



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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Warning on Aspirin Use to be Updated

An article in the recent *Current Problems in Pharmacovigilance* (Vol 28: April 2002), published by the Medical Control Agency and the Committee on Safety of Medicines, backs the conclusions of the BPSU's Reye's syndrome (RS) survey (Hall SM, Lynn RM: Reye's syndrome. BPSU 15th Annual Report 2001). Data collected through the BPSU showed that, between June 1986, when the first warning about the association between aspirin and RS was made public and April 2001, when the survey ended, there were 17 reports of cases of RS associated with aspirin, 10 of whom were aged 12 years and over.

Following consideration of the data submitted by Dr Susan Hall, the principal investigator, a new warning has been put out, as follows: *Do not give aspirin to children under 12 years unless medically indicated, and avoid in children aged up to and including 15 years if feverish.* A publicity campaign is to be initiated in the near future and clinicians are reminded to report any cases of Reye's syndrome on the MCA Yellow Card. On hearing the news Dr Hall said "this is another example of the contribution that the BPSU has made to public health and we are most grateful to paediatricians who participated in the survey."

BPSU Successfully Hosts the Second INoPSU Conference

Following a similar meeting in Ottawa two years ago, the British Paediatric Surveillance Unit has successfully hosted the second INoPSU conference. This was held over two days at York University, in conjunction with the Annual Scientific meeting of the College. The first day brought together 20 representatives from 11 of the 14 national surveillance units. Professor Mike Preece, Dr Chris Verity and the BPSU Scientific Co-ordinator, Richard Lynn represented the UK. Countries represented at the meeting included Germany, Netherlands, Australia, New Zealand, Republic of Ireland, Wales, Switzerland, Canada, Malaysia, Portugal and Greece/Cyprus. The aims of INoPSU were reiterated, to facilitate communication between existing units; encourage the sharing of information between researchers and to assist in the development of new units. With the final aim in mind the Portuguese and Irish Paediatric Surveillance Units were accepted as full INoPSU members whilst the Greece/Cyprus Unit was accepted as an affiliate until such time as it has fulfilled the requirements for entry.

Topics discussed included funding problems, the difficulties with data collection and handling and the need for multi-national rare disease surveillance. To this end several disorders were considered for such targeting, including haemolytic uraemic syndrome, and congenital toxoplasmosis. Ways in which communications can be improved by national research teams were also proposed and it is hoped that this will stimulate the use of multi-national surveillance protocols.

A series of lectures on the second day demonstrated the work of the INoPSU. Around 100 paediatricians attended the open session. Following an introduction by Professor Elizabeth Elliott of the Australian Paediatric Unit on the workings of the INoPSU the session continued with a presentation by Dr Jodie McVernon of the Oxford Vaccine Group on *Haemophilus b* vaccination strategies (Hib). Particular concerns were raised over the recent increase in Hib vaccine failures. Several theories for this have been proposed which will require further study and the question arose about the need for placing Hib back onto the BPSU orange card. This was followed by a telling presentation from Dr Elizabeth Miller of the PHLS on how the hypothesis linking MMR with a myriad of disorders including, Crohn's colitis, and autism has continually evolved to try and fit with new evidence. However there continues to be no evidence to show any causal associations. This was followed by Dr Marie Louise Newell of the ICH London who spoke on HIV mother to child transmission rates in the UK and worldwide, and how effective screening and appropriate interventional procedures can help to reduce such rates.

INOPSU Conference, contd.

The fifth lecture presented by Professor Bhupinder Sandhu of the RHSC Bristol outlined the BPSU survey of inflammatory bowel disease proposing that this may be increasing in the paediatric population. Dr Sarah Muirhead outlined the Canadian surveillance on cerebral oedema following DKA. Dr Chris Verity then presented results from the BPSU study of progressive intellectual and neurological deterioration (PIND) study. Effectively being used to identify paediatric vCJD in the UK, it was reported that 1299 cases of suspected PIND had been reported; of these 6 (4 confirmed, 2 probable) have been identified as vCJD.

