



Royal College of Paediatrics and Child Health

The British Paediatric Surveillance Unit (BPSU) is part of the Research Division of the Royal College of Paediatrics and Child Health

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British Paediatric Surveillance Unit Report Card

NOTHING TO REPORT March 2003 [2003-03]

Specify in box the number of cases seen CODE No []

<input type="checkbox"/>	HIV & AIDS
<input type="checkbox"/>	Progressive Intellectual & Neurological Deterioration
<input type="checkbox"/>	Congenital Rubella
<input type="checkbox"/>	Suspected Fatal Adverse Drug Reactions
<input type="checkbox"/>	Congenital Toxoplasmosis
<input type="checkbox"/>	Severe Complications of Varicella
<input type="checkbox"/>	Invasive fungal infection in VLBW infants

In order to simplify reporting on the orange card the layout has been slightly altered. If you have a case to report please tick the box to the left of the disorder adding the number of cases if more than one. Please do not identify the case on the card but complete the clinicians' tear-off section, **retaining** as a reminder for when you are contacted by the investigators. Please remember if you do not have a case to report tick the nothing to report box

The new card is being brought in alongside the new BPSU epidemiology programme. This system will hopefully improve still further the reliability of the data handling and will allow more focussed analysis of regional returns. As always the success of the studies we survey is very much dependent on the contribution of the clinicians reporting cases and completing the short questionnaires and we are very grateful for this continued support.

RCPCH Bursary available for BPSU study applicants

The RCPCH is offering paediatricians the opportunity to win a Bursary to undertake an epidemiological study using the BPSU. The successful applicant will receive £15,000 towards costs for a one-year surveillance study.

The purpose of the bursary:-

- To encourage paediatricians who are not research active to undertake a study of a rare disease or condition which affects children and which is of scientific or public health importance
- To promote the role of the BPSU in the surveillance of rare diseases affecting children
- To support the Royal College of Paediatrics and Child Health's objective to build and strengthen research in paediatrics.
- To enable paediatricians to further develop their research knowledge and skills.
- To add to the body of knowledge of rare childhood diseases and conditions.

Who is eligible to apply for this bursary? Paediatricians of Specialist Registrar or consultant grade (FT or P/T) with NHS contracts and who have not held research grants or have not previously been involved in a major research study. Clinicians with university appointments, joint NHS/Academic appointments or those who have previously undertaken a BPSU study are **not** eligible to apply.

Applicants should be RCPCH members and have access to administrative/research support for the duration of the study. Closing date for initial application is **11 July 2003**

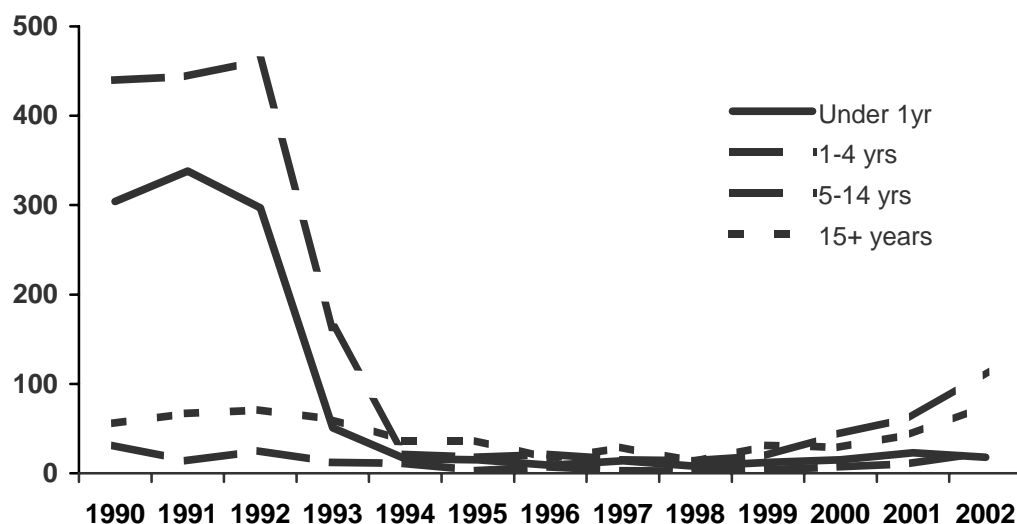
Further information is available on the BPSU website at <http://bpsu.inopsu.com/methodol.htm> or from Richard Lynn, Scientific Coordinator, Tel: 020 7307 5671 or Email: bpsu@rcpch.ac.uk.

