EPI-INSIGHT

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IN THE NEWS!

Wild Poliovirus Eradication

Through the efforts of the World Health Organisation (WHO) polio should be eradicated from the last remaining reservoirs of wild poliovirus in Africa and Asia within the next few years. Once the global eradication of polio has been achieved the only remaining source of wild poliovirus will be from laboratories. The risk of wild poliovirus escaping from laboratories into the community is exceedingly small. Were this to occur, however, it would represent a major threat to public health, particularly once the use of polio vaccine is suspended following global eradication.The WHO has produced a global action plan for the laboratory containment of poliovirus. Each country must complete a survey of laboratories and ensure that poliovirus infectious, or potentially infectious, materials are stored under appropriate biosafety conditions (BSL-2/polio). At a later stage, once global eradication has been achieved, all materials containing poliovirus will be destroyed or transferred to maximum containment facilities (BSL-4).A national plan for the laboratory containment of poliovirus in Ireland has been drawn up and was recently presented to the regional WHO polio eradication committee. Over the next 12 months any laboratory that stores biological materials for more than one month will be asked to complete an inventory of materials that may contain poliovirus. It is likely that few, if any, laboratories in Ireland will possess poliovirus-infectious material. It is important, however, that this detailed inventory is carried out to ensure that Ireland remains polio-free. Copies of the WHO global action plan for laboratory containment of poliovirus can be downloaded from www.who.ch/gpv-documents/DocsPDF/www9829.pdf.

SRSV Outbreak

The investigation of an extensive outbreak of gastrointestinal illness associated with a hotel in the Southern Health Board (SHB) region over the Christmas/New Year period is nearing completion. Over 400 people are known to have been affected. Eight cases were hospitalised. Early evidence suggested that the cause was likely to be viral in origin. Small Round Structured Virus (SRSV) infection was subsequently confirmed by polymerase chain reaction (PCR) of stool samples. The hotel closed voluntarily for a period. Control measures recommended by the Outbreak Control Team included very specific recommendations on environmental decontamination of the premises. These were based on recently published expert advice reported by the Public Health Laboratory Service (PHLS) in Bristol, UK.[1] SRSVs may be spread from person-to-person by the faecal-oral route and by vomiting, probably by causing widespread aerosol dissemination of virus particles, environmental contamination and subsequent indirect person-to-person spread. SRSVs can also be transmitted via contaminated water and food.

1.Management of hospital outbreaks of gastro-enteritis due to small round structured viruses. Report of the Public Health Laboratory Service Viral Gastroenteritis Working Group. *Journal of Hospital Infection* 2000; **45**: 1-10

Dr M O Sullivan, Specialist in Public Health Medicine, SHB(on behalf of the Outbreak Control Team)

EPIET training fellowships for intervention epidemiology in Europe

The European Programme for Intervention Epidemiology Training (EPIET) started in 1995 and is funded by the European Commission and various EU member states as well as Norway. A seventh cohort of fellows is planned, starting in September 2001. The programme invites applications of eight fellowships for this 24-month training programme in communicable disease field epidemiology. Applicants for the 2001 cohort should have experience in public health, a keen interest in field work and be pursuing a career involving public health infectious disease epidemiology. They should have a good knowledge of English and of at least one other EU language, and be prepared to live abroad for a period of 24 months. The appropriately experienced professional is likely to be below 40 years of age. The aim of the training is to enable the fellow to assume service responsibilities in communicable disease epidemiology. The in-service training will focus on outbreak investigations, disease surveillance, applied research, and communications with decision makers, the media, the public and the scientific community. Fellows will attend a 3-week intensive introductory course and then be located in a host institute in one of the 15 participating countries.

Detailed information can be obtained from the EPIET programme office at the address below. Letters of application accompanied by a curriculum vitae should be submitted by **28 February, 2001**.

European Programme for Intervention Epidemiology Training, Institut de Veille Sanitaire, 12, rue du Val d'Osne 94415 Saint-Maurice Cedex, France, Fax :+33 1 55 12 53 35, email: EPIET@invs.sante.fr

Rotavirus in Ireland: 1997-1999.

