

# BPSU

21<sup>st</sup> Annual Report  
2006-2007



British Paediatric Surveillance Unit  
Royal College of Paediatrics and Child Health

Supported by the Department of Health



# Aims of the British Paediatric Surveillance Unit

To:

- Facilitate research into uncommon childhood infections and disorders for the advancement of knowledge and to effect practical improvement in prevention, treatment and service planning
- Allow paediatricians to participate in surveillance of uncommon disorders and to lessen the burden on reporting doctors of such requests arising from numerous different sources
- Increase awareness within the medical profession of the less common disorders studied and respond rapidly to public health emergencies.

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## **British Paediatric Surveillance Unit Annual Report 2006/2007**

Compiled and edited by Mr Richard Lynn, Ms Jennifer Ellinghaus, Dr Rachel Knowles and Dr Chikwe Ihekweazu

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# Foreword

This year the average number of conditions on the orange card is up on the previous two years to nine, with a further five in the pipeline. As usual there is a mix of studies coordinated from the Health Protection Agency, the Institute of Child Health and individual paediatricians. Amongst the latter are those of the Sir Peter Tizard Bursary award holders: Shamez Ladhani's study on imported malaria and Scott Williamson's on thyrotoxicosis are now complete, Yim Yee's study on intra-cranial hypertension and Shazia Adalat and Tom Dawson's on toxic shock syndrome are about to go on the card. This annual bursary, funded by the RCPCH, is now firmly embedded in the work of the BPSU. This year there were 17 applications and, although only one can win the help of the bursary funds, a number of others will hopefully be worked up for the orange card. A further development was our first study in collaboration with the UK Obstetric Surveillance System (UKOSS) on fetomaternal alloimmune thrombocytopenia (FMAIT). UKOSS was launched in 2004 and we hope there will be further collaborative studies, initiated by obstetricians and/or paediatricians. In order to encourage applications further, the BPSU held a second workshop at the College offices in April 2007. Attended by over 40 doctors and researchers, subjects such as questionnaire design, patient involvement, data collection and consent and confidentiality were considered.



Prof A Colver  
Chair, BPSU Executive Committee

I was aware that some paediatricians have wondered how many and for what reasons some conditions remain on the card for many years. The Executive Committee therefore discussed this formally and determined some principles. The issues were also addressed by Pat Tookey (HIV/AIDS, congenital rubella) and Chris Verity (PIND) in our Summer edition of the Quarterly News Bulletin.

This year Sue Banton and Ann Seymour have joined the committee on behalf of the RCPCH Patient and Carers' Advisory Group in order to promote public involvement in health related research. Their wide experience was described in the March Quarterly Bulletin. The committee has benefited enormously from their expertise. As part of the Unit's self-evaluation we are now assessing the degree of parent and support group involvement in past studies; the application form for an orange card study now asks applicants to state how they have considered involving voluntary groups and patients or parents; and the user's workshop and study day included a session illustrating how helpful involvement of the public can be. There is always the danger of tokenism and we are pleased that Sue and Ann tell us we are avoiding this.

For each of the last three years a day has been set aside for strategic thinking and an issue discussed this year was electronic communication. For practical reasons (non-delivery of emails, blocking by NHS Trusts, keeping email lists up to date), we decided now is not the right time to send the orange card electronically. However we think that reporting the details of a case to the investigator could be via online questionnaires on secure websites, and hope to pilot this over the coming year.

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There are 12 other active international paediatric surveillance units, most influenced by or copying BPSU methodology and working together under the acronym INOPSU ([www.inopsu.com](http://www.inopsu.com)). Following a successful meeting last year, INOPSU applied this April for funds from European Commission Research Framework 7 to develop its collaborative work and engage with other European groupings such as the European Centre for Disease Control; by the time of publication of this report we should have heard the outcome of the application.

After 12 years Denis Gill, representing the Royal College of Physicians (Ireland) has stepped down. The BPSU is very grateful to him for so enthusiastically promoting the involvement of Ireland in surveillance. I also thank Martin Richardson and Neil McIntosh for all the work they have done for the committee and welcome Terence Stephenson representing the College and Ted Wozniak representing the Department of Health.

I would like to thank Jennifer Ellinghaus, research facilitator, Richard Lynn, scientific coordinator, and Linda Haines, head of the RCPCH research unit for all their work on behalf of the BPSU. Thanks also go to Claire Brunert, College press officer and Sophie Auckland, College patient involvement officer, who regularly assist the work of the BPSU.



# Introduction

Rare diseases and infections are, paradoxically, a numerically important cause of morbidity and mortality in childhood. Individually uncommon, together they number thousands, and many result in severe sequelae. Many are characterised by chronicity, high rates of disability or death. These conditions pose a large financial and emotional burden for affected children, their families and health systems.

To address this problem in the UK and Ireland, in July 1986 the British Paediatric Surveillance Unit (BPSU) was set up, enabling paediatricians to participate in the surveillance and further study of rare disorders affecting children.

The BPSU's work primarily concerns epidemiological surveillance, defined as 'the collection, analysis and dissemination of high quality data relevant to the understanding, prevention and control of medical conditions of public health importance so as to satisfy the needs of health care professionals, science, government, voluntary organisations and the public at large'. (Adapted from: Bulletin of the World Health Organisation, 1994; 72).

Several agencies founded and continue collaborating to support the work of the BPSU: the Royal College of Paediatrics and Child Health (RCPCH), the Health Protection Agency (HPA), the Centre for Epidemiology and Biostatistics at the Institute of Child Health (London), Health Protection Scotland (HPS) and the Faculty of Paediatrics of the Royal College of Physicians of Ireland. As the BPSU monitors conditions of public health importance, an observer from the Department of Health attends the BPSU's Executive Committee, which meets every eight weeks to consider individual applications and the progress of studies.

The aims and key challenges of the Unit are summarised on the inside front cover.

This report mainly focuses on activities undertaken during the year 2006. Reference is also made to studies and activities, which commenced in the year 2007.

## 2 How the Surveillance System Works

### Selection of studies for inclusion in the scheme

A study is eligible for participation in the scheme if the subject is a rare childhood disorder (or rare complication of a commoner disease) of such low incidence or prevalence as to require cases to be ascertained nationally in order to generate sufficient numbers for study. All studies have to conform to high standards of scientific rigour and practicality. The system is open to any clinician or research group, but applicants are encouraged to approach the BPSU with, or through, a paediatrician or department of paediatrics/child health.

The number of conditions under surveillance is usually limited to 12 and there is keen competition for places on the BPSU card. The BPSU application procedure consists of two phases: a screening phase based on an outline of the study and a detailed consideration of the full application. Details about the BPSU application procedure can be downloaded from the website at <http://bpsu.inopsu.com/methodol.htm> or are available on request from the BPSU office.

Factors that increase the likelihood of a study being accepted include scientific importance, rarity of the condition, proposals with outcomes of clear importance to public health, clear achievable objectives and a clear and easily applied case definition. Once approved by the BPSU Executive, studies require Multi Research Ethics Committee (MREC) and Patient Information Advisory Group (PIAG) approval under Section 60 of the Health and Social Care Bill (2000) before commencement.

### The reporting system

Those participating in the reporting system include consultant paediatricians who are either members of the RCPC or the Faculty of Paediatrics of the Royal College of Physicians of Ireland.

Surveillance is 'active' as the BPSU Office actively sends out cards to clinicians asking for cases to be reported on the BPSU orange card (Figure 1). Each month, all clinicians participating in the surveillance scheme are sent the orange card listing the conditions currently under surveillance; follow-up reminders are sent to those who have not returned their

British Paediatric Surveillance Unit Report Card  
NOTHING TO REPORT  2006  
Specify in the box number of cases seen CODE No [ ]

- AIDS/HIV
- Congenital rubella
- Progressive Intellectual & Neurological Deterioration
- Neonatal Herpes Simplex Virus (HSV) Infection
- Medium chain acyl CoA dehydrogenase deficiency
- Early onset eating disorder in children <13 years
- MRSA
- Scleroderma
- Malaria in childhood
- Vitamin k deficiency bleeding
- Feto-maternal alloimmune thrombocytopenia

Figure 1: Orange Card Side A

Clinicians Section – Please Keep if Necessary British Paediatric Surveillance Unit Report Card for cases seen in 2006

Please NOTE the patient's name(s) or other identification and **KEEP THIS SLIP** for easy reference when you are contacted by the investigator.

Condition	Patient	Hospital No.

Detach this Section Before Posting

Figure 2: Orange Card Side B

card for two consecutive months. A set of instructions for completing the card, including case definition of the conditions listed on the card is also circulated. When a new study begins, the mailing also includes a specially produced study protocol card and other information about the study.

When reporting a case, respondents are also asked to make a note of the case (Figure 2) and keep the details for future reference as they will later be contacted by the study team with a questionnaire about each case.

Participants are also expected to return cards even if they have no cases to report - there is a 'nothing to report' box on the card for them to tick. This allows us to measure compliance to the system. The BPSU also regularly updates the list of consultant paediatricians who are eligible to participate and compliance rates are continually monitored, thus ensuring good coverage of the paediatric surveillance scheme across the whole of the UK and Ireland.

## Follow-up and confirmation of case reports

On receiving a case report the BPSU informs the relevant study team. The study team then contacts the reporting clinician for further information about the case, usually through a short questionnaire. Particular care is taken to ensure that questionnaires sent to reporting clinicians are as short as possible, clear, straightforward and not excessive in their demands. As the questionnaire cannot be fully anonymised, the amount of patient identifiable data collected is strictly limited to preserve patient confidentiality. The study investigators report back to the BPSU, indicating when cases have been confirmed or are duplicate case reports (Figure 3). Duplication of reporting is most likely to occur when the condition requires referral to another clinician, but this is encouraged, as it is better to receive duplicate reports than to miss a case.

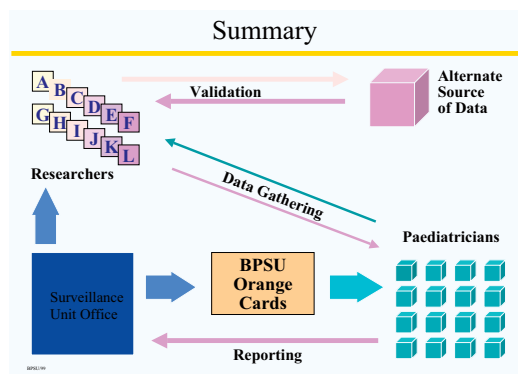


Figure 3: Surveillance Mechanism

Table 2 (page 9) shows the number of cases reported to the BPSU from its inception until the end of year 2006 for conditions under surveillance at October 2006. The extent to which investigators receive survey data, identifying incorrect reports and duplicates and the speed in which this is done is known as the 'completion rate'. The number of cases which have so far been subsequently confirmed as meeting the case definition are also shown.

The time taken to follow-up a case report varies greatly between conditions and may be longer if microbiological or pathological details are required to confirm a case. The completion rate is high. For example, as of June 2007, only 488 (5%) of the 9272 case reports had yet to be followed-up. The final completion rate normally averages between 90-95%.

Table 3 (page 10) summarises the outcome of the follow-up of all cases reported to the BPSU by the end of year 2006 and provides evidence for the level of accuracy of reporting by participating clinicians.

To improve case ascertainment for specific studies where a child may see specialist clinicians, consultants working in a number of other specialties have been invited to participate in the scheme. Pathologists have been included in the BPSU reporting scheme since 1992 and most studies of paediatric infections involve laboratory reporting by microbiologists. For the past two years child psychiatrists have been involved in a parallel reporting system for the study of early onset eating disorders. Apart from helping to improve ascertainment such complementary data sources help to validate the surveillance system (Figure 4). The impact of such alternate data sources has recently been examined and the findings published. (Using multiple sources to improve and measure case ascertainment in surveillance studies: Knowles RL, Smith A, Lynn R, Rahi J. 20 years of the British Paediatric Surveillance Unit. J Public Health 2006 Jun;28(20): 157-65).

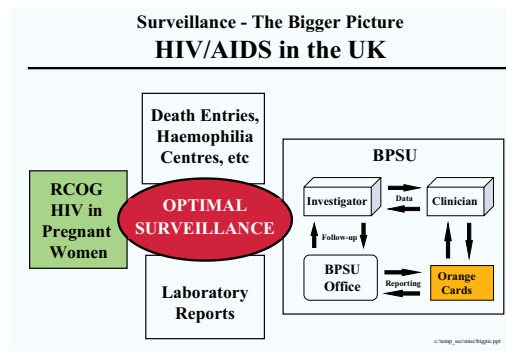


Figure 4: Surveillance - the bigger picture

## Funding

The BPSU continues to be in receipt of a grant from the Department of Health to cover the majority of the running costs of the unit. In addition, the BPSU asks surveillance teams to contribute a sum to cover the administrative costs of coordinating their study. These funds permit us to undertake other activities such as holding workshops to support current and potential investigators, most recently in April 2007. Funds were also used to hold a conference to mark the 20<sup>th</sup> anniversary of the BPSU and cover our international commitments to the International Network of Paediatric Surveillance Units (INoPSU). The BPSU is also grateful for the ongoing support that it receives from the Royal College of Paediatrics and Child Health, the Institute of Child Health (London), and the Health Protection Agency.

### 3 Scientific Coordinator's Yearly Review of Activities

This past year has seen the commencement of three new BPSU studies. The first, malaria in childhood, commenced in January 2006. The investigator for this study, Dr Shamez Ladhani, was the Sir Peter Tizard bursary 2004 recipient. The second study, vitamin k deficiency bleeding (VKDB), commenced in September 2006. This study has appeared on the orange card three times in the past, and the principal investigator is Dr Alison Busfield. The third study on foeto-maternal alloimmune thrombocytopenia (FMAIT) commenced in October 2006, and is being lead by Dr Marian Knight. This study is the first BPSU facilitated study to be undertaken in collaboration with the UK obstetric surveillance system.

Six studies had their period of surveillance extended for a further year in 2006: HIV, congenital rubella, progressive intellectual and neurological deterioration (PIND), medium chain acyl CoA dehydrogenase deficiency (MCADD), neonatal herpes simplex virus and childhood scleroderma. Surveillance of early onset eating disorders (EOED) ended in May 2007, though a one- year follow is currently underway.

One study has so far commenced in 2007 - genital herpes in children under 11 years of age presenting to secondary care (April), investigator Richard Reading. The third Sir Peter Tizard Bursary, awarded to Dr Yim Yee Matthews for her proposed study of Idiopathic Intracranial Hypertension (IIH), received the appropriate ethical approval and will commence soon. The 2006 bursary was awarded jointly to Dr Shazia Adalat and Dr Tom Dawson to undertake a study on Toxic Shock Syndrome (TSS). The bursary has now become established as a major source of research funding for doctors in training wishing to undertake research into rare paediatric disease. Details for those wishing to apply for the Sir Peter Tizard Bursary are available from the BPSU office or via the BPSU website.

Between the inception of the BPSU in 1986 and December 2006, 60 studies have been completed (Appendix A). During 2006/2007, there were 22 publications and 54 presentations relating to BPSU studies (Appendices B and C).

Last year we reported that all BPSU facilitated studies must now apply for approval under Section 60 from the Patient Information Advisory Group (PIAG) to allow the collection of minimal identifier data without consent. All current BPSU studies

(Photo by Joe Spinoza, aged 9)



Richard Lynn  
Scientific coordinator

have now received such approval and the BPSU has set up a process with PIAG to facilitate swift review of applications which appears to be working well. As yet, no extra delays have been experienced and the BPSU and PIAG will continue to work together to ensure that this remains the case.

As part of the BPSU's strategy to engage with the patients, carers and the public in general the membership of the BPSU Executive Committee now includes two representatives from the College's Patient and Carers Advisory Group. Mrs Sue Banton, who is a founder & director of a national charity STEPS (<http://www.steps-charity.org.uk>) which supports individuals and their families with lower limb conditions and Mrs Ann Seymour whose remit includes ensuring the participation of children, young people, their parents and carers in the work of the College joined in 2006. Both Sue and Anne are voting members of the BPSU Executive Committee and are involved in activities such as reviewing BPSU paperwork so as to ensure that it reflects the importance of researchers engaging with those with a non-clinical background.

The BPSU continues to disseminate information on its activities to clinicians and the public alike. This is achieved mainly through this report, the quarterly bulletin and increasingly through the BPSU website. The website (<http://bpsu.inopsu.com>) has recently been improved and updated and now contains information on each condition under study, research protocols, copies of publications, details of parent support groups and information regarding involving the public in research.

As liaison officer to the International Network of Paediatric Surveillance Units (INoPSU) it is my job to keep the units in contact, inform them of each other's work and put investigators in different countries in touch with each other in order to

facilitate collaboration. In the past year, over 90 different conditions have been investigated across the 13 member surveillance units. The BPSU office continues to manage the INoPSU website (<http://www.inopsu.com>) where information on INoPSU's work is available. A short report of the 4<sup>th</sup> INoPSU conference, held in London in May 2006 was included in the 2005/6 annual report. The next meeting will be held in Munich, Germany, in September 2008.

### Participation in the scheme during the year 2006

The BPSU ascertains the names of new consultants primarily through the RCPCH advisory appointment committees, membership office, personal communication and the ongoing College

workforce. During the year, 157 consultants were placed on the mailing list whilst 110 were removed mainly following retirement or due to moving overseas. The number of consultant paediatricians participating in the scheme as of December 2006 rose to 2681, an increase of 1.0% on the previous year. The BPSU mailing list also includes selected groups of consultants other than paediatricians such as cardiologists, clinical geneticists and pathologists. In order to help in the ascertainment of cases pathologists continue to be included in the surveillance system, and our thanks are extended to the Royal College of Pathologists for supporting this initiative. Our thanks also go to the child psychiatrists who contributed significantly to the early onset eating disorder study. Such was the interest that there is now the real possibility of the development of a child psychiatric surveillance system.

**Table 1 Regional response rate 2005 and 2006**

Region	Rank 2006	Rank 2005
Northern	11	5
Yorkshire	8	8
Trent	7	12
East Anglia	6	10
NWT	17	16
NET	20	19
SET	12	8
SWT	18	15
Wessex	10	9
Oxford	3	3
South Western	2	11
West Midlands	9	13
Mersey	19	17
North Western	5	7
Wales	1	1
North Scotland	14	4
South Scotland	16	14
West Scotland	13	15
Northern Ireland	4	2
Republic of Ireland	15	20

Reporting rates for returning the orange cards remain high - the overall card return compliance rate for the year 2006, calculated as a proportion of orange cards returned, was 93.7% (32,070/30,059), an increase of 0.1% from 2005. Monthly response rates ranged from 95.5% in January to 91.5% in November, with a median of 93.8%. To maintain this compliance rate respondents who have not returned cards for two consecutive months are sent letters, as much to verify postal address as to act as a reminder. This return rate remains higher than any equivalent UK scheme and ranks highly against other national paediatric surveillance units (**Table 15 page 62**).

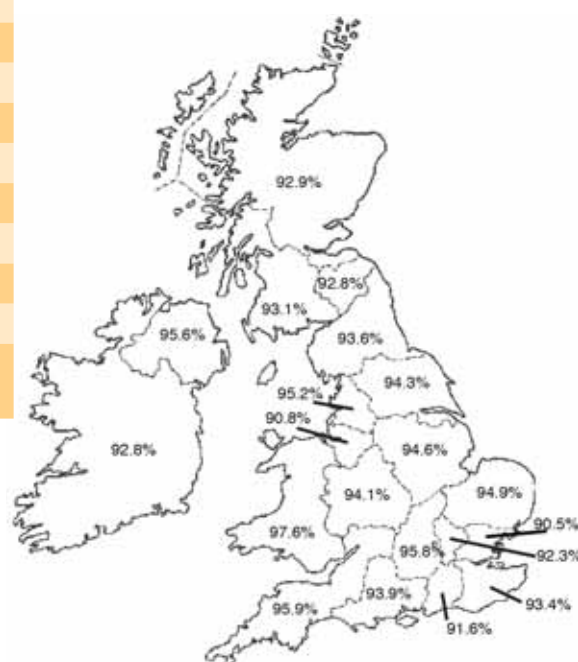


Figure 5: Average orange card return rate (%) by area, 2006

Wales continues to achieve the highest average yearly response rate – 97.6% - with South Western showing the highest move in the rankings up nine to rank second with 95.9%, just ahead of Oxford with 95.8%. The Thames area showed a cumulative response rate of 91.8%, down 0.8% on 2005 but still over 3% higher than in 2004. The ranking for Scotland continues to fall with North Scotland falling 10 places. Full details of regional response rates are provided in **Table 1**. Overall the response rate is still exceptional and is a testament to the willingness of clinicians to support the BPSU reporting scheme.

### Workload of those reporting in the scheme

The BPSU continually monitors the workload of participants in the scheme in terms of the number of suspected cases reported. 78% (2089) of participants reported no cases in 2006, 14% (368) reported a single case, 6% (153) reported between two and four cases and 2% (52) reported five or more cases. The greatest numbers of cases reported were by HIV/AIDS specialists, one of whom reported 108 cases and another 35. Specialties that had a particularly high level of reporting were paediatric neurologists (PIND), neonatologists and infectious disease specialists (AIDS/HIV, malaria, MRSA). Community paediatricians continue to make a significant contribution to the reporting, particularly to the PIND and HIV/AIDS studies and their continued involvement in the scheme is very much welcomed.

**Table 2 Cases reported from June 1986 - December 2006 for conditions under surveillance at May 2007**

Reports (confirmed cases)						
	Date when reporting began	June 1986- Dec-95	Jan-96 Dec-00	Jan-01 Dec-03	Jan-04 Dec-05	2006
Conditions under surveillance						
HIV	Jun-86	991 (691)	1017(705)	1774 (1382)	1434(1212)	723(491)
Congenital rubella	Jun-91	72(39)	49 (25)	26 (6)	9 (3)	4(1)
PIND	May-97		1066 (633)	610(338)	350 (232)	152(88)
Neonatal Herpes Simplex	Feb-04				118 (68)	64 (7)
MCADD	Jun-04				168 (114)	99 (57)
EOED*	Mar-05				345 (133)	160 (75)
MRSA	Jun-05				53 (26)	72 (43)
Scleroderma	Jun-05				33 (12)	49(28)
Malaria	Jan-06					190 (140)
FMAIT	Oct-06					17 (10)
VKDB	Oct-06					7 (1)
<b>Total</b>		<b>1063 (730)</b>	<b>2132 (1363)</b>	<b>2410 (1726)</b>	<b>2510 (1800)</b>	<b>1537 (941)</b>

HIV Human immunodeficiency virus: reports of AIDS in June 1986 include cases previously seen; case definition extended to include HIV infection in January 1990

PIND Progressive Intellectual and Neurological Degeneration

EOED Early onset eating disorders in children aged 5-12 years. \* Includes reports received through the child psychiatrist yellow card monitoring system.

