



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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Survey of invasive fungal infections in low birth weight infants to commence in New Year

A survey of invasive fungal infections in very low birth weight (VLBW) infants is due to commence in the coming months. Dr W McGuire, the lead investigator stated, "Invasive fungal infection is an increasingly common cause of substantial morbidity and mortality in very low birth weight infants. This one-year prospective descriptive study aims to provide national data on the incidence, patterns of presentation, and the outcome of invasive fungal infection in very low birth weight infants in the British Isles. These data may inform practice with regard to investigation, management, counselling, and assist in the evaluation of new preventative strategies."

The case definition is:-

Live born VLBW infant with confirmed invasive fungal infection as determined by one or more of the following:

- culture from a sterile site: CSF, blood, or urine (supra-pubic aspirate), bone or joint, peritoneal or pleural space
- pathognomonic findings on ophthalmological examination
- pathognomonic findings on renal ultrasound examination
- Infants with an autopsy diagnosis of invasive fungal infection.

Further information and the protocol card will be made available nearer the commencement of the study. In the meantime for further details contact Dr W McGuire, Senior Lecturer, Tayside Institute of Child Health, Ninewells Hospital and Medical School, Dundee.

Email: w.mcguire@dundee.ac.uk or visit the BPSU website at <http://bpsu.inopsu.com>.

Founder of the BPSU steps down

Professor Catherine Peckham, one of the founders of the BPSU, attended her last meeting of the BPSU Executive in November as representative of the Institute of Child Health - London (ICH), one of the BPSU's parent bodies. Catherine was involved right from the start in 1985 and her guidance and advice particularly during her time as chairperson has been invaluable to the success of the BPSU. Catherine's replacement as Head of the Centre for Epidemiology, Professor Carol Dezateux, will take over as representative for the ICH on the Executive. As well as maintaining continuity Carol has close knowledge of the BPSU gained in her role as principal investigator of the congenital dislocation of the hip survey.

BPSU Executive seeks new committee member

A vacancy has arisen on the BPSU Executive, to replace Dr Patricia Hamilton. Applicants should be a fellow of the College and in current good standing, aware of the work of the BPSU and have some experience in research. Members are expected to take an active role in the Committee, which meets every two months to review study applications and oversee the general running of the Unit.

Nomination details for the committee membership have been sent out with this month's College newsletter pack. For further details contact Professor Mike Preece Tel: 020 7242 9789 or the BPSU Scientific Coordinator on Tel: 020 7307 5671. For general information on the BPSU visit its website at <http://bpsu.inopsu.com>

Study Updates

Thrombosis in Childhood (Age >1 month – 16 years)

The first national prospective epidemiological study of childhood thrombosis in the UK began collecting cases in February 2001, by reporting to the BPSU via the monthly report card. The study was initially to run for a period of 13 months, but due to concerns of sub-optimal reporting, it was agreed to extend the study for a further 12 months, to the end of February 2003. In an effort to collect all possible cases, during this latter period specific clinician groups who are most likely to see thrombotic events in children, but who may not be members of the RCPCH, were targeted. These include paediatric anaesthetics, paediatric intensivists, and paediatric cardiac and general surgeons.

Objectives of the study

- 1 To determine the incidence and epidemiology of thrombosis in the UK in children aged between one month and 16 years.
- 2 To determine which risk factors predispose to thrombosis in childhood, and in particular, the role of thrombophilia, both inherited and acquired.
- 3 To determine current diagnostic and therapeutic practice in childhood thrombosis and to assess if there is sufficient available information on which to develop management guidelines.

The criteria for entry is – 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** are children with stroke, whether this is arterial or due to sino-venous thrombosis.

Preliminary analysis: 259 thrombotic episodes have been reported in the 21 months to November 2002, and data collection forms sent to reporting clinicians. 202 forms have been completed and returned and of these 128 fit the study criteria. 74 (36%) were excluded for various reasons, including duplicate reporting, non-fulfilment of the study criteria, events occurring during the neonatal period and those outside of the study period. 89 six-monthly follow up mailing forms have been sent to clinicians and 72 have been completed and returned.

Site of Thrombus: Of the 128 cases analysed 105 (82%) were venous related. 57% of all cases occurred in the lower limbs, 23% in the upper limbs, jugular and subclavian veins. 11% were cardiac related (SVC and IVC, and post cardiac surgery) and 9% occurred in various other sites.

Risk factors: The main risk factors were – central venous/femoral lines (42%), Sepsis and immobility (31%), malignancy (21%). In only seven cases were there no risk factors reported.

Diagnostic investigations: doppler ultrasound, echocardiogram, venogram, angiogram and CT scans were the main method of diagnosis, with ultrasound being the most common at 64%. In over 30% of cases more than one diagnostic investigation proved to be abnormal.