Introduction:

Rotavirus is the commonest cause of severe gastroenteritis in children aged less than 5 years. It results in significant morbidity in developed countries, and is responsible for over 500,000 deaths per year in developing countries.[1] Rotavirus disease is characterised by vomiting and watery diarrhoea for 3-8 days and fever and abdominal pain occur frequently. The incubation period for rotavirus disease is approximately two days. The primary mode of transmission is faecal-oral, with the highest rates of infection among infants and young children. Diagnosis of infection may be made by rapid antigen detection or by electron microscopy for the characteristic wheel-like appearence of rotavirus in stool (Figure 1). Rotavirus gastroenteritis is a self-limiting illness and treatment is non-specific and consists of oral rehydration therapy. The use of oral rehydration solutions has led to some reduction in diarrhoeal morbidity and mortality in developing countries but has little impact in developed countries. Improvements in water and food safety that are effective in preventing diseases caused by other enteric pathogens are ineffective in preventing rotavirus disease.[2] This has led to the pursuit of safe and effective rotavirus vaccines.

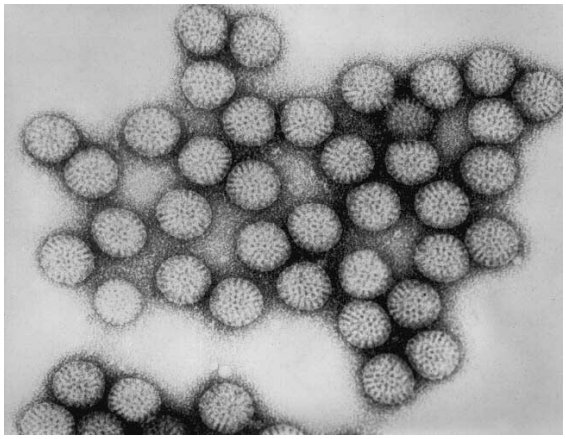

Figure 1. Electron micrograph of rotavirus (courtesy of PHIL, CDC).

The first rotavirus vaccine, a tetravalent rhesus-based vaccine (RRV-TV) was licensed in the United States in 1998. In clinical trials, vaccine efficacy was found to be 50% against all rotavirus-related diarrhoea and 70-100% against severe diarrhoea and hospitalisation. This vaccine was subsequently withdrawn by the Centers for Disease Control and Prevention (CDC) because of a possible association with intussusception.[3] An investigation was initiated to examine the possible association of RRV-TV with intussusception. The results of this will soon be available. There are other candidate vaccines at advanced stages of development.[4]

Surveillance systems in individual countries are needed to examine the disease burden of rotavirus, and to determine whether a rotavirus vaccine is needed in each country. In January 1997, at Cork University Hospital, we began a prospective national study on laboratory-confirmed rotavirus infections in Ireland. This report describes our results to date.

Methods:

We obtained data from two sources for this study; 1) national laboratory surveillance collating incidence data for laboratory-confirmed rotavirus infection, as well as detailed demographic data on each patient and, 2) data from INFOSCAN, a regional surveillance system of all enteric pathogens for one-third of the Irish population, showing the overall proportion of rotavirus to laboratory-confirmed gastrointestinal infections.

Figure 2. Rotavirus testing centres in Ireland.

1) National laboratory surveillance: In 1996, all 50 medical microbiology laboratories in Ireland were sent a questionnaire to determine whether they routinely tested faecal specimens from children with diarrhoea for rotavirus, and if so, what criteria and methods were used for testing. All the laboratories responded and 16 reported that they routinely tested for rotavirus. These laboratories were well distributed throughout Ireland, (Figure 2). Rotavirus investigation and referral in areas without testing centres was not assessed. While all 16 laboratories routinely tested faecal specimens throughout the year for rotavirus in children < 2 years, only a few tested specimens from children who were older. Therefore, we selected 2 years as an upper limit for our review so that results from all centres could be combined. Fifteen of the laboratories screened specimens by enzyme immunoassay and only one centre used electron microscopy. For 1997, 1998, and 1999, each laboratory reported the number of rotavirus detections each month to our centre (Cork University Hospital), where the data were collated and analysed. Obvious duplicates were removed. Demographic data collected on each patient included: date of birth, sample date, laboratory, and, for most, sample source (hospital vs outpatient). These data were used to estimate the annual incidence of laboratory-confirmed rotavirus disease in children aged less than 2 years, based on 1996 population census data.

