



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



Royal College of Paediatrics and Child Health

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Using the BPSU for Long Term Surveillance

You may have noticed that a few of the conditions on the orange card have been there for some time. Why is this? Are the studies preventing surveillance of *other* rare childhood diseases? Do paediatricians get tired of filling out questionnaires about these conditions?

Well the BPSU Executive Committee been considering these issues for some time and have even put these questions to the investigators, who must submit regular extension requests in order to continue surveillance.

Most studies stay on the card for between 1-3 years the surveillance period dependent on whether significant numbers of cases can be reported to address the research objectives. However where there is thought to be a public health need consideration for longer period of surveillance will be given. In the following extended articles Dr Pat Tookey (HIV, congenital rubella) and Dr Chris Verity (PIND) explain further why such long term surveillance is required for these conditions.



Dr Pat Tookey

Paediatric AIDS appeared on the orange card from the beginning in 1986. When parallel obstetric surveillance of all pregnancies in HIV-infected women was set up through the Royal College of Obstetricians and Gynecologists in 1990, the BPSU case definition was expanded to include all HIV-infected children, and all infants born to infected women regardless of the child's own infection status.

We seek paediatric notification of all infants born to infected women, not just infected infants, in order to get robust data on postnatal prophylaxis and reliable confirmation of infection status for all infants (confirming absence as well as presence of infection), which is not available from obstetric sources. Before antenatal HIV testing was routinely recommended from 2000 onwards, most infected women were not diagnosed prior to delivery, and paediatricians reported cases from fewer than 50 units each year. Detection rates have soared since then, and over 90% of infected women are now diagnosed in time to take advantage of interventions which reduce the risk of transmission from 15-30% to around 1%.

Births to diagnosed women now exceed 1000 a year (see Table 1 overleaf); paediatricians reported infants from at least 150 units in 2006, and over half of all reports in England were from outside London, compared with only 20% in 2000. To simplify reporting and reduce the burden on individual paediatricians, direct reporting arrangements have been established with some clinics with large case-loads. Nevertheless, over 50% of all paediatric reports still come through the BPSU which remains a vital component of the surveillance system, particularly with respect to capturing cases seen in non-specialist centres all over the country.

Long Term Surveillance of BPSU Studies – continued

Table 1: Children born in UK/Ireland to women diagnosed before delivery, all reports from all sources to end March 2007

About 50% of all reports have come through the BPSU

	infected	indeterminate	uninfected	Total
Pre 1990	20	20	144	184
1990-1996	76	90	343	509
1997-1998	11	21	213	245
1999-2000	10	48	540	598
2001-2002	21	130	1151	1302
2003-2004	21	221	1883	2125
2005-2006	19	901	1332	2252
All years	178	1431	5606	7215

In addition, to date reports have been received for

- 642 infected children born UK or Ireland, with infection acquired from their mothers who were undiagnosed at delivery
- 763 children born abroad, infection acquired from their mothers
- 323 children, infection acquired through blood products (most before 1990, in the UK or Ireland)
- 65 infected children, other/unknown exposure (most born abroad)

Among the 100+ infected children currently diagnosed each year, about 25% were born to diagnosed and another 25% to undiagnosed women in the UK or Ireland; the remainder were born abroad. Follow-up data on infected children are now collected through CHIPS (Collaborative HIV Paediatric Study). We work closely with CHIVA (Children's HIV Association) and NSHPC data are widely used at national, regional and local levels. Recent publications have focused on exposure to antiretroviral therapy and congenital abnormalities, prematurity, follow up of exposed uninfected children, and clinical management and outcomes for infected children.

Comprehensive long-term surveillance through the BPSU, together with the obstetric system, has provided invaluable national data on the changing epidemiology and management of obstetric and paediatric HIV, the impact of these changes on transmission rates, the natural history of HIV in children, and the longer term outcomes for both

infected and uninfected children. We really appreciate your continued support, and especially thank the 600 or more paediatricians who have completed case report forms over the last 20 years. For further information and the latest NSHPC data, visit our website at <http://www.ucl.ac.uk/paediatric-epidemiology/nshpc/nshpc.html>.

Ethics and Funding: MREC approved the NSHPC in 2004, and there is PIAG approval for paediatric HIV surveillance through the BPSU. The NSHPC is a collaboration between the Institute of Child Health, the Health Protection Agency Centre for Infections, and Health Protection Scotland. Funding is currently through the HPA.

Congenital rubella: After rubella vaccine became available in 1970, the number of congenital rubella (CR) cases in the UK declined from about 250 each year to about 40 a year in the 1980s. Rubella-associated terminations also reduced substantially in number.

After MMR was introduced in 1988, CR became really rare, and won a place on the orange card in 1990. Only about 60 CR cases have been identified since then, with 75% reported through the BPSU. A third of these infants had mothers who acquired infection abroad (most in their country of origin) in early pregnancy, another third had mothers who were born abroad but caught rubella in the UK, and the rest had UK-born mothers infected in the UK. CR cases in the Republic of Ireland are also reported through the BPSU, and also remain at low levels.

