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ORIGINAL ARTICLES

Euro roundup

VARICELLA ZOSTER VIRUS VACCINATION POLICIES AND SURVEILLANCE STRATEGIES IN EUROPE

A Pinot de Moira, A Nardone*

The incorporation of varicella zoster virus (VZV) vaccination in childhood immunisation schedules is becoming an increasingly common option in Europe. The current study forms part of the European Sero-Epidemiology Network 2 (ESEN2) organisational analysis for VZV and describes current passive immunisation policies, as well as current and proposed active immunisation strategies, and existing surveillance systems for diseases caused by the varicella zoster virus in ESEN countries.

A questionnaire was compiled and distributed to 23 participating countries. A VZV vaccine is currently licensed in 14 of the 20 participating ESEN countries. Germany is the only country to have incorporated VZV vaccination into its routine childhood immunisation programme. Three further countries currently recommend vaccination of children against VZV and five countries are also considering introducing routine immunisation against VZV for children. However, of the eight countries with or considering introducing childhood VZV immunisation, only six have case-based mandatory notification of varicella, and only two countries have primary care surveillance data available for herpes zoster.

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Introduction

Varicella is a self-limiting and relatively mild disease of childhood, although it is frequently more severe and complicated amongst neonates (severe neonatal varicella), adults, pregnant women (potentially leading to congenital varicella syndrome in the child) and the immunocompromised. In addition, after an initial infection, the varicella zoster virus (VZV) lays dormant in dorsal root ganglia and may reactivate with declining cellular immunity to cause herpes zoster, particularly in the elderly and immunocompromised [1].

There are two methods of varicella infection control using immunisation: post-exposure passive antibody prophylaxis in the form of varicella zoster immunoglobulin (VZIG or VARITECT) and active vaccination. The varicella vaccine, which was developed in the early 1970s using a live attenuated form of the varicella zoster virus [2], has been licensed for use in some countries since the mid 1980s and has been part of the routine childhood immunisation schedule in the United States (US) since 1995 [3]. The cost-effectiveness of mass vaccination against varicella has, however, been questioned [4,5].

Universal vaccination programmes may cause an increase in the average age of infection, which may lead to increased adult morbidity and incidence of congenital varicella syndrome (CVS) and severe neonatal varicella. Studies have also suggested that re-exposure to exogenous varicella zoster virus protects against herpes zoster [6,8], thus, a reduction in the transmission of VZV (through vaccination) could result in an increased incidence of zoster.

Many European countries have already introduced targeted VZV vaccination for risk groups, and others are considering recommending either targeted vaccination or routine mass childhood immunisation. Only Germany has recently introduced VZV vaccination into the routine vaccination schedule. This is, therefore, an opportune moment to catalogue current passive immunisation policies, as well as current and proposed active immunisation strategies, and existing surveillance systems for diseases caused by the varicella zoster virus.

Methods

The European Sero-Epidemiology Network 2 (ESEN2) is a network of 22 European countries and Australia that aims to coordinate and harmonise the serological surveillance of immunity to a variety of vaccine preventable diseases in participating countries, including VZV [9]. This study formed part of the ESEN2 organisational analysis for VZV, the aim of which was to collate information regarding immunisation strategies and surveillance systems for the diseases under investigation.

A descriptive questionnaire was compiled, querying current and proposed VZV vaccination strategies and current surveillance of VZV. The questionnaire was split into three sections:

1. Current licensing of a VZV vaccine plus vaccine contraindications, current targeted vaccination of risk groups and mass vaccination, and also current use of VZIG.
2. Proposed mass childhood immunisation and targeted vaccination of specific groups. Questions included details of vaccination schedules, age and risk groups targeted, and catch-up campaigns being considered.
3. Current surveillance strategies for varicella, herpes zoster, congenital varicella syndrome and neonatal varicella, in particular mandatory notification, national hospital morbidity data and national primary care databases.