MCADD Medium chain Acyl Co A dehydrogenase deficiency

MRSA Methicillin-resistant *Staphylococcus aureus* bacteraemia

FMAIT Feto-maternal alloimmune thrombocytopenia

VKDB Vitamin K deficiency bleeding

**Table 3 Outcome of follow-up of the cases reported in 2006 for conditions under surveillance at May 2007**

Condition under surveillance	Date when reporting began	Valid reports		Invalid Reports			Not yet known		Total
		reports	(%)	Duplication	Errors	(%)	known	(%)	
HIV/AIDS	Jun-86	4,481	75	572	587	20	299	5	5939
Congenital rubella	Jun-91	74	46	30	54	53	2	1	160
PIND	May-97	1291	59	259	599	39	29	1	2178
Neonatal Herpes Simplex	Feb-04	75	41	24	22	25	61	34	182
MCADD	Jun-04	171	64	47	30	29	19	7	267
EOED	Mar-05	208	41	103	144	505	51	10	505
MRSA	Jun-05	69	55	12	23	28	21	17	125
Scleroderma	Jun-05	40	49	4	19	28	19	23	82
Malaria	Jan-06	140	74	10	3	7	37	19	190
FMAIT	Oct-06	10	59	1	6	41	0	0	17
VKDB	Nov-06	1	14	1	5	86	0	0	7
All		6560	68	1063	1492	26	538	6	9653

**Table 4 Case report table**

<p><b>Valid reports:</b></p> <p>Cases confirmed at follow-up as being both unique (i.e. not a duplicate) and satisfying the diagnostic criteria set out in the case definition. Confirmed cases reported to the BPSU but already known to the research worker from another source are included.</p>	<p><b>Invalid reports:</b></p> <p>These include:</p> <p><b>duplicate reports</b> of cases already reported to the BPSU, and</p> <p><b>reporting errors</b> arising as a result of a misdiagnosis, the wrong box on the orange card being ticked, the case not meeting the diagnostic criteria set out in the case definition or an inability to follow-up a case.</p>
<p><b>Outcome not yet known:</b></p> <p>Outcome of follow-up not yet received by BPSU (by May 2007).</p>	

## 4 Report from the RCPCH Patient & Carers' advisory group representatives

Last year the Executive Committee of the BPSU appointed two new patient and carer representative members, to help to initiate public involvement in its work. It is therefore early days but next year we hope to be able report on some tangible achievements.

### Sue Banton

I am founder & director of a national charity, STEPS, which supports individuals and their families with lower limb conditions. I have been involved in research projects for over 10 years and am currently chairing the steering committee of a Big Lottery Funded collaborative research project on supporting the positive development and well-being of children and young people with prostheses: the influence of the appearance of the prosthesis and individual choice ([www.steps-charity.org.uk/links/6-25-research.pphp](http://www.steps-charity.org.uk/links/6-25-research.pphp)). I am also a member of the Department of Health funded organisation INVOLVE ([www.invo.org.uk](http://www.invo.org.uk)) and the Medicines for Children Research Network (MCRN) Consumer Involvement Steering Group.

In a previous life I was also a teacher and hospital play specialist so I am very interested in active participation with children.

### Ann Seymour

I am a lay member of the Patient and Carers Advisory Group of the RCPCH, whose remit includes ensuring the participation of children, young people, their parents and carers in the work of the College. I am also a lay member of the Board of CEMACH (Confidential Enquiry into Maternal and Child Health) and the National Collaborating Centre for Women's and Children's Health which produces NICE guidelines. My interest in children's healthcare began over 20 years ago when I joined the National Association for the Welfare of Children in Hospital (NAWCH).

### What is public involvement?

- It is **active** involvement between people who use services - carers and researchers
- It can be described as involvement doing research **with** or **by** people who use services.



Sue Banton



Ann Seymour

INVOLVE defines members of the public as:

- patients and potential patients
- people who use health and social services
- informal (unpaid) carers
- parents / guardians
- disabled people
- members of the public who are potential recipients of health promotion programmes, public health programmes, and social service interventions
- groups asking for research because they believe they have been exposed to potentially harmful substances or products (e.g. pesticides or asbestos)
- organisations that represent people who use services.

Involving the public is central to the Department of Health's new national health research strategy. The report says,

*"We know from our experience that engaging patients and members of the public leads to research that is more relevant to people's needs and concerns, more reliable and more likely to be put into practice. To achieve this, patients and the public must be involved in all stages of the research process:*

- *Priority setting*
- *Defining research outcomes*
- *Selecting research methodology*

- 
- *Patient recruitment*
  - *Interpretation of findings*
  - *Dissemination of results.”*

Department of Health, (2006) Best Research for Best Health.

### What we have started to do.

We presented some ideas for the future to the BPSU Executive Committee at its Strategy Day in November 2006. At this meeting we considered how the public could be more involved in and better informed about the work of the BPSU.

The BPSU has over a period of years engaged with support groups, many of which have funded BPSU studies. However the degree of participation and involvement has not been clearly documented and this is something we aim to address. We have started to review the BPSU application forms to encourage researchers to consider how they might involve the public and also so that we can audit the type and range of involvement more formally.

We are also working with Sophie Auckland, the College's Children's Participation Project Manger, and hope to look at ways we can involve children and young people. To this end we have already had a group of children commenting on the BPSU public information leaflets and we aim to put their comments into practice.

## 5 Main findings of studies undertaken in 2006

Surveillance for **congenital rubella** (page 15) has been underway in the UK continuously since 1971 and importantly is the only source of surveillance for this condition in the UK. Fourteen infants born in the UK and Ireland since 1997 have been reported as having congenital rubella; in seven of these cases the maternal infection was acquired abroad. Women who have come to the UK as adults have higher rates of rubella susceptibility than women who were born and brought up in the UK and will be at higher risk of acquiring infection in pregnancy if rubella outbreaks occur. Although there is no evidence of rubella circulating at present, the uptake of MMR in infants continues to be low and the risk of future rubella outbreaks in the UK remains an important public health concern.

*Principal investigators: Dr P Tookey and Professor C Peckham, Dr E Miller – ICH London, HPA.*

A study on **early onset eating disorders in children** (page 20) aged between 5 and 12 inclusive commenced in March 2005 and ended in May 2006. This was the first BPSU study to involve members of the Royal College of Psychiatrists in the ascertainment of cases. After 15 months of surveillance 505 suspected cases had been reported, of these 208 were confirmed. Psychiatrists reported 168 (80%) of the cases. 171 were females and 37 were male. 76 fitted the criteria for anorexia nervosa, the youngest being nine years old. Six children had a binge eating disorder and three had bulimia nervosa. 83 had eating disorders not specified and there were 40 who fitted no category. Though these numbers are higher than expected the majority of children have improved.

*Principal investigators: Dr D Nicholls, Mr R Lynn, Dr R Viner, Professor P Lelliott – ICH/GOS, RCPCH, The Middlesex Hospital, RCPsychs.*

Undertaken in collaboration with the UK obstetric surveillance system a study on **feto-maternal alloimmune thrombocytopenia** (FMAIT) (page 24) commenced in October 2006. The study aims to assess the incidence of FMAIT in the UK, to describe current obstetric and paediatric management and outcome as well as informing on the ongoing review of the case for antenatal screening for this condition. By February 2007 21 cases have been reported of which 11 have so far been confirmed.

*Principal investigator: Dr M Knight, National Perinatal Epidemiology Unit, University of Oxford.*

The BPSU survey of **HIV infection in children** (page 27) is the prime source of paediatric data on this condition in the UK and Ireland. Publications resulting from this study have greatly informed current UK antenatal screening policy and clinical practice. Almost all new infections are acquired through mother to child transmission and although just over half of all reports continue to come from the London area, cases are increasingly being notified from all parts of the country. Reports of infants born to HIV infected women have increased substantially year on year since 2000 but the proportion of infants born to HIV infected women who are themselves infected has declined. In spite of greatly improved antenatal detection rates and high uptake of interventions to prevent transmission, infected infants born in the UK and Ireland to both diagnosed and undiagnosed women are still being reported. Finally, the proportion of infected children reported who were born abroad has increased in recent years; these children tend to be older at diagnosis than those born in the UK and Ireland.

*Principal Investigators: Dr P Tookey, Dr F Ncube, Professor D Goldberg – ICH London, HPA, HPS.*

The second Sir Peter Tizard bursary study commenced in January 2005 for 13 months. The study into **malaria in children** (page 31) has so far received 206 notifications, of which 134 have been confirmed. Numbers are lower than expected and more cases may arise when a comparison is made with the Malaria Reference Laboratory database. *P. falciparum* (83%) was the most commonly reported species.

*Principal investigator: Dr Shamez Ladhani, Queen Mary University of London.*

Surveillance of **medium chain acyl CoA dehydrogenase deficiency** (MCADD) (page 35) commenced in June 2004. The objectives of the study are to ascertain all cases of diagnosed MCADD and to determine clinical outcome to two years of age, with the further aims of determining the detection rate of screening for MCADD in a UK setting and informing future national screening policy. The BPSU study is linked to a national screening pilot for MCADD. So far, 265 cases have been reported to the BPSU, of which 177 cases have been confirmed.

The Department of Health recently announced a ministerial decision to introduce universal screening for MCADD in England by April 2009 (Gateway number 7801).

*Principal Investigators: Professor C Dezateux, Dr J Oerton, Ms P Phillips, Dr G Shortland – ICH London, University Hospital Wales.*

Surveillance on **Methicillin-resistant Staphylococcus aureus (MRSA)** (page 39) commenced in June 2005. The study aimed to document the incidence in children and the clinical features and patterns of presentation. To April 2007 144 cases have been notified to the BPSU, and so far 74 have been confirmed of which 70% were under the age of one. 119 other confirmed cases have been reported through the HPA and voluntary reporting of isolates from hospital microbiologists to Labbase2.

*Principal Investigators: Ms C Goodall, Dr A Johnson, Department of Healthcare Associated Infection & Antimicrobial Resistance, HPA Centre for Infections. Dr M Sharland, St George's Hospital.*

Surveillance of **Neonatal herpes simplex virus (HSV)** (page 43) infection commenced in February 2004 for a period of three years. During this period 86 with confirmed neonatal HSV were reported 83 through the BPSU. Virus has been typed in 90% of cases reported to date, and about half of infants had HSV-1 infection. Diagnosis of maternal infection prior to delivery was extremely rare; in about 20% of cases a possible postnatal source of infection was identified retrospectively, usually a close relative of the infant. Neonatal HSV remains an extremely rare condition, although the number of confirmed reports in the first two years of reporting suggests an increase in prevalence since the last national surveillance study was carried out through the BPSU nearly 20 years ago.

*Principal Investigators: Dr P Tookey, Professor C Peckham, Dr D Brown, Mr R Lynn – ICH London, HPA, RCPCH.*

Despite the complexity of the conditions involved in the survey of **progressive intellectual and neurological deterioration in children (PIND)** (page 46) has proved successful. A primary objective of the study is to identify new cases of variant Creutzfeldt-Jakob disease (vCJD) in UK children. Over 2200 cases of suspected PIND have been reported. Among them 953 cases are confirmed diagnoses, comprising of 114 known degenerative conditions. Six cases of vCJD have

been identified. Active surveillance will continue to 2008.

*Principal Investigators: Dr C Verity, Mrs A-M Winstone, Mrs L Stellitano, Professor A Nicoll, Professor R Will – Addenbrooke's Hospital, ECDC, CJDSU.*

Commencing in July 2005 the study on **scleroderma** (page 50) aims to assess incidence, examine presenting features, and consider current management. In order to ascertain as many cases as possible, members of the British Society for Paediatric and Adolescent Rheumatology, the British Association of Dermatologists, and the UK Scleroderma Study Group are also being asked to report cases. Of the 99 cases reported 47 have so far been confirmed. The small number of notifications has been disappointing, perhaps reflecting that childhood scleroderma is even less common than previously thought. All efforts are being made to maximise ascertainment during the forthcoming months and awareness of the study is being raised through discussion at professional meetings.

*Principal investigators: Dr E Baildam, Liverpool Children's Hospital, Dr AL Herrick, Professor AJ Silman, University of Manchester, Dr Bhushan, Hope Hospital.*

September saw the commencement of the fourth BPSU survey of **vitamin K deficiency bleeding (VKDB)** (page 54). The reason for repeating this study is that since the withdrawal of Konakion Neonatal, the only product now licensed for intramuscular (IM) prophylaxis is Konakion MM. Published data about the long-term protection conferred by a single IM dose of this preparation, which has a completely different formulation from Konakion Neonatal, is very limited. This study will look for any change in incidence; assess the effectiveness of prophylactic regimens in use, particularly Konakion MM 1mg IM as a single dose at birth, to examine treatment and outcome. In the first five months of the study one case has been confirmed.

*Principal investigators: Dr A Busfield, Dr A McNinch, Dr J Tripp, Royal Devon & Exeter NHS Foundation Trust.*

*Please note the data presented are provisional, not peer reviewed and definite conclusions should not be drawn from them.*

# 6 Surveillance Studies Undertaken in 2006

## Congenital Rubella

### Key Points

- Since 1997 13 congenital rubella births have been reported in the UK, and one in Ireland.
- Five of the 14 mothers caught rubella in the British Isles; the other nine cases were imported infections where, although the birth occurred in the UK or Ireland, the maternal infection was acquired abroad.
- In almost all recent cases, maternal rubella infection was not diagnosed in pregnancy, and the diagnosis of congenital rubella infection in the newborn baby was unexpected.
- Women who have come to the British Isles as adults are more likely than women who were born and/or brought up here to be rubella susceptible. They will be at higher risk of acquiring infection in pregnancy if rubella outbreaks occur.



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Protection Agency (HPA) or Health Protection Scotland (HPS), and has remained at a very low level in recent years (<10 a year). Women with diagnosed first trimester infection usually opt for termination of pregnancy in the UK; most mothers of congenitally infected infants are unaware of their infection until their baby is diagnosed.

The World Health Organisation Regional Office for Europe has set a target for the elimination of measles and rubella, and prevention of congenital rubella infection (<1 case of congenital rubella syndrome per 100,000 births) by 2010<sup>1</sup>. Long-standing rubella vaccination programmes (**Table 5**) have already led to the virtual elimination of congenital rubella in the UK and Ireland<sup>2</sup>. Nevertheless, sub-optimal MMR coverage and migration within Europe have been identified as major challenges to reaching this target, and maintaining control in the long term<sup>3</sup>.

Between 1997 and 2003 there was a decline in MMR uptake from about 92% to about 80% in the UK overall, with a similar decline occurring in Ireland. Although uptake rates have subsequently improved to about 85% by the end of 2006<sup>4,5</sup>, years

### Background

The National Congenital Rubella Surveillance Programme was established in 1971 to monitor congenital rubella births in England, Scotland and Wales. Active surveillance through the BPSU started in 1990, and since then reports have also been received from Ireland and Northern Ireland. Diagnosed rubella infection in pregnancy is monitored through laboratory reports to the Health

**Table 5. Rubella vaccination strategy in the UK and Ireland**

From 1970	Rubella vaccine introduced for schoolgirls and susceptible women. Provided individual protection against infection in pregnancy while rubella infection still circulated freely and most children acquired natural infection.
1988	Triple vaccine against measles, mumps and rubella (MMR) introduced for children aged 12-15 months. Protects women from infection in pregnancy by preventing circulation of infection.
1992	MMR 2 <sup>nd</sup> dose for boys and girls aged 10-14 years introduced in Ireland, replacing schoolgirl only programme.
1994	Measles/rubella vaccine offered to all 5-16 year olds in the UK (one-off). Similar programme in Ireland in 1995
1996	MMR 2 <sup>nd</sup> (pre-school entry) dose introduced in the UK, replacing schoolgirl only programme.
1999	Age at MMR 2 <sup>nd</sup> dose reduced to 4-5 years in Ireland.
2004 onwards	Local and national initiatives to improve MMR uptake in childhood, and offer MMR to students and young adults.

of inadequate vaccine uptake with no wild virus circulating mean that there must be a substantial number of susceptible children in the community. In addition, migration into the UK and Ireland from countries without long-standing high uptake rubella vaccination programmes will have led to greater concentrations of susceptible individuals in some areas, often those where MMR uptake has been low (e.g. parts of London). If vaccine coverage is not maintained at higher levels in the long term it is possible that rubella could once again start to circulate in the British Isles, as it still does in many parts of the world.

## Objectives

To monitor the effectiveness of the rubella immunisation programme by determining the incidence of congenital rubella and investigating the circumstances surrounding any new cases.

## Surveillance period

Surveillance through the BPSU began in January 1990 and is reviewed annually.

## Methodology

### Case definition

Any infant (live or still born) or child up to 16 years of age who, in the opinion of the notifying paediatrician, has suspected or confirmed congenital rubella with or without defects, based on history, clinical, and/or laboratory findings. This includes "imported cases", i.e. children born in the British Isles where the maternal infection occurred abroad, AND children who were born abroad, as well as British-born infants whose mothers acquired infection in the British Isles.

### Reporting instructions

Any live or still born infant, or child, seen for the first time in the past month who meets the case definition, regardless of country of birth. The reporting instructions were changed in 2005 to include reports of children born abroad: this has been instituted as part of the enhanced surveillance necessary to monitor progress towards the European elimination target.

### Additional data sources

No active additional sources, but reports are occasionally made direct to the investigator (e.g. from virologists, audiologists), and there is close liaison with the HPA, HPS and the Health Protection Surveillance Centre in Ireland.

### Expected number of cases

Currently less than five births a year, but could increase if there were renewed circulation of rubella infection in the community. Rubella-associated terminations of pregnancy are monitored through reports to the Office for National Statistics, but the annual number is not currently published because there are so few cases.

### Denominator source

Routine national statistics on number of live and still births.

**Table 6. Congenital rubella reports to BPSU 1990-2006 (includes births occurring in earlier years)**

	Confirmed or compatible	Possible cases	Cases already reported	Duplicate error or lost	Total
Place of birth					
England, Scotland and Wales	50	4	13	66	136
NI and Ireland	4	1	2	9	16
Elsewhere (2005 reports only)	2	1	0	1	4

## Analysis

Only one confirmed case was reported in 2006. The infant's mother was born abroad, but had lived in the UK for several years; there was no history of travel in pregnancy. There were four reports through the BPSU, three of which related to the confirmed case; the fourth report was made in error.

The number of reported congenital rubella births and rubella associated terminations declined from, on average, 50 births and 740 terminations a year in 1971-75 to 22 births and 54 terminations a year in 1986-90. Since the beginning of active surveillance in 1990, 156 reports have been made through the BPSU (Table 6). Of the 136 from England, Scotland and Wales, 50 are confirmed or compatible, previously unreported cases of congenital rubella, four are possible cases, and 13 had already been reported from another source; the remaining reports were duplicates (24), reporting errors (41) and five where further information could not be obtained. Sixteen reports were from Northern Ireland or Ireland, and included

**Table 7. Confirmed and compatible congenital rubella births reported in the UK and Ireland 1990-2006**

year of birth	Primary source of notification		Total
	BPSU	Other	
1990*	8	4	12
1991	2	1	3
1992**	5	2	7
1993	2	1	3
1994	5	2	7
1995	1	0	1
1996	11	3	14
1997	0	0	0
1998	0	0	0
1999	0	1	1
2000	4	0	4
2001	3	0	3
2002	0	0	0
2003	2	0	2
2004*	1	1	2
2005	1	0	1
2006	1	0	1
Total	46	15	61

\*Includes a still born infant

\*\*Includes a set of triplets, one of whom was still born

four children with confirmed congenital rubella (one born in 1989, two in 1996 and one in 2004), and a fifth possible case (born in 1983).

Since 2005 reports of children born abroad have been eligible for notification, and three (all under the age of three years at notification) were reported in 2005, but none in 2006. In previous years reports of children who were born abroad were not requested, and any such reports were categorised as errors.

*Congenital rubella 1990-2006:* Fifty-eight children and three stillborn infants with confirmed or compatible congenital rubella have been born and reported in the UK and Ireland since the beginning of active surveillance in 1990; 46 of these (79%) were first reported through the BPSU (Table 7). Overall, about one third of their mothers acquired infection abroad. Another third were born to women who, although they acquired infection in the British Isles, were recent immigrants<sup>6,7</sup>. Three British-born women had confirmed reinfection in pregnancy. There were 75 terminations for rubella disease or contact in pregnancy recorded by the Office for National Statistics in England and Wales during the period 1990-2003<sup>8</sup>.

## Recent reports

Fourteen infants with congenital rubella were born and reported between 1999 and 2006, including one born in Ireland, and one stillborn infant. Although nine were imported cases with maternal infection acquired abroad (five in Southern or South Eastern Asia, four in Africa), five infants were born to women whose infection occurred in the UK. One British-born woman acquired rubella in Scotland, although the infection was epidemiologically linked to an outbreak in Greece in 1999<sup>9</sup>. Four maternal infections were acquired in England, one by a British-born woman, and three by women who were born abroad, but who had all been resident in the UK for several years<sup>10</sup>.

CDC-Public Health Image Library



Figure 6: Cataracts due to congenital rubella syndrome

## Discussion

The number of reported cases of congenital rubella has remained at a very low level over the last ten years, but virtually all reports concern infants with serious rubella-associated defects present at birth (**Figure 6**). It is possible that some infants with less specific or serious signs of congenital rubella, or those with later onset, are not diagnosed and reported.

Rubella susceptibility in pregnant women in the UK varies by ethnic group, with women from many parts of Asia and Africa having particularly high susceptibility rates especially if they are having their first baby<sup>11</sup>. Women who have come to the UK and Ireland from countries without comprehensive and long-standing vaccination programmes are likely to be at higher risk if there is renewed circulation of rubella here. Even while rubella infection is rare in the British Isles, susceptible women who travel abroad during early pregnancy may come into contact with infection. Awareness of rubella infection and congenital rubella among paediatricians and other health professionals must be maintained.

Comprehensive national surveillance through the BPSU remains extremely valuable. Please continue to notify all infants with suspected congenital rubella, whether or not they have the associated typical defects, and regardless of country of birth. Timely reporting by paediatricians will help us to recognise any resurgence in numbers at an early stage, and will also assist in the implementation of appropriate control measures. Congenitally infected infants excrete rubella virus for an extended period of time, and it is important that they are managed in such a way as to avoid the risk of contributing to further community transmission.

Please note the data presented are provisional, not peer reviewed and definitive conclusions should not be drawn from them.

## Funding

The Health Protection Agency makes a contribution towards the costs of the surveillance. Additional support is received from Sense and from the Centre for Paediatric Epidemiology and Biostatistics at the UCL Institute of Child Health.

## Ethics approval

The London Multicentre Research Ethics Committee reaffirmed approval in 2005 (Ref: 05/MRE02/2). Surveillance of congenital rubella through the BPSU also has PIAG approval (PIAG/BPSU 2-10(f)/2005).

## Support group

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Tel: 020 7272 7774, Text: 020 7272 9648;  
Fax: 020 7272 6012;  
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## Acknowledgements

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## References

1. World Health Organisation Europe. Eliminating measles and rubella and preventing congenital rubella infection. WHO European Region strategic plan 2005-2010. Available from <http://www.euro.who.int/document/E87772.pdf>
2. Cotter S, Gee S, Connell J. Rubella and congenital rubella infection in Ireland. *Epi-Insight* 2005; **6(5)**: 2-3. Available from <http://www.ndsc.ie/hpsc/EPI-Insight/Volume62005/File,1091,en.PDF>
3. Crowcroft N, Pebody R. Prevention of congenital rubella infection: a challenge for every country in Europe. *Editorial. Eurosurveillance Monthly* 2004; **9(4)**: 1-2. Available from <http://www.eurosurveillance.org/em/v09n04/0904-221.asp>
4. Health Protection Agency. COVER programme: July to September 2006. *Commun Dis Rep CDR Wkly [serial online]* 2006; 16 (12): immunisation. Available from <http://www.hpa.org.uk/cdr/archives/2006/cdr5106.pdf>
5. Health Protection Surveillance Centre. Immunisation uptake report for Ireland, Q3 2006. Available from <http://www.ndsc.ie/hpsc/A-Z/VaccinePreventable/Vaccination/ImmunisationUptakeStatistics/2006/File,2192,en.pdf>

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6. Tookey PA, Peckham CS. Surveillance of congenital rubella in Great Britain, 1971-96. *BMJ* 1999; **318**:769-70
  7. Tookey P. Rubella in England, Scotland and Wales. Surveillance Report. *Eurosurveillance Monthly* 2004; **9(4)**:21-22. Available from <http://www.eurosurveillance.org/em/v09n04/0904-231.asp>
  8. Abortion Statistics 2001: series AB No 28. London: Stationery Office, 2002 [http://www.statistics.gov.uk/downloads/theme\\_health/AB28\\_2001/AB28\\_2001.pdf](http://www.statistics.gov.uk/downloads/theme_health/AB28_2001/AB28_2001.pdf) (data for 2002 and 2003, personal communication from ONS)
  9. Tookey P, Molyneaux P, Helms P. UK case of congenital rubella can be linked to Greek cases. *BMJ* 2000; **321**: 766-67
  10. Thomas RM and Mehta NM. Cases of congenital rubella may be the tip of the iceberg. *BMJ* 2002;**325**:596-97
  11. 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

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# Early onset eating disorder in children under 13 years

## Key Points

- This is the first prospective surveillance of pre-adolescent eating disorders presenting to secondary care in the United Kingdom and Ireland.
- This is also the first joint paediatric/psychiatric surveillance study to be undertaken by the BPSU.
- In the fifteen months 208 cases were reported; 76 have been classified with anorexia nervosa, three with bulimia nervosa, six with binge eating disorder, and 83 with 'eating disorder not otherwise specified' (EDNOS). Most EDNOS cases had features of anorexia nervosa but were not below the weight threshold at the time of reporting.
- Determined food avoidance was the most common presenting feature.

