



### 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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## BPSU 17th Annual Report Published

The BPSU 17th Annual Report 2002-2003 has recently been published. College members will receive their copies with the College newsletter that should be reaching you shortly. A limited number of additional copies are available from the BPSU office, alternatively the report can be viewed on the College's website at <http://www.rcpch.ac.uk/publications/bpsu.html>. We hope you will find this an interesting read and worthy of storage on your overcrowded bookshelves. Alternatively do feel free to circulate it within the department or pass it on to the hospital library.

This year the report concentrates more on the disorders under surveillance, with a reduction to the sections on the administrative workings of the Unit, this information is now available on the BPSU website (<http://www.bpsu.inopsu.com>), and the international section which will be highlighted in a separate INoPSU report which will be available soon. This year's report contains feedback on the 11 undertaken over the past year, as well as the yearly Unit analysis. Here the willingness of paediatricians to continue to contribute to the system is reflected in an average monthly response rate of 92% which has led to over 760 confirmed case reports, one of the highest ever for a single year. Even so case ascertainment is an area the BPSU is acutely concerned with and we would encourage all to report cases even if they are not sure they fitted the case definition and even if they feel a colleague may have already done so. This, with the increased use of alternate sources of ascertainment, will improve still further the number of cases reported. On behalf of the Unit and the investigators we thank you for this magnificent response.

The inaugural report on the activities of INoPSU is also now available on-line as a pdf (<http://bpsu.inopsu.com/publicat.htm>) though a limited number of hardcopies are available on request. The report covers activities undertaken between 1999 and 2002, highlighting the activities of individual units comparing data for studies undertaken across several units, notably the vitamin K deficiency bleeding, haemolytic uraemic syndrome, congenital rubella and PIND.

## BPSU Announces RCPCH/BPSU Bursary Winner

The call for applications for the RCPCH/BPSU bursary was well received. The BPSU Executive considered 12 applications, all of a very high standard. After some deliberation the unanimous winner was Dr Scott Williamson an SpR from Ninewells Hospital. Dr Williamson wishes to study the epidemiology of Grave's disease in childhood in the UK with particular emphasis on its incidence, the presenting features, the initial management of the condition and any severe complications of initial treatment or of the disease itself. We are currently working with Dr Williamson in order to develop the appropriate methodology to undertake surveillance, and we aim to commence surveillance in 2004. Many thanks to all those who applied we wish you good luck with your search for funding. We hope we can secure funding to make this an annual award.

## Severe Hyperbilirubinaemia in the Newborn

Following a slight confusion over the case definition Dr Manning wishes to clarify matters. *"Thanks to all who have reported cases. We still await completed questionnaires for some babies reported in June and July and would be very grateful if these could be returned. I apologise for some confusion with the case definition. The June and July reporting instructions gave a definition of 'severe hyperbilirubinaemia (serum bilirubin >510 micromol/L during the first month of life)'. This should have read 'unconjugated serum bilirubin >510 micromol/L. I apologise again to those paediatricians who have reported cases with a total bilirubin >510 micromol/L but with unconjugated bilirubin below this level."*

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## Study News - Invasive Fungal Infection in Very Low Birth Weight Infants

### Background

Invasive fungal infection is an increasingly common cause of morbidity and mortality in very low birth weight infants (VLBW: birth weight less than 1500 grams).<sup>1</sup> The increase in incidence over the past 20 years is likely to be due to the improved survival rates for very small and immature infants, and the invasive and intensive nature of the care that these infants need. The estimated incidence is 2% in VLBW infants in referral centres in North America. In these centres, systemic fungal infection now accounts for about 10% of all cases of acquired sepsis diagnosed in VLBW infants.<sup>2,3</sup>

We are undertaking a one-year population-based prospective survey to describe the epidemiology, clinical features, and mycology of invasive fungal infection in VLBW infants in the UK and Eire. Invasive fungal infection is defined as the presence of one or more of the following:

- culture from a sterile site: blood (peripheral site), “long-line” tip, urine (supra-pubic aspirate or “in-out” catheter), cerebro-spinal fluid, bone or joint, peritoneal or pleural space
- pathognomonic findings on ophthalmological or renal ultrasound examination
- infants with an autopsy diagnosis of invasive fungal infection.

