PAEDIATRIC ACTIVE ENHANCED DISEASE SURVELLANCE (PAEDS)

Study Protocol – Varicella

BACKGROUND

Varicella zoster is a highly contagious and infectious virus causing varicella on primary infection and herpes zoster on subsequent reactivation. Approximately 90% of varicella cases occur in children less than 15 years of age with the highest incidence among children aged 1 to 4 years (1, 2). Although generally a mild disease in previously healthy children, in at least 1% of children under the age of 15 years there are severe complications including secondary bacterial infections, central nervous system manifestations, pneumonitis and death (3). A study by the German Paediatric Surveillance Unit showed that 6.7% of patients have long-term sequelae including persistent neurological deficits (4). Higher rates of complications are reported among children with compromised T cell immunity including children with leukaemia and tissue transplant recipients. Other described risk factors for severe complications include asthma, malnutrition, intense exposure and smoking. Analysis of ICD codes for hospital admissions in Australia for the years 1971 to 1993, show that 37% of all admissions for chicken-pox are for children under the age of 15 years (5). There are no systematic prospectively collected data on the severe complications of varicella in Australia.

From 1 November 2005, a live attenuated vaccine has been made available by the Australian Government Department of Health and Ageing and is recommended for all children born after 1 May 2004 (6). The vaccine is to be administered at age 18 months. A catch-up vaccination is available to a cohort of children aged 10 to 13 who have not been vaccinated previously and who have not had the disease. The vaccine has been shown to prevent varicella in 85% of immunised children, with 97% protection against moderately severe and severe disease (7).

Little is known about the distribution of VZV genotypes and their virulence in Australia (8). Literature from the UK and the USA suggests that there are two European genotypes, an African/Asian genotype, and a Japanese genotype (9). Immunity to one genotype was thought to be completely cross protective, against recurrent clinical varicella infection. However, a recent study found that up to 13% of children with varicella had a previously well-documented history of varicella illness suggesting that second attacks are more common than previously thought (10).
We propose to genotype viruses from children who develop severe or complicated varicella infection to distinguish vaccine complications from wild virus infection and to identify the genotypes of VZV that cause severe complications of varicella in Australia. This information may have an impact on the future development of varicella vaccines.

STUDY OBJECTIVES

- To document the incidence of children aged between 1 month and 15 years requiring hospitalisation due to varicella infection
- To describe the demographics of affected children: age group, birth order, ethnicity, geographical distribution
- To document vaccination status and any underlying conditions
- To describe the management of the disease, complications and short term outcomes
- To describe the genotype(s) of varicella zoster viruses that is associated with severe complications of varicella infection in Australia

CASE DEFINITION AND REPORTING INSTRUCTIONS

Report any child aged 1month or more, up to 15 years, hospitalised due to varicella. Varicella cases in hospitalised children may be complicated by one or more of the following:

- Bacteraemia/septic shock
- Toxic shock syndrome/toxin mediated disease
- Necrotising fasciitis
- Septic arthritis
- Other focal purulent collection
- Encephalitis
- Ataxia
- Purpura fulminans
- Disseminated coagulopathy
- X-ray evidence of pneumonia
- Fulminant varicella (multi-organ involvement)
- Reye's syndrome
- Hepatitis
- Zoster
- Other

SPECIMEN COLLECTION
All cases of varicella requiring hospitalisation are to have a PAEDS varicella questionnaire completed and a specimen collected.

To collect the specimen, a fresh vesicle is de-roofed and a skin scraping obtained from the base of the vesicle with a sterile swab. The specimen is then placed into viral transport medium (VTM) and stored in a refrigerator. Specimens can be stored up to 5 days in a refrigerator but for longer storage it is preferable that the specimens be stored in a minus 70^{o}C refrigerator or is one is not available a minus 20^{o}C refrigerator can be utilised. Samples should be couriered in a cold environment preferably in an esky on dry ice to prevent the specimens thawing. Specimens should be processed locally before being forwarded to Westmead Hospital for genotyping. The following information should accompany all specimens:

- DOB
- Sex
- Date of sample
- Site of specimen (eg upper left arm)

PLEASE SEND GENOTYPING SPECIMENS TO:
Cheryl Toi
Clinical Virology
Centre for infectious Diseases and Microbiology
ICPMR
Level 3
Westmead Hospital
Hawkesbury Road
WESTMEAD NSW 2145

INVESTIGATORS
Prof Robert Booy
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