Finally to put rare disease into context the audience heard a talk from Ms Carol Youngs of the European Organisation for Rare Disease, an umbrella organisation for parent support groups. The importance of appropriate communication with parents when treating such disorders was emphasised as well as bringing to attention the difficulties faced by the family once a child has been diagnosed with a rare disease.

The meeting was considered a great success and will be repeated in 2004 in Portugal. Copies of the abstracts are available via the BPSU office, Tel: (020) 7307 5671, Email: bpsu@rcpch.ac.uk or online at <http://bpsu.inopsu.com/Whatsnew.htm>. Further information on INoPSU is available from <http://www.inopsu.com>

The Royal College of Paediatrics and Child Health, the Wellcome Trust and Wyeth Vaccines deserve grateful thanks for their support.

New Studies

Several studies have recently been approved. The survey on **suspected fatal adverse reactions**, principal investigator Professor Terence Stephenson, in association with the MCA starts this month. You should have received the protocol card for this study with the orange card. If not let us know and we can send another copy. In July the second survey of **congenital toxoplasmosis** commences, principal investigator Dr Ruth Gilbert (see below). The autumn sees the commencement of studies on **severe complications of varicella**, investigator Dr Claire Bramely and **Langerhan cell histiocytosis**, investigator Dr Louise Parker. This study will also involve pathologists, haematologists and dermatologists and those not already receiving the orange card are, with the help of the speciality groups, being actively recruited into the system.

Information on applying to the BPSU is now available on our website at <http://bpsu.inopsu.com/methodol.htm>, alternatively contact the BPSU at bpsu@rcpch.ac.uk

Congenital toxoplasmosis (CT):

Due to commence this summer this will be the second survey of CT undertaken through the BPSU. The first survey identified 17 cases born during the study period 1989-90. At the time it was concluded that there was little to justify the introduction of screening. Since then, neonatal screening has been shown to be feasible and changes in travel and diet may have led to an increase in the incidence of maternal infection. This study will determine birth prevalence of symptomatic CT detected by clinicians in the British Isles and the severity of clinical manifestations. Results will be compared with findings from a similar study conducted 12 years ago informing on prevention strategies such as neonatal screening in the UK, which is already carried out in the US and Europe. The study will also examine the feasibility and usefulness of testing stored Guthrie card bloodspots to detect toxoplasmosis specific IgM/IgA antibodies in children with suspected CT infection. To improve ascertainment the BPSU will be collaborating with the British Ophthalmological Surveillance Unit.

An information flyer is included in this months mailing and the protocol card will distributed in the July mailing.

For further information contact: Dr Ruth Gilbert, Institute of Child Health, 30 Guilford Street, London WC1N 1EH
Tel: 020 7242 29789 E-mail: r.gilbert@ich.ucl.ac.uk

North London surveillance of status epilepticus:

May 1st 2002 marked the start of the two year data collection phase of the *North London convulsive Status Epilepticus in childhood Surveillance Study (NLSTEPSS)*. Though not a BPSU survey and thus not on the orange card, considerable input into the study design has been supplied through the BPSU scientific coordinator.

This regional surveillance study, restricted to North London, has been approved by the London Multi-Centre Research Ethics Committee, and seeks to determine the incidence, seizure types, treatment strategies, and short term mortality of convulsive status epilepticus in a population of children aged between 29 days to 15 years.

Twenty -two centres are involved in the study. A Research Collaborative Group has been established and is constituted of representatives from each of the twenty-two centres, along with other collaborators from the Neurosciences Unit, and the Paediatric Epidemiology & Biostatistics Unit, Institute of Child Health, London.

Further information on the study can be obtained through the principal investigators, Dr Richard Chin, Professor Brian Neville, and Dr Rod Scott, at the Wolfson Centre, Mecklenburgh Square, London WC1N 2AP. E-mail: R.Chinn@ich.ucl.ac.uk

STOP PRESS

Orange card design: Due to the impending start of several new studies and the recent completion of several long term studies the card design will revert back to its original format of two columns with no dividing line. Please check carefully before completing.

