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Outbreak of Marburg Haemorrhagic Fever in Angola

As of 20 April 2005, 266 cases of Marburg haemorrhagic fever have been reported in Angola. There have been 244 deaths, a case fatality rate of 91.7%.[1] Most of the cases in the early stages of the outbreak were in children but increasingly cases are occurring in adults. The outbreak is believed to have begun in Uige Province in October 2004. Although several other provinces (Luanda, Cabinda, Malange and Kuanza Norte) have reported cases, most of these cases have been linked directly to the outbreak in Uige. This is the largest reported outbreak of Marburg haemorrhagic fever to date and the first to occur in an urban setting.[2]

WHO and its partners are using the Global Outbreak and Response Network (GOARN) to support the Ministry of Health in Angola in strengthening infection control in hospitals, intensifying case finding and contact tracing activities, and improving public understanding of the disease and its transmission.[2]

Clinical Features

Marburg virus causes a severe acute illness with sudden onset of fever, malaise, myalgia and headache followed by vomiting and diarrhoea and maculopapular rash. Many patients develop severe haemorrhagic manifestations and multiorgan failure between five and seven days after the onset of symptoms. The incubation period is three to nine days.

Diagnosis

The diagnosis is made by antigen detection employing enzyme linked immunosorbent assay (ELISA), viral genome detection by PCR, by the demonstration of IgM antibody or a four-fold rise in IgG antibody in serum. Virus isolation should take place in a Containment Level 4 laboratory as Marburg virus is highly pathogenic.

Occurrence

Marburg virus belongs to the same virus family, filoviridae, as the virus which causes Ebola haemorrhagic fever. Marburg virus was first recognised in 1967 when outbreaks of haemorrhagic fever occurred in Marburg and Frankfurt in Germany, and in Belgrade in the former Yugoslavia. Thirty seven people (seven fatalities) were infected as a result of being exposed to African green monkeys imported from Uganda. Outbreaks and sporadic cases have been reported in Angola, Democratic Republic of Congo, Kenya, and South Africa (index case had been infected in Zimbabwe).[3]

Reservoir of Infection

The reservoir of infection is unknown despite extensive studies.

Transmission

Person-to person transmission occurs through direct contact with infected blood and body fluids. Risk is highest during the later stages of illness when the patient is vomiting, having diarrhoea or haemorrhaging, and also during funerals with unprotected body preparation. Risk is low during the incubation period. Nosocomial infections have been frequent.[3]

Treatment

Treatment is supportive. There is no specific treatment or vaccine against Marburg haemorrhagic fever.

The risk of epidemic spread of Marburg haemorrhagic fever in the general population in Ireland is negligible. However, the speed and volume of international travel have increased the risk that persons incubating the disease may present after returning from high risk areas. For guidelines on the management of viral haemorrhagic fever in Ireland see www.hpsc.ie/Publications/ViralHaemorrhagicFever/

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Rubella and Congenital Rubella Infection in Ireland

Background

Rubella is usually a mild febrile illness with a diffuse punctuate and maculopapular rash.[1] It is frequently mistaken for other infections (e.g. measles, parvovirus B19, scarlet fever). Children usually present with few or no constitutional symptoms. Adults may experience non-specific symptoms of low-grade fever, headache, fatigue, upper respiratory symptoms (runny nose, sore throat), and conjunctivitis for 1-5 days before the onset of rash. Cervical and occipital lymph node swelling is characteristic of infection and may precede the rash by 5-10 days. Approximately 50% of infections are sub-clinical.

Complications, although uncommon, are more likely to occur in adults and include arthralgia or arthritis (up to 70% of adult females), encephalitis (1 in 6,000 cases), or haemorrhagic manifestations (1 in 3,000 cases).

Epidemiology of Rubella in Ireland

Rubella has been a statutory notifiable disease since 1948. Clear case definitions for rubella (both acute rubella infection and congenital rubella infection [CRI] in an infant resulting from rubella infection in utero) were introduced under the Infectious Diseases (Amendment) (No 3) Regulations 2003 (SI No 707 of 2003).[2]

Frequent large outbreaks were reported during the 1950s and 1960s with thousands of cases being reported during each outbreak.[3] The most recent outbreak occurred in 1996 (602 cases). Since 2001, approximately 50 cases are reported annually (Figure 1).