### Results to date

The study started in February 2003. By the end of July 2003 (5 months surveillance), 57 reports of suspected cases have been received. 27 cases have been confirmed to fulfil the case definition. 21 reports were duplicates or errors (mainly infants diagnosed outside the study period).

	Total reports	Cases confirmed	Error/duplicate report	Awaiting confirmation	
2003					These reports are consistent with an estimated birth prevalence of 1- 1.2% of VLBW infants (based on reported cases for the first 4 months).
February	20	9	10	1	
March	9	3	3	4	
April	11	8	2	0	
May	8	4	2	2	
June	9	2	3	4	
Totals	57	26	20	11	The median gestational age of confirmed cases is 25 weeks (range 23 – 30 weeks), and the median birth weight 800 grams (range 520-1200 grams). The median age at diagnosis is 11 days (0 - 126 days).

The identified organism was *Candida albicans* in 65% of cases and *Candida parapsilosis* in 19%. There have been three reports of invasive infection with other non-albicans *Candida spp.* and one case of invasive *Aspergillus spp.* infection. The organisms were isolated from blood in 85% of cases, urine in 19% cases, cerebro-spinal fluid in 8%, peritoneal space in 1 case, pleural space in 1 case and line tips in 58% (only 1 case of an infant with a positive line tip culture and negative blood cultures).

	No of cases (%)	Anti-fungal treatment
Amphotericin	5 (19)	34% of infants received monotherapy (liposomal amphotericin 15% and fluconazole 19%), the others received two or more drugs serially or in combination. 38% of cases had received prophylactic antifungal agents. There is a single case of reported drug resistance; fluconazole resistance of a non-albicans <i>Candida spp.</i>
Liposomal Amphotericin	18 (69)	
Fluconazole	13 (50)	
Itraconazole	0 (0)	
Flucytosine	8 (31)	

### Aims of this work

The full dataset will provide an estimate of incidence unaffected by referral bias, define the population most at risk, and describe the pattern of presentation. These data will also inform further research in this area, particularly in the development of pragmatic randomised controlled trials to assess the impact of preventative and therapeutic interventions for invasive fungal infection in VLBW infants. This national study also aims to determine the outcome at term. This information may be important in the counseling of parents whose infants develop invasive fungal infection.

### References

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2. Stoll BJ, Gordon T, Korones SB, *et al.* Late-onset sepsis in very low birth weight neonates: a report from the National Institute of Child Health and Human Development Neonatal Research Network. *J Pediatr* 1996; **129**: 63-71.
3. Saiman L, Ludington E, Pfaller M, *et al.* Risk factors for candidemia in Neonatal Intensive Care Unit patients. The National Epidemiology of Mycosis Survey Study Group. *Pediatr Infect Dis J* 2000; **19**:319-324.

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## Survey News

**Study Extensions:** Two studies, symptomatic toxoplasmosis and congenital rubella, have recently received approval for a further year's surveillance, details of which are highlighted below.

The national surveillance study to determine the incidence of **symptomatic toxoplasmosis in children** has been extended from July 2003 for a further year. The aim of the study is determine the burden of disease due to congenital toxoplasmosis to guide policy decisions on screening and other preventive strategies in the UK. Paediatricians, Ophthalmologists, and referring laboratories are being asked to report cases of symptomatic toxoplasmosis in children. Symptoms are most commonly manifest as ocular symptoms due to retinochoroiditis which can be due to congenital or postnatally acquired infection. Other presentations include neurological symptoms which indicate congenital infection except in immune deficiency disease, or signs of disseminated infection in fetal losses or in early infancy.