Past Study Revisited

HiB Catchup for BPSU

The United Kingdom introduced routine immunisation against *Haemophilus influenzae* type b (Hib) in October 1992 as a three dose primary course at 2, 3 and 4 months of age without a booster dose. A concurrent catch-up campaign, in which a single dose of vaccine was given to children less than four years old, facilitated rapid control of disease. The BPSU was involved in enhanced surveillance for invasive *Haemophilus influenzae* infections until October 2000, in collaboration with the Oxford Vaccine Group (OVG) and Public Health Laboratory Service (PHLS). Cases of invasive Hib infection are defined by isolation of *Haemophilus influenzae* from a normally sterile site, with confirmation as type b at the PHLS *Haemophilus* Reference Unit, using serotyping and PCR methods. Vaccination status is confirmed by each child's general practitioner, or using immunisation records held on the local child health computer system. A marked reduction in Hib disease confirmed the success of this intervention (Figure 1). Unfortunately this has not been sustained, with a more recent increase in the number of confirmed reports of serious Hib infections, the vast majority occurring in fully vaccinated children.

Figure 1 : Invasive Hib infections by age group, 1990-2002
England and Wales, combined PHLS HRU/CDSC data



Studies conducted by the PHLS and OVG in order to better understand the causes underlying this increase have identified a number of factors may have contributed to lower population immunity against Hib over time. These include a 'wearing off' of the effect of the catch-up campaign, and more recently the use of less immunogenic Hib vaccines. An acute shortage of the whole cell pertussis combination vaccine (DTwP-Hib) in 2000/2001 necessitated replacement with acellular pertussis containing preparations (DTaP-Hib). These have been shown to reduce immunogenicity of the Hib component¹, but the relevance of this finding to efficacy has been questioned². Recent UK surveillance data has shown that children who have received at least two of their three primary doses of Hib vaccine as DTaP-Hib are at increased risk of vaccine failure (Personal communication, Dr M Ramsay).

All children aged between six months and four years at 1st April 2003 will be given an additional dose of Hib vaccine in a nationwide catch-up campaign scheduled to begin in April or May of this year³. Meanwhile, clinicians are advised to remain vigilant for evidence of invasive Hib infection in any of its manifestations, including meningitis, bacteraemia and epiglottitis. Once again, the importance of long term surveillance to identify unexpected late effects of immunisation programmes is reinforced, particularly at times of change to the routine schedule.

References: 1. Vidor E, Hoffenbach A, Fletcher MA. *Haemophilus influenzae* type b vaccine: reconstitution of lyophilised PRP-T vaccine with a Pertussis-containing paediatric combination vaccine, or a change in the primary series immunisation schedule, may modify the serum anti-PRP antibody responses. *Curr Med Res Opin* 2001; **17**: 197-209.
2. Eskola J, Ward J, Dagan R, Goldblatt D, Zepp F, Siegrist C-A. Combined vaccination of *Haemophilus influenzae* type b conjugate and diphtheria-tetanus-pertussis containing acellular Pertussis. *Lancet* 1999; **354**: 2063-2068.
3. Added protection planned against Hib. *Booster vaccine to be offered following increase in cases. Press release 2003/0071.* London: Department of Health, 18 February 2003.