## Background

Early-onset eating disorders (EOED: defined here as onset before 13 years of age) are equally as likely to present to paediatricians as child psychiatrists in the UK<sup>1</sup>. Management of these frequently extremely ill children is complicated by a lack of knowledge of the breadth of the problem, difficulties with recognition of eating disorders in this age group<sup>2</sup> and ongoing debate over the role of paediatricians versus mental health professionals. Nevertheless, clinical experience suggests that children with EOED are frequently admitted to paediatric wards before referral to child mental health services.

Epidemiological studies suggest that the incidence of eating disorders, including anorexia nervosa, has been fairly static over the last few decades, but there is some suggestion that cases are presenting earlier in adolescence<sup>3</sup>. Work has focused on the peak ages of onset (15 years for anorexia nervosa and older for bulimia nervosa). Specialist services are often asked whether they are seeing increasing numbers of EOED cases, but these samples are not representative. As yet no incidence estimates are available for this specific age group. The only recent incidence data for eating disorders in the UK were obtained from a GP register study of all age groups undertaken in the early 1990s. Incidence of anorexia nervosa



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was estimated as 17.5/100,000 in 10-19 year olds, and 0.3/100,000 in 0-9 year olds. For bulimia nervosa the rates are 20.5/100,000 and 0/100,000 respectively<sup>4</sup>. Retrospective studies from the US and Denmark have suggested higher figures, e.g. 9-27 per 100,000 10-14 year girls and 3.7 per 100,000 for boys<sup>5,6</sup>.

Eating disorders in prepubertal and peripubertal children frequently require paediatric admission and long-term medical monitoring as well as psychiatric management. This study, supported by the Royal College of Psychiatrists, aims to quantify the problem and also examine the circumstances surrounding onset of illness as well as current management regimens. A one-year follow up will assess short-term outcomes.

## Objectives

The study aims to:

- estimate the incidence of early onset eating disorders in children in the UK and Ireland.
- describe the age, sex and family history of children presenting with eating disorders.
- describe the range of clinical features at presentation including other psychiatric illness.
- delineate patterns of professional involvement (paediatric & child mental health).
- characterise the range of acute medical complications experienced by children with early onset eating disorders.
- identify the range of therapeutic interventions used in management of eating disorders.

## Surveillance period

March 2005– May 2006 (inclusive).

## Methodology

### Case definition

Any child aged 5 –12 years inclusive, newly diagnosed with early onset eating disorder which is defined as:

#### TWO OR MORE OF THE FOLLOWING

- weight loss or failure to gain weight during a period of expected growth, not due to any identifiable organic cause.
- determined food avoidance.
- fear of weight gain.
- preoccupation with body weight or energy intake.
- self induced vomiting.
- excessive exercising.
- recurrent episodes of binge eating or abuse of laxatives.

Excessive exercising has been defined in the questionnaire using the following definition: "Exercise may be considered to be excessive when it significantly interferes with important activities, when it occurs at inappropriate times or in inappropriate settings, or when the individual continues to exercise despite injury or other medical complications." (American Psychiatric Association. DSM-IV-TR: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision. Washington, D.C.: American Psychiatric Association; 2004; pp. 590-591.)

### Reporting instructions

To report any new cases meeting the surveillance definition seen by you for the first time, even if you believe the case may have been reported from elsewhere.

### Denominator source

The total population of children between the ages of 5 and 13 years identified by the Office of National Statistics (UK) and the Central Statistics Office (Ireland).

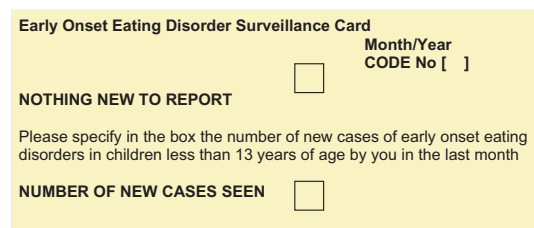
### Number of expected cases

Approximately 100 cases were expected to be reported using the case definition.

### Alternative data sources

As it is known that cases are seen by child psychiatrists, a parallel monthly card surveillance system was set up for the child psychiatrists. All psychiatrists who were members of the Faculty of Child Psychiatry of the Royal College of Psychiatrists and likely to see such cases were asked to participate. Those that agreed were sent a monthly yellow report card (Figure 7). Over the 15 month surveillance period the study return rates for the card were 80%, slightly lower than for the BPSU but comparable with other specialist surveillance units using this methodology.

Paediatricians and psychiatrists reporting a case were sent a questionnaire seeking demographic details and clinical features. For all valid cases a second questionnaire will be sent to the reporting paediatrician one year after the case is first reported.



The image shows a yellow surveillance card titled "Early Onset Eating Disorder Surveillance Card". It includes a box for "Month/Year CODE No [ ]", a checkbox for "NOTHING NEW TO REPORT", and a box for "NUMBER OF NEW CASES SEEN". Below the boxes is a note: "Please specify in the box the number of new cases of early onset eating disorders in children less than 13 years of age by you in the last month".

Figure 7: Early Onset Eating Disorders Surveillance Card

## Analysis

After fifteen months of surveillance, 505 suspected cases have been reported; 379 (75%) reported by psychiatrists and 126 (25%) by paediatricians. Details on 424 reports have been collected through questionnaires to clinicians. 303 reports fitted the case definition. Following de-duplication there were 208 individual cases, giving an incidence of 3.01/100,000 (CI 1.63-4.96), with a clear association between increasing incidence and increasing age. 164 (54%) cases were reported solely by psychiatrists and 42 (14%) solely by paediatricians. 127 cases were reported by both psychiatrists and paediatricians (Figure 8). There were 117 erroneous reports, mainly due to the diagnosis being made before the reporting period.

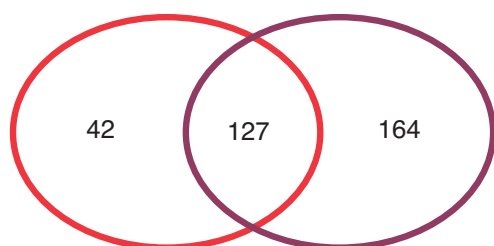


Figure 8 Multiple source case ascertainment

Of the 208 cases 171 (79%) were female and 37 (18%) were male. Operational criteria for eating disorder subtypes were devised from weight/height data and symptom reports. On the basis of these, 76 were classified as having anorexia nervosa giving an incidence of 1.1/100,000 (CI 0.4-2.37), three as having bulimia nervosa (BN), six as having binge eating disorder (BED), 83 as having eating disorder not specified (EDNOS). 40 met the case definition, but did not show the features of weight and shape concern or fear of weight gain necessary for diagnosis of an eating disorder. These were classified as "Other" eating difficulties. The nature of these cases needs further clarification. (Figure 9).

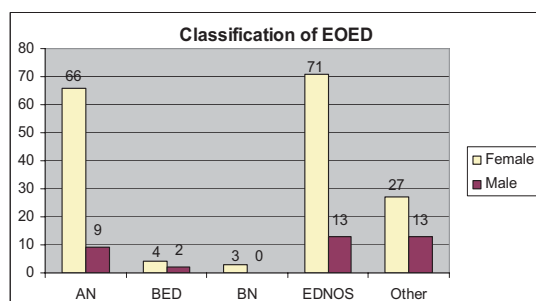


Figure 9 Classification of EOED cases by sex

The median age of reported cases is 137 months (11.5 years, SD 1.3), the youngest being a male of 75 months (6.25 years). The majority (89%) of cases are ethnically white.

On presentation determined food avoidance was the most common feature, seen in 95% of cases. Nearly 40% excessively exercised as a means of controlling weight and 16% self-induced vomiting. 79% had a pre-occupation with food, but there was no relationship with concern about weight and shape.

The one year follow-up is incomplete and further analyses, including outcomes at one year after diagnosis, will be reported next year.

This is the first prospective study, involving a unique collaboration between members of the Royal College of Paediatrics and Child Health and the Child and Adolescent Faculty of the Royal College of Psychiatrists, to examine the incidence of eating disorders presenting to secondary care in this particular age group in the British Isles. Use of a dual reporting system aimed to maximise case ascertainment.

Overall numbers were significantly higher than expected. The proportion of cases reported in boys (18%) is higher than the literature for adolescent populations would predict (around 10%).

A key criteria for the diagnosis of anorexia nervosa is weight below 85% of ideal body weight for height; 76 cases fitted categorisation for anorexia nervosa, while those above 85% weight for height were categorised as EDNOS. However the dynamic nature of weight loss and gain means that some children categorised as EDNOS will go on to develop anorexia nervosa, and some may have met full criteria for anorexia nervosa but put on weight at the time of reporting. Retrospective reporting of minimum weight would have partially addressed this issue, but can be unreliable and requires an accurate simultaneous height measurement. This is a recognised methodological difficulty in eating disorders research. Initial outcome showed that 50% of the children showed signs of improvement; this figure may well increase once the one year outcome data has been fully analysed.

In the view of the investigators, this joint surveillance project has been a success. Many eating disorders services are designed to target adolescents and the data collected during this study should therefore enable the needs of younger patients to be quantified and specified in terms of clinical profile.

Following completion of the study an evaluation form was sent to the psychiatrists taking part in reporting. Over 90% said that they would be willing to take part in future surveillance studies. Of these, 25% wished to report via electronic means. Difficulties in completing the questionnaire were highlighted, especially when working on a split site or where the case notes were held in another location.

Finally, as the research protocol has been based on studies undertaken through the Australian and the Canadian Paediatric Surveillance Units, it is hoped that comparative analysis will also be possible.

Please note the data presented are provisional, not peer reviewed and definitive conclusions should not be drawn from them.

## Funding

The Hyman Wingate Foundation is funding this study. The Royal College of Psychiatrists and the RCPCH research division are providing further support.

## Support group

Beating Eating Disorders (BEAT), 103 Prince of Wales Road, Norwich NR1 1DW. Tel: 0845 1414. B-eat youth line Tel: 0845 634 7650 E-mail: <http://www.b-eat.co.uk>

## Ethics approval

The London MREC (04/MRE02/77) has approved this study as has the Patient Information Advisory Group (PIAG/BPSU 2-10(h)/2005).

## Acknowledgements

We are extremely grateful to all the participating paediatricians and psychiatrists, especially those who have notified cases and completed questionnaires. Thanks also go to the Royal College of Psychiatrists for allowing the researchers to approach their membership and especially to the membership department who helped facilitate this.

## References

1. Fosson A, Knibbs J, Bryant-Waugh R, Lask B. Early onset anorexia nervosa. *Arch Dis Child* 1987; **62**:114-8.
2. Bryant WRJ, Lask BD, Shafran RL, Fosson AR. Do doctors recognise eating disorders in children? *Arch Dis Child* 1992; **67**(1):103-5.

3. Lucas AR, Beard CM, O'Fallon WM, Kurland LT. Fifty year trends in the incidence of anorexia nervosa in Rochester, Minnesota: a population-based study. *American Journal of Psychiatry* 1991; **148**:917-22.
4. Turnbull S, Ward A, Treasure J, Jick H, Derby L. The demand for eating disorder care. An epidemiological study using the general practice research database. *Br.J Psychiatry* 1996; **169**(6): 705-12.
5. Pfeiffer RJ, Lucas AR, Ilstrup DM. Effect of anorexia nervosa on linear growth. *Clinical Pediatrics* 1986; **25**:7-12.
6. Joergensen J. The epidemiology of eating disorders in Fyn County, Denmark, 1977-1986. *Acta Psychiatr. Scand* 1992; **85**(1): 30-4.

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# Feto-maternal Alloimmune Thrombocytopenia (FMAIT)

## Key Points

- FMAIT is associated with significant fetal and infant morbidity and mortality.
- First pregnancies are often severely affected and the diagnosis is usually made with the birth of a first affected infant.
- There is a debate about the utility of antenatal screening for the condition.
- This study will provide a national picture of the incidence of the disease, its epidemiology and management and provide information for the assessment of the case for a screening programme.

## Background

Feto-maternal Alloimmune Thrombocytopenia (FMAIT), also known as neonatal alloimmune thrombocytopenia or NAIT, is the most common cause of severe neonatal thrombocytopenia in otherwise well term infants<sup>1</sup>, and is analogous to the fetal/neonatal anaemia caused by haemolytic disease of the newborn (HDN). The condition results from a fetomaternal incompatibility in platelet alloantigen, most commonly HPA-1a, and can lead to serious bleeding, intracranial haemorrhage and sometimes death of the fetus or infant<sup>2</sup>. In contrast to HDN, first pregnancies are often severely affected and the diagnosis is usually made with the birth of a first affected infant. There is therefore a current debate about the utility of screening for the condition. A recent evaluation against the National Screening Committee criteria for appraising a screening programme has identified a number of deficiencies in basic epidemiological information needed to assess the utility of antenatal screening<sup>3</sup>. This study aims to address three of these deficiencies: 1) to determine the true incidence of severe haemorrhage associated with FMAIT, 2) to describe the clinical outcome of affected cases and 3) to identify prognostic factors.

Additionally, there are considerable controversies in the optimal management of FMAIT-affected pregnancies<sup>3</sup>. There is no clear approach to the antenatal management of first affected pregnancies, and several questions remain in the approaches to managing second and subsequent affected pregnancies<sup>4</sup>. This is the first study to be conducted simultaneously through the BPSU and the UK Obstetric Surveillance System (UKOSS). The combined use of both obstetric and paediatric



Dr M Knight

reporting systems will help to ensure identification of cases is as complete as possible and will allow collection of comprehensive antenatal and postnatal information. We will also be able to assess the outcomes following different antenatal management strategies. The study results will be used to inform ongoing review of the case for antenatal screening for this condition.

## Objectives

- To combine the use of existing obstetric, paediatric and National Blood Service reporting systems to assess the incidence of Fetomaternal Alloimmune Thrombocytopenia (FMAIT) in the UK.
- To describe the current obstetric and paediatric management of FMAIT in the UK.
- To describe the outcomes of affected infants.
- To use the information gained to inform ongoing review of the case for antenatal screening for this condition.

## Surveillance period

October 2006 to October 2007 (inclusive).

## Methodology

### Case definition

Any infant live born during the study period with a documented maternal/fetal platelet antigen incompatibility, usually in the presence of maternal antibodies, AND at least **one** of the following:

- i. Cord platelet count at birth  $<50 \times 10^9/l$
- ii. Haemorrhagic complications before or after birth (e.g. intraventricular haemorrhage, GI bleed, bruising or petechiae)
- iii. Antenatal therapy with either maternal steroids, IVIg or fetal platelet transfusion.

### Reporting instructions

Paediatricians are asked to report any infant born since the beginning of October 2006 in the UK with newly-diagnosed FMAIT (confirmed or suspected). All cases of FMAIT should be reported irrespective of whether the condition was diagnosed before or after birth or whether the case has also been reported to UKOSS through a hospital obstetrician or midwife.

### Additional data sources

Cases are also being sought in a parallel study conducted through UKOSS. In addition, cases reported through the surveillance studies will be compared with cases referred for investigation to the National Blood Service or Welsh Blood Service.

### Expected number of cases

Incidence of severely affected infants is estimated to be 1 in 15,000 births (approximately 50 cases per year in the UK). The incidence of clinically detected infants (including those more mildly affected) is estimated to be up to 1 in 2800 births (approximately 250 cases per year in the UK)<sup>2,5</sup>.

### Denominator source

The denominator used will be all births in the UK, identified by the Office of National Statistics.

### Interim Analysis

Over the period October 2006 to February 2007 there were 21 cases reported. We have received further information on 17 of these infants (81%). Five cases were excluded because they did not meet the case definition and there was one duplicate report, leaving 11 confirmed cases. Two cases were diagnosed antenatally and nine cases were diagnosed postnatally. These cases have not been further analysed at this early stage of the study.

At the end of the study case reports received through the BPSU will be compared with those received through UKOSS and with infants referred to the National Blood Service or Welsh Blood Service. Capture-recapture analyses will be undertaken to determine case ascertainment through the different surveillance sources and to gain a complete picture of case numbers.

### Discussion

This study is currently at an early stage. These interim results suggest that the incidence of clinically detected infants may be lower than that estimated from a screening study of 24,417 pregnancies in East Anglia<sup>2</sup>. However, the low number of cases reported at this stage may simply be a chance phenomenon and we will be able to present more robust results at the conclusion of the study.

Please note the data presented are provisional, not peer reviewed and definitive conclusions should not be drawn from them.

### Funding

This study has been funded by the charity Wellbeing of Women:

[www.wellbeingofwomen.org.uk](http://www.wellbeingofwomen.org.uk)

### Ethical approval

The study has been approved by the London MREC (study ref 06/MRE02/53) and the Patient Information Advisory Group (ref BPSU PIAAG 03-04(FT4)/2006).

### Acknowledgements

We would like to thank UK paediatricians for their continued support for this study.

### References

1. Dreyfus M, Kaplan C, Verdy E, Schlegel N, Durand-Zaleski I, Tchernia G. Frequency of immune thrombocytopenia in newborns: a prospective study. Immune Thrombocytopenia Working Group. *Blood* 1997; **89**(12):4402-6.
2. Williamson LM, Hackett G, Rennie J *et al*. The natural history of fetomaternal alloimmunization to the platelet-specific antigen HPA-1a (PIA1, Zwa) as determined by antenatal screening. *Blood* 1998; **92**(7):2280-7.
3. Murphy MF, Williamson LM, Urbaniak SJ. Antenatal screening for fetomaternal alloimmune thrombocytopenia: should we be doing it? *Vox Sang* 2002; **83** Suppl 1:409-16.

- 
4. Rayment R, Brunskill SJ, Stanworth S, Soothill PW, Roberts DJ, Murphy MF. Antenatal interventions for fetomaternal alloimmune thrombocytopenia. *Cochrane Database Syst Rev* 2005; **(1)**:CD004226.
  5. Serrarens-Janssen VM, Steegers EA, van den Bos A, van Heijst AF, Pereira R, Semmekrot BA. Experiences with fetomaternal alloimmune thrombocytopenia in the Netherlands over a 2-year period. *Acta Obstet Gynecol Scand* 2005; **84(2)**:203.

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*Study Administrator: Mrs Carole Harris, National Perinatal Epidemiology Unit.*

## HIV infection in childhood

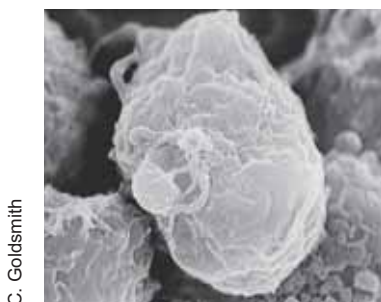
### Key points

- Reports from all regions of the UK and Ireland have increased in recent years; this highlights the valuable role of the BPSU in capturing cases seen in non-specialist centres.
- Despite greatly improved antenatal detection rates and high uptake of interventions to prevent transmission, infected infants are still being born in the British Isles to both diagnosed and undiagnosed women.
- Changing trends in the demographic profile of HIV infected children and young people living in the UK and Ireland have implications for current, and future, health and social service provision.

### Background

National surveillance of paediatric HIV infection and AIDS began in 1986 and is based on complementary paediatric, obstetric and laboratory reporting schemes. Reporting is voluntary and confidential and data from all sources are combined as the National Study of HIV in Pregnancy and Childhood (NSHPC) at the Institute of Child Health<sup>1</sup>.

Most children currently living with HIV in the UK and Ireland, whether born here or abroad, acquired their infection through mother to child transmission. Combining NSHPC with unlinked anonymous survey data<sup>2</sup> shows that in the UK the number of exposed infants increased substantially from about 300 in 1997 to about 1200 in 2005. Antiretroviral treatment, delivery by elective caesarean section and the avoidance of breastfeeding reduce transmission rates to around 1% in comparison with a likely transmission rate of about 25% without interventions. Women must be diagnosed in time to be able to access these interventions, and antenatal HIV testing is now routinely recommended to all pregnant women throughout the UK and Ireland<sup>3</sup>. The proportion of women diagnosed before delivery



C. Goldsmith

Figure 10: Scanning EM of HIV, grown in cultured lymphocytes. Virions are seen as small spheres on the surface of the cell.



Dr P Tookey and team

increased from an estimated 32% in 1997 in the UK to over 90% in 2004 and 2005<sup>2</sup>.

Children with confirmed HIV infection who were born abroad and reported in the British Isles are usually diagnosed because they are symptomatic or because another member of their family, often the mother, is diagnosed with HIV infection.

### Objective

The surveillance of paediatric HIV infection and AIDS in the United Kingdom and Ireland.

### Surveillance period

Surveillance began in June 1986 and is reviewed annually.

### Methodology

#### Case definition

Any child less than 16 years of age who has AIDS, or has been diagnosed with HIV infection. Any child born to a woman known to be HIV infected at the time of delivery regardless of the child's infection status.

#### Reporting instructions

Clinicians are asked to report children diagnosed with HIV infection before their 16<sup>th</sup> birthday, and all infants born to HIV infected women (i.e. exposed infants).

#### Additional data sources

Paediatric reports made directly to the NSHPC, pregnancy reports made through a parallel scheme run under the auspices of the Royal College of Obstetricians and Gynaecologists, laboratory reports to the Health Protection Agency (HPA) Centre for Infections and Health Protection Scotland (HPS), and in earlier years cases reported through the UK Haemophilia Centre.

### Expected number of cases

The number of infants born to HIV infected women in the UK and Ireland has exceeded 1000 each year since 2003. Over 100 infected children are currently being diagnosed each year. Direct reporting arrangements have been established with some centres in order to simplify reporting and reduce the burden on individual paediatricians.

### Denominator source

Routine national statistics on number of live births, obtained from the Office of National Statistics. Irish birth rate obtained from the Irish Census 2002 (Central statistics office, Ireland).

### Follow up

Information is sought for all exposed infants to establish infection status. Follow-up data on infected children are subsequently collected through the Collaborative HIV Paediatric Study (CHIPS), a collaboration between the NSHPC, the MRC Clinical Trials Unit and participating clinics.

### Routine use of data

NSHPC data contribute to the overall national surveillance of HIV infection. UK summary tables appear quarterly in the Health Protection Report formerly Communicable Disease Report ([www.hpa.org.uk](http://www.hpa.org.uk)) and the HPS Weekly Report ([www.hps.scot.nhs.uk](http://www.hps.scot.nhs.uk)). Regional data are also regularly provided to HIV commissioners, public health and HIV specialists.