In recent years (2000-2004), the majority of rubella cases notifed were among children in the 0-4 year age group (63%) (figure 2).

Public Health Importance

Despite its mild clinical presentation in most cases, rubella is considered to be a disease of major public health importance due to its potential to cause congenital rubella syndrome (CRS), and the fact that it is a vaccine preventable disease.

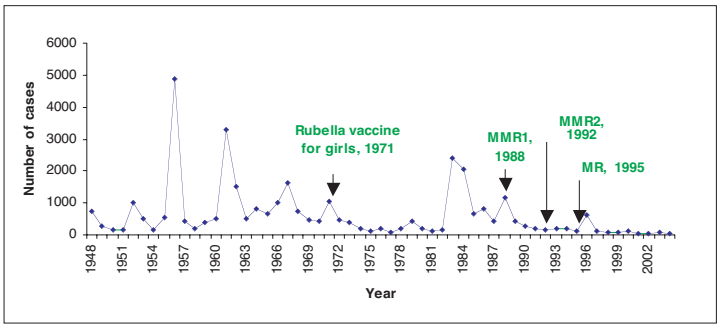

*Figure 1. Rubella notifications in Ireland, 1948 to 2004**
*Preliminary data

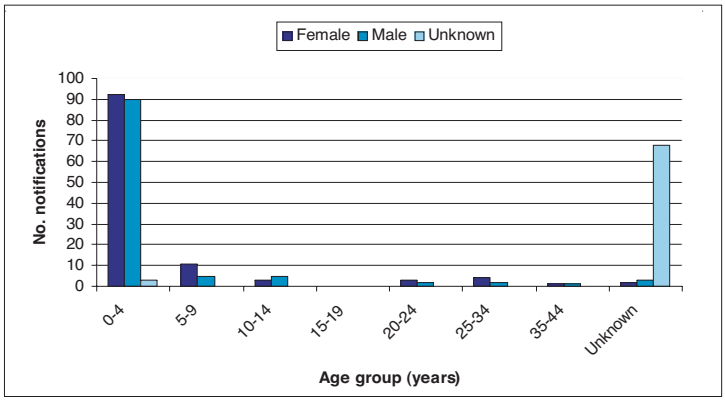

Figure 2. Rubella notifications in Ireland by age group and gender, 2000-2004 (n = 295)
*2004 data are provisional

Congenital Rubella Syndrome

Rubella infection in a non-immune pregnant woman may cause severe teratogenic effects in the foetus. The spectrum of CRS depends upon the gestational age of the foetus at the time of infection. Up to 85% of infants infected during the 1st trimester of pregnancy will be found to be affected if followed after birth. Defects are rare when infection occurs after the 20th week of gestation.

One or all of the following abnormalities may be present in the CRS infant:

- Deafness
- Cataracts
- Heart defects
- Microcephaly
- Mental retardation
- Bone alterations
- Liver and spleen damage.

Few cases of congenital rubella have been reported in Ireland in recent years in contrast to the substantial numbers reported between 1975-1990 (106 cases reported).[3] Since 1990, a total of four cases of CRS were reported to the British Paediatric Surveillance Unit (personal communication). This unit was established in 1986 and undertakes active surveillance of rare but important conditions that affect the health of children. Irish paediatricians contribute to the surveillance of identified conditions (including CRS). Each month the BPSU sends a surveillance form to each paediatrician in Ireland and the UK.[4,5] The

Table 1. The history of rubella containing vaccine usage in Ireland and the age groups targeted.