Study News

National Surveillance Study on UK Congenital Toxoplasmosis: The study aims to determine the birth prevalence of symptomatic congenital toxoplasmosis (CT) and started on 1st August 2002. It will also assess the severity of clinical manifestations in children presenting with suspected CT. Up to date information on birth prevalence and severity of CT provides an estimate of the clinical burden of this disease which is useful for consideration of prevention strategies such as neonatal screening. The surveillance study is based on active monthly reporting from three sources: paediatricians (through the BPSU), ophthalmologists (through the BOSU), and the toxoplasma reference laboratories.

By mid February 2003, 31 reports of suspected cases of CT had been made (16 through BPSU, 11 through the BOSU and four through reference laboratories). Excluding reports in error and duplicates, three children presented during the study period (after 1 July 2002) with toxoplasma retinochoroiditis reported by ophthalmologists. A further 9/12 children who presented with toxoplasma infection prior to 1st July 2002 had retinochoroiditis.

At present, only eight children are classified as definitely having congenital as opposed to postnatally acquired toxoplasmosis. Further serological information may be available from testing of stored Guthrie card blood spots for toxoplasma-specific IgM. In view of the small number of cases, a request will be made to continue surveillance for a second year.

Contact: Dr R Gilbert, Mrs S Cliffe, Centre for Paediatric Epidemiology and Biostatistics, Institute of Child Health, 30 Guilford Street, London WC1N 1EH Tel: 0207 813 8142 Email: S.Cliffe@ich.ucl.ac.uk

Suspected Fatal Adverse Drug Reactions in Children: In June 2002, a study commenced to monitor the incidence and nature of suspected fatal adverse drug reactions in children. The principal investigator is Professor Terence Stephenson and the study is run by the Medicines Control Agency.

To date, eight reports of suspected fatal adverse drug reactions have been received of which three have been confirmed. This number is **less** than the BPSU and investigators would have expected and we encourage any outstanding cases back to June 2002 to be reported.

Please continue to report any suspected adverse drug reactions with a fatal outcome. Adverse drug reactions include suspected reactions to any therapeutic agent, including drugs, self prescribed and prescribed, vaccines, blood products, x-ray contrast media, dental or surgical materials and herbal products. Drug administration errors or deliberate drug ingestion (self-harm) should **not** be reported. For further information please contact Dr Katharine Cheng at Tel: 020 7273 0101. Email: katharine.cheng@mca.gsi.gov.uk

Studies end: Congenital Cytomegalovirus (cCMV) was put on the orange card in February 2001, and remained there for 25 months. All infants born in 2001 or 2002 and diagnosed with confirmed or suspected congenital CMV should have been reported. Laboratory reports to PHLS and SCIEH have also been monitored. The study was established to ascertain the population prevalence of congenital CMV disease, current management strategies, and the clinical disease outcome, and to explore the feasibility of using routinely collected neonatal dried blood spots to confirm or exclude a diagnosis of congenital CMV infection in infants who present after 3 weeks of age.

By the end of February 2003, 279 reports had been made through the BPSU (Table 1). Of these, 89 were confirmed and 67 possible cases (diagnosis after three weeks of age). There were 37 duplicates and 44 error reports, and 42 are currently outstanding. Among the 89 confirmed cases, 20 received antiviral drugs, and eight are known to have died. Follow-up questionnaires are being sent to notifying paediatricians to establish the outcome for the survivors after their first birthday. An additional 25 confirmed cases have only been reported through the laboratory reporting system, and there is no information on them at present.

Table 1. cCMV cases reported to the BPSU by status and country to the end of February 2003

Please make sure that all infants with suspected or confirmed congenital CMV born in 2001 or 2002 have been reported on the orange card. If you have any outstanding reports contact Pat Tookey at p.tookey@ich.ucl.ac.uk directly. The investigators thank all those who reported cases during this study, and will present further information from the study as soon as possible.