## Analysis

*Number and geographical distribution of reports:* By the end of December 2006 there had been 5652 BPSU reports, of which 4196 were confirmed cases of HIV infection or exposed infants at risk of vertical transmission, 639 were duplicates and 566 reporting errors; the remaining 299 reports were still being investigated. A further 4753 confirmed cases were reported through other sources (see methods). **Table 8** shows the likely source of infection or exposure risk for all confirmed cases.

In recent years, the annual number of reports from every region of the UK and Ireland has increased. Before 2000, paediatricians reported cases from fewer than 50 units each year; this rose to over 150 units in 2006. In England, the proportion of cases reported from outside London increased from 20% in 2000, to over 50% in 2006.

*Children born to infected women:* Most reported children (8561/8949 96%) were born to infected women. By the end of 2006, 1553 (18%) of these children were known to be infected, and 5393 (63%) uninfected; infection status for the remaining 1615 (19%) had not been reported (**Table 9**). While less than 10% were born abroad, they accounted for nearly 50% of confirmed mother to child infections.

Over 80% of the 6951 children born to diagnosed women in the UK or Ireland (**Table 10**) were born between 2000 and 2005. Although the infection status of many of these children has yet to be reported, most will be uninfected.

**Table 8: HIV infection and infants born to HIV infected women (all reporting sources) (notified by 31 December 2006)**

Exposure / likely source of infection	BPSU reports	Reports from other sources	Total
Children born to HIV infected women	4089	4472	8561
<b>Likely source of infection for other infected children</b>			
Haemophilia treatment	48	219	267
Blood transfusion/products	36	20	56
Other/not yet established	23	42	65
<b>Total</b>	<b>4196</b>	<b>4753</b>	<b>8949</b>

\*1553 known to be infected (see table 9)

**Table 9: Children born to HIV infected women\* Infection status and region of first report (notified by 31 December 2006)**

Region of first report	Infected	Indeterminate	Not infected	Total
England Total	1389	1443	4379	7211
London	918	727	2824	4469
North	153	198	464	815
Midlands & East	184	291	677	1152
Midlands & East	134	464	414	775
Wales	17	19	38	74
Northern Ireland	5	8	14	27
Scotland	65	65	264	394
Ireland	77	80	698	855
<b>Total</b>	<b>1553</b>	<b>1615</b>	<b>5393</b>	<b>8561</b>

\*Includes children born abroad

*Infected children:* Since surveillance started, 1941 infected children have been reported to the NSHPC. Overall 43% were born outside the UK and Ireland but the proportion has changed over time: 27% of children diagnosed before 2000 were born abroad, compared with 63% of those diagnosed 2000-2006. In 4% of cases it was not possible to ascertain the route of transmission; these were mainly children diagnosed at older ages whose mothers' HIV status at delivery was unknown.

Three hundred and twenty nine (17%) infected children are known to have died, 76 (4%) to have gone abroad and 406 (21%) are either reported as lost to follow up or have not had follow up information reported since 2004.

Over 1100 infected children and young people reported as paediatric cases were known to be alive and receiving care in the UK or Ireland at last follow up in 2005 or 2006: about a quarter had been diagnosed with at least one AIDS indicator disease at some time and an additional 40% had other HIV symptoms reported. At the end of 2006, 139 (12%) were aged 16 years or over and 379 (34%) were aged 11 to 15.

Of the 810 children known to have acquired infection from their mothers in the UK or Ireland, most (78%) were born to undiagnosed women; 130 infants born since 2002 (78 to undiagnosed and 52 to diagnosed women) were confirmed infected by the end of 2006.

**Table 10: Year of birth and infection status of children born in the UK and Ireland to HIV diagnosed women. (notified by 31 December 2006)**

Year of Birth	Infected	Indeterminate	Not infected	Total
1982-1999	111	147	899	1157
2000	6	32	341	379
2001	8	69	490	567
2002	13	61	660	734
2003	10	95	914	1019
2004	11	146	946	1103
2005	10	473	713	1196
2006*	8	527	261	796
<b>Total</b>	<b>177</b>	<b>1550</b>	<b>5224</b>	<b>6951</b>

\*Reports for 2006 expected to rise substantially

## Discussion

The number of births to HIV infected women in the UK and Ireland has increased substantially each year since 2000. Most of these infants were born to diagnosed women, who were able to take advantage of interventions to reduce the risk of transmission. However, despite high uptake of antenatal testing and interventions, some infants are still acquiring HIV infection from their mothers. An audit of cases occurring in England between 2002 and 2005 was carried out in 2006 and the resulting report will be available in 2007.

Changing trends in the demographic profile of HIV infected children and young people living in the UK and Ireland have implications for current, and future, health and social service provision. The introduction of highly active antiretroviral therapy (HAART) in 1997 has substantially improved the prognosis for HIV infected children, with most surviving into their teens and some now reaching adulthood. There are now several hundred young teenagers living with HIV, and currently being seen in paediatric clinics, who will need appropriate and specialised services to support their transition into adult care.

Reports to the NSHPC from all areas of the UK and Ireland have increased in recent years. The wide geographical distribution of the newly reported cases highlights the important role of the BPSU in identifying infected children diagnosed outside the specialist paediatric HIV centres, as well as exposed infants born to infected women in lower prevalence areas.

Recent publications drawing on NSHPC data, including that collected through the BPSU, have focused on ART and congenital abnormalities, prematurity, the follow up of exposed uninfected children, and clinical management and outcomes of infected children (see Appendix 1,2).

Please note the data presented are provisional, not peer reviewed and definitive conclusions should not be drawn from them.

## Funding

This study is funded by the HPA; additional support has come from the collaborating institutions and the Medical Research Council.

## Ethics approval

The London Multicentre Research Ethics Committee reviewed and approved the NSHPC and the associated CHIPS study on 28 January 2004 (Refs: London MREC/04/2/009; MREC/04/2/010). Paediatric

surveillance of HIV through the BPSU also has PIAG approval (ref PIAG/BPSU 2-10(a)/2005).

## Support groups

Barnardos Positive Options, William Morris Hall, 6 Somers Road, London, E17 6RX.

Web: <http://www.barnardos.org>

Positively Women, 347-349 City Road, London, EC1V 1LR.

Web: <http://positivelywomen.org.uk>

## Acknowledgements

We are very grateful to the BPSU and all members of the RCPCH, particularly those paediatricians who have reported cases and completed questionnaires, for their continued support and diligence.

## References

1. Duong T, Ades AE, Gibb DM, Tookey PA, Masters J. Vertical transmission rates for HIV in the British Isles: estimates based on surveillance data. *BMJ* 1999; **319**:1227-29
2. The UK Collaborative Group for HIV and STI Surveillance. A Complex Picture. HIV and other Sexually Transmitted Infections in the United Kingdom: 2006. London: Health Protection Agency Centre for Infections, November 2006
3. Department of Health. Reducing mother to baby transmission of HIV. Health Service Circular 1999/183. London: Department of Health, 1999

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## Malaria in childhood

### Key Points

- Imported malaria is a preventable disease, yet over 2000 cases are reported in the United Kingdom, of which around 15% occur in children under 16 years of age.
- Between 01 January 2006 and 31 January 2007, 206 cases of imported malaria have been reported through the BPSU.
- *Plasmodium falciparum* (83%) remains the most prevalent species responsible for imported malaria in children in the UK and Ireland.
- Although many children are very ill at presentation, serious complications are uncommon and none of the children in this study died.

### Background

The United Kingdom currently has the highest incidence of imported malaria cases among industrialised countries<sup>1</sup>. Between 1997 and 2001, the National Malaria Reference Laboratory (MRL), London, received an average of 240 notifications of children below 15 years of age with malaria each year<sup>2</sup>. The incidence of paediatric malaria in the UK has tripled over the past 30 years<sup>3,4</sup>. Particularly concerning is the proportion of cases due to *Plasmodium falciparum* (**Figure 11**), responsible for most of the complications of malaria (shock, severe anaemia, acute renal failure, convulsions, coma, long-term neurological damage and death,<sup>5</sup>) has increased exponentially over the past three decades. In England, the proportion of *P. falciparum* cases reported to the MRL has increased from 17% in 1977 to 40% in 1987 and

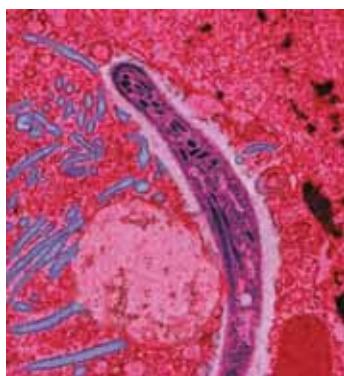


Figure 11: This thin film blood smear micrograph depicts a *Plasmodium falciparum* parasite microgametocyte.



Dr S Landhani

77% in 2001 in both adults and children<sup>2</sup>. Many parents who have immigrated to industrialised countries continue to take their children back to their home countries, often with no prophylaxis<sup>6</sup>. In addition, because children with malaria often present with symptoms of common childhood illnesses, the diagnosis is often missed initially. A recent six-year retrospective study of children with malaria in East London found that only 15% took appropriate antimalarial prophylaxis<sup>7</sup>. Furthermore, malaria was suspected by the General Practitioner at the first visit in only 32% of children and a further 25% of children were referred to the Emergency department with a diagnosis other than malaria<sup>7</sup>. Many studies have consistently shown that delay in diagnosis is the single most important determinant of an adverse outcome in imported malaria<sup>8,9</sup>.

Despite the potentially fatal nature of the disease, there is a lack of robust data on children with imported malaria in industrialised countries. National statistics on paediatric imported malaria in the United Kingdom are currently derived from official notifications to the MRL but it is unclear how accurately they reflect the true incidence of paediatric malaria. Furthermore, because MRL data are based on laboratory notifications, current knowledge on the clinical features of imported malaria is limited to small retrospective case series. In addition, the management of paediatric malaria is based on national guidelines, but it remains unclear whether they are followed and whether the recommended therapy is effective. The public health importance of this project cannot be over-emphasised. Imported malaria is a preventable disease. This study will help us understand the epidemiology and risk factors for imported malaria and provide crucial information upon which future public health measures can be modeled. It is hoped that this study will enable us to identify high risk populations and regions within the United Kingdom and allow us to develop strategies to target such populations in order to prevent imported malaria by, for example, improving antimalarial prophylaxis uptake.

## Objectives

For children with imported malaria, this study will aim to:

- Estimate the incidence in the United Kingdom and Ireland.
- Describe the clinical and laboratory features, management, complications and outcome at discharge.
- Identify risk factors for imported cases of severe malaria.

## Surveillance period

January 2006 - January 2007 (inclusive).

## Methodology

The BPSU forwarded all notifications to the Centre for Child Health, Royal London Hospital. A pre-drafted introduction letter, study information sheet, questionnaire and a stamped, addressed return envelope were then sent to the reporting paediatrician. Completed questionnaires were returned to the Centre for Child Health. If no response was received after four weeks, a reminder letter along with another copy of the questionnaire was sent to the paediatrician. The first page of the four-page questionnaire requested contact details of the reporting consultant and minimal information about the patient to allow cross-reference with the MRL database without revealing the identity of the patient. Data collected included first and second initials of the patient, date of birth, sex, ethnicity and the first-part of the postcode which, along with the hospital admitted to and the date of diagnosis should provide sufficient identifiers to allow comparison with the MRL database, which is being used as an additional alternative data source. Less than six adult and paediatric malaria cases are notified to the Health Protection Surveillance Centre in Ireland every year and, unlike the MRL database, it will not be possible to link the notifications with the cases reported to the BPSU from Ireland.

The second and third pages of the questionnaire sought information on previous history of malaria, travel history, antimalarial prophylaxis, delay in diagnosis, presenting features, laboratory investigations, concurrent infections, and management, including the need for specialist or intensive care.

## Case definition

Any child less than 16 years of age who is diagnosed with malaria through either microscopic examination of thick and thin blood smears or malaria antigen detection in the blood using commercially available assays.

## Alternative data sources

The MRL database was used as an alternate source of case notification.

## Denominator source

Children under 16 years of age identified by the Office of National Statistics.

## Number of cases expected

Around 240 paediatric cases are notified to the MRL every year and, assuming only 75% of the cases are notified to the MRL, it is estimated that approximately 320 cases will be reported by paediatricians through the BPSU.

## Analysis

There were 206 cases of imported malaria notified to the BPSU over the 13 month study period. Eighty-five percent of cases (175/206 cases) occurred in England, with 106 cases (51%) reported from London. Of the 206 notifications, 134 have been confirmed as imported malaria, ten were duplicates and three were reported in error. Questionnaires from the remaining 59 cases are awaited. The number of cases notified by month are shown in **Figure 12**. The *Plasmodium* species responsible for infection were *P. falciparum* (83%), *P. vivax* (6%) *P. ovale* (3%) and *P. malariae* (1%). Four other children had dual infections while, in one case, the species responsible was not reported. Fever was the most common presenting symptom, and 5% presented with convulsions. The median *P. falciparum* parasitaemia count was 2% (range, 0.1-21%) – interestingly, 24% of cases presented with a parasitaemia >5%. Twelve children (8%) required admission to a paediatric intensive care unit, but none of the children in this study died.

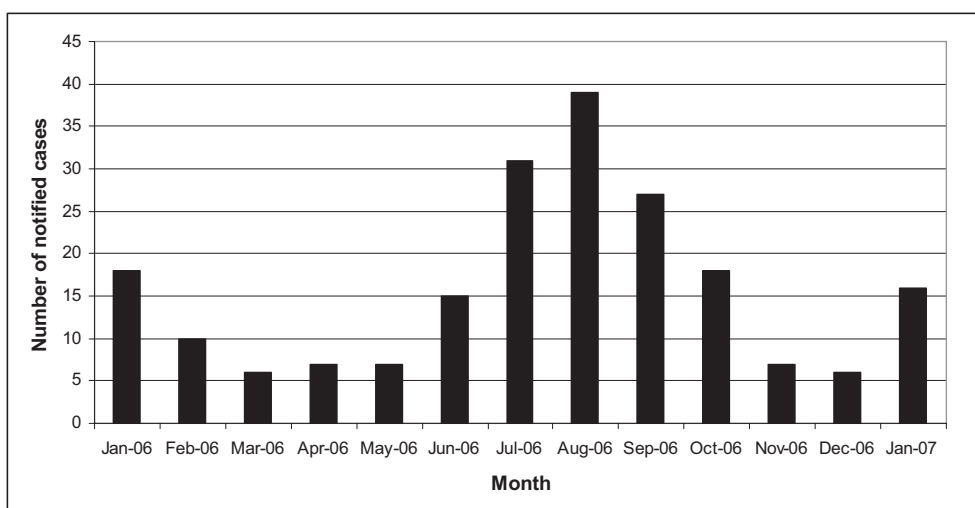


Figure 12: Number of cases notified to the BPSU

## Discussion

The number of imported malaria cases reported through the BPSU was lower than expected. At present, it is unclear whether this is due to under-reporting or due to a true reduction in the incidence of imported childhood malaria in the UK and Ireland. Comparison with the Malaria Reference Laboratory database for 2006 may provide further information. It is essential that paediatricians complete the remaining questionnaires so that the data can be analysed properly. So far, however, it is reassuring to note that, although many of the children with imported malaria are very ill at presentation, few have had any serious complications and none died.

Please note the data presented are provisional, not peer reviewed and definitive conclusions should not be drawn from them

## Funding

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## Ethical approval

This study was approved by the Leicestershire, Northamptonshire and Rutland Multi-centre Research Ethics Committee (Reference: 05/Q2502/120).

## Acknowledgements

We are grateful to the BPSU for their support and all members of the RCPCH who reported cases of imported malaria and completed the questionnaires.

## References

1. Muentener P, Schlagenhauf P, Steffen R. Imported malaria (1985-95): trends and perspectives. *Bull World Health Org* 1999; **77**: 560-6.
2. Health Protection Agency (HPA). Illness in England, Wales and Northern Ireland associated with foreign travel: a baseline report to 2002. London: Health Protection Agency, 2002. ([http://www.hpa.org.uk/infections/topics\\_az/travel/pdf/full\\_version.pdf](http://www.hpa.org.uk/infections/topics_az/travel/pdf/full_version.pdf)).
3. Sabatinelli G, Ejov M, Joergensen P. Malaria in the WHO European Region (1971-1999). *Euro Surveill* 2001; **6**: 61-5.
4. Williams JP, Chitre M, Sharland M. Increasing falciparum malaria in southwest London: a 25 year observational study. *Arch Dis Child* 2002; **86**: 428-430.
5. World Health Organisation. Management of severe malaria: a practical handbook. 2<sup>nd</sup> Edition. Geneva: World Health Organisation; 2000. <http://mosquito.who.int/docs/hbsm.pdf>
6. Brabin BJ, Ganley Y. Imported malaria in the UK. *Arch Dis Child* 1997; **77**: 76-81.
7. Ladhani S, El Bashir H, Patel VS, Shingadia D. Childhood malaria in East London. *Pediatr Infect Dis J* 2003 Sep; **22(9)**:814-9.
8. Lynk A, Gold R. Review of 40 children with imported malaria. *Pediatr Infect Dis J* 1989; **8**: 745-750.
9. Viani RM, Bromberg K. Pediatric imported malaria in New York: delayed diagnosis. *Clin Pediatr* 1999; June: 333-6.

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# Medium Chain Acyl CoA Dehydrogenase Deficiency (MCADD)

## Key Points

- Medium chain acyl CoA dehydrogenase deficiency (MCADD) is an autosomal recessive disease of fatty acid oxidation that may cause hypoglycaemia, encephalopathy, hepatic dysfunction and sudden death<sup>1</sup>.
- It is estimated that of those presenting clinically, up to one quarter will die at first clinical presentation, with one third of survivors sustaining significant neurological damage.
- The Department of Health and the National Screening Committee funded a two year pilot newborn screening service for MCADD from March 2004 to February 2006, with a concurrent research evaluation to December 2008. Screening commenced in six laboratories, covering half of all UK births each year. Interim funds have since been made available from the DH for screening to continue within the six laboratories from March 2006 to March 2008.
- The concurrent evaluation will estimate test performance, including the predictive value, specificity and detection rate of screening for MCADD, and will examine clinical outcomes in affected children diagnosed clinically or through screening.
- The Department of Health recently announced a ministerial decision to introduce universal screening for MCADD in England by April 2009 (Gateway number 7801).

## Background

Medium chain acyl CoA dehydrogenase deficiency (MCADD) is a recessively inherited metabolic disorder, which has been identified as a candidate for newborn screening through three systematic reviews commissioned by the Health Technology Assessment Programme<sup>2,3,4</sup>. The reviews concluded that more information was needed on test performance and clinical outcomes in a UK setting. Subsequently the Department of Health and the National Screening Committee have funded a pilot newborn screening service for MCADD. They have also commissioned a concurrent research study to evaluate the service. Although primary studies of MCADD screening in other countries have been carried out<sup>5,6,7,8,9,11</sup>



Prof C Dezateux

important questions remain unanswered<sup>10,12,13,14</sup>. Specifically, uncertainty remains over the clinical outcome following detection through newborn screening. Furthermore, the findings of these studies may not be generalisable to a UK setting; screening is carried out several days later in the UK and the population is ethnically more diverse than countries that have previously reported MCADD screening.

## Objectives

- To ascertain all cases of MCADD diagnosed during the study period in order to determine clinical outcomes up to two years of age.
- To estimate test performance, predictive value, specificity and detection rate of screening for MCADD.

## Surveillance period

April 2004 – April 2008 (inclusive).

## Methodology

### Case definition

MCADD is an inherited fatty acid oxidation disorder resulting from the lack of an enzyme required to convert fat stores into energy. During an intercurrent illness, such as gastroenteritis, there may be progressive encephalopathy with drowsiness, lethargy and hypotonia progressing to coma. Severely ill children may be hypoglycaemic. Without screening, children with MCADD usually present clinically before the age of two. It is predicted that the birth prevalence is about 1 in 10,000<sup>1</sup>.

Diagnosis of MCADD will be accepted if one or more of the following criteria are met:

- Elevated octanoyl carnitine in the presence of normal free carnitine levels on blood test using tandem mass spectrometry.

- Characteristic urine profile of organic acids with hexanoyl, suberyl and phenylpropionyl glycine.
- Molecular genetic studies confirming the presence of a mutation characteristic of MCADD.
- Enzyme studies based on skin fibroblasts showing reduced activity of MCAD.

All valid notifications reported up to February 2006 were reviewed by an independent diagnostic review panel.

### Reporting instructions

Diagnosis of MCADD can be made through newborn screening, clinical presentation, investigation of children with an affected family member or through post mortem investigation. If the diagnosis is uncertain or awaiting confirmation, the case should still be reported.

### Additional data sources

A Biochemical Surveillance Scheme for MCADD (BioSS–MCADD) has been set up through UK laboratories providing diagnostic testing for MCADD, in order to increase ascertainment of cases. Cases are also notified to the study through the six laboratories currently undertaking MCADD screening.

### Expected number of cases

Approximately 65 cases are expected per year.

### Denominator source

The total number of births in the UK over the study period, obtained from the Office for National Statistics.

## Analysis

Final report will include:

- Prevalence of MCADD in screened and unscreened areas of the UK.
- Age and clinical manifestation at diagnosis.
- Clinical outcome at one and two years post diagnosis.
- False negative rate of newborn screening for MCADD in screened areas.

### Numbers of cases notified to the BPSU

Between April 2004 and the end of December 2006, 265 notifications of MCADD had been received by the BPSU. Of these, 59 were confirmed clinically diagnosed cases of MCADD, 118 were detected by newborn screening, 54 were duplicates, twelve were notifications made in error (not MCADD or diagnosed outside surveillance period), and 22 are as yet unknown, pending return of follow-up questionnaires.

Of the 59 diagnosed clinically, 35 presented with clinical symptoms (including 10 diagnosed after death), one was investigated due to behavioural problems, and 19 were investigated because of affected siblings.

Of those who presented with clinical symptoms 12, (34%) were female, with a median age at diagnosis of 15.8 months (range 0 to 173). Of the 19 who were confirmed as having MCADD following diagnosis of an affected sibling, 11 (31%) were female, with a median age at diagnosis of 22.4 months (range 0 to 140).

Ninety-two follow-up forms have been sent to clinicians to ascertain clinical outcome in infants diagnosed over one year ago. Ninety of these have been returned. No deaths or major encephalopathic events were reported in the year following diagnosis. Given the natural history of clinically diagnosed MCADD, longer term systematic follow up is needed to obtain reliable estimates of MCADD mortality and morbidity. Preliminary data on two year follow-up will be included in next year's (2007-08) annual report.

### Number of cases by source of data

The three sources of data are:

- British Paediatric Surveillance Unit
- Newborn screening laboratories currently undertaking MCADD screening, which notify screened cases
- Biochemical Surveillance Scheme for MCADD (BioSS – MCADD)

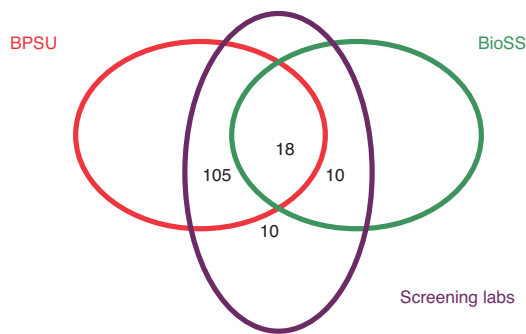


Figure 13: Number of confirmed cases by source of data  
Screened (presumptive) positives, N=143

## Reports

As the third year of surveillance draws to a close, we are pleased to have received 265 notifications through the BPSU. Our data are consistent with reports of a higher frequency of MCADD diagnoses in screened compared to unscreened populations.