2) INFOSCAN: INFOSCAN is an infectious disease bulletin and database for one-third of the Irish population (1.25 million). It collates data on all laboratory-confirmed pathogens, in all age groups, from hospitalised patients and outpatients. Six of the 16 laboratories reporting to the national laboratory surveillance report to INFOSCAN. From this bulletin, we reviewed reports of pathogens identified in faecal specimens from children <5 years for 1997-1999, to assess the relative contribution of rotavirus to diarrhoeal diseases.

Results:

1) National laboratory surveillance: Between January 1997 and December 1999, the 16 laboratories reported 4643 rotavirus detections: 1418 in 1997, 1712 in 1998, and 1513 in 1999 (Children aged<2 years = 97428, 1996 census data). The annual rate of laboratory-confirmed rotavirus infections was 14.5/1000 in 1997 in children less than 2 years; 17.6/1000 in 1998 and 15.5/1000 in 1999 . Each year, there were more detections in boys than in girls, (53% in 1997, 51% in 1998, and 54% in 1999).

2) INFOSCAN: Rotavirus accounted for 50% of laboratory-confirmed faecal pathogens in children <5 years (Figure 3), followed by *Campylobacter spp* at 14%.

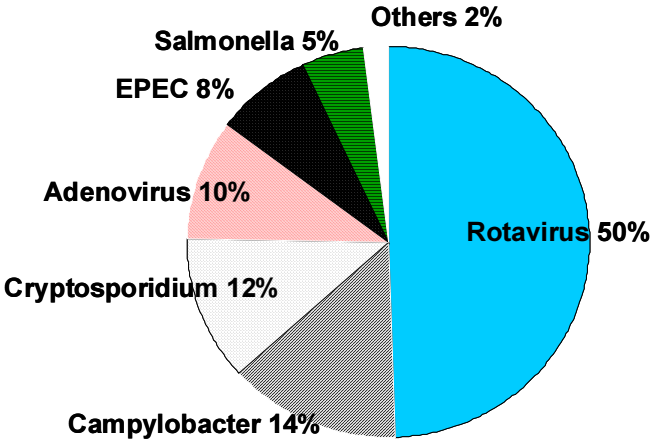

Figure 3. Faecal pathogens in children <5 years. INFOSCAN 1997-1998. EPEC= Enteropathogenic Escherischia coli. *Others* = Shigella spp, Escherischia coli *0157*, Giardia lamblia, Clostridium difficile.

Laboratory reports for rotavirus disease were seasonal and were most numerous from November to June, with peaks from February to May (Figure 4). The cumulative frequency by age in months of laboratory-confirmed rotavirus infections was similar for 1997 and 1998 (Figure 5). In 1999, fewer infections were reported in the first three months of life.

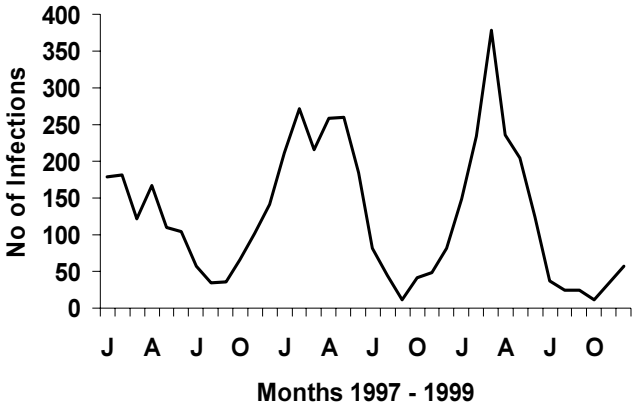

Figure 4. Rotavirus seasonality in Ireland, 1997-1999.