	Confirmed	Possible	Duplicate or error	Outstanding	Total
England	74	59	61	32	226
Wales	2	2	5	2	11
Scotland	8	4	9	4	25
NI	0	1	2	1	4
RoI	5	1	4	3	13
Total	89	67	81	42	279

Study News, contd

Studies end contd. The first national prospective epidemiological study of **childhood thrombosis (Age >1 month – 16 years)** in the UK, (principal investigator Dr B Gibson, Yorkhill Hospital) which began collecting cases in February 2001, has after two years now ended. To date 309 cases have been reported and 153 have met the study criteria. The two year study on **internal abdominal injuries**, (principal investigator Professor J Sibert, Llandough Hospital) ended this February. To date 72 cases have been reported 18 of which have been confirmed. Details of this study will be presented at the RCPCH scientific meeting this April.

On behalf of the investigators we would like to thank all those who have reported cases and completed the questionnaire. If you have any outstanding questionnaires or have seen cases that have yet to be reported please can we encourage you to do so?

New studies: A 13-month study on **invasive fungal infection in VLBW infants** (principal investigator Dr W McGuire, Ninewells Hospital) commenced this February. You should by now have received the protocol card for this, if not contact the BPSU office and we can dispatch a copy, information is also available from the BPSU website at <<http://bpsu.inopsu.com>>.

The BPSU Executive has approved two further studies to commence. Start dates will be confirmed once MREC approval has been obtained. The studies in question are the first UK survey of **Langerhan Cell Histiocytosis** (principal investigator Professor L Parker, Newcastle) and a second BPSU study on **neonatal herpes simplex virus** (principal investigator Dr P Tookey, London).

Monthly Analysis

TABLE 2 - % RESPONSE RATE
May-October 2002

Region	% retd	Rank (Feb-July 2002)
North	90.9	15 (15)
Yorks	94.6	7 (9)
Trent	92.9	11 (13)
EAngl	94.9	6 (3)
NWT	86.9	18 (19)
NET	81.9	20 (20)
SET	89.0	17 (16)
SWT	86.7	19 (18)
Wessex	91.7	14 (12)
Oxford	95.1	5 (2)
SWest	92.9	13 (11)
WMids	89.9	16 (17)
Mersey	93.6	10 (6)
NWest	96.1	3 (8)
Welsh	95.9	4 (5)
NScot	98.1	1 (1)
SScot	93.6	9 (14)
WScot	92.9	12 (10)
NIRE	94.5	8 (7)
RIRE	96.8	2 (4)
Total	91.5	

TABLE 3 - ALL CASES REPORTED AND FOLLOW-UPS TO 28/02/2003

Condition	Started	I					as % of total			
		VALID	II INVALID		NYK	Ttl	I	II	III	
HIV/AIDS	1986	2117	346	Ila	Ilb	159	3083	69	26	5
CR	1990	66	24	44	6	140	47	49	4	
PIND	1997	891	161	365	85	1502	59	35	6	
VKDB	2001	4	3	11	24	42	10	35	57	
Thrombosis	2001	153	27	64	65	309	51	30	18	
CMV	2001	130	26	40	83	279	47	24	30	
IAI	2001	18	17	20	17	72	25	51	24	
SFADR	2002	3	0	4	1	8	50	37	13	
Con Toxo	2002	0	1	12	6	19	0	68	32	
Varicella	2002	0	0	1	45	46	0	2	98	
Total		3382	605	1022	490	5499	62	29	9	

I = confirmed/already known

Ilb = reporting error or revised diagnosis

Ila = duplicate

III = status not yet reported to BPSU by investigator

AIDS/HIV - Acquired Immunodeficiency Syndrome / Human Immunodeficiency Virus

CR - Congenital Rubella

PIND - Progressive Intellectual Neurological Degeneration

VKDB - Vitamin k deficiency bleeding

CMV - Congenital Cytomegalovirus

IAI - Internal abdominal injuries due to child abuse -in children under 14 yrs

SFADR - Suspected fatal adverse drug reactions

Con Toxo - Congenital Toxoplasmosis

ALL DATA IS PROVISIONAL AND IS CONTINUALLY BEING UPDATED