, in Lausanne and in Berne, and elsewhere in Europe [25,26,37,38]. In addition to reluctance to vaccinate, missed opportunities certainly contribute to the accumulation of non-immune people. However, they seem to relate in particular to the second dose in children and catch-up vaccination for adults born after 1963.

Although they are still insufficient, interventions to control outbreaks of measles have continuously increased throughout this epidemic. In general they are well accepted by the population, but still have to be extended to the country as a whole. The prior aim of the measures is to stop the transmission of the virus rapidly, if not to prevent it. To this end, rapid notification of cases is crucial. This is why the delay for notification was reduced from one week to 24 hours in 2006. However, sometimes physicians are slow in notifying or do not notify cases at all. In these instances intervention is more difficult and its effectiveness reduced. Where implemented, measures such as exclusion of susceptible contacts from school have encouraged vaccination: parents have preferred to vaccinate their children rather than risking their eviction.

Consequences for the elimination of measles

Despite its magnitude, the current epidemic has only slightly (-1.4%) decreased the proportion of non-immune people in Switzerland aged less than 20 years. Although the epidemic is now over, a new one could start at any time. Therefore, it is essential to achieve very high vaccination coverage (≥95%) of each new birth cohort with two doses of MMR vaccine; but this will not be enough to eliminate measles in Switzerland: in parallel, catch-up vaccination has to be intensified for susceptible people born after 1963 ensuring that they are vaccinated with two doses of MMR.

The situation in Switzerland is a national challenge and a threat for the elimination of measles from the WHO European Region, as shown by the numerous exportations of measles. Further efforts are necessary and are planned by the national and cantonal health authorities so that with the help of partners and of the population, vaccination coverage can be increased to ≥95% and measles can be eliminated in Switzerland.

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