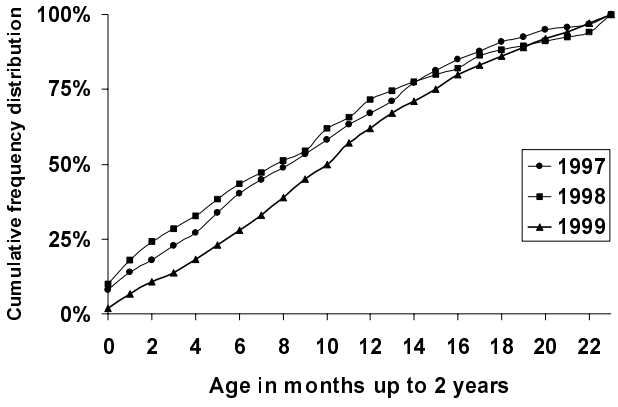

Figure 5. Cumulative frequency by age in months of laboratory-confirmed rotavirus infections in Ireland (children<2 years only).

Discussion:

This is the first national study of laboratory-confirmed rotavirus infections in Ireland. From this study the rate of laboratory-confirmed rotavirus infections in children < 2 years, annually, ranged between 14.5/1000 in 1997 and 17.6/1000 in 1998. This is likely to underestimate the level of infection, as data from laboratory-based studies depends on the rate of stool submission, laboratory testing policies, the sensitivity of laboratory tests used, and the completeness of laboratory reporting.[5] In Ireland, microbiology laboratories test for rotavirus on a year-round basis. Age-based policies vary in different laboratories. A recent laboratory study showed that in children less than 5 years, 16% of infections occur in the 2-5 year age group.[5]

We have recently combined our laboratory results with those of national diarrhoeal hospitalisations in children less than 5 years for 1997-1998[6]. The disease burden of rotavirus is much greater than laboratory-based estimates suggest, and likely an enormous cost to our healthcare system. In our study,[6] we found that in children less than 5 years, 16% of rotavirus hospitalisations occur in the 2-5 year age group. We combined laboratory and hospitalisation data and from these we estimate that the incidence of a child being hospitalised for rotavirus is 12/1000/yr in children less than 5 years. This compares with 5/1000/yr in the United Kingdom,[7] 6/1000/yr in Finland[8] and 3.5/1000/yr in the United States.[9] The relatively high rate in Ireland may be explained by the long epidemic season and a greater tendency to hospitalise children with rotavirus diarrhoea.

In conclusion, this study has included patients with severe rotavirus disease, those who sought medical attention, and those who were hospitalised. These are the patients most likely to benefit from a safe and effective rotavirus vaccine. National surveillance is essential to estimate disease burden, and to monitor the impact of a vaccine.

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RSV BRONCHIOLITIS AND AVAILABLE PROPHYLAXIS

Respiratory Syncytial Virus (RSV) is ubiquitous, easily transmissible and virulent and is the most common cause of lower respiratory tract disease in infants and small children.[1] Traditionally, certain groups of infants are considered to be at high risk of developing more severe RSV bronchiolitis. These high risks groups include infants born prematurely and those with chronic lung disease of prematurity, other underlying cardiorespiratory disease or immunodeficiency. However the great majority of infants admitted are previously normal babies. During winter epidemics RSV infections places a major burden upon both primary and hospital paediatric care.

RSV is a member of the paramyxovirus family, others include the measles, mumps and parainfluenza viruses. It was given the name Respiratory Syncytial Virus in 1957 by Chanock and Finberg describing the unusual cytopathological changes induced by the virus in cell culture.[2] It is a single stranded RNA virus, is encapsulated, helical in shape and 120 – 300 micrometers in diameter. It produces at least ten polypeptides, including the fusion protein (F) and the attached protein (G). Strains have been divided into two major groups (A and B) on the basis of antigenic differences between the attachment (G) protein. The (G) protein allows RSV to attach itself to a whole cell and is variable across both RSV strains (A and B). The (F) protein allows the infected cell to fuse, facilitating cell to cell spread, and is highly conserved across strains. Further heterogeneity has been demonstrated by RNA sequencing, and it may be that this heterogeneity plays a role in the susceptibility to re-infection. It is common for more than one strain to coexist within any single epidemic.

RSV is transferred by droplet infection, is highly contagious and humans are the only known reservoir. The incubation period is four to eight days and the infectious period lasts for about seven days after the onset of symptoms (this period can be considerably longer).