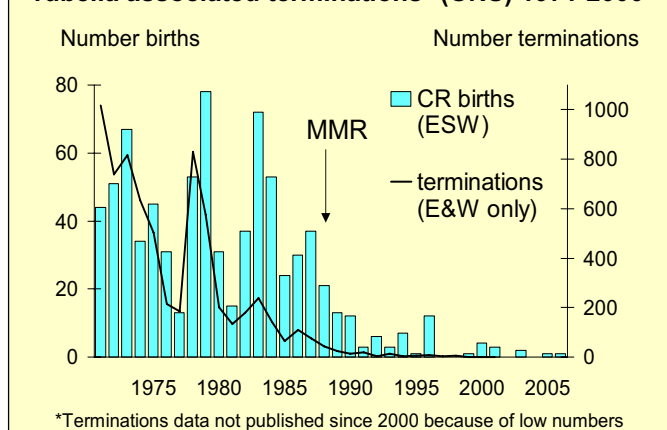
Unfortunately, because of the long-standing inadequate coverage of MMR, there is the potential for rubella to become re-established. The areas of low MMR uptake are also often areas with substantial ethnic minority populations, and rubella could be reintroduced by visitors from, or travel to, parts of the world where the virus continues to circulate.

If this does happen, we need to be able to recognize the problem as soon as possible, and respond rapidly to reduce the on-going risk. Most CR births in the UK are unexpected, as women with diagnosed infection in early pregnancy usually opt for termination because of the very high risk of serious damage to the baby. In the context of the WHO Europe goal of eliminating endemic rubella (and measles) by 2010, and reducing CR births to <1 case per 100,000 births, comprehensive active surveillance remains vital; we are therefore extremely grateful for the continued support of paediatricians reporting through the BPSU.

Case definition, ethics and funding: London MREC last approved the National Congenital Rubella Surveillance Programme in 2005; the reporting definition was extended to include all infants diagnosed with CR in the UK/Ireland, wherever they were born, to optimize case ascertainment. BPSU surveillance also has PIAG approval. The HPA currently pays the orange card fee.

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Congenital rubella births (NCRSP) 1971-2006 and rubella associated terminations* (ONS) 1971-2000



Long Term Surveillance of BPSU Studies – continued

Surveillance for **PIND (Progressive intellectual and neurological deterioration)** commenced following the discovery of the human form of BSE in 1996. What is the justification for continuing surveillance for this length of time?

- Variant CJD could have a very long incubation period (cases of Kuru, another prion disease affecting humans, have appeared after incubation periods of more than 50 years).
- There is no screening test.
- Transmission of vCJD via blood transfusion has now been reported.
- vCJD could spread via surgical instruments because sterilisation has proved to be very difficult where ‘unstable’ prion proteins (the vCJD culprit) are concerned.
- The ‘gold standard’ for diagnosis is neuropathological study of the brain but autopsies are rarely performed.
- Good response has been maintained throughout the study (see Figure). Notifications come from the whole of the UK, from consultants reporting for the first time and from those who have previously notified cases.
- It would be difficult to reinstate the study once it had been stopped.
- Variant CJD is a relatively novel disease that could present in a number of different ways.



PIND Team

All this reinforces the need for continuing surveillance

We ask paediatricians to report children fitting a broad case definition so that all possible cases are notified; hence PIND – Progressive Intellectual & Neurological Deterioration.

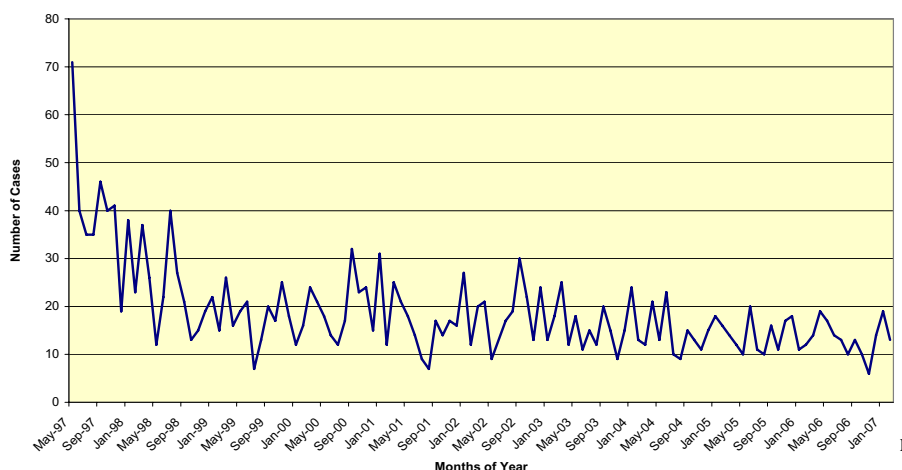
After almost ten years of surveillance **2200** children have been notified. PIND surveillance yields a complex caseload, hence the need for an Expert Group. **1568** cases have been discussed by the Group of seven paediatric neurologists. There have been **953** children with a known diagnosis other than vCJD, and in this diagnosed group there are 117 different neurodegenerative conditions. Because of the heterogeneity of PIND cases it is a very complex process to ensure that all of them have been comprehensively investigated.