An improvement has been seen from the previous year in the number of notifications initially notified through BioSS, now also being reported through the BPSU. An advantage of the BPSU over laboratory based surveillance is the ability to follow up clinical outcome through clinicians, so it is important to report all cases to the BPSU, irrespective of whether they have been notified through the other schemes. All clinicians are encouraged to continue to report any new cases of MCADD, particularly those which present clinically or have been diagnosed at post mortem. The return of any outstanding questionnaires is also encouraged.

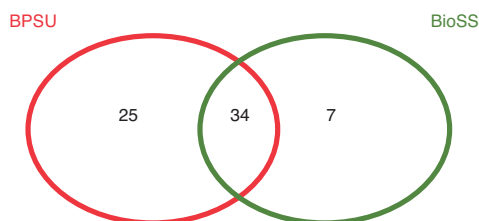


Figure 14: Confirmed cases clinical.  
Clinically diagnosed, N=66

## Discussion

From preliminary data comparing screened and unscreened populations in the UK, the estimated prevalence of MCADD identified after clinical diagnosis appears to be a half to two-thirds of that after newborn screening. This suggests under-diagnosis and/or variable penetrance and has also been reported in other countries and screening programmes<sup>14</sup>. Of those presenting clinically, over 80% are homozygous for common mutation 985A>G, whereas this falls to 55% for those diagnosed through newborn screening.

Since 2004, in one of the largest pilot studies of newborn screening carried out worldwide, more than one million babies have been screened for MCADD in England. The study has shown that newborn screening reliably identifies affected children before they are likely to develop symptoms, enabling parents to use simple measures to avoid fasting and thereby reduce the chances of severe illness or death.

Please note the data presented are provisional, not peer reviewed and definitive conclusions should not be drawn from them.

## Conclusions

Interim results from this study together with international evidence from other screening programmes were reviewed by the National Screening Committee in May 2006. This led to the ministerial announcement on Feb 7<sup>th</sup> 2007, that newborn screening for MCADD is to be implemented throughout England by April 2009 (Gateway reference number: 7801).

## Funding

The Department of Health and the National Screening Committee.

## Ethical approval

This study was approved in April 2004 by the London GOS MREC (04/Q0508/2 with no local investigator status); it also has approval from the Patient Information Advisory Group (PIAG/BPSU 2-10(e)/2005).

## Support group

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Web: <http://www.climb.org.uk/climb>

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## References

1. Pollitt, R.J., Leonard, J.V. Prospective surveillance study of medium chain acyl-CoA dehydrogenase deficiency in the UK. *Arch Dis Child* 1998; **79**:116-119
2. Seymour, C. A, Thomason, M. J, Chalmers, R. A, Addison, G. M, Bain, M. D, Cockburn, F, Littlejohns, P, Lord, J, and Wilcox, A. H. Newborn screening for inborn errors of metabolism: a systematic review. *Health Technology Assessment* 1997 1, 1-97.
3. Pollitt, R. J, Green, A, McCabe, C. J, Booth, A, Cooper, N. J, Leonard, J. V, Nicholl, J, Nicholson, P, Tunaley, J. R, and Viridi, N. K. Neonatal screening for inborn errors of metabolism: cost, yield and outcome. *Health Technology Assessment* 1997 1, 1-203.
4. Pandor, A, Eastham, J, Beverley, C, Chilcott, J, Paisley, S. Clinical effectiveness and cost-effectiveness of neonatal screening for inborn errors of metabolism using tandem mass spectrometry: a systematic review. *Health Technology Assessment* 2004, 8: No.12
5. Wilcken, B, Wiley, V, Hammond, J, Carpenter, K. Screening Newborns for Inborn Errors of metabolism by tandem Mass Spectrometry. *N Engl J Med* 2003, **348**:2304-12
6. Zytovicz, T. H. et al. Tandem Mass spectrometric analysis for amino, organic, and fatty acid disorders in newborn dried blood spots: A two year summary from the New England Newborn Screening Program. *Clin Chem* 2001 **47**:1, 1945-1955
7. Schultze, A, Lindner, M, Kohlmuller, D, Oglemoller, K, Mayatepek, E, Hoffmann, G. Expanded newborn screening for inborn errors of metabolism by electrospray ionization-tandem mass spectrometry: results, outcome, and implications. *Pediatrics* June 2003;Vol 111 No.6;1399-1406
8. Pourfarzam, M, Morris, A, Appleton, M, Craft, A, Bartlett, K. Neonatal screening for medium-chain acyl-CoA dehydrogenase deficiency. *Lancet* Sept 29, 2001; **358**:1063 –1064
9. Waisbren, S, Albers, S, Amato, S, et al. Effect of expanded newborn screening for biochemical genetic disorders on childhood outcomes and parental stress. *JAMA* 2003; **290**:2564-2572
10. Holtzman, N. Expanded newborn screening. How good is the evidence? *JAMA* 2003; **290**:2606-2608
11. 'Sudden Unexpected Death in Infancy: The report of a working group convened by The Royal College of Pathologists and The Royal College of Paediatrics and Child Health' The Royal College of Pathologists and the Royal College of Paediatrics and Child Health, September 2004
12. Wilcken, B, Haas, M, Joy, P, et al. Outcome of neonatal screening for medium-chain acyl-CoA dehydrogenase deficiency in Australia: a cohort study. *Lancet* 2007;**369**:37-42
13. Grosse, S D, Dezateux, C. Newborn screening in inherited metabolic disease. *Lancet*. 2007;**369**:5-6
14. Grosse, S D, Khoury, MJ, Greene CL, et al. The epidemiology of medium chain acyl-CoA dehydrogenase deficiency: An update. *Gen Med* April 2006; Vol **8**, No.4:205-212

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## Methicillin-Resistant *Staphylococcus aureus* (MRSA) Bacteraemia

### Key Points

- 144 notifications have been received from the BPSU, of which 74 have currently been confirmed as meeting the case definition.
- The majority of confirmed BPSU case notifications (70%) concern infants less than one year old.
- 55 of the isolates (77%) referred to the HPA Staphylococcal Reference Unit were characterised as healthcare-associated strains (EMRSA 15/16).

### Background

Routine national surveillance has identified a worrying increase in Methicillin-Resistant *Staphylococcus aureus* (MRSA) bacteraemia in children, with the number of reported cases rising from four in 1990 to 77 in 2000<sup>1</sup>. 53% of the 376 cases of MRSA bacteraemia in children reported between 1990 and 2001 involved infants less than 12 months of age, although substantial numbers of infected infants aged one to four years were also reported. As the above data were derived from voluntary reporting of cases, they almost certainly reflect an under-estimate of the true incidence of infection.

The aims of this study are to obtain a robust estimate of the incidence of MRSA bacteraemia in children, and to define the demographic and clinical features of the patient population, with particular regard to the proportion of cases that are healthcare or community-associated.

Historically, infections due to MRSA have been primarily acquired in hospitals, however, in the last few years, there have been reports from other countries, particularly the USA, of MRSA



Dr A Johnson



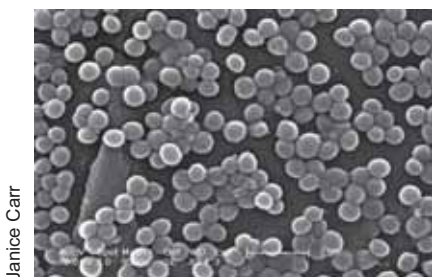
Ms C Goodall

infections in children that have been acquired in the community with no demonstrable links to the hospital setting<sup>2-5</sup>. In this study, isolates of MRSA from children are characterised in terms of their antibiotic resistance pattern, strain type and biological properties (particularly virulence traits). Possible associations between organism type and clinical features of infection are investigated. The consolidation of microbiological, epidemiological and clinical information will allow us to determine if community-associated MRSA as a cause of bacteraemia has emerged in the UK. These findings will have significant implication for the management of severe paediatric infections due to *S. aureus* in the community.

### Objectives

The study aims to determine

- the incidence of MRSA bacteraemia in children aged <16 years.
- whether the incidence of MRSA bacteraemia varies between children of different ages.
- the spectrum of clinical features and patterns of presentation of MRSA bacteraemia in children.
- whether MRSA bacteraemia in children is mainly due to healthcare- or community-associated MRSA and whether acquired nosocomially or in the community.
- whether cases of MRSA bacteraemia in children tend to occur in particular hospital units or specialties.
- whether strains of MRSA that cause bacteraemia in children have particular biological characteristics.



Janice Carr

Figure 15: Scanning EM numerous clumps of MRSA: x9560.

In particular:

- (i) Are the isolates similar to those found in hospitalised adults?
- (ii) Are the isolates representative of true community-associated MRSA reported in the UK and other countries?
- (iii) Do the strains possess particular virulence traits, such as Panton Valentine leukocidin?

#### Additional data sources

In addition to cases ascertained through the BPSU, cases were also sought using the following sources:

1. Reports of MRSA bacteraemia routinely reported to the Health Protection Agency (HPA) from hospitals in England, Wales and Northern Ireland.
2. Cases of MRSA bacteraemia in children reported to the Health Protection Agency, Health Protection Scotland or the National Disease Surveillance Centre (Dublin) by hospitals participating in the European Antimicrobial Resistance Surveillance System (EARSS), a pan-European surveillance programme looking at antimicrobial resistance in a number of pathogenic bacteria including *S. aureus*. About 30 hospitals in England and Wales, and all hospitals in Scotland and Northern Ireland participate in EARSS.
3. Cases identified following referral of blood culture isolates of MRSA from children to reference laboratories including the HPA Laboratory of Healthcare Associated Infection or the HPA Antimicrobial Resistance Monitoring and Reference Laboratory (based on the same site in London), the Scottish MRSA Reference Laboratory (Glasgow) or the National MRSA Reference Laboratory (Dublin).

### Surveillance period

June 2005 – May 2007 (inclusive).

### Methodology

Paediatricians were asked to report all cases meeting the case definition via the orange card system on a monthly basis. Paediatricians were then sent a questionnaire seeking demographic details and clinical information

#### Case definition

Isolation of methicillin-resistant *Staphylococcus aureus* (MRSA) from blood culture(s) of children less than 16 years of age.

#### Reporting instructions

Clinicians are asked to report any cases seen within the last month that meet the case definition. However this surveillance does not replace other forms of routine *S. aureus* reporting to the HPA.

Microbiology laboratories that have not submitted the associated isolate to Laboratory of Healthcare Associated Infection will be asked to do so. Data from these sources will be pooled and reconciled to identify a unique set of cases.

**Table 11: Reports made to the BPSU between June 2005 and March 2007**

	Confirmed	Duplicates/ or errors	Outstanding	Total
England	58	34	24	116
Wales	3	3	0	6
Scotland	6	0	1	7
Northern Ireland	3	0	1	4
Ireland	4	3	4	11
<b>Total</b>	<b>74</b>	<b>40</b>	<b>30</b>	<b>144</b>

**Table 12: Patient's age at the date the specimen was taken**

	<1 year	1-4 years	5-9 years	10-15 years	unknown	Total
Confirmed BPSU Cases	52	15	3	4	0	74
Reference Laboratory Isolates	32	10	3	5	16	66
LabBase 2 reports	83	28	10	11	0	132

*Expected number of cases*

Approximately 100-120 each year.

*Denominator source*

Resident population estimates: live births taken from Office of National Statistics tables and the Ireland census 2002 data (Central statistics office, Ireland).

**Analysis**

By the end of March 2007, 144 notifications of MRSA bacteraemia have been received (Table 11). However, 24 notifications were made in error (for example MRSA isolated from skin swabs not blood), and 16 duplicate notifications have been received.

At present there are 74 confirmed cases with 30 outstanding questionnaires yet to be returned. Of the 74 confirmed cases notified by paediatricians, 78% (56/74) were submitted by paediatricians in England, 8% (6/74) from Scotland, 5% from Ireland and 4% from both Northern Ireland and Wales (Table 11).

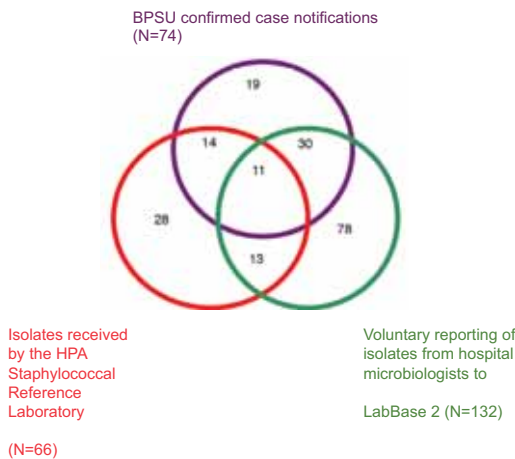
Irrespective of the notification source, reports were concentrated in children less than one year old (BPSU, 70%; Reference Laboratory, 48%; LabBase, 63%), although a substantial proportion of cases was reported in infants aged 1-4 years (BPSU, 20%; Reference Laboratory, 15%; LabBase, 21%) (Table 12).

Voluntary routine reporting to LabBase identified 132 cases while 66 cases were detected following referral of an isolate to the Reference Laboratory; eleven cases were confirmed by all three reporting routes (Figure 16).

Characterisation of the referred isolates in the Reference Laboratory indicated that the majority were representatives of EMRSA-15, the most prevalent healthcare-associated MRSA seen in the UK (Table 13).

**Table 13: Strain characterisation of isolates submitted to the HPA Staphylococcal Reference Laboratory (England & Wales data only)**

MRSA Strain type	Total
EMRSA-15	46
EMRSA-16	9
Distinct strain	11
<b>Total</b>	<b>66</b>



## Conclusions

The results suggest that

1. MRSA bacteraemia in children remains rare in contrast to the situation in adults (where more than seven thousand cases were reported via the mandatory enhanced MRSA surveillance scheme in 2005).
2. The provisional finding that when MRSA bacteraemia in children does occur it involves healthcare-associated strains has implications for potential control measures aimed at reducing further the frequency of infection.

Please note the data presented are provisional, not yet peer reviewed and so definitive conclusions should not be drawn from them.

## Ethical approval

This study has been approved by the Eastern MREC. This study has Patient Information Advisory Group approval through the HPA (PIAG 03-c)/2001.

## Funding

Department of Health.

## Acknowledgements

We are very grateful to the BPSU and all participating paediatricians and microbiologists for their continued support, especially those who have notified cases and completed questionnaires.

## References

1. Khairulddin N, Bishop L, Lamagni TL, Sharland M, Duckworth G. Emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) bacteraemia among children in England and Wales, 1990-2001. *Arch Dis Child*. 2004 Apr; **89**(4):378-9.
2. Groom, A.V. *et al*. Community-acquired methicillin-resistant *Staphylococcus aureus* in a rural American Indian community. *JAMA* 2001; **286**: 1201-1205.
3. Fey, P.D. *et al*. Comparative molecular analysis of community- or hospital-acquired methicillin-resistant *Staphylococcus aureus*. *Antimicrob Agents Chemother* 2003; **47**: 196-203.
4. Dietrich, D.W. *et al*. Community-acquired methicillin-resistant *Staphylococcus aureus* in Southern New England Children. *Pediatrics* 2004; **113**: 347-352.
5. PHLS. *Staphylococcus aureus* bacteraemia: England, Wales and Northern Ireland, February to December 2002. *Commun Dis Rep CDR Wkly [serial online]* 2003; **13**:Bacteraemia.

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# Neonatal herpes simplex virus infection

## Key points

- Over the three year surveillance period, 83 infants born 2004-2006 were reported through the BPSU with confirmed neonatal HSV. Three additional cases were reported directly to the study investigators. The number of confirmed cases is likely to increase as outstanding reports are clarified.
- Virus was typed in over 90% of cases; about half the infants had HSV-1 infection; 70% had disseminated and/or CNS infection, and over half of those did not have typical skin, eye or mouth lesions.
- Maternal genital herpes infection was rarely diagnosed prior to delivery, although it was retrospectively recognised in about 20% of cases. In about 25% of cases a possible postnatal source of infection was identified, usually a close relative of the infant.
- Neonatal HSV remains extremely rare, although the number of confirmed reports suggests prevalence has increased over the last 20 years.

## Background

Neonatal herpes simplex virus (HSV) infection is rare but potentially devastating. It can follow primary or recurrent maternal infection, or be acquired postnatally through direct contact with infected secretions. Transplacental transmission is unusual, and perinatal infection is usually acquired during vaginal delivery through an infected birth canal. Early diagnosis is vital as antiviral therapy can significantly affect outcome<sup>1</sup>.

Surveillance of neonatal HSV was previously undertaken through the BPSU between 1986 and 1991<sup>2</sup>. Seventy-six cases were reported over the five and a half year period, an estimated prevalence of 1.65/100 000 (CI 1.3-2.0/100 000); approximately equal proportions of infections were HSV-1, HSV-2 and untyped. There has subsequently been an increase in the prevalence of sexually transmitted diseases, as well as demographic and social changes within the general population which may have contributed to a change in the prevalence and serotype distribution of neonatal HSV<sup>3</sup>. Improvements in diagnostic techniques may also have had an impact on the reported prevalence of neonatal infection.



Dr P Tookey

## Objectives

The aim of the study was to:

- estimate the current prevalence of neonatal herpes simplex infection in the British Isles, and to distinguish the proportion attributable to HSV-1 and HSV-2.
- explore the presentation of neonatal HSV infection, and management of diagnosed cases.
- assess subsequent morbidity and mortality through the notifying paediatrician.
- compare findings with the 1986-91 BPSU cohort, and with other INOPSU studies of HSV.
- inform the debate on antenatal screening.

## Surveillance period

January 2004 to January 2007 (inclusive).

## Methodology

### Case definition

### Surveillance definition

- 1) Any infant under one month of age
  - a) with a diagnosis of HSV infection based on virus detection by culture, polymerase chain reaction (PCR) or immunofluorescence (IF), or serology – IgM and/or seroconversion, or
  - b) treated with antiviral drugs for suspected HSV infection.
- 2) Any stillborn infant in whom HSV is suspected.

*Analytic definition*

*Confirmed case of neonatal HSV:*

- a) virus detection by culture, PCR or IF, or serology – IgM and/or seroconversion on a specimen taken within four weeks of birth,

or

- b) typical clinical manifestations with maternal infection confirmed by either seroconversion during pregnancy or virus isolation around the time of delivery.

*Suspected/possible case of neonatal HSV:*

Typical clinical manifestations in an infant treated with antiviral drugs for suspected HSV infection.

*Reporting instructions*

Any live or stillborn infant born between 1<sup>st</sup> January 2004 and 31<sup>st</sup> December 2006 in the UK or Ireland with confirmed or suspected neonatal HSV infection.

*Alternative data sources*

Alternative data sources included paediatric reports made directly to the study investigators.

*Denominator source*

Routine national statistics on number of live and still births, obtained from the Office of National Statistics. Irish birth rate obtained from the Irish census 2002 (Central statistics office, Ireland).



Judith Faulk

Figure 17: Neonate displaying maculopapular outbreak on feet due to congenitally acquired HSV.

*Number of cases expected*

On the basis of the previous study, and allowing for a modest increase in prevalence, it was expected that there would be 10-25 confirmed cases a year.

**Analysis**

*Number of reports:* By the end of February 2007 there had been 191 reports through the BPSU, of which 83 were confirmed cases of neonatal HSV infection, 13 were suspected, and 65 were duplicates or reporting errors. Three reports could not be followed up, and 27 were still being investigated. A further three confirmed cases were reported directly to the study investigators.

*Confirmed cases:* About half of the 86 infants with confirmed and typed infection had HSV-1 infection (Table 14). Infection was localised to the skin (Figure 16), eye or oral mucosa (SEM) in about 30%; among those with disseminated and/or CNS infection, about 60% had no SEM involvement. About a quarter of the mothers were aged under 21 years at delivery; about 40% delivered prematurely, at <37 weeks. Diagnosis of maternal genital infection prior to delivery was extremely rare, although after the neonatal diagnosis about 20% of mothers reported a history of genital herpes prior to pregnancy, or symptoms indicating primary or recurrent infection in pregnancy, or there was retrospective laboratory confirmation of recent maternal genital infection. There were no reports of hospital acquired infection, but in about 25% of cases a possible source of postnatal infection was

**Table 14: Year of birth, virus type and % with no reported SEM involvement**

Year of birth	HSV 1	HSV 2	Type unknown	Total
2004	11	13	2	26
2005	15	16	3	34
2006*	9	15	2	26
2004-2006*	35	44	7	86
% with no SEM involvement	31%	51%	~50%	43%

\* Outstanding reports still to be clarified, number likely to rise.

identified, usually a close relative of the infant. About 25% of infants were reported to have died, most in the neonatal period. Among the survivors, about 15% were believed to have neurological damage, but most were too young at last report for an assessment of outcome to be made.

Follow up: Outstanding reports will be clarified, and summary follow-up information on outcome in the second or third year of life will be sought for surviving children.

## Discussion

More confirmed cases were reported in each of the three years than in any year in the previous study period<sup>1</sup>; these data are consistent with an approximate doubling of prevalence, although a robust estimate of prevalence cannot yet be made since some reports are still outstanding, and denominator data are not yet available. Virus type is available for almost all cases in the current survey; in terms of the nature of infection and the lack of maternal history the current findings are similar to the previous survey. Analysis of the relationship between virus type, presentation, timing of treatment, and outcome will be undertaken when data collection is completed.

Please note the data presented are provisional, not peer reviewed and definitive conclusions should not be drawn from them.

## Funding

The National Screening Committee paid for neonatal HSV to appear on the orange card. Other costs are being met by the Centre for Paediatric Epidemiology and Biostatistics, Institute of Child Health, London.

## Ethics approval

The London Multicentre Research Ethics Committee reviewed and approved the study on 18<sup>th</sup> December 2003 (London MREC/03/2/080). PIAG approval has been given (PIAG/BPSU 2-10(g)/2005).

## Support group

The Herpes Viruses Association, 41 North Rd, London N7 9DP. Telephone helpline 0845 1232305. E-mail: [info@herpes.org.uk](mailto:info@herpes.org.uk). Web: <http://www.herpes.org.uk>

## Acknowledgements

We are very grateful to the BPSU and all members of the RCPCH, particularly those paediatricians who have reported cases and completed questionnaires, for their continued support. We also thank Sooria Balasagaram, Icina Shakes and Janet Masters for technical and administrative support.

## References

1. Herpes infection in pregnancy. International Herpes Management Forum. 1999 <http://www.ihmf.com/guidelines/summary9.asp> (accessed 17 March 2007).
2. Neonatal Herpes Simplex virus infection in the British Isles. Tookey P and Peckham C. *Paediatric and Perinatal Epidemiology* 1996, **10**: 432-442.
3. Vyse AJ, Gay NJ, Slomka MJ, Gopal R, Gibbs T, Morgan-Capner P, Brown D. The burden of infection with HSV-1 and HSV-2 in England and Wales: implications for the changing epidemiology of genital herpes. *Sex Transm Inf* 2000; **76**:183-87

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# Progressive Intellectual and Neurological Deterioration in Children

## Key Points

- After almost ten years of surveillance 2200 children have been notified. Of these, 1568 cases have been discussed by the Expert Group of seven paediatric neurologists. There have been 953 children with a known diagnosis other than vCJD, and in the diagnosed group there are 114 different phenotypic conditions.
- Six cases of variant Creutzfeldt-Jakob disease have been reported to the study since December 1998. Of these, four have been classified as “definite” and two “probable” according to the National Creutzfeldt-Jakob Disease Surveillance Unit criteria. All have now died.
- Further active surveillance is planned until April 2008.
- Even if you have made a diagnosis we still want to hear about all children with progressive intellectual and neurological deterioration.

## Background

Active prospective surveillance of UK children with progressive intellectual and neurological deterioration (PIND) commenced in May 1997. Funded by the Department of Health, it is being carried out via the British Paediatric Surveillance Unit (BPSU) in conjunction with the National Creutzfeldt-Jakob Disease Surveillance Unit in Edinburgh (NCJDSU) and the Health Protection Agency.