Management: In over 50% of cases Heparin/LMWH followed by Warfarin was the treatment of choice. A further 36% received Heparin alone. Of the patients with central/femoral lines insitu 52% were removed. Thrombectomy was performed in 11 patients.

Outcome: 43 patients achieved complete resolution (34%) and 51 partial resolution (40%). At the time of completing the forms there was no resolution in 16 patients, and in 17 patients this was not known. The overall mortality has remained low (7%) with no death attributed to venous thromboembolism.

Conclusions: This study is nearing completion, with only three months to run. For the study to give realistic and accurate data on which to base future diagnostic and therapeutic practice, it is important to collect information on as many thrombotic episodes as possible. So if you are aware of any unreported cases occurring during the surveillance period please let us know. We are grateful to all reporting physicians and would encourage continued support of the study.

Contact: Dr Brenda Gibson, Diane Henderson, Dept of Haematology, Yorkhill Hospital, Glasgow G3 8SJ.
Email: diane.henderson@yorkhill.scot.nhs.uk

Suspected fatal adverse drug reactions

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, two reports of suspected fatal adverse drug reactions have been received. One of these was a teenage girl with congenital heart disease, taking enalapril for heart failure, who developed liver failure and died. Details of the second case are awaited.

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

Study Updates, continued

Vitamin K Deficiency Bleeding

Dr Andrew McNinch reports “The third 2–year BPSU survey will finish at the end of December 2002. To date there have been 35 notifications, for which 27 questionnaires have been returned; of these, three were duplicate notifications, 12 have been classified as “no case” and seven require further details to allow classification. Of the five confirmed cases, 2 had liver disease (associated with cystic fibrosis in one; biliary atresia in the other). In two other cases the bleeding was/may have been provoked by other factors (circumcision in one, intestinal haemorrhage associated with campylobacter enteritis in the other), so-called secondary VKDB. Two cases received oral vitamin K prophylaxis, three had none. There has been no death or confirmed case of intracranial haemorrhage.

Comments: The 12 “no cases” (one third of notifications) and three duplicates imply that paediatricians have a low threshold for notifying possible cases, for which we are grateful. The previous 2-year surveys found about 15 confirmed/probable cases per year and about five per year suffered intracranial haemorrhage; the preliminary results of the current survey suggest that the incidence and associated mortality of VKDB have fallen. This may be the result of many factors, including changes in the use of vitamin K prophylaxis; we plan to repeat a national survey of prophylaxis policies in 2003. We thank all our colleagues for their continuing co-operation with the surveys.”

Contact: Dr A. McNinch/Dr J. Tripp, Royal Devon and Exeter Hospital, Barrack Road, Exeter, Devon, EX2 5DW.
Tel: 01392 402676. E-mail: awmcninch@doctors.org.uk

Yearly Review

Once again we have reached the time of year when it is traditional to look back over the year’s activities. During 2002 the BPSU Executive Committee met six times to discuss surveillance proposals and applications. A few changes to the Committee membership were seen this past year. Most notable was the retirement of Professor Catherine Peckham, one of the founders of the BPSU, after 17 years. Dr Carol Dezateux, the new head of the Centre of Epidemiology at the ICH (London) will be taking over as ICH representative on the Executive. This year also saw Professor Ian Jones of SCIEH stepping down to be replaced by Dr Claire Bramley, Professor Neil McIntosh in his capacity as Head of Research took over from Professor Richard Cooke and finally Dr Patricia Hamilton after five years steps off the committee. A replacement is currently being sought.

Ten studies are currently being undertaken, three of which commenced this year: fatal adverse drug reactions, congenital toxoplasmosis and severe complications following varicella infection. Two further studies have received provisional approval, invasive fungal infection in very low birth weight infants and Langerhan cell histiocytosis. Hopefully these will commence in the New Year.

This year there have been 11 general study enquiries; seven phase one applications and seven full applications have been considered. Full guidelines for applying to the BPSU can now be downloaded from the BPSU website at <<http://bpsu.inopsu.com/methodol.htm>> or alternatively the BPSU scientific coordinator can be contacted. In terms of case reports, of the 22,000 cards returned from 24,000 sent, there were just over 1,000 case reports of which 600 have been confirmed to date.

The International forum supplied the Unit with its main highlight of the year, with the hosting of the second INoPSU conference. Representatives from 12 countries attended the business meeting, whilst over 120 paediatricians attended the open session. At the following RCPCCH scientific meeting, six BPSU study papers were presented and eight publications appeared in peer review journals this year. Data coming out of the BPSU has also been mentioned several times in the national press this year.