Year	Vaccine	Target population		Comment
		Age	Sex	
1971	Rubella only	12-14 years	Female only	Rubella only vaccine introduced 1971
1988	MMR*	15 months-2 yrs	Both	MMR introduced 1988
1988	MMR*	10-14 yrs	Female only	MMR introduced 1988 for girls aged 10-14 years
1992	MMR*	15 months & 10-14 yrs	Both	2nd dose MMR introduced 1992
1995	Rubella and measles (MR)	5-12 years	Both	Part of a measles/rubella campaign for 5-12 yr olds
1999	MMR*	15 months & 4-5 yrs	Both	Age at 2nd dose MMR reduced from 10-14 to 4-5 yrs
2002	MMR*	12-15 months & 4-5 yrs	Both	Age at 1st dose reduced to 12-15 months

*MMR = Measles/Mumps/Rubella vaccine

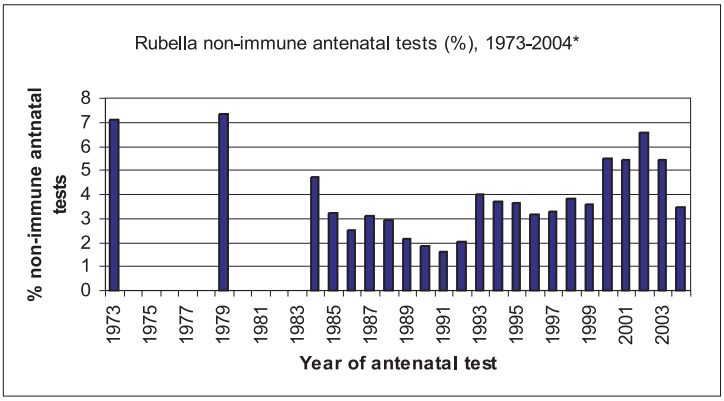

Figure 3. Proportion of antenatal tests that demonstrate rubella non-immunity, 1973 - 2004 (source NVRL).

completeness of reporting through this system is not known.

It is hoped that recent changes to ID legislation and case definitions will assist in the surveillance of rubella and clearly identify those cases which are CRS cases. Following this identification it is important that enhanced data are routinely collected on each of these cases to document the impact of this disease, and identify risk factors for infection in the mother (i.e. non-immunisation).

The impact of CRS on the developing foetus is clearly evident from information obtained from enhanced surveillance.[3] In the most recent case reported in Ireland, the infant was born with bilateral deafness, microcephaly and cranial calcifications. The infant's mother had never received a rubella containing vaccine and reported an illness, consistent with rubella, during the 4th - 5th month of pregnancy.

Rubella Vaccination in Ireland

Vaccination against rubella has been routinely recommended for schoolgirls (12-14 years of age) since 1971, and for all young children (15 -24 months) since 1988. In 1992, a second dose of MMR was introduced for all school children (10-14 years of age). In 1995, a rubella containing vaccine (MR) was administered to all children aged 5-12 years of age as part of the measles control campaign. The age for administration of the second dose of MMR was dropped to 4-5 years of age in 1999 (table 1).

Levels of Rubella Immunity Among Irish Women

In Ireland, all women are routinely screened during the first antenatal visit for rubella immunity. The National Virus Reference Laboratory (NVRL) test approximately three quarters of antenatal samples. In recent years, the proportion of antenatal women that are rubella sero-nonimmune has ranged from 3.5 to 6.5% (figure 3).

Recent results of a serological survey conducted in Ireland on approximately 2600 individuals during 2002-2003 as part of the European Seroepidemiology Study 2 [ESEN2] provide additional information on the rubella immunity of women in the child bearing age groups and indicate a level of non-immunity similar to that found by the NVRL. On average, 3.6% of women between 15-39 years of age are non-immune. The proportion of non-immunity differs by age group (range 1.6%-4.7%) (figure 4).

Discussion

Clinical rubella notifications have decreased dramatically following the routine usage of rubella containing vaccines as part of the childhood immunisation programme. In 1998, the European Region (EUR) of the World Health Organization (WHO) committed itself to a reduction in the incidence of CRS in all countries to <1 per 100,000 live births by 2010 in tandem with a measles elimination strategy.[6] Ireland has committed itself to realising this goal.