The main aim is to determine whether or not any children in the PIND group have developed variant Creutzfeldt-Jakob disease (vCJD). This new disease was first described by Will et al<sup>1</sup> in 1996. vCJD has been described in patients as young as 12 years of age<sup>2</sup> and it could occur in younger children. It is possible that the clinical presentation of vCJD in young children might differ from that described in adults. The strategy is to detect suspected vCJD cases by looking at a broader group of conditions causing progressive intellectual and neurological deterioration (PIND) in children. It is only by carefully examining the clinical details in all these PIND cases that we can be reasonably sure that vCJD is not being missed among the numerous rare neurodegenerative disorders that



The PIND Expert Group

affect children. An Expert Group of seven paediatric neurologists independently reviews the anonymised clinical details for all the PIND cases. The unique epidemiological data provide the opportunity to detect vCJD cases and highlight the variety of PIND conditions in the UK<sup>3</sup>.

The surveillance team use a detailed questionnaire to gather information via a telephone interview or site visit to review the case notes; alternatively the notifying paediatrician may wish to complete the questionnaire. There is further follow up of undiagnosed cases via the local paediatricians.

## Objectives

The study aims to:

- carry out active prospective surveillance of UK children with paediatric neurological conditions (including those with specific diagnoses) defined by their common presentation – progressive intellectual and neurological deterioration (PIND) - to determine the incidence and distribution of PIND.
- evaluate cases presenting with PIND in order to classify them and investigate the possibility that vCJD is occurring in children.

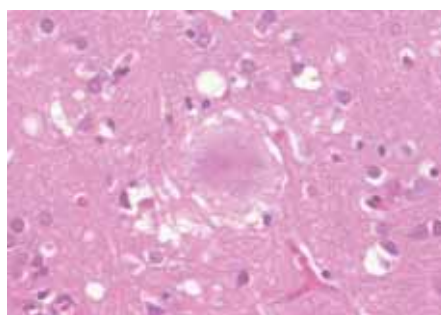


Figure 18: Florid plaque in vCJD x 400 haematoxylin/eosin stain

## Surveillance period

Surveillance commenced in May 1997 and continues.

## Methodology

### Case definition

Any child under 16 years of age at onset of symptoms who fulfils all of the following three criteria:

- Progressive deterioration for more than three months

With

- Loss of already attained intellectual/developmental abilities

And

- Development of abnormal neurological signs.

Excluding: Static intellectual loss, e.g. after encephalitis, head injury or near drowning.

Including:

- Children who meet the case definition even if specific neurological diagnoses have been made.
- Metabolic disorders leading to neurological deterioration.
- Seizure disorders if associated with progressive deterioration.
- Children that have been diagnosed as having neurodegenerative conditions but who have not yet developed symptoms.

### Reporting instructions

Cases seen in the last month but including those whose conditions began earlier (i.e. including “old cases” of children in follow-up (if seen in that month).

### Additional sources of data

All cases are being ascertained only through the paediatricians.

### Number of cases expected

Approximately 200 suspected cases of PIND a year.

### Denominator source

National population figures for children under 16 obtained from the Office for National Statistics and in Ireland from the census 2002 (Central Statistics Office, Ireland).

## Analysis

By the end of February 2007 a total of 2200 children had been reported via the BPSU (**Figure 19**). There were 953 PIND children with a definite underlying diagnosis, 128 in whom no diagnosis had been made and 120 who were still under investigation. There were 919 “No Cases” including those who did not fulfil the criteria for PIND, reporting errors, duplicate notifications etc. The 74 outstanding cases await data collection. The six cases of definite/probable vCJD are discussed below.

*Definite/probable cases of vCJD: Six cases of vCJD*

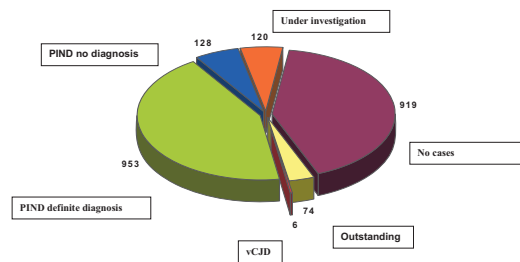


Figure 19: PIND study - current status

have been notified - the youngest was a girl aged 12 years at onset. There were three other girls and two boys. One child was notified in 1998, two in 1999, one in 2000 and two in 2001. All have now died and neuropathology has confirmed vCJD in four of them (classified as “definite” cases). Two have died without neuropathological study (classified by the NCJDSU criteria as “probable” cases”).

*Children who have definite PIND diagnoses other than vCJD:* The study is producing unique population-based data on the causes of PIND. The majority of reported children with PIND have a known degenerative diagnosis or a likely underlying diagnosis that is not vCJD. In the 953 children with a confirmed diagnosis other than vCJD there were 114 different neurodegenerative conditions. The eight most commonly occurring diagnoses are shown in **Figure 20**.

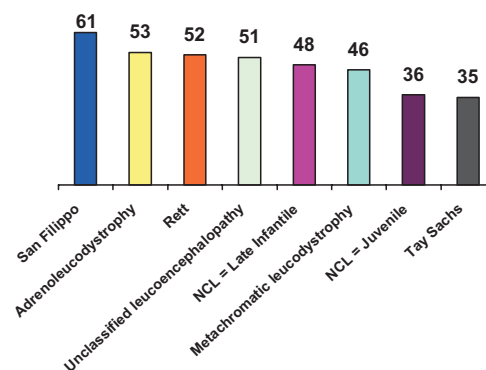


Figure 20: Eight most commonly reported PIND diagnoses of the 953 with a known diagnosis

*Variation in reporting by district:* Geographical analysis by hospital of report and by residence reveals significant variations. A few hospitals have not reported any cases. There are some areas with considerably higher numbers of children with PIND. Yorkshire remains the highest reporting BPSU region (264 cases) with West Midlands (246 cases) followed by North East Thames (231 cases).

*Variation in reporting by category of referring paediatrician:* General paediatricians notified the largest number of children followed by paediatric neurologists then community paediatricians.

(Figure 21)

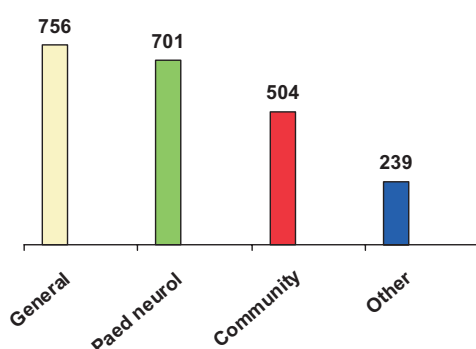


Figure 20: Category of referring paediatrician

## Discussion

PIND surveillance has been running for almost ten years now. Six cases of vCJD in children under 16 years of age at first presentation have been notified to the study. There were four cases of definite vCJD and two cases of probable vCJD. One girl was age 12 years at onset, the youngest ever reported case of vCJD. There have been no other children with the clinical features of vCJD, however there is concern that more childhood cases may appear.

Ten years is a short time to perform surveillance for a disease about which there are still many unanswered questions - for example, the number of children who may be incubating vCJD, the length of the incubation period and the exact nature of transmission. In 2004 Peden et al reported a case of preclinical vCJD discovered at autopsy. The patient had received blood from a donor who later developed vCJD<sup>4</sup>. This preclinical case had a methionine/valine genotype at codon 129 of the prion protein gene. All previously confirmed cases of vCJD have been methionine homozygous at this site. Methionine/valine genotypes make up 51% of the general population. It is possible that methionine/valine genotypes might develop vCJD with a longer incubation period than the methionine

homozygotes resulting in a “second wave” of vCJD cases.

“It is important to note that although a peak has been passed, it is possible that there will be future peaks, possibly in other genetic groups. There is also the possibility of ongoing person to person spread as seen with four cases of transfusion associated vCJD infection to date, who received blood from earlier cases”<sup>5</sup>.

Please note the data presented are provisional, not peer reviewed and definitive conclusions should not be drawn from them.

## Funding

This study is funded by the Department of Health.

## Ethics approval

Initial approval in 1997 was given by the Local Research Ethics Committee, Addenbrooke’s Hospital (ref: 97/010) and the Public Health Laboratory Service Ethics Committee and the Patient Information Advisory Group (PIAG/BPSU 2-10(c)2005).

## Acknowledgements

PIND surveillance continues to work very well and is yielding valuable information about the conditions that lead to PIND in children. Many thanks to the UK paediatricians who are still responding enthusiastically with a median number of 17 notifications per month. The PIND surveillance team is very grateful to the members of the paediatric neurology Expert Group (Prof J. Aicardi, Dr P. Baxter, Dr. M. Pike, Prof. R. Robinson, Prof. R. Surtees and Dr J. Wilson) for all their work in classifying cases. We will be welcoming Dr. J. Livingston to the team this year.

We were deeply saddened by the sudden death of Dr. Stuart Green who had given his time generously in support of the study. He will be greatly missed by us all.

## Support groups

1. Creutzfeldt-Jakob Disease Support Network, PO Box 346, Market Drayton, Shropshire TF9 4WN. Web:<http://www.cjdsupport.net>
2. Batten Disease Family Association, c/o Heather House, Heather Drive, Tadley, Hampshire, RG26 4QR. Web:<http://www.bdfa-uk.org.uk>

3. The Society for Mucopolysaccharide Diseases, MPS House, Repton Place, White Lion Road, Amersham, Buckinghamshire, HP7 9LP. Tel: 0845 389 9901
4. Climb National Information and Advice Centre for Metabolic Diseases. 176 Nantwich Road, Crewe, CW2 6BG. Tel: 0800 652 3181 Freephone Family Service Helpline, 0870 770 0326. E-mail: info@climb.org.uk. Web: <http://www.climb.org.uk>
5. Adrenalleukodystrophy (ALD) Aid Family Support Trust, 30-32 Morely House, 320 Regent Street, London W1R 5AB. Web: <http://www.aldfst.org.uk>
4. Peden AH, Head MW, Ritchie DL, Bell JE, Ironside JW. Preclinical vCJD after blood transfusion in a PRNP codon 129 heterozygous patient. *Lancet* 2004;**264**:527-29.
5. Incidence of Variant Creutzfeldt-Jakob Disease Deaths in the UK, January 1994 – December 2006, N J Andrews, Senior Statistician, Statistics Unit, Centre for Infections, Health Protection Agency, 2nd February 2007

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*Prof. R. Will, The National Creutzfeldt-Jakob Disease Surveillance Unit, Western General Hospital, Edinburgh, EH4 2XU*

## References

1. Will RG, Ironside JW, Zeidler M et al. A new variant of Creutzfeldt-Jakob Disease in the UK. *Lancet* 1996;**347**: 921-5
2. Verity CM, Nicoll A, Will RG, Devereux G, Stelitano L. Variant Creutzfeldt-Jakob disease in UK children: a national surveillance study. *Lancet* 2000;**356**:1224-7
3. Devereux G, Stelitano L, Verity CM, Nicoll A, Rogers P. Variations in neurodegenerative disease across the UK: findings from the national study of Progressive Intellectual and Neurological Deterioration (PIND). *Arch Dis Child* 2004;**89**:8-12

# Scleroderma

## Key points

- At the time of this report (March 2007) the study has been recruiting for 21 months: recruitment ends in July 2007.
- Twelve month questionnaires are currently being sent out (and will be sent out until July 2008).
- Linear scleroderma and systemic sclerosis are rare in childhood.



Dr A Herrick

## Background

Scleroderma may affect children as well as adults, and is associated with significant morbidity and mortality<sup>1-3</sup>. While some children with scleroderma have systemic sclerosis (SSc), more commonly scleroderma in children is localised in that it is primarily confined to the skin and underlying tissues. Two large international studies documenting clinical and immunological features of juvenile systemic sclerosis<sup>4</sup> and of juvenile localised scleroderma<sup>5</sup> have been published in the last year, reflecting the increased recognition of the importance of identifying and treating these conditions.

*Systemic Sclerosis.* There are two main subtypes of SSc - limited cutaneous and diffuse cutaneous (Figures 22, 23, 24). SSc is rare in children and while there have been no epidemiological studies specifically of SSc in children, it has been estimated that fewer than 2% of patients with SSc have onset younger than 10 years of age, and fewer than 9% onset between 10-20 years of age<sup>6</sup>. Even if rare, SSc in children is an important condition because its internal organ involvement can be life-threatening.

*Localised scleroderma.* Although localised scleroderma, unlike SSc, is not a multisystem connective tissue disease, it can be severely debilitating, especially the linear form of disease (which includes the “coup de sabre” variant). Subcutaneous tissues, muscle and bone as well as skin can be affected. Further, if the affected area crosses a joint, for example knee or elbow, then contracture and growth retardation can occur (Figure 25). In addition, the lesions can be very disfiguring, especially if the face is involved. Similarly to in SSc, little is known about the epidemiology of localised scleroderma in children. One study in the United States (the Rochester Epidemiology Project), reviewed medical records of patients seen between 1960-1993 and reported an incidence of localised morphea across all age groups of 2.7/100000, 28% of whom were



Figure 22: Limited cutaneous



Figure 23: Diffuse cutaneous



Figure 24: Diffuse cutaneous



Figure 25: Localised

aged less than 18 years (0.8/100000)<sup>7</sup>. If this was the incidence in the UK, then approximately 450 children per year would be diagnosed as having localised scleroderma of whom in the order of 40% (180) would have the linear form of the disease. The paucity of data on localised scleroderma incidence reflects difficulties in diagnosis, referral to different specialists, and perhaps the incorrect perception that localised scleroderma is a 'mild' disease not requiring specific treatment. However, we know that the early lesions of localised scleroderma are inflammatory and a recent study has reported extracutaneous features in a significant proportion of children<sup>8</sup>. Therefore there is a rationale for early diagnosis and intervention.

## Objectives

The primary aim is to ascertain the incidence of scleroderma, concentrating upon linear scleroderma (a sub type of localized scleroderma) and SSc. In addition we aim to identify the

- usual presenting symptoms.
- delay between symptom onset and diagnosis.
- pattern of care that is received by affected children before and after diagnosis.
- age at which most children are affected.
- sex ratio of affected children and whether this varies with age.
- regional or ethnic variations in incidence.

## Surveillance period

July 2005 - July 2007 (inclusive).

## Methodology

### Case definition

The reporting case definition is 'All cases of abnormal skin thickening newly diagnosed in the past month (the skin will usually be difficult to pinch normally) suspected by the reporting paediatrician to be linear scleroderma or systemic sclerosis (age up to 16 years).' For confirmation of cases, the 12 month follow up questionnaire asks if the diagnosis has been confirmed by a dermatologist or paediatric rheumatologist.

### Reporting instructions

Paediatricians are asked to report any cases, as defined above, seen for the first time since 1<sup>st</sup> July 2005.

### Alternative data sources

Although the BPSU is the main source of case ascertainment, some children with scleroderma are referred directly to adult rheumatologists or dermatologists with an interest in scleroderma. Members of the British Society for Paediatric and Adolescent Rheumatology (BSPAR), the British Association of Dermatologists (BAD), and the UK Scleroderma Study Group (UKSSG) have also been informed about the study and asked to notify cases. The reporting system for these three organisations is different from the BPSU reporting system in that members of the three organisations are mailed and are asked to contact the University of Manchester directly if a case is identified. The questionnaires that are sent to BPSU respondents are also sent to clinicians from other sources who notify cases directly.

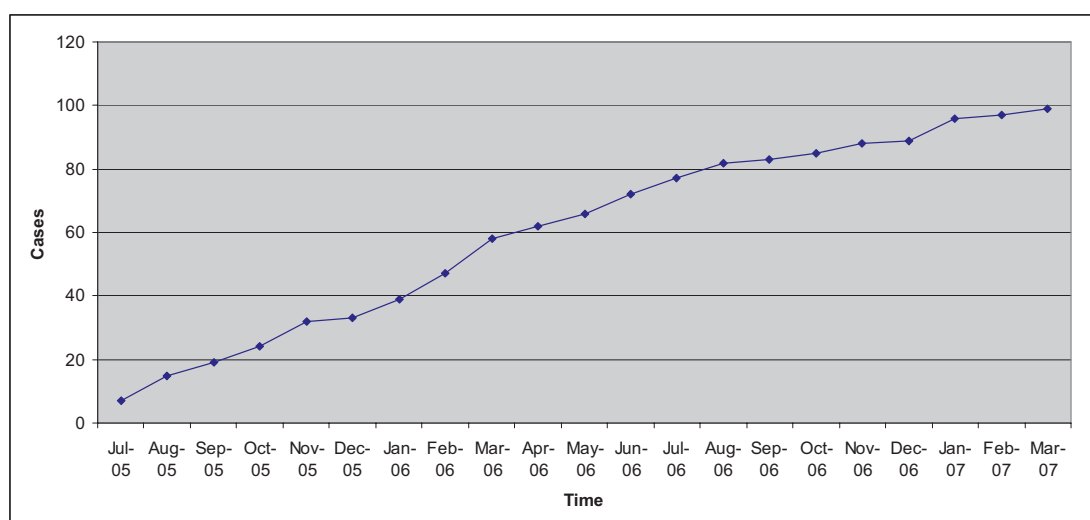


Figure 26: The number of notifications July 2005 - March 2007

### Number of cases expected

Initially it was anticipated that approximately 180 patients per year would be notified with localised scleroderma and approximately 20 with systemic sclerosis. However our experience, as outlined below, indicates that numbers notified have been very much lower than expected.

### Denominator Source

Office of National Statistics

### Analysis

#### Case notification and questionnaire return rate

From the commencement of the study until the middle of March 2007, 99 cases had been notified. Of these 99 notified cases, 65 questionnaires have been returned, 31 questionnaires remain outstanding, and three cases were excluded for not meeting the study criteria. Several cases notified at the outset of the study were excluded because the child had presented prior to the study period, that is prior to July 2005 (Figure 27).

By March 2007, 17 of the 12 month follow-up questionnaires had been sent out and eight of these returned

As anticipated, the majority of case notifications are through the BPSU. Only 13 notifications have come through other reporting sources, namely the British Society for Paediatric and Adolescent Rheumatology (BSPAR), the British Association of Dermatologists (BAD), and the UK Scleroderma Study Group (SSG). This may reflect differences between the systems for surveillance set up through alternative reporting sources, particularly regarding the frequency of mailings to medical practitioners which is not undertaken on a monthly basis as through the BPSU. However, early practical difficulties in the mailing of other organisations have been resolved (Figure 27).

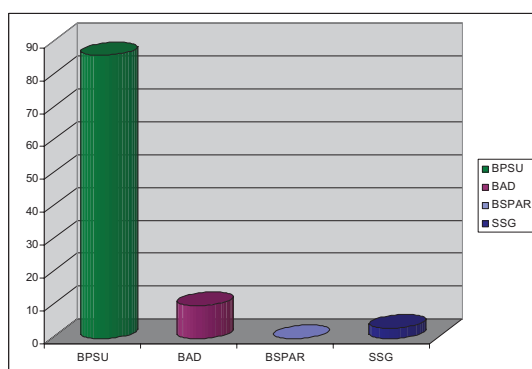


Figure 27: Notifications by reporting source

Of the 65 questionnaires returned, 47 cases are eligible for inclusion whilst 18 cases were excluded as not meeting the case definition. Of the eligible cases, 44 (94%) have localised scleroderma and three (6%) have systemic sclerosis. Seventeen (36%) are male and 30 (64%) are female. The mean age of included cases identified before March 2007 is 10 years (range 4 to 16 years).

Further analyses will be undertaken at a later date when case reporting is complete.

### Discussion

As described in the previous BPSU annual report, the rate of notifications has been unexpectedly low. This may be due to a higher number of children than expected attending specialists who are not BPSU members and so escaping notification to the study; however this low rate has not been affected by maintaining awareness of the study through presentations at professional meetings and the repeated provision of information about the study to different specialty organisations.

Findings so far suggest that childhood scleroderma, at least linear scleroderma and systemic sclerosis, are even rarer than originally thought.

### Conclusions

The main conclusions so far are as follows:

1. Childhood linear scleroderma and systemic sclerosis are rare.
2. BPSU notifications are higher in number than those from other clinical specialist groups, which may reflect the longer experience of paediatricians in surveillance and the active surveillance methods used by the BPSU.
3. Analysis of the study will be completed shortly after July 2008 when the last of the 12 month questionnaires is returned.

Through the study it is hoped that awareness of paediatricians about this rare condition has been increased by this surveillance study.

Please note the data presented are provisional, not peer reviewed and definitive conclusions should not be drawn from them.

## Funding

The study is being funded by the Raynaud's and Scleroderma Association. Funding has been extended until the end of July 2008.

## Support group

The Raynaud's and Scleroderma Association, 112 Crewe Road, Alsager, Cheshire ST7 2JA.  
Tel: 01270 8727756. Freephone: 0800 9172494 (for UK enquiries only).  
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Web: <http://www.raynauds.org.uk>

## Ethics approval

The study has been approved South Manchester Research Ethics Committee.

## Acknowledgements

We are extremely grateful to all paediatricians who have already notified cases and/or expressed interest in the study. The 12 month questionnaires, which ask for follow-up data and (if appropriate) whether the diagnosis has been confirmed by a rheumatologist or dermatologist, are an important part of the study and we are grateful also to paediatricians for completing these.

## References

1. Uziel Y, Miller ML, Laxer RM. Scleroderma in children. *Paed Clin N America* 1995; **42**: 1171-1203.
2. Garty BZ, Athreya BH, Wilmott R, Scarpa N, Doughty R, Douglas SD. Pulmonary function in children with progressive systemic sclerosis. *Pediatrics* 1991; **88**: 1161-7.
3. Foeldvari I. Scleroderma in Children. *Curr Opin Rheumatol* 2002; **14**: 699-703.
4. Martini G, Foeldvari I, Russo R et al. Systemic sclerosis in childhood. *Arthritis Rheum* 2006; **54**: 3971-8.
5. Zulian F, Athreya BH, Laxer R et al. Juvenile localized scleroderma: clinical and epidemiological features in 750 children. An international study. *Rheumatology* 2006; **45(5)**: 614-20.
6. Cassidy JT, Petty RE. The sclerodermas and related disorders. In: Textbook of Pediatric Rheumatology. 2nd Edition. Churchill Livingstone, New York 1990.
7. Peterson LS, Nelson AM, Su WP, Mason T, O'Fallon WM, Gabriel SE. The epidemiology of morphea (localized scleroderma) in Olmsted County 1960-1993. *J Rheumatol* 1997; **24**: 73-80.
8. Zulian F, Vallongo C, Woo P et al. Localized scleroderma in childhood is not just a skin disease. *Arthritis Rheum* 2005; **52**: 2873-81.

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# Vitamin K Deficiency Bleeding

## Key Points

- Since the withdrawal of Konakion Neonatal, the only product now licensed for intramuscular (IM) prophylaxis is Konakion MM. Published data about the long-term protection conferred by a single IM dose of this preparation, which has a completely different formulation from Konakion Neonatal, are very limited.
- Four of the seven cases of Vitamin K deficiency bleeding (VKDB) that occurred during the 2000-02 BPSU surveillance study received no prophylaxis because parents withheld their consent for IM prophylaxis.
- In equivocal cases of VKDB, measurement of PIVKA-II in as little as 10microlitres of serum/plasma allows retrospective confirmation of vitamin K (VK) deficiency days, even weeks, after presentation and treatment.

## Background

VKDB is a rare, potentially-handicapping or fatal condition (**Figure 28**), preventable by a combination of VK prophylaxis and surveillance for predisposing conditions, particularly liver disease<sup>1,2</sup>.