The virus multiplies in the mucus membranes of the nose and throat. It can also invade the bronchioles and lower respiratory tract, causing oedema and necrosis of the bronchiolar epithelium. This can lead to plugging of the airways, air trapping and hyperinflation of the lungs. Young infants are particularly at risk due to the narrow diameter of their bronchioles. It is also believed that the lack of mature immune system may also be implicated in the severity of RSV in infancy. RSV causes sharply defined epidemics, mainly over the late winter and early spring.

Treatment of RSV bronchiolitis is supportive care in the form of adequate nutrition and oxygen therapy if required.It is now widely accepted that bronchodilators, steroids and ribavirin have no overall significant benefit.[3] There is no effective vaccine available as yet.

Pooled hyperimmune RSV intravenous immunoglobulin (RSV IVIG, Respigam) was licensed after the PREVENT study.[4] Monthly prophylaxis over the RSV season with RSV IVIG led to an overall reduction of 41% in admissions for RSV bronchiolitis in high-risk group. However RSV IVIG required regular intravenous infusions of a high volume and protein load from pooled donors, with the risk of transmission of blood borne pathogens.

Palivizumab (Synagis) is a recombinant humanised mouse monoclonal antibody directed against the (F) protein of the RSV virus. It acts by binding to the (F) protein neutralising a broad range of clinical RSV isolates. Clinical safety and efficacy of palivizumab was demonstrated in IMpact trial published in September 1998. This trial was a phase III, multi-centre, randomised, double blind; placebo controlled study designed to provide safety and efficacy data for Synagis as intramuscular prophylaxis against serious RSV disease in high-risk children. The dosage used was 15 mg/kg administered at 30 day intervals during the epidemic season, each child receiving five injections.

The primary efficacy endpoint was the incidence of hospitalisation due to RSV infection. The Synagis group showed a 55% reduction in the incidence of hospitalisation when compared to placebo (10.6 % versus 4.8%).[5] Adverse effects reported in studies were similar in both palivizumab and placebo groups.The study was not powered to detect reduction in mortality. Subsequent studies in the first year post licensure in the USA affirms the earlier safety and efficacy results found in the investigational studies.

Palivizumab is currently being marketed for premature babies less than or equal to 35 weeks gestational age and who are born less than six months prior to the onset of the RSV season. It is also indicated for children less than 2 years of age with bronchopulmonary dysplasia (BPD), which have required treatment for BPD within the last six months. Clinical trials are currently underway in children with congenital heart disease, cystic fibrosis and bone marrow transplant children. Reimbursement for Synagis occurs under the High Tech Medicinal scheme. Overall costs will depend on body weight and will therefore vary from patient to patient. Individual vial costs are £424 for 50 mgs and £706 for 100 mgs. As a recombinant derived product, palivizumab presents no risk of transmission of blood borne infections.

In conclusion, RSV is a major cause of respiratory illness in children and places enormous burden on health services globally. Prevention in future may be achieved with the development of a safe effective vaccine.[6] In the meantime the cost effectiveness of palivizumab needs to be considered in those infants most at risk of developing severe RSV bronchiolitis.

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Dr Louise Kyne

Salmonella Monthly Report (December 2000):

Strains are allocated to months based on the date of receipt of the isolate from the referring laboratory. These figures are provisional as work may not be finished on particular strains at the time of publication. Data are provided courtesy of Prof Martin Cormican and Dr Geraldine Corbett-Feeney, INSRL.

Health Board	E	M	MW	NE	NW	SE	S	W	Total
S.Typhimurium	2	2	1	0	3	0	0	0	8
S.Enteritidis	3	1	0	0	1	1	3	4	13
S.Agona	1	0	0	0	0	0	0	0	1
S.Braederup	1	0	0	0	0	0	0	0	1
S.Bredeney	0	1	0	0	0	1	0	0	2
S.Corvallis	1	0	0	0	0	0	0	0	1
S.Kentucky	3	0	0	2	0	0	0	0	5
S.Schwarzengrund	0	0	0	0	0	0	0	1	1
S.Stanley	1	0	0	0	0	0	0	0	1
Total	12	4	1	2	4	2	3	5	33