Study Extensions

Thrombosis in childhood:

During the first 12 month period 138 thrombotic episodes have been reported and data collection forms sent to reporting clinicians. 112 forms have been completed and returned and of these 68 fit the criteria for the study for which we report. 59 (87%) were venous related, five cases were cardiac related. 61% occurred in the lower limbs, 29% in the upper limbs, jugular and subclavian veins and 10% in various other sites. 52 cases (76.5%) had achieved complete or partial resolution at the time the forms were completed. In 16 cases (23.5%) resolution had either not been achieved or this was unknown. The six-month follow up mailing forms will give a more accurate picture of the incidence of complete resolution. Bleeding complications in only four cases were noted, and these were all minor. The overall mortality is low in these patients (5.8%) with no death attributed to venous thromboembolism. The number reports received is lower than anticipated and to address possible concerns over under ascertainment other clinical groups most likely to be involved in the management of thromboembolic episodes in children will be more actively targeted. These include paediatric anaesthetists, paediatric intensivists, paediatric cardiac and general surgeons. However please report cases even if you feel a colleague has already done so as duplicates can be identified.

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Internal abdominal injuries due to child abuse:

This study commenced in March 2001 and will now end in March 2003. To date of the 49 reports received, 15 have been confirmed, 16 were errors (for example, accidental injuries or external abdominal bruising alone) and 14 duplicates. We await details on four. The mean age of those confirmed was 3 years 11 months, 46% were males. In presenting, for eight of the 15 (54%), there were signs of new or recent fractures and in four (27%) no external bruising was reported. Sadly in six cases (40%) the child died through internal abdominal injury. In 11 of 15 cases notified (73%), small bowel injury (including duodenum) was reported and in nine of these, rupture of small bowel / duodenum was evident (60% of all cases).

It is important to consider that only the most severe cases, where the diagnosis is obvious, are being reported, and that other perhaps less severe cases with different patterns of internal abdominal injury may not have abuse considered as a possible cause. Though it is reassuring to note that duplicate notifications are being received, which indicates that cases are being picked up through the BPSU.

Contact: Professor J Sibert, Department of Child Health, University of Wales College of Medicine, Llandough Hospital, Penarth, Wales CF64 2XX. Tel: 02928 350140 E-mail: sibert@cf.ac.uk

Congenital rubella:

Following concerns over the continued falling MMR uptake rate and the increase in imported rubella cases, the BPSU has agreed to continue surveillance of congenital rubella for a further year. Dr Pat Tookey reports further:-

“National surveillance (England, Scotland and Wales) of congenital rubella began in 1971 with passive reporting by audiologists, paediatricians and microbiologists. After the rubella vaccination programme was implemented, there was a dramatic decline in the number of cases from an average 50 births and 740 terminations a year in 1971-75 to 20 births and 55 terminations a year in 1986-90. Active surveillance was needed to monitor cases at this low level, and congenital rubella was put on the orange card in 1990. BPSU reports from Ireland are also followed up, but not usually included in published figures”.

Seven infants with congenital rubella have been reported for 2000/2001. Five were imported cases with women acquiring infection in their countries of origin (Bangladesh, Pakistan, Sri Lanka, Nigeria and Zambia). In 1999 a major rubella epidemic in Greece led to isolated outbreaks of infection in the UK. The only reported case of congenital rubella that year, an infant born in December 1999 in Scotland, was epidemiologically linked to one of these outbreaks, although the maternal infection was acquired in Scotland. No congenital rubella births were reported in 1997 and 1998.

Table 1 Congenital rubella births and terminations 1990-2001

Year of birth	Congenital rubella cases			Terminations associated with rubella disease or contact (ONS, E&W only)
	First reported through:		Total CR cases	
	BPSU	Other source~		
1990-98	32	13	45*	73
1999	0	1	1	1
2000	4	0	4	1
2001	3	0	3	n/a

~ includes notifications first made known to the NCRSP via the laboratory reporting systems

* includes a set of triplets in 1992

Rubella continues to circulate in many parts of the world; the decline in MMR uptake rates in the UK (currently 84%) means that infection could once again start to circulate here. Awareness of rubella infection and congenital rubella among paediatricians, and health professionals looking after pregnant women must be maintained. Hence continued surveillance of congenital rubella is vital.”