The three previous BPSU studies of VKDB have certainly informed practice. All UK units now provide VK prophylaxis<sup>3</sup> and there is greater awareness of the importance of investigating 'warning bleeds' and prolonged jaundice.

The third study (2000-02) found the rate of VKDB in the UK/Ireland to be the lowest recorded with no death or long-term morbidity, comparing favourably with published rates from abroad. Only seven cases of VKDB were reported; four received no prophylaxis (the parents having withheld consent for IM VK), one was reported to have received IM prophylaxis and two, oral prophylaxis<sup>2</sup>.



Figure 28: Bleeding from umbilicus due to VKDB



Dr A Busfield

At that time Konakion Neonatal was used by most of the 60% of units recommending IM prophylaxis. With exceedingly rare exceptions, a single 1mg IM dose of that preparation at birth was known to protect against VKDB for several months<sup>4</sup>. However, withholding of parental consent reduced the effectiveness of IM prophylaxis, calculated according to 'intention to treat', to a level similar to that of oral prophylaxis intended to continue beyond seven days<sup>3</sup>.

Since this study: first, Konakion Neonatal has been withdrawn; second, guidelines from the National Institute for Health and Clinical Excellence have recommended IM in preference to oral prophylaxis<sup>5</sup>. It seems inevitable that the use of IM prophylaxis with Konakion MM will increase, there now being no alternative, although published data about the 'long-term' protection it confers seems to be confined to an abstract of a study of 40 babies (half of them controls given Konakion Neonatal or equivalent) followed for only 14 days – hardly adequate when VKDB is so rare and the late form (which includes most cases of intracranial bleeding) has a peak incidence at six weeks<sup>6</sup>.

The Medicines and Healthcare Product Regulatory Agency advised surveillance following withdrawal of Konakion Neonatal. This fourth BPSU study, with data from a contemporaneous survey of VK prophylaxis practices in the same population, will provide the efficacy data required and not available elsewhere.

## Objectives

The study aims to document:

- Incidence of VKDB following the withdrawal of Konakion Neonatal.
- Effectiveness of prophylactic regimens in use, particularly Konakion MM 1mg IM as a single dose at birth.

- Outcomes following VKDB - death, intracranial bleed, significant sequelae.
- Risk factors in cases – maternal medication, breast feeding, liver disease, failure to thrive etc.
- Clinical presentation – warning bleeds, timing, site of bleed.
- Treatment given to correct bleeding.
- When parents withhold consent for VK, whether an alternative route of administration was offered.

## Surveillance period

October 2006 – October 2008 (inclusive).

## Methodology

### Case definition

Any infant under six months of age with spontaneous bruising, bleeding or intracranial haemorrhage associated with prolonged clotting (prothrombin time at least twice control value) and normal or raised platelet count, NOT due to an inherited coagulopathy or disseminated intravascular coagulation.

Cases will be classified as 'confirmed', 'possible' or 'no case' by the criteria used in the previous studies.

To allow international comparison, cases of *late* VKDB will also be classified in accordance with more stringent internationally-agreed criteria, which are:

Infants older than seven days with spontaneous bruising, bleeding or intracranial haemorrhage NOT due to an inherited coagulopathy or disseminated intravascular coagulation but associated with prothrombin time at least four times the control value AND at least one of the following:

- Platelet count normal or raised AND normal fibrinogen and/or absent fibrin degradation products.
- Normal prothrombin time after vitamin K administration.
- Concentration of undercarboxylated prothrombin (i.e. PIVKA-II) above normal controls.

### Reporting instructions

Please report any infant presenting with a bleeding disorder in the first six months of life where no alternative firm diagnosis (e.g. haemophilia, septicaemia with DIC) has been established; if there is suspicion of VKDB, please report the case.

### Expected numbers (per year)

0 -70 confirmed cases per year.

If current prophylaxis provided no protection we would expect an incidence of VKDB of about 1 in 10,000 (70 cases/year) amongst 'low risk' infants; the incidence in 'high risk' babies given no prophylaxis is unknown<sup>1</sup>.

### Denominator source

A contemporaneous survey of units in the study area will be undertaken to document the VK prophylaxis policies and annual delivery rate in each.

## Analysis

During the first six months of surveillance, October 2006 to March 2007, there have been 10 notifications of possible cases of VKDB. Of these, five fell outside the study period and are therefore excluded, leaving two confirmed case of VKDB, one duplicate report and two questionnaires not yet returned.

## Discussion

It is not possible to draw any conclusions at this early stage in the study, particularly as the incidence of the condition is so low and prophylaxis practices have not yet been surveyed.

It is very important any possible case of VKDB is notified; in such a rare condition the loss of even a single case from the study will significantly alter the calculated results for incidence of the condition and for effectiveness of prophylaxis.

In previous BPSU studies of VKDB, cases have occurred following omission of intended prophylaxis. In the most recent study, 2000-02, the reason for omission in each case was lack of parental consent for the recommended IM prophylaxis. Unfortunately information about whether an oral alternative was offered (and also refused) was not requested by investigators or offered by reporting clinicians. With the reduction in the incidence of VKDB this issue has become more significant and so in this study we request more information in cases not given prophylaxis.

Establishing a diagnosis of VKDB can be difficult. It should be emphasised that measurement of serum PIVKA-II can (with high specificity) give *retrospective* confirmation of VK deficiency days, even weeks, after treatment and normalisation of clotting. In VKDB intravenous VK alone may significantly improve clotting and stop bleeding in as little as 20-30 minutes<sup>7</sup> - however the exceedingly high serum PIVKA-II levels are unaffected by VK (or blood products) and, with a half life of about 60 hours, remain elevated for a long time (personal communication, Dr Martin Shearer). Dr Shearer can measure both VK and PIVKA-II levels in 0.5ml of serum/plasma, or PIVKA-II alone in as little as 10microlitres of serum/plasma, and is happy to offer this service to any contacting paediatrician – contact details, and the website for more about sample requirements, are given below<sup>8</sup>.

Please note the data presented are provisional, not peer reviewed and definitive conclusions should not be drawn from them.

## Funding

Roche Pharmaceuticals Ltd.

## Ethical approval

Obtained from the Cornwall Research Ethics Committee (ref.06/Q2101/74), site-specific approval for Trusts reporting cases is not required. The study also has Patient Information Advisory Group approval (ref. BPSU PIAG 03-04(FT5)/2006).

## Acknowledgements

We are grateful to the BPSU and all participating Paediatricians for their continued support. We would like to thank Roche for funding the study.

## References

1. McNinch AW, Tripp JH. Haemorrhagic disease of the newborn in the British Isles: two year prospective study. *BMJ* 1991;**303**:1105-9.
2. McNinch AW, Busfield A and Tripp JH. Vitamin K deficiency bleeding in infants in the Great Britain and Ireland: British Paediatric Unit Surveys 1993-94 and 2001-02. *Arch Dis Child*. – provisionally accepted for publication.
3. Busfield A, McNinch AW and Tripp JH. Neonatal vitamin K prophylaxis in Great Britain and Ireland: the impact of perceived risk and product licensing on effectiveness. *Arch Dis Child*. – provisionally accepted for publication.

4. Cornelissen M, von Kries R, Loughnan P, Schubiger G. Prevention of vitamin k deficiency bleeding: efficacy of different multiple oral dose schedules of vitamin k. *Eur J Paediatr* 1997 Feb;**156**(2):126-30.
5. National Institute for Health and Clinical Excellence. Postnatal care: Routine postnatal care of women and their babies. Clinical guideline CG37. July 2006.
6. Joubert P, Bolton K, Shearer M, Kneer J. Comparison of the effects of a mixed micellar and cremophor formulation of vitamin K, given intramuscularly to healthy neonates. *J Clin Pharmacol* (thirty-third annual ACCP meeting abstracts). 2004:1195.
7. Sutor AH, Kunzer W. Time interval between vitamin K administration and effective hemostasis. In: Perinatal Thrombosis and Haemostasis. Suzuki S, Hathaway WE, Bonnar J, Sutor AH, eds. Springer-Verlag, Berlin, Heidelberg, New York, London, Tokyo, Hong Kong 1991, pp 257-262.
8. Dr Martin J Shearer, Consultant Clinical Scientist & Honorary Senior Lecturer, Centre for Haemostasis and Thrombosis, 1st Floor North Wing, St Thomas' Hospital, London SE1 7EH. Tel: 020 7188 2801 (office), 020 7188 6815 (lab). E-mail: martin.shearer@gstt.nhs.uk Website: <http://keqas.com>

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# 7 New Studies 2007

## Genital Herpes in Children Under 11 years of Age Presenting to Secondary Care

### Background

Genital herpes in prepubertal children is rare, and when it occurs, raises the question of possible sexual abuse. Paediatricians currently have very little evidence on which to base an opinion on possible mode of transmission, yet their advice is key to whether or not a child protection investigation proceeds. A recently published literature review highlights both the inconsistency in current guidelines and the weakness of epidemiological data on this condition (Reading and Ranaan-Eliya, 2006).

This study will provide data on the incidence of genital herpes in young children in the UK, and describe clinical, social and other features which might point to possible modes of transmission (sexual and non-sexual). It will not be able to confirm the mode of transmission because there is no way of definitively ascertaining whether sexual abuse has occurred or not. However, indicative data on anything more than a handful of cases are currently not available.

A national surveillance study is necessary to provide such data because of the rarity of the condition, the need to collect true population based data to eliminate referral bias, and because most cases will be referred to a paediatrician at some stage in the initial presentation because of the child protection implications.

### Objectives

The study aims to

- estimate the incidence of genital herpes in children < 11 years in the UK and Ireland by age and sex
- describe the clinical presentation of cases
- describe clinical, developmental and social features which might indicate possible modes of transmission
- describe the extent and outcome of child protection enquiries consequent on a diagnosis of genital herpes.

### Surveillance period

April 2007 - April 2008 (inclusive).

### Methodology

Paediatricians reporting a case through the orange card system will be asked to complete a questionnaire seeking information on infant diagnosis, management and outcomes. A further follow-up questionnaire will be sent when the infant is one year of age.

### Case definition

Children age one month to ten years inclusive with typical herpetic vesicular lesions in genital or perineal area presenting as new cases to secondary care (includes recurrent cases seen for the first time in secondary care).

- Proven cases: Herpes simplex isolated by viral culture, or PCR in association with typical lesions.
- Suspected cases: Supportive evidence in addition to typical clinical lesions, e.g. rising paired antibody titres, viral culture from lesions elsewhere (such as oral lesions), giant multinuclear cells on cytology or positive viral culture in a physical contact.

**Exclude:** Recurrent lesions previously identified and seen in secondary care. No viral isolation and no supportive clinical or virological evidence.

### Reporting instructions

Please report any case first seen or known to reporting clinician in the last month that meets the case definition even if you believe it may have been reported by someone else. This particularly applies if you have been consulted by a non-paediatrician, e.g. a forensic medical examiner or a genito-urinary physician. Please note that notification to the BPSU does not replace other forms of reporting genital herpes infection to the HPA.

### Expected numbers

20 – 30 cases per year.

### Source of denominator data

Office of National Statistics population estimates for the <11 population.

### Funding

Birmingham Children's Hospital Research Fund.

### Support group

The Herpes Viruses Association,  
41 North Road, London N7 9DP  
Telephone helpline: 0845 1232305  
Web:<http://www.herpes.org.uk>

### Ethics approval

This study has been approved by the London MREC (Ref: 07/MRE02/9) and has been granted PIAG Section 60 Support (Ref: 4-06(FT6)/2006).

### References

1. Health Protection Agency. STI data resource page. Retrieved Sep 14th 2005 from [http://www.hpa.org.uk/infections/topics\\_az/hiv\\_and\\_sti/epidemiology/dataresource.htm](http://www.hpa.org.uk/infections/topics_az/hiv_and_sti/epidemiology/dataresource.htm)
2. Reading R, Rannan-Eliya Y. Evidence for sexual transmission of genital herpes in children. *Arch Dis Child* 2006 ADC Published Online First: 5 December 2006. <http://dx.doi.org/10.1136/adc.2005.086835>
3. Scoular A. Using the evidence base on genital herpes: optimising the use of diagnostic tests and information provision. *Sexually Transmitted Infections* 2002;**78**:160-165

### Supporting information for paediatricians

1. Department for Education and Skills. Working together to safeguard children. (2006) The Stationary Office <http://www.everychildmatters.gov.uk/resources-and-practice/IG00060>
2. Royal College of Paediatrics and Child Health. *Child Protection Companion*. RCPCH, 2006 <http://www.rcpch.ac.uk/publications/publications-list-by-title#c>
3. Royal College of Physicians. Physical signs of sexual abuse. London: RCP, 1997 Thomas A, Forster G, Robinson A, Rogstad K, Clinical Effectiveness Group. (2003) National guideline for the management of suspected sexually transmitted infections in children and young people. *Sex Transm Inf* 2002;**78**:324-331.

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# Idiopathic Intracranial Hypertension (IIH)

## Background

Idiopathic intracranial hypertension (IIH), previously known as pseudotumour cerebri or benign intracranial hypertension, is a rare condition of raised cerebrospinal fluid (fluid within the cavities of the brain and spine) pressure without any identifiable pathology. Although IIH is most common in obese young women, it is also well recognized that both genders in children are equally affected<sup>1</sup>. Despite intervention, the clinical course of IIH is often prolonged and fluctuating with potential complications of distressing headache and blindness<sup>2-8</sup>. The overall (including children and adult) incidence of IIH is one to three in every 100,000 people per year<sup>9,10</sup>, however the epidemiological data on childhood IIH to date are sparse and limited to hospital based retrospective case series<sup>11,12</sup>.

## Objectives

The research objectives for this study are to determine the:

- incidence of IIH in children aged 1 to 16 years in the UK and Ireland
- age specific patterns of clinical presentation of IIH in children
- national incidences of established association factors (in particularly with obesity) at presentation
- frequency and spectrum of visual disturbances at presentation
- current various initial clinical management of children with IIH
- clinical course of the headache and spectrum of the visual outcome in this national cohort one-year post diagnosis following various treatment modalities. We aim to use an additional follow-up joint paediatrician and ophthalmologist questionnaire to facilitate this prospective review.

## Surveillance period

July 2007 – July 2008.

## Methodology

### Case definition

Any child aged 1 to 16 years (not including 17<sup>th</sup> birthday) who fulfils at least two of the key features and all of the three essential criteria.

Key features (at least two have to be satisfied):

- Symptoms of raised cerebrospinal fluid (fluid within the cavities of the brain and spine) pressure i.e. headache, nausea, vomiting or irritability and/or visual symptoms of double or blurring vision, or transient visual loss
- Papilloedema, swelling of the optic disc (at the back of the eye where the optic nerve enters) of one or both eyes
- Raised opening cerebrospinal fluid pressure above 20 cm by lumbar puncture (spinal tap into the lower back).

### AND

Essential criteria (all three have to be satisfied):

- Normal level of consciousness
- Brain neuroimaging (including computerised tomography, magnetic resonance imaging and magnetic resonance venography i.e. radiological studies of veins) does not reveal a structural cause to explain the presenting symptoms or signs of raised cerebrospinal fluid pressure e.g. dilatation of ventricles (of a series of connecting cavities in the brain), cerebral or vascular lesion
- Normal cerebrospinal fluid contents (for atraumatic tap, white cell count less or equal to 5 x 1,000,000/L, protein less than 0.4 g/L and ratio of cerebrospinal fluid glucose to plasma glucose more than or equal to 0.6).

### Excluding

- \* Sinus venous thrombosis whose neuroimaging appearances can be difficult to distinguish from venous obstruction related to raised intracranial pressure. Please report if in doubt or if case was excluded due to sinus venous thrombosis.

### Caution

Optic nerve head Drusen (a degenerative condition consists of deposits of hyaline material within the

optic nerve head which results in an apparent elevation or swelling of the optic disc) can mimic papilloedema. However, papilloedema can occur in Drusen, their differentiation can be made by optic ultrasound and/or orbital CT scan.

### Reporting instructions

Any child aged 1-16 years (not including 17<sup>th</sup> birthday) seen in the past month who fulfil at least two of the three key features and all of the three essential criteria:

### Expected numbers

390 cases are expected. This estimate is based on the local survey in Coventry over the past three years (2002-05) where an average of two children were diagnosed of IIH per year.

### Source of denominator data

Office of National Statistics ([www.statistics.gov.uk](http://www.statistics.gov.uk)).

### Funding

Sir Peter Tizard Bursary.

### Ethical approval

This study has been approved by the East London and the City Research Ethics Committee (Ref: 07/Q0603/47) and the Patient Information advisory Group (Ref:PIAG/BPSU-2-05(FT3/2007)).

### References

1. Scott IU, Siatkowski RM, Eneyni M, Brodsky MC, Lam BL. Idiopathic intracranial hypertension in children and adolescents. *Am J Ophthalmol* 1997;**124**(2):253-5.
2. Salman MS, Kirkham FJ, MacGregor DL. Idiopathic "benign" intracranial hypertension: case series and review. *J Child Neurol* 2001; **16**(7):465-70.

3. Youroukos S, Psychou F, Fryssiras S, Paikos P, Nicolaidou P. Idiopathic intracranial hypertension in children. *J Child Neurol* 2000;**15**(7):453-7.
4. Phillips PH, Repka MX, Lambert SR. Pseudotumor cerebri in children. *J Aapos* 1998;**2**(1):33-8.
5. Babikian P, Corbett J, Bell W. Idiopathic intracranial hypertension in children: the Iowa experience. *J Child Neurol* 1994;**9**(2):144-9.
6. Lessell S, Rosman NP. Permanent visual impairment in childhood pseudotumor cerebri. *Arch Neurol* 1986;**43**(8):801-4.
7. Couch R, Camfield PR, Tibbles JA. The changing picture of pseudotumor cerebri in children. *Can J Neurol Sci* 1985;**12**(1):48-50.
8. Baker RS, Carter D, Hendrick EB, Buncic JR. Visual loss in pseudotumor cerebri of childhood. A follow-up study. *Arch Ophthalmol* 1985;**103**(11):1681-6.
9. Durcan FJ, Corbett JJ, Wall M. The incidence of pseudotumor cerebri. Population studies in Iowa and Louisiana. *Arch Neurol* 1988;**45**(8):875-7.
10. Radhakrishnan K, Ahlskog JE, Garrity JA, Kurland LT. Idiopathic intracranial hypertension. *Mayo Clin Proc* 1994; **69**(2):169-80.
11. Gordon K. Pediatric pseudotumor cerebri: descriptive epidemiology. *Can J Neurol Sci* 1997 **24**(3):219-21.
12. Craig JJ, Mulholland DA, Gibson JM. Idiopathic intracranial hypertension; incidence, presenting features and outcome in Northern Ireland (1991-1995). *Ulster Med J* 2001;**70**(1):31-5.

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## 8 International Network of Paediatric Surveillance Units (INoPSU)



Figure 29: International Network of Paediatric Surveillance Units (INoPSU)

### Background

Following the success of the BPSU, the same methodology was adopted and adapted in the 1990s to other countries who wished to set up active paediatric surveillance systems. In 1992, surveillance units were established in the Netherlands and Germany and in 1994 Switzerland. The European paediatric surveillance units then met and communicated regularly in order to discuss surveillance protocols.

The European initiative was also the stimulus for the development in 1992 of an Australian unit and later the Malaysian unit (1994) to be followed by units in Canada (1996), Papua New Guinea (1996), New Zealand and Latvia (1997), Portugal (2001) and Greece/Cyprus (2003). Wales (1994) and Republic of Ireland (1996) developed surveillance units using a similar methodology to the BPSU, but are including on more common disorders in their surveillance (Table 15).

Through the use of active ascertainment, the aforementioned units provide an efficient, effective framework for case finding for investigators who wish to study rare conditions in children. Conditions under surveillance include infections, infection-related conditions, vaccine-preventable diseases, congenital and inherited (genetic) diseases, unusual injuries or therapies and rare complications of common

diseases. The units frequently encourage, facilitate or elicit studies undertaken by clinical investigators but only occasionally undertake research themselves.

In 1998 an International Network of Paediatric Surveillance Units (INoPSU) was formed by existing units during the 22<sup>nd</sup> International Congress of Paediatrics in Amsterdam, The Netherlands. The first INoPSU conference was held in June 2000 in Ottawa, Canada, the second in April 2002 in York, UK and the 3<sup>rd</sup> in May 2004 in Lisbon, Portugal. Two non-paediatric surveillance units have affiliated to INoPSU, these being the British Ophthalmology Surveillance Unit and UK obstetric surveillance system. Now all the units contact each other for results, sharing of protocols and to put researchers in different countries in touch with each other. A common website [www.inopsu.com](http://www.inopsu.com) and yearly international report is shared as part of the national reports.

The mission of INoPSU is the advancement of knowledge of rare and uncommon childhood infections and disorders and the participation of paediatricians in surveillance on a national and international basis so as to achieve a series of benefits to clinical practice and health policy. A document, known as the Amsterdam-Ottawa Note, details the functions and structure of the network and has been posted on the INoPSU website.

The 4<sup>th</sup> INoPSU conference was held in London in May 2006 alongside the BPSU's 20th anniversary celebrations (Figure 30). At this meeting Rudi von Kries stepped down as convenor to be replaced by Rob Rodrigues Pereira of The Netherlands and he will be supported by Daniel Virella from the Portuguese Unit. At the meeting it was reported that unfortunately, due to a lack of support, the Malaysian, and Papua New Guinea units have ceased surveillance.

At the INoPSU business meeting the units agreed to fund a part-time administrator to take forward the objectives of INoPSU.

Table 15: National paediatric surveillance units

Country	Child population (10 <sup>6</sup> - aged 0-15 years)	Established	Respondents	Card &/or Email	Response rate
Australia	3.9	1992	1110	C/E	89%
British Isles	12.8	1986	2550	C	93%
Canada	7.5	1996	2550	E	82%
Germany	12.0	1992	462	C/E	98%
Greece/Cyprus	1.6	2001	110	C	93%
Ireland	1.0	1996	150	C	80%
Latvia	0.4	1996	8	E	70%
Netherlands	3.0	1992	640	C/E	100%
New Zealand	0.8	1997	208	C/E	94%
Portugal	1.8	2001	1800	C/E	33%
Switzerland	1.3	1995	100	C	100%
Wales	0.65	1994	158	C	100%

(A report of the conference is included in the 20th BPSU annual report.)

A funding application to the EU Framework 7 programme has been submitted, which we hope will be considered favourably. The funds will allow us to improve collaboration between the units and increase networking between other rare disease organisations.

Over the past two years, INoPSU countries have facilitated the surveillance of 70 different rare conditions (Table 16) and have now undertaken over 150 studies, covering a child population of over 50 million and involving over 10,000 clinicians. Details on all the activities of each surveillance unit is available from their respective websites and also from the INoPSU website ([www.inopsu.com](http://www.inopsu.com)).