- Six cases of variant Creutzfeldt-Jakob disease have been reported to the study since December 1998. Of these 4 have been classified as “definite” and 2 “probable” by the National Creutzfeldt-Jakob Disease Surveillance Unit criteria. All have now died.
- Further active surveillance is planned until April 2008.

Even if an **underlying diagnosis has been made** we still want to hear about **all** children with **progressive intellectual and neurological deterioration**.

Ethical approval is given for us to obtain clinical information about patients who meet the PIND criteria from local paediatricians by telephone interview, postal questionnaire or site visit to extract information from the hospital notes. In those tertiary centres where there are multiple notifications a site visit reduces the burden on the notifying paediatricians.

Monthly Notifications



As expected relatively large numbers were reported in the first few months because we were notified of prevalent cases. Since then incident cases have been notified and this number has remained fairly static throughout the study period.

PIND surveillance continues to work very well and is yielding valuable information about the conditions that lead to PIND in children.

Many thanks to UK paediatricians who are still responding enthusiastically with a median number of 17 notifications per month.

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News in Brief

New studies

The study on idiopathic intracranial hypertension is due to start in July, details will be circulated with the orange card. Studies on intussusception, congenital adrenal hyperplasia and anaphylaxis following vaccination have been approved; start dates will be confirmed following MREC/PIAG approval. Further details are available at <http://bpsu.inopsu.com/studies/index.html>

Recent publications

Rising incidence of type 2 diabetes in children in the United Kingdom. Haines L, Wan KC, Lynn R, Barrett TG, Shield JP. *Diabetes Care.* 2007; **30(5)**: 1097-1101

Pneumococcal infection surveillance in (almost) real time!

Paediatricians are encouraged to visit the [pneumococcal pages of the HPA website](http://www.hpa.org.uk/infections/topics_az/pneumococcal/default.htm) (http://www.hpa.org.uk/infections/topics_az/pneumococcal/default.htm) where information on pneumococcal disease, vaccines, management of vaccine failures and weekly updated surveillance graphs showing the **impact** of the new conjugate vaccine are now available.

Analysis

As you can see from **Table 2** Wales continues to be the highest ranked reporting area. Northern region has moved up 15 places over the past six months, while the ranking for Mersey region continues to freefall. Overall the response rate for 2006 was 93.7% a similar level to that of 2005. This reflects the continued support for the system, and we thank you for this. **Table 3** highlights the current reports; on reporting a case can I remind you to make a note of the case on the tear off section of the card and for you to keep this safe. We have on several occasions of late had clinicians not being able to remember cases they have reported because they did not keep a note of whom they were reporting. The MRSA study will end in June and the scleroderma study in July.

TABLE 2 - % RESPONSE RATE

Region	% rtd Oct 06 – Mar 07	Rank (previous rank)
North	93.1	2 (17)
Yorks	91.9	9 (11)
Trent	90.5	12 (6)
EAnGl	93.0	3 (5)
NWT	85.7	20 (13)
NET	85.9	18 (20)
SET	89.4	14 (12)
SWT	98.5	16 (16)
Wessex	92.2	7 (9)
Oxford	93.0	4 (7)
SWest	92.8	5 (2)
WMids	90.4	13 (8)
Mersey	85.8	19 (15)
NWest	91.8	10 (4)
Wales	96.2	1 (1)
NScot	91.1	11 (19)
SScot	92.0	8 (18)
WScot	88.7	15 (14)
Nlre	92.4	6 (5)
Rlre	86.8	17 (10)
Total	90.3%	

TABLE 3 - ALL CASES REPORTED AND FOLLOW-UPS TO MAY 2007

Condition	Started	VALID				NYK	Total	as % of total		
		C/R	D	E	X			C&R	D&E	X
HIV	1986	4531	572	591	423	6117	74	19	7	
CR	1990	74	30	54	7	165	45	51	4	
PIND	1997	1291	259	599	74	2223	58	39	3	
NNH	2004	75	24	22	69	190	39	24	36	
MCADD	2004	171	47	30	36	284	60	27	13	
MRSA	2005	76	16	23	38	153	50	25	25	
Scleroderma	2005	41	4	19	25	89	46	26	28	
Malaria	2006	140	10	32	55	208	67	7	26	
VKDB	2006	2	1	5	3	11	18	55	27	
FMAIT	2006	16	1	7	18	42	38	19	43	
Genital Herpes	2007				1	1	0	0	100	
Total		6417	964	1353	749	9483	68	24	8	

C/R = confirmed/already known
E = reporting error or revised diagnosis
D = duplicate
X = status not yet reported to BPSU by investigator

HIV Human Immunodeficiency Virus In Childhood
CR Congenital Rubella
PIND Progressive Intellectual Neurological Degeneration
NNH Neonatal Herpes Simplex Virus infection
MCADD Medium chain Acyl CoA dehydrogenase deficiency
MRSA Methicillin-resistant Staphylococcus aureus
VKDB Vitamin K Deficiency Bleeding
FMAIT Fetomaternal Alloimmune Thrombocytopenia

ALL DATA IS PROVISIONAL & CONTINUALLY BEING UPDATED