Contact: Dr P Tookey, Dept of Epidemiology, Institute of Child Health, Guilford Street, London W1N1EH.

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In the News

SPARKS Award: Congratulations goes to our very own Dr Jugnoo Rahi, BPSU medical adviser, who was awarded the prestigious SPARKS award for young investigator of the year, at this year's RCPCH scientific meeting. Jugnoo was nominated by the Institute of Child Health for her work into severe visual impairment and blindness in children.

New GOSH website: Children will be able to get health advice on a new website recently launched by Great Ormond Street Children's Hospital (GOSH). The site has been designed by experts at the world-famous hospital and the Institute of Child Health, but is also based on the experiences of children. It is aimed at children aged five to 16, and will have separate areas for young children and teenagers. The website is at <http://www.goshkids.nhs.uk>.

Consent & Confidentiality: Drs Verity and Nicoll outline their thoughts on seeking consent and the importance of confidentiality in relation to public health surveillance. Consent, confidentiality and the threat to public health surveillance. Verity C, Nicoll A; *BMJ* 2002; **24**:1210-3. Also available at <http://bpsu.inopsu.com/Whatsnew.htm#Publication>

Monthly Analysis

Preliminary analysis of the 2001 returns suggest an overall orange card return rate of 92.7%, this is a similar level to that seen in 2000 and stems the decline in responses seen since 1997. One thing we can't be sure about is whether any negative cards are being returned when in fact a reportable disorder was seen; we would hope that this is not the case. The figure in brackets in **Table 2** shows your regions overall position on the year, North Scotland and Wales were the highest responders with Oxford the highest English region. **Table 3** outlines the report received for the current studies. There are still a considerable number of outstanding questionnaires for the cerebralvascular disease/stroke survey, so if you have yet to return your questionnaire, could you please do so. If you require a new questionnaire please let us know.

**TABLE 2 –
% RESPONSE RATE
Sept 2001 - Feb 2002**

Region	% ret'd	Rank (Jan-Dec 2001)
North	90.4	13 (8)
Yorks	91.9	7 (18)
Trent	88.8	18 (17)
EAnagl	92.2	6 (14)
NWT	87.1	19 (7)
NET	81.3	20 (20)
SET	89.6	15 (16)
SWT	89.7	14 (11)
Wessex	91.9	8 (4)
Oxford	93.1	2 (3)
SWest	91.1	11 (15)
WMids	92.4	4 (5)
Mersey	89.2	16 (6)
NWest	91.3	10 (9)
Welsh	93.0	3 (2)
NScot	98.4	1 (1)
SScot	91.6	9 (13)
WScot	91.1	12 (12)
Nlre	92.3	5 (4)
Rlre	89.1	17 (19)
Total	90.0	

TABLE 3 - ALL CASES REPORTED AND FOLLOW-UP at 25/5/02

Condition	Started	I VALID		II INVALID		NYK	Ttl	as % of total		
		I	Ia	Ib	III			I	II	III
HIV/AIDS	1986	1720	314	400	134	2568	67	28	5	
CR	1990	66	24	41	4	135	49	48	3	
PIND	1997	795	138	314	60	1307	61	35	5	
CVD/S	2001	168	12	36	95	311	54	15	31	
VKDB	2001	6	2	1	21	30	20	10	70	
Thrombosis	2001	67	15	31	42	155	43	30	27	
CMV	2001	77	15	31	42	165	47	28	25	
IAI	2001	14	13	18	8	53	26	58	15	
Total*		2913	533	872	406	4724	62	30	9	

* All data is provisional & continually being updated

Key to table / abbreviations

I	= confirmed/already known	IIa	= duplicate
IIb	= reporting error or revised diagnosis	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		
Enceph	Encephalitis in children (2-36months)		
GBS	Group B streptococcus disease		
CV/S	Cerebrovascular disease/stroke & like illness		
CMV	Congenital Cytomegalovirus		
IAI	Internal abdominal injuries due to child abuse in children under 14 yrs		