The questionnaire was distributed in February 2004 to lead epidemiologists in all 23 countries participating in the ESEN2 project. After three weeks a reminder was sent to participants to improve the response rate. Responses were received from 20 countries (87% of countries contacted) with a representative spread across Europe. Results were discussed at a one day workshop and returned to all participants for validation and feedback.

Results

Passive immunisation strategies

Eleven of the 20 countries responding (Australia, Cyprus, England and Wales, Germany, Greece, Ireland, Israel, Italy, Lithuania, Malta, the Netherlands) currently use passive antibody prophylaxis for exposed risk groups. Groups for which prophylaxis is recommended include neonates and premature infants, pregnant women, and the immunocompromised.

Various VZV susceptibility screening procedures have been adopted for risk groups. For example, screening procedures for exposed pregnant women include either a verbal screen (Israel, Cyprus, and Malta), a serological screen (Australia, Germany, Italy, and the Netherlands) or a combination of the two (Greece, England and Wales, and Ireland).

Active immunisation strategies

A VZV vaccine is currently licensed in 14 of the 20 responding countries; the six countries without a licensed vaccine are Bulgaria, Greece, the Netherlands, Romania, Slovakia and Slovenia.

Germany is the only country in Europe with routine childhood immunisation against VZV: VZV vaccination was incorporated into the routine immunisation schedule in July 2004, as a single dose at the age of 11-14 months [10].

In Lithuania, Cyprus, and Israel, VZV vaccination is recommended for children and is available either privately, or, as in Israel, through Health Maintenance Organisations (HMOs), but is not yet part of the routine childhood immunisation schedule. For Israel and Cyprus, the intention is to incorporate VZV vaccination into the routine childhood immunisation schedule in the short to medium term. Cyprus intends to vaccinate infants aged 13-18 months and children aged 11-12 years with no history of varicella, whereas Israel intends to administer the vaccine at the same time as the MMR vaccine, as a single dose at 12 months.

In Italy, there are no national recommendations for routine childhood immunisation, but, since July 2002, one of the twenty regions (Sicily) has offered free vaccination in the second year of life and for all anti-VZV negative 12 year olds.

Australia, Slovenia and Malta are also considering introducing recommendations for childhood immunisation against VZV in the short to medium term. Slovenia and Malta intend to combine vaccination with the MMR vaccine first dose, whilst Australia proposes to offer vaccination at 18 months with a catch-up at 10-13 years.

Eleven countries (Belgium, England and Wales, Finland, Germany, Israel, Ireland, Italy, Luxembourg, Malta, Slovenia and Spain) currently have targeted vaccination of specific groups, and one country (Slovakia) intends to issue guidelines for vaccination of specific groups [TABLE 1]. All of these countries, but England and Wales, either currently, or intend to, vaccinate immunocompromised patients. Susceptible healthcare workers are vaccinated in eight countries, with one further country (Israel) intending to introduce vaccination for healthcare workers. Interestingly, Belgium and Germany also recommend vaccination for susceptible child care workers.

Surveillance systems

Table 2 displays current surveillance systems for varicella in participating countries. Of the five countries with some degree of childhood immunisation in place (Cyprus, Germany, Israel, Italy and Lithuania), Cyprus, Israel and Italy have case-based mandatory notification of varicella, and Lithuania has mandatory notification of varicella epidemics, as did Israel between 1949 and 2003. Italy also has a sentinel surveillance system based on paediatricians, estimated to cover roughly 4% of children aged 0-14 years. None of these countries, however, have primary care based sentinel surveillance data for herpes zoster, although data from HMOs are available in Israel [11]. Israel also has hospital morbidity data available for both varicella and herpes zoster, as does Italy. In Germany, there are plans for a sentinel surveillance scheme, based on that currently in place for measles, to be in place by 2005 for both varicella and herpes zoster.