So as you can see the work and reputation of the BPSU goes from strength to strength and this is wholly attributable to the contribution given by members of the RCPCCH. On behalf of the investigators and the BPSU we thank you all.

News in brief

Aspirin warning update: Our summer bulletin highlighted the fact that data supplied by the BPSU Reye study to the Medicines Control Agency had led, in April, to a change in the advice on the administration of aspirin. This extended the 1986 warning that children under 12 should not be administered aspirin. It would now also cover those less than 16 years. but for children 13-15 years this was only if they were presenting with fever. However, the Committee subsequently had concerns about confusing the public over administration to teenagers. So in October they announced that the warning would state "Do not give to children aged under 16 years, unless on the advice of a doctor". Consultation is currently under way <<http://www.mca.gov.uk/>> and the legal process should be complete by March 2003. The administration of aspirin to children under 16 for certain conditions such as Kawasaki disease and juvenile chronic arthritis will be permissible if required.

Enhanced Surveillance of Haemolytic Uraemic Syndrome (ENSHURE) and other presentations of Thrombotic Microangiopathy (TMA): A clinically driven system for enhanced surveillance of all cases of HUS and other presentations of TMA will be launched in Scotland on 1 January 2003, co-ordinated by SCIEH (the Scottish Centre for Infection & Environmental Health). More detailed information is being sent to paediatricians and other potential case reporters in Scotland.

For more information please contact us, or visit our website: Mary Locking/Kevin Pollock, Epidemiologists (mary.locking@scieh.csa.scot.nhs.uk or kevin.pollock@scieh.csa.scot.nhs.uk) SCIEH, Clifton House, Clifton Place, GLASGOW G3 7LN (Tel 0141-300-1100; Fax 0141-300-1170) <http://www.show.scot.nhs.uk/scieh/#infectious/infgastro.html>

Correction: In the last quarterly bulletin the articles on Rett syndrome and hepatitis C virus (HCV) may have given the impression that the BPSU was still surveying for these disorders, this is **not** so. However, registers do exist for these disorder and case reports can be made direct. For further information on the Rett Syndrome register contact Dr Alison Kerr – email: amk5m@clinmed.gla.ac.uk and for the HCV register contact Dr Helen Harris - email: hharris@phls.nhs.uk.

Monthly Analysis

TABLE 1 – % RESPONSE RATE

Feb-July 2002		
Region	% ret'd	Rank (Dec-May 2002)
North	89.2	15(14)
Yorks	93.8	9 (9)
Trent	90.1	13 (16)
EAngl	95.6	3 (1)
NWT	85.9	19 (19)
NET	80.6	20 (20)
SET	89.1	16 (18)
SWT	88.2	18 (17)
Wessex	91.7	12 (12)
Oxford	95.8	2 (2)
SWest	92.4	11 (10)
WMids	89.0	17 (15)
Mersey	94.5	6 (7)
NWest	93.3	8 (6)
Welsh	95.0	5 (5)
NScot	97.7	1 (3)
SScot	89.3	14 (13)
WScot	93.1	10 (4)
NIRE	93.6	7 (8)
RIre	95.0	4 (11)
Total	90.6	

TABLE 2 - ALL CASES REPORTED AND FOLLOW-UP at 16/11/02

		I VALID		II INVALID		NYK	as % of total		
Condition	Started	I	Ia	Ib	III	Ttl	I	II	III
HIV/AIDS	1986	1993	337	440	159	2929	68	27	5
CR	1990	66	24	44	5	139	47	49	4
PIND	1997	865	149	342	81	1437	60	34	6
VKDB	2001	4	2	11	20	37	11	35	54
Thrombosis	2001	128	18	54	54	254	50	28	22
CMV	2001	124	23	39	56	242	51	26	23
IAI	2001	17	17	19	10	63	27	57	16
SFADR	2002	2	0	1	2	5	40	20	40
Con Toxo	2002	0	0	0	15	15	0	0	100
Total*		3410	582	1007	436	5435	63	29	8

* All data is provisional & continually being updated

Key to table / abbreviations

I	= confirmed/already known	IIa	= duplicate
Ib	= reporting error or revised diagnosis	III	= status not yet reported to BPSU by investigator
AIDS/HIV	Acquired Immunodeficiency Syndrome/ Human Immunodeficiency Virus	CMV	Congenital Cytomegalovirus
CR	Congenital Rubella	IAI	Internal abdominal injuries due to child abuse in children under 14 yrs
PIND	Progressive Intellectual Neurological Degeneration	SFADR	Suspected Fatal Adverse Drug Reactions
VKDB	Vitamin k Deficiency Bleeding	Con Toxo	Congenital Toxoplasmosis