The investigators have received a total of 79 reports between 1.8.02 and 31.5.03. Most relate to reports before the prospective surveillance period (starting 1.7.02). During the prospective phase of the study (1.7.02 to 31.5.03) 11 children presented for the first time and there were 6 miscarriages (all 6 were classified as possible CT). Six of the 11 children presented before 15 months of age and were classified as definite or probable congenital toxoplasmosis (CT). The remainder presented at 10 or more years old and may have congenital or postnatally acquired infection. Eight of the 11 children presented with ocular symptoms or signs. A larger sample size will help to better define the two populations of early and late presenters. Both groups will be used to derive upper and lower estimates for the birth prevalence of symptomatic congenital toxoplasmosis.

Please report all stillbirths or under 16 seen in the last month where CT is **suspected**. CT may be suspected in any of the following:

1. toxoplasma specific IgM/IgA antibodies under 2 years of age in peripheral blood (or cord blood)
2. any child with toxoplasma IgG detected between approximately 6-18 months
3. any child with toxoplasma DNA or parasite detected in body tissues or placenta
4. any child with unexplained retinitis and toxoplasma IgG antibodies
5. any infant (<12 months) with unexplained hepatosplenomegaly or lymphadenopathy and toxoplasma IgG antibodies or serological results compatible with maternal toxoplasma infection during pregnancy
6. any child with unexplained hydrocephalus, intracranial calcification, microcephaly or microphthalmia and toxoplasma IgG antibodies or serological results compatible with maternal toxoplasma infection during pregnancy

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**Congenital Rubella** Only one infant with congenital rubella has been reported so far during 2003 and there is little evidence at the moment of rubella infection circulating in the UK. However, the decline in MMR uptake rates (only 79% in the UK overall in the first quarter of this year, with considerable regional variation) has already led to well-publicised outbreaks of measles and mumps. About half of the infants with congenital rubella reported to the National Congenital Rubella Surveillance Programme in the last decade (including the most recent case) were born to women who, although they caught rubella in the UK, had arrived in the country relatively recently (1). Rubella susceptibility continues to vary considerably by ethnic group, and women coming from countries with less successful or disrupted vaccination programmes are likely to be at higher risk if there is renewed circulation of rubella (2). Health professionals looking after pregnant women should be aware of the guidelines for the management of rash infection in pregnancy (3); paediatricians should be aware that further cases of congenital rubella might occur.

**Contact:** Dr Pat Tookey, National Congenital Rubella Surveillance Programme, ICH, London. E-mail: p.tookey @ich.ucl.ac.uk

1. Tookey P. Congenital rubella: down but not out (letter). *Lancet* 2002; **360**: 803
2. Tookey PA, Cortina-Borja M, Peckham CS. Rubella susceptibility among pregnant women in North London, 1996-1999. *J Public Health Medicine* 2002; **24**(3): 211-16
3. Morgan-Capner P, Crowcroft NS. Guidelines on the management of, and exposure to, rash illness in pregnancy (including consideration of relevant antibody screening programmes in pregnancy). *Commun Dis Public Health*. 2002 Mar; **5**(1): 59-71. Also available at [http://www.phls.org.uk/topics\\_az/rashes/rash.pdf](http://www.phls.org.uk/topics_az/rashes/rash.pdf)

**Study Ends:** The first national prospective epidemiological study of **childhood thrombosis** in the UK has now closed. The study ran for 25 months (February 2001 – February 2003). The criteria for entry were – any child aged between one month (or 44 weeks post conceptional age) and 16 years, newly diagnosed with an objectively documented venous or arterial thrombosis. **Excluded** were children with stroke, whether this was arterial or due to sino-venous thrombosis.

342 thrombotic episodes have been reported and 310 first mailing forms have been completed and returned. Of these 192 fit the study criteria. 118 (38%) were excluded for various reasons, including duplicate reporting, non- fulfillment of the study criteria, events occurring during the neonatal period and those outwith the study period. Six-monthly follow-up mailing forms have been sent to clinicians and 136 have been completed and returned. Overall mortality has been low (7%). 3 deaths (1.5%) were directly attributed to thrombosis, and in 4 cases (2.2%) it was a contributory factor. Preliminary analysis is taking place, but can we please urge those physicians who have not returned their forms to do so as soon as possible in order that all data can be analysed with a view to publication. Dr Brenda Gibson, study investigator, is grateful to all reporting physicians for their co-operation and support of the study.