TABLE 2

Current surveillance strategies for varicella in 19 European countries and Australia, 2004

Country	Mandatory Notification		Sentinel surveillance of primary care	
	Year established	Case-based or aggregate	Year established	Estimated coverage
Countries with childhood vaccination (where childhood VZV vaccination is currently recommended or where routine vaccination is undertaken in one major region of the country)				
Cyprus	2004	Case-based	-	-
Germany	-	-	2005	-
Israel	1949	Case-based†	†	†
Italy	1961	Case-based	2000	4% <14yrs
Lithuania	1973	Aggregate	-	-
Countries intending to introduce childhood vaccination				
Australia	n/r	Case-based*	n/r	n/r
Malta	n/r	Case-based	-	-
Slovenia	1977	Case-based	Unknown	Unknown
Other countries				
Belgium	-	-	-	-
Bulgaria	1940	Aggregate	-	-
England & Wales	-	-	1967	1%
Finland	-	-	n/r#	n/r#
Greece	1950	Aggregate\$	2000	n/r
Ireland	2004	Case-based**	2000	3%
Latvia	1999	Case-based	-	-
Luxembourg	-	-	-	-
Netherlands	-	-	2000	1%
Romania	1978	Aggregate	-	-
Slovakia	1953	Case-based	-	-
Spain	1904	Aggregate	-	-

† Databases owned by HMOs

‡ Case-based notification introduced in 2003

* State of South Australia only

** Case-based mandatory notification of outbreaks

Local primary care varicella databases (no national sentinel surveillance) mandatory laboratory reporting

\$ Replaced by notification of 'varicella with complications' in 2004

n/r not reported

TABLE 1

Current and proposed targeted vaccination against Varicella Zoster Virus (VZV) in 12 European countries, 2004

Country	Immuno-compromised	Contacts of immunocompromised	Susceptible healthcare workers	Susceptible child care workers	Susceptible adolescents	Susceptible women of childbearing age
Belgium	+/-	+/-	+/-	+/-	+/-†	
England & Wales			+			
Germany	+	+	+	+	+	+
Italy	+				*	
Luxembourg	+/-	+/-	+/-			+/-
Malta	+		+			
Slovenia	+		+			
Spain	+		+		*	
Finland	+/-	+/-			+/-	
Ireland	*		+			
Israel	+/-	+/-	*			+/-
Slovakia	*					

+ free or reimbursed vaccination currently in place

+/- vaccination available privately (in Israel, through HMOs)

* under consideration

† Also recommended for healthy seronegative adults

Of the countries intending to introduce childhood immunisation against varicella (Australia, Slovenia and Malta), only Slovenia currently has primary care surveillance data for herpes zoster. In addition to this, Slovenia has varicella primary care data and case-based mandatory notification of varicella, for which data on attendance at daycare facilities and hospitalisation are collected [12]. Malta also has case-based mandatory notification of varicella. In Australia, although only the state of South Australia has mandatory varicella notification, data are also collected via sentinel surveillance of family doctors through the Australian Sentinel Practice Research Network.

Within those countries with neither childhood vaccination nor any current intentions to introduce it, Greece, Latvia and Slovakia have mandatory notification of varicella. In Greece, mandatory notification of 'varicella with complications' replaced notification of 'varicella' in 2004. Slovakia is the only participating country that has case-based mandatory notification of herpes zoster. Bulgaria, Ireland, Romania and Spain have mandatory notification of varicella epidemics. The Netherlands, Ireland, and England and Wales have primary care sentinel surveillance data for both varicella and herpes zoster.

Discussion

Since its development in the early 1970s, the VZV vaccine has been licensed in numerous countries and incorporated into the US routine childhood immunisation schedule. Many European countries have targeted VZV vaccination of susceptibles for whom VZV infection poses a particular risk either to themselves (e.g. immunocompromised patients) or to others (e.g. healthcare workers), with many more considering introducing either targeted or mass childhood immunisation. Germany is the only country to have recently incorporated VZV vaccination into their routine childhood immunisation schedule, but several other countries plan to do so in the near future. Cyprus, Israel and Lithuania currently recommend VZV vaccination for children, and routine mass childhood immunisation has already been introduced in the Sicily region of Italy.