Measles and rubella vaccines can induce long-term immunity with

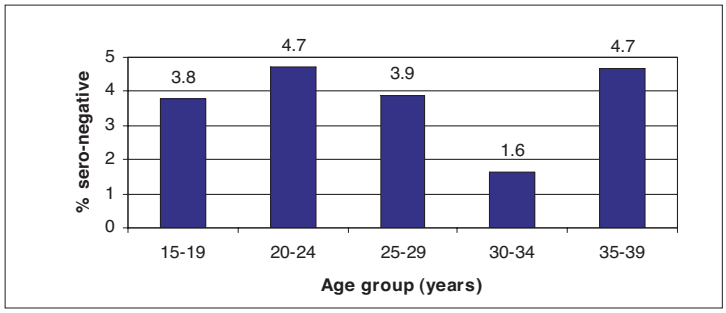

Figure 4. Rubella sero-negative profile for women, by age group (ESEN2)

an effectiveness of 90-95%. Successful reduction in the incidence in congenital rubella infection (CRI) requires maintaining low levels of susceptibility among women of childbearing age and ensuring high levels of herd immunity, thus preventing unnecessary transmission to susceptible non-immune women.

In recent years, MMR coverage in Ireland has been sub-optimal, well below the 95% level required to ensure herd immunity to rubella transmission. Countries (such as Ireland) with low immunisation coverage typically will see a reduction in rubella virus circulation among children. However, a larger proportion of unvaccinated children will reach adolescence and adulthood without being infected, creating an increased pool of susceptible women of childbearing age. During a rubella outbreak, these women will have an increased risk for infection, increasing the number of children with CRS compared with countries where rubella vaccine has never been used. Countries such as Ireland, with low levels of coverage with rubella vaccine have an opportunity to markedly reduce the risk and burden of CRI by linking prevention activities with accelerated control of measles using MMR vaccine.[1]

The National Measles Elimination Committee (convened under the Department of Health and Children) is developing a strategy of measles elimination in Ireland, to be achieved by 2010. Part of this strategy will include ensuring high levels of MMR uptake so that CRS rates are maintained at <1 case per 100,000 live births.

As part of the WHO European Region rubella control strategy it is recommended that all countries collect enhanced information on all rubella cases (including CRS). Enhanced CRS surveillance is an important adjunct to monitoring the success of the rubella control programme. An enhanced questionnaire has been developed which can be used to ensure standard investigation of any CRS case that might be identified in Ireland.

- **Clinicians are reminded that all cases of rubella are notifiable.**
- **An enhanced CRS surveillance system, collecting additional data on risk factors for infection and infant outcomes is recommended. This information will assist in identifying women at risk of infection and can inform strategies to improve coverage amongst this population.**
- **A standardised template (form) for collecting this information has been developed as part of the measles/rubella control strategy.**

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Immunisation Uptake in Ireland, 2004

Introduction

The current Irish childhood immunisation schedule recommends that newborns should receive one dose of BCG and infants receive three doses of DTaP/IPV/Hib and MenC at 2, 4 and 6 months of age. Between 12 and 15 months these children should receive the first dose of MMR. In this report immunisation uptake statistics for 2004 are presented. These statistics relate to children who were 12 and 24 months of age in 2004, i.e. birth cohorts born between 01/01/2003 & 31/12/2003 and 01/01/2002 & 31/12/2002 and who completed the immunisation schedule outlined above.

Immunisation uptake rates at 12 months

In 2004, national immunisation uptake rates at 12 months were 83% for D_3, P_3, T_3, Hib_3, $Polio_3$ and $MenC_3$. This was an improvement of 2.5% when compared to 2003. Immunisation uptake rates in Ireland have been steadily rising each year since 2001, when uptake of vaccines was 68-70%. Uptake of the above vaccines in 2004 ranged from 79% in the Eastern Area to 90% in the Midland Area. Five of the eight HSE Areas had uptake rates greater than 85% (table 1). Last year (2004) was the first entire year that BCG uptake rates were available, with five of the eight HSE Areas in a position to provide figures (representing a third of the national birth cohort). BCG uptake in these areas was 90.5%.

Immunisation uptake rates at 24 months

In 2004, an improvement in immunisation uptake rates was also seen in those 24 months of age. National uptake for D_3, P_3, T_3, Hib_3 and $Polio_3$ was 89%, 88% for $MenC_3$ and 81% for MMR_1 (figure 1). Compared with 2003, uptake of D_3, T_3, Hib_3 and $Polio_3$ improved by 3%, P_3 by 3.6%, $MenC_3$ by 4% and MMR_1 by almost 3%. MMR_1 uptake in 2004 was the highest recorded since the collation of these statistics commenced in the current format, in 1999. Uptake of D_3, P_3, T_3, Hib_3, $Polio_3$ and $MenC_3$ ranged from 85-86% in the Eastern Area to 93-95% in the North Western Area, while MMR_1 uptake ranged from 76% in the Eastern Area to 91% in Midland Area (table 1).