## Study News, contd

A thirteen-month survey of **Langerhans Cell Histiocytosis (LCH)** in the UK and Ireland began in July. LCH is a rare cancer-like disease that affects the lives of around one in 200,000 children and adults. It can be fatal in very small children and can leave sufferers with serious long-term physical disabilities.

The study aims to describe the incidence of LCH and the extent of disease at diagnosis and also to raise awareness of the disease to encourage early diagnosis and treatment. The study team at the University of Newcastle has so far received 18 notifications. Questionnaires are sent out for all notifications requesting further information about patients including presenting symptoms, referral history, diagnosis and diagnostic procedures, systems involved and related problems. Follow-up information will be collected one year after diagnosis.

Please report any new or suspected cases you have seen in the past month. If you need any clinical advice regarding the eligibility of a particular case for inclusion in the study, please contact Dr Vasanta Nanduri (Tel.01923 217992, E-mail: Vasanta.Nanduri@whht.nhs.uk) or Dr Kevin Windebank (Tel: 0191 202 3037, E-mail: k.p.windebank@ncl.ac.uk).

Further information about the study including case definition can be found at <http://bpsu.inopsu.com/current.htm#LCH>. An illustrated information leaflet in pdf format is also available.

## Monthly Analysis

**TABLE 1 - % RESPONSE RATE**  
Jan-June 2003

Region	% retd	Rank (July- Dec 2002)
North	90.6	14 (15)
Yorks	92.8	7 (7)
Trent	90.7	13 (11)
EAnGl	94.2	3 (6)
NWT	85.9	19 (18)
NET	81.9	20 (20)
SET	87.8	17 (17)
SWT	86.4	18 (19)
Wessex	91.4	11 (14)
Oxford	92.6	8 (5)
SWest	93.5	5 (13)
WMids	90.2	16 (16)
Mersey	91.3	12 (10)
NWest	93.3	6 (3)
Welsh	94.7	2 (4)
NScot	98.1	1 (1)
SScot	91.7	10 (9)
WScot	90.3	15 (12)
NIRE	92.4	9 (8)
RIre	93.9	4 (2)
<b>Total</b>	<b>90.3</b>	

**TABLE 2 - ALL CASES REPORTED AND FOLLOW-UPS TO 12/9/2003**

Condition	Started	I					Ttl	as % of total		
		VALID	INVALID		NYK	I		II	III	
HIV/AIDS	1986	2370	363	494	238	3465	68	25	7	
CR	1990	67	24	46	5	142	47	49	4	
PIND	1997	933	176	390	103	1602	58	35	6	
SFADR	2002	6	3	3	4	16	38	38	25	
Con Toxo	2002	2	1	13	6	22	9	64	27	
Varicella	2002	90	6	4	65	165	55	6	39	
IFInfect	2003	26	8	13	24	71	37	30	34	
Se. Hyperbil	2003	3	2	8	18	31	10	32	58	
LCH	2003	0	0	0	19	19	0	0	100	
<b>Total</b>		<b>3497</b>	<b>582</b>	<b>971</b>	<b>482</b>	<b>5533</b>	<b>63</b>	<b>28</b>	<b>9</b>	

I = confirmed/already known

IIb = reporting error or revised diagnosis

AIDS/HIV - Acquired Immunodeficiency Syndrome / Human Immunodeficiency Virus

CR - Congenital Rubella

PIND - Progressive Intellectual

Neurological Degeneration

SFADR - Suspected fatal adverse drug reactions

IIa = duplicate

III = status not yet reported to BPSU by investigator

Con Toxo - Congenital Toxoplasmosis

IFInfect - Invasive Fungal Infection in VLBW infants

Se Hyperbil - Severe Hyperbilirubinaemia

LCH - Langerhans Cell Histiocytosis

**ALL DATA IS PROVISIONAL AND IS CONTINUALLY BEING UPDATED**