As with most universal mass vaccination, childhood immunisation against VZV could have a negative impact should it be introduced without sufficient coverage to induce herd immunity. Low vaccine coverage can result in an increase in the average age of primary infection, with a concomitant increase in severity of varicella in adult age groups [13], and especially in pregnant women, where infection can have adverse sequelae for both the mother and unborn child [14]. The levels of coverage estimated in countries with current VZV vaccination (approximately 25%), will have little impact on the age distribution of disease [15]. However, with increasing coverage, morbidity amongst adults is likely to increase, and vaccination is only predicted to decrease morbidity in both adults and children at around 70% coverage [16]. Thus, it is important that universal vaccination against VZV is introduced in a region or country only if the attainment of very high coverage can be assured. Furthermore, it is important that the age distribution of varicella disease is monitored, and this is best done through case-based surveillance of varicella. Of the eight countries that have or are considering introducing childhood VZV immunisation, only six have case-based mandatory notification of varicella. Initially, while disease incidence remains high, a well managed sentinel surveillance system could be an acceptable alternative: of the two countries without case-based mandatory notification of varicella, one is intending to implement such a surveillance system.

Exogenous exposure to varicella is thought to protect against zoster through boosting specific immune responses [6]. Therefore, the impact VZV vaccination will have on herpes zoster also needs to be considered. In the US, where mass childhood immunisation has been in place since 1995, no change in herpes zoster incidence was reported amongst 10-14 year olds, but the incidence of zoster in this

age group is low, and declines in exogenous VZV exposure would have been both recent and not immediate [17]. Mathematical modelling of a mass childhood immunisation strategy against VZV has predicted that there would be a significant rise in zoster morbidity, which is predicted to last more than 60 years [14]. Any country considering mass vaccination, should, therefore, have suitable surveillance for herpes zoster. Only two of the eight countries that have or are proposing to introduce childhood vaccination have primary care surveillance data available for herpes zoster.

Many countries have opted to limit vaccination to specific groups who are at increased risk of developing severe varicella disease or infecting risk groups (for example, healthcare workers). Targeted strategies have been predicted to have little impact on varicella incidence [16], and, consequently, are predicted to have little impact on herpes zoster [18], and the age distribution of primary disease [15]. Mass vaccination against VZV should be introduced only if very high coverage can be assured. With the introduction of routine childhood immunisation against VZV, however, adequate surveillance systems for both varicella and herpes zoster are advisable.

* ESEN2 group:

Australia: J Backhouse, L Gilbert. Belgium: P van Damme, L De Cock, H Theeten, N Thiry, R Vranckx. Bulgaria: N Gatcheva, V Voynova. Cyprus: C Hadjianastasiou, M Zarvous. Finland: I Davidkin, S Jokinen. Germany: W Hellenbrand, S Reiter, A Tischer. Greece: C Anastassopoulou, T Georgakopoulou, A Hatzakis, T Panagiotopoulos. Ireland: M Carton, S Cotter, D O'Flanagan. Israel: D Cohen, L Moerman, Z Smetana. Italy: P Crovari, G Gabutti, MC Rota. Latvia: I Lucenko, J Perevoscikovs, I Velicko. Lithuania: V Bakasenas, J Surauciene. Luxembourg: J Mossong, F Schneider. The Netherlands: G Berbers, H de Melker. Malta: A Amato-Gauci, C Barbara. Romania: A Pistol. Slovakia: J Lancová, M Sláčíková. Slovenia: A Kraigher, K Prosenec. Spain: C Amela, F de Ory. UK: E Miller, RG Pebody.

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