Discussion

An improvement in immunisation uptake rates at both 12 and 24 months was observed in 2003. This improvement continued in 2004, with even higher rates recorded. The 2004 uptake figures at both 12 months and 24 months are the highest reported since collation of these data commenced in 2001 and 1999, respectively. For all the vaccines with the exception of MMR_1, immunisation uptake rates at 24 months were 90% or greater in four of the eight HSE Areas. These improvements are very encouraging and are a reflection of the work done by health care professionals and allied staff in the regions in promoting immunisation, making updates to the immunisation registers, and undertaking data cleaning on these systems. It is vital that these improvements can be built on, so that the required 95% target rate can become a reality. Initiatives currently being undertaken by the Programme of Action for Children which include defining the requirements of a proposed national IT system to register and track immunisations, producing immunisation health promotion materials and providing support for regional immunisation initiatives, will undoubtedly have a very positive impact in maximising immunisation uptake in Ireland.

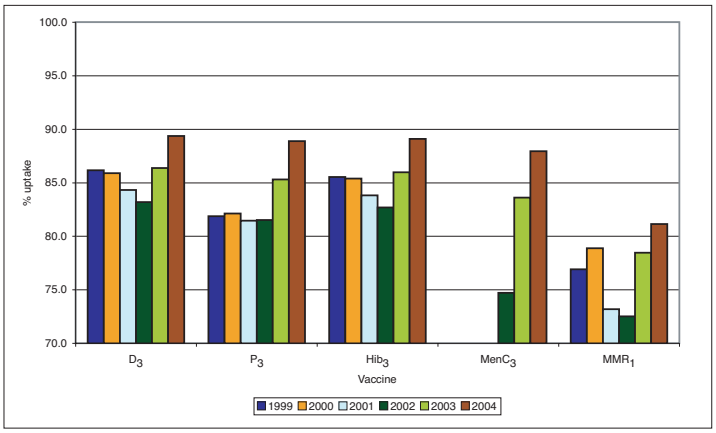

Figure 1. National annual immunisation uptake rates at 24 months
Note scale ranges from 70-100%
Since T_3 uptake identical to D_3, only D_3 uptake figures presented and $Polio_3$ uptake almost identical to Hib_3 figures, only Hib_3 data presented

Quarterly immunisation uptake reports are available at www.hpsc.ie/Publications/Immunisation/

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Acknowledgements
HPSC would like to thank the HSE Areas for providing these data. Particular thanks to the specialists in public health medicine, surveillance scientists, immunisation co-ordinators and system analysts for their help.

HSE Area	% Uptake at 12 months			% Uptake at 24 months			
	Cohort born 01/01/2003 - 31/12/2003			Cohort born 01/01/2002 - 31/12/2002			
	D_3*	Hib_3**	$MenC_3$	D_3*	Hib_3**	$MenC_3$	MMR_1
Eastern	79.0	79.0	78.5	86.1	85.9	84.5	76.1
Midland	89.9	89.9	89.8	94.0	94.0	93.9	91.0
Mid-West	86.2	86.1	86.0	89.2	88.8	88.2	83.7
North Eastern	86.3	86.2	85.8	93.3	92.7	92.1	82.6
North Western	89.2	88.7	88.5	95.1	94.1	93.4	87.0
South Eastern	86.4	86.2	85.8	91.5	91.3	90.3	86.6
Southern	83.3	83.2	82.9	89.3	89.1	88.4	83.5
Western	81.0	80.9	79.4	89.8	89.7	86.5	77.5
Ireland	**83.1**	**83.0**	**82.6**	**89.4**	**89.1**	**87.9**	**81.1**

* Since P_3 and T_3 uptake almost identical to D_3, only D_3 uptake figures presented
** Since $Polio_3$ uptake almost identical to Hib_3 figures, only Hib_3 data presented