Figure 30: INoPSU Delegates

**Table 16: Conditions under surveillance 2006-07**

Condition	Country
Acquired demyelinating syndromes of the central nervous system	Canada
Acute encephalitis and encephalomyelitis	Portugal
Acute flaccid paralysis	Australia, Canada, New Zealand, Switzerland
Acute rheumatic fever	Australia, Canada, Switzerland
Adverse drug reactions – serious and life-threatening	Canada, New Zealand
Alcohol intoxication	Netherlands
Ambiguous genitals	Netherlands
Anaphylaxis in childhood	Germany, Switzerland
Anorexia nervosa	Netherlands
Arthritic syndrome	Latvia
Bleeding complications after adenotomy/tonsillectomy in children	Germany
Cerebral palsy among 5-years-olds	Portugal
Child abuse	Netherlands
Child death review pilot	Wales
Chronic fatigue syndrome	Netherlands
Chronic interstitial lung disease	Germany
Complications of measles	Germany
Congenital adrenal hyperplasia - Non CAH Primary Adrenal Insufficiency	Ireland
Congenital cytomegalovirus	Australia, Canada, Portugal
Congenital hydronefrosis	Netherlands
Congenital myotonic dystrophy	Canada
Congenital rubella (with defects)	Australia, British Isles, Netherlands, New Zealand, Switzerland
Congenital toxoplasmosis	Greece, Portugal
Congenital varicella	Australia
Craniosynostosis	Wales
Cystic fibrosis	Netherlands
Diabetes mellitus under 5 years / Insulin-dependend Diabetes mellitus	Germany, Netherlands
Early onset eating disorder	Australia, British Isles
Fatal and near-fatal asthma	Germany
Fetal Alcohol Syndrome	Netherlands
FMAIT	British Isles
Gall stones in childhood	Wales
Genetic-based severe early hearing impairment	Portugal
Haemoglobinopathies	Australia, Netherlands
Haemolytic uraemic syndrome	Greece, New Zealand, Portugal, Switzerland
Head injury secondary to suspected child maltreatment (abuse or neglect)	Canada
Hepatitis C virus infection	Australia
Hereditary periodic fever syndrome	Germany
Genital herpes in under 11 year olds	British Isles
HIV	British Isles, New Zealand
Hyperbillirubinaemia	Canada, Netherlands, Switzerland
Hyperinsulinaemic hypoglycaemia	Australia, New Zealand
Hypernatraemia	Wales

**Table 16 Cont: Conditions under surveillance 2006-07**

<b>Condition</b>	<b>Country</b>
Inherited neuromuscular disorders	Australia
Intussusception	Australia ,British Isles, Latvia
Idiopathic intracranial hypertension	British Isles
Inborn errors of metabolism	New Zealand
Influenza-associated intensive care and death cases among children and adolescents	Germany
Intractable asthma	Netherlands
Invasive Haemophilus influenzae infections (all types)	Germany
Juvenile idiopathic arthritis	Wales
Kawasaki disease	Portugal
Long term ventilation	Wales
Malaria	British Isles, Portugal
MCADD	British Isles, Canada, Netherlands
Morbid obesity	Netherlands
MRSA	British Isles
Multiple sclerosis	Netherlands
Neonatal group B streptococcus sepsis	Australia, Portugal
Neonatal herpes simplex virus infection	Australia, British Isles, Switzerland
Neonatal sinus venous thrombosis	Germany
Neonatal varicella	Australia
Nephrotic syndrome	Germany
Neuroborreliosis	Netherlands
Neural tube defects	Switzerland
Non CF bronchiectasis	Ireland
Non tuberculosis mycobacterial infection (NTMI)	Australia
Non-type 1 diabetes mellitus	Canada, Latvia, Wales
Nosebleeds in Infancy	Wales
Peanut allergy	Ireland
Perinatal exposure to HIV	Australia
Perinatal infection after exposure to HIV	Australia
Pertussis	Switzerland
Progressive Intellectual and Neurological Deterioration	British Isles
Pneumococcal sepsis/Meningitis	Germany ,New Zealand
Rett syndrome	Australia
Scleroderma	British Isles
Serious seatbelt injuries	Australia
Severe bronchiolitis requiring ICH/HUD care	Ireland
Severe combined immunodeficiency	Canada
Severe complications of varicella infection	Australia, Ireland, Netherlands
Severe retinopathy of prematurity	Latvia
Shaken baby syndrome	Switzerland
Stroke & transient ischaemic attacks	Ireland
Systemic lupus erythematosus	Germany
Transfusion-related acute lung injury	Canada
Varicella zoster complications	Netherlands
Vitamin D deficiency rickets	Australia, Ireland
Vitamin K deficiency bleeding	Australia, British Isles, New Zealand, Switzerland
VVZ among hospitalized children and adolescents	Portugal

## APPENDIX A - Completed Studies 1986-2006

By mid-2006 the BPSU had completed 60 studies. Information about these studies has been included in previous annual reports of the BPSU, which are available from the BPSU office and are also listed on the BPSU website.

### **X-linked anhydrotic ectodermal dysplasia**

Surveillance Period: June 1986 - August 1986  
Investigator: Dr A Clarke  
Published paper: X-linked anhydrotic ectodermal dysplasia. Clarke D. BPSU 2nd Annual Report 1987. BPSU London

### **Haemorrhagic shock encephalopathy syndrome**

Surveillance Period: June 1986 - December 1988  
Investigator: Dr S Hall  
Published paper: Haemorrhagic Shock Encephalopathy Syndrome in the British Isles. Bacon CJ, Hall SM. *Arch Dis Child* 1992; **67**: 985-993

### **Haemolytic uraemic syndrome**

Surveillance Period: June 1986 - December 1989  
Investigators: Dr C M Taylor, Dr D Milford, Dr S Hall  
Published paper: Haemolytic Uraemic Syndrome in the British Isles 1985-88; Association with Verocytotoxin-Producing *E.coli*: Milford DV, Taylor CM, Guttridge B, Hall SM, Rowe B, Kleanthous H. *Arch Dis Child* 1990; **65**: 716-72.

### **Kawasaki disease**

Surveillance Period: June 1986 - December 1992  
Investigator: Dr S Hall  
Published paper: Kawasaki Disease in the British Isles. A survey of management: Dhillon R, Newton L, Rudd PT, Hall SM *Arch. Dis. Child* 1993; **69**: 631-638  
Kawasaki disease - Lessons for Britain: Bissenden JG, Hall SM. *BMJ* 1990; **300**: 1025-1026.

### **Low syndrome**

Surveillance Period: June 1986 - February 1988  
Investigator: Dr C McKeown  
Published paper: Lowe Syndrome. McKeown C. BPSU 2<sup>nd</sup> Annual Report. 1987. BPSU London

### **Neonatal herpes**

Surveillance Period: June 1986 - December 1991  
Investigators: Ms PA Tookey, Professor C S Peckham, Dr R Dinwiddie  
Published paper: Neonatal herpes simplex virus infection in the British Isles: Tookey P, Peckham CS. *Paediatr Perinat Epidemiol* 1997; **10**: 432-442.

### **Insulin dependent diabetes in under fifteens**

Surveillance Period: January 1988 - December 1988  
Investigator: Professor J D Baum  
Published paper: Incidence of Insulin Dependent Diabetes in Children Aged Under 15 Years in the British Isles During 1988: Metcalfe MA, Baum JD. *BMJ* 1991; **302**: 443-447.

### **Drowning and near drowning**

Surveillance Period: January 1988 - December 1989  
Investigators: Professor J Sibert, Dr A Kemp  
Published paper: Drowning and near drowning in children in the United Kingdom: lessons for prevention: Kemp A, Sibert JR. *BMJ* 1992; **306**: 291-297  
Outcome in Children Who Nearly Drown: a British Isles Study: Kemp AM, Sibert JR. *BMJ* 1991; **302**: 931-933.

### **Haemorrhagic disease of the newborn**

Surveillance Period: March 1988 - February 1990  
Investigators: Dr AW McNinch, Dr H Tripp  
Published paper: Haemorrhagic Disease of the Newborn in the British Isles: a two year prospective study: McNinch AW, Tripp JH. *BMJ* 1991; **303**: 1105-1109.

### **Galactosaemia**

Surveillance Period: January 1988 - September 1991  
Investigators: Mrs A Green, Dr J Holton, Dr M Honeyman, Professor J Leonard  
Published paper: Galactosaemia, Results of the British Paediatric Surveillance Study 1988-90: Honeyman MM, Green A, Holton JB, Leonard JV. *Arch Dis Child* 1993; **69**: 339-341.

### **Congenital toxoplasmosis**

Surveillance Period: June 1989 - May 1990  
Investigator: Dr S Hall  
Published paper: Screening for Toxoplasmosis during pregnancy: Peckham CS, Logan S. *Arch Dis Child* 1993; **68**: 3-50.

### **Higher order births**

Surveillance Period: January 1989 - December 1989  
Investigator: Professor M Levene  
Published paper: Higher multiple births and the modern management of infertility in Britain. For the British Association of Perinatal Medicine: Levene MI, Wild J, Steer P. *Br J Obst Gynaecol* 1992; **99**: 607-613.

### **Acute rheumatic fever**

Surveillance Period: January 1990 - December 1990

Investigators: Dr C Boyd-Scobie, Dr S Hall

Published paper: BPSU 5<sup>th</sup> Annual Report 1990. BPSU London 1990

### **Rett syndrome**

Surveillance Period: April 1990 - June 1990

Investigator: Dr A Kerr

Published paper: Rett Syndrome: British Longitudinal Study (1982-1990) and 1990 Survey. In Mental Retardation and Medical Care. Roosendaal JJ (ed.). Uitgeverij Kerckebosch, Zeist 1991

### **Measles, mumps, rubella-meningococcal meningitis**

Surveillance Period: January 1990 - December 1991

Investigator: Dr N Begg

Published paper: Meningoencephalitis associated with MMR vaccine: Maguire HC, Begg NT, Handford SC. *Communicable Disease Report* 1991; **1** (6): R57-R59.

### **Chemistry set poisoning**

Surveillance Period: January 1991 - April 1992

Investigator: Dr E Mucklow

Published paper: Chemistry Set Poisoning: Mucklow ES. *Internat. Journ. Clin. Pract* 1997; **51.5**: 321-23.

### **Acute flaccid paralysis**

Surveillance Period: July 1991- June 1994

Investigator: Dr N Begg

Published paper: Polio Eradication: Surveillance Implications for the United Kingdom: Salisbury DM, Ramsay ME, White JM, Brown DW. *Infect. Dis* 1997; **175** (Suppl 1): S156-9.

### **Androgen insensitivity syndrome**

Surveillance Period: September 1991 - August 1993

Investigator: Professor IA Hughes

Published paper: Androgen Insensitivity syndrome: a survey of diagnostic procedures and management in the UK. Viner RM, Teoh Y, Williams DM, Patterson MN, Hughes IA. *Arch Dis Child* 1997; **77**: 305-309.

### **Long term parenteral nutrition**

Surveillance Period: February 1992 - April 1992

Investigators: Professor D Candy, Professor E Ross, Dr S P Devane

Published paper: Survey of children on long term parenteral nutrition, UK and Eire 1992. Devane S P. Abstract RCPCH Scientific Meeting 1993.

### **Insulin dependent diabetes in under fives**

Surveillance Period: January 1992 - December 1992

Investigators: Professor JD Baum, Ms E Wadsworth

Published Paper: Insulin dependent diabetes in children under five: incidence and ascertainment validation for 1992. *BMJ* 1995; **67**: 700-703.

Dermatoglyphics, fetal growth and insulin dependent diabetes in children under five: Shield JP, Wadsworth EJ, Hobbs K, Baum JD. *Arch Dis Child* 1995 **72**(2): 159-60.

### **Juvenile dermatomyositis**

Surveillance Period: June 1992 - December 1993

Investigators: Dr D Symmons, Dr A Sills

Published paper: The incidence of juvenile dermatomyositis: results from a nationwide study: Symmons DP, Sills JA, Davis SM. *Br J Rheumatol* 1995; **34**: 732-736.

### **Congenital dislocation of the hip**

Surveillance Period: April 1993 - July 1993

Investigators: Dr C Dezateux, Dr S Godward

Published paper: A national survey of screening for congenital dislocation of the hip: Dezateux C, Godward S. *Arch Dis Child* 1996; **74**: 445-448.

Screening for congenital dislocation of the hip in the newborn and young infants. Dezateux C, Godward S. Edinburgh 1997; Churchill Livingstone

### **Haemophagocytic lymphohistiocytosis**

Surveillance Period: September 1991 - August 1994

Investigators; Professor S Strobel, Dr M Taylor,

Dr J Pritchard

Published paper: 10<sup>th</sup> BPSU Annual Report 1995/96. BPSU London 1995

### **Non-accidental poisoning/ Munchausen syndrome by proxy**

Surveillance Period: September 1992- August 1994

Investigator: Dr P Davis, Professor J Sibert, Professor SR Meadow, Dr R McClure

Published paper: The epidemiology of Munchausen Syndrome by Proxy, Non-accidental poisoning and Non-accidental suffocation: McClure RJ, Davis PM, Meadow SR, Sibert JR. *Arch Dis Child*. 1996; **75**: 57-61.

### **Neonatal necrotising enterocolitis**

Surveillance Period: October 1993 - October 1994

Investigators: Professor A Lucas, Ms R Abbott

Published Paper: Neonatal necrotising enterocolitis: 11<sup>th</sup> BPSU Annual Report 1996/7. London 1997

### **Vitamin K deficiency bleeding II**

Surveillance Period: January 1993 - December 1994  
Investigators: Dr A McNinch, Dr J Tripp  
Vitamin K Deficiency Bleeding: McNinch A, Tripp J  
Published paper: 9<sup>th</sup> BPSU Annual Report 1993/94.  
BPSU London 1994

### **Biliary Atresia**

Surveillance Period: March 1993 - February 1995  
Investigators: Dr JP McKiernan, Dr D Kelly,  
Dr AJ Baker  
Published paper: Thr frequency and outcome of  
biliary atresia in the UK and Ireland. McKiernan  
JP, Baker AJ, Kelly D. *Lancet* 2000; **355**: 25 - 29.

### **Transient and permanent neonatal diabetes**

Surveillance Period: July 1994- August 1995  
Investigator: Dr J Shield, Professor JD Baum,  
Ms E Wadsworth  
Published paper: Aetiopathology and genetic  
basis of neonatal diabetes: Shield JP, Gardner  
RJ, Wadsworth EJ, Whiteford ML, James RS,  
Robinson DO, Baum JD, Temple IK. *Arch Dis  
Child* 1997; **76**: F39-F42.

### **Adverse neonatal outcomes of delivery or labour in water**

Surveillance Period: April 1994- April 1996  
Investigators: Ms P Tookey, Dr R Gilbert  
Published paper: Labour and birth in water in England  
and Wales. Aldernice F, Renfrew M, Marchant S,  
Ashurst H, et al. *BMJ* 1995; **310**: 837  
Perinatal mortality and morbidity among babies  
delivered in water: surveillance study and postal survey  
Gilbert R E and Tookey P A. *BMJ* 1999; **319**: 483-487.

### **Congenital syphilis**

Surveillance Period: July 1993 - July 1996  
Investigators: Dr A Nicoll, Dr T Lissauer  
Published paper: Syphilis in pregnant women and  
their children in the United Kingdom: results from  
national clinician reporting surveys: Hurtig A-K,  
Nicoll A, Carne C, Lissauer T et al. *BMJ* 1998; **317**:  
1617-9.

### **Congenital cataract**

Surveillance Period: October 1995 - October 1996  
Investigator: Dr J Rahi  
Published paper: National cross sectional study of  
detection of congenital and infantile cataract in the  
United Kingdom: role of childhood screening and  
surveillance:  
Rahi JS, Dezateux C. *BMJ* 1999; **318**: 362-365  
Capture-recapture analysis of ascertainment  
by active surveillance in the British Congenital  
Cataract Study: Rahi JS, Dezateux C, for the  
British Congenital Cataract Interest Group: *Invest.  
Ophthalmol. Vis. Sci.* 1999; **40**: 236-239.

### **Medium chain acyl-CoA dehydrogenase**

Surveillance Period: March 1994 - March 1996  
Investigators: Dr R J Pollitt, Prof J Leonad  
Published paper: Prospective surveillance study of  
medium-chain CoA dehydrogenase deficiency in  
the United Kingdom: Pollitt RJ, Leonard JV. *Arch  
Dis Child* 1998; **79**: 116-119.  
Neonatal screening for inborn errors of metabolism:  
cost, yield and outcome: Pollitt R J, Green A,  
McCabe CJ, et al. Health Technology Assessment  
Report 1997

### **Pyroxidine dependent seizures**

Surveillance Period: September 1995 - October 1996  
Investigator: Dr P Baxter  
Published paper: Epidemiology of pyridoxine  
dependent and pyridoxine responsive seizures in the  
UK. Baxter P. *Arch Dis Child.* 1999; **81(5)**: 431-3.

### **Neonatal meningitis**

Surveillance Period: July 1996 - December 1997  
Investigators: Dr D Holt, Mrs S Halkett  
Published paper: Neonatal meningitis in England  
and Wales: 10 years on. Holt DE, Halket S, de  
Louvois J, Harvey D. *Arch Dis Child Fetal Ed*  
2001; **84**:F85-F89.

### **Cerebral oedema and death following diabetic ketoacidosis**

Surveillance Period: October 1995 - September  
1998  
Investigators: Dr J Edge, Dr M Hawkins  
Published paper: The risk and outcome if cerebral  
oedema developing during diabetic ketoacidosis.  
Edge JA Hawkins MA, Winter DL, Dunger DB.  
*Arch Dis Child* 2000; **85**: 16-22.

### **Hepatitis C virus (HCV) infection**

Surveillance Period: March 1997 - March 1999  
Investigators: Dr D Gibb, Ms P Neave  
Published paper: Active surveillance of hepatitis C  
infection in the UK and Ireland.  
Gibb DM, Neave PE, Tookey PA, Ramsay M,  
Harris H, Balogun K, Goldberg D, Mieli-Vergani G,  
Kelly D. *Arch Dis Child* 2000; **82(4)**: 286-91.

### **Congenital brachial palsy**

Surveillance Period: March 1998- March 1999  
Investigators: Dr G Evans-Jones, Mr S P J Kay,  
Professor M Weindling  
Published paper: Congenital brachial palsy:  
incidence, causes, and outcome in the United  
Kingdom and Republic of Ireland. Evans-Jones  
G, Kay S P J, Weindling A M, Cranny G, Ward  
A, Bradshaw A, Herson C. *Arch Dis Child Fetal  
Neonatal Ed.* 2003; **88**: F185-F189.

### **Subdural haematoma and effusion**

Surveillance Period: April 1998- April 1999

Investigators: Dr C Hobbs, Dr J Wynne, Dr A M Childs

Published paper: Subdural haematoma and effusion in infancy: an epidemiological study. *Arch Dis Child* 2005 Sep; **90(9)**: 952-5.

### **Inflammatory bowel disease in under 20 year olds**

Surveillance Period: June 1998-June 1999

Investigators: Professor B Sandhu, Dr A Sawczenko  
Published paper: Prospective survey of childhood inflammatory bowel disease in the British Isles  
Sawczenko A, Sandhu B K Logan, R F A, Jenkins H, Taylor C J, Mian S, Lynn R. *Lancet* 2001; **357**: 1095-96.

### **Fatal/Severe allergic reactions to food ingestion**

Surveillance Period: March 1998 - February 2000

Investigators: Dr A Colver, Dr A Cant, Dr C MacDougall

Published paper: How dangerous is food allergy in childhood? The incidence of severe and fatal allergic reactions across the UK and Ireland. Macdougall CF, Cant AJ, Colver AF. *Arch Dis Child* 2002; **86**: 236-239.

### **Invasive Haemophilus influenzae infection**

Surveillance Period: October 1992-October 2000

Investigators: Dr P Heath, Dr J McVernon, Professor R Booy

Published paper: Vaccine failures after primary immunisation with Haemophilus influenza type-b conjugate vaccine without booster. Booy R, Heath PT, Slack MPE, Begg, N, Moxon ER. *Lancet* 1997; **349**:1197-202.

### **Severe Visual Impairment /Blindness**

Surveillance Period: September 1999- December 2000

Investigator: Dr JS Rahi, N Cable, on behalf of the British Childhood Visual Impairment Study Group (BCVISG)

Published paper: Severe visual impairment and blindness in children in the UK. Rahi JS, Cable N. on behalf of the British Childhood Visual Impairment Study Group (BCVISG). *Lancet* 2003; **362**: 1359-65.

### **Haemolytic Uraemic Syndrome II**

Surveillance Period: February 1997- February 2001

Investigators: Dr M Taylor, Dr D Milford, Dr B Adak, Mr R Lynn, Dr M Locking, Dr S O'Brien

Published paper: Childhood hemolytic uremic syndrome, United Kingdom and Ireland. Lynn RM, O'Brien SJ, Taylor CM, Adak GK, Chart H, Cheasty T, Coia JE, Gillespie IA, Locking ME, Reilly WJ, Smith HR, Waters A, Willshaw GA. *Emerg Infect Dis* 2005 Apr; **11(4)**: 590-6.

### **Group B Streptococcal Disease**

Surveillance Period: March 2000 - March 2001

Investigator: Dr P Heath

Published paper: Group B streptococcal disease in UK and Irish infants younger than 90 days. Heath PT, Balfou G Weisner AW, Efstratiou A, Lamagni, TL, Tighe H, O'Connell LAF, Cafferkey M, Verlander NQ, Nicoll A, McCartney CA, on behalf of the PHLS GBS Working Group. *Lancet* 2004; **363**: 292-94.

### **Reye's Syndrome**

Surveillance Period: June 1986 - June 2001

Investigators: Dr S Hall, Mr R Lynn

Published paper: 15<sup>th</sup> BPSU Annual Report 2000/01. BPSU London 2001

### **Subacute Sclerosing Panencephalitis**

Surveillance Period: June 1986 - June 2001

Investigator: Dr E Miler

Published paper: The epidemiology of subacute sclerosing panencephalitis in England and Wales 1990-2002. Miller C, Andrews N, Rush M, Munro H, Jin L, Miller E. *Arch Dis Child* 2004; **89(12)**: 1145-8.

### **Encephalitis in Early Childhood (2 months – 3 years)**

Surveillance Period: October 1998 – September 2001

Investigators: Dr K Ward, Professor E Ross

Published paper: Human herpesviruses-6 and -7 each cause significant neurological morbidity in Britain and Ireland. Ward K N, Andrews N J, Verity C M, Miller E, Ross E M. *Arch Dis Child* 2005; **90**: 619-623.

### **Cerebrovascular disease, stroke and like illness**

Surveillance Period: January 2001 - January 2002

Investigators: Dr F Kirkham, Dr A Williams

Published paper: 17<sup>th</sup> BPSU Annual Report 2002/03. BPSU London 2003

### **Vitamin K deficiency bleeding III**

Surveillance Period: January 2002 - January 2003

Investigators: Dr A W McNinch, Dr J H Tripp

Published paper: Vitamin K deficiency bleeding in Great Britain and Ireland; British Paediatric Surveillance Unit Surveys, 1993-94 and 2001-02 McNinch A, Busfield A, Tripp JH. *Arch Dis Child* online 30 May 2007; doi:10.1136/adc.2006.104752

### **Congenital cytomegalovirus (cCMV)**

Surveillance Period: February 2001 - February 2003

Investigators: Dr P Tookey, Professor M-L Newell, Dr M Sharland

Published paper: 17<sup>th</sup> BPSU Annual Report 2002/03. BPSU London 2003

### **Thrombosis in childhood**

Surveillance Period: February 2001 - February 2003

Investigators: Dr B Gibson, Dr P Bolton-Maggs

Published paper: 17<sup>th</sup> BPSU Annual Report 2002/03. BPSU London 2003

### **Internal abdominal injury due to child abuse**

Surveillance Period: March 2002 - March 2003

Investigators: Dr P M Barnes, Dr C A Norman, Dr A M Kemp, Professor J Sibert

Published paper: Abdominal injury due to child abuse. Barnes PM, Norton CM, Dunstan FD, Kemp AM, Yates DW, Sibert JR. *Lancet*. 2005 Jul 16-22; **366**(9481): 234-5.

### **Suspected fatal adverse drug reaction in children**

Surveillance Period: June 2002 - June 2003

Investigators: Professor T Stephenson, Dr K Cheng

Published paper: Identification of suspected fatal adverse drug reactions by paediatricians: a UK surveillance study. Cheng K, Masters S, Stephenson T et al. *Arch Dis Child*. online 22 June 2007 doi: 10.1136/adc.2006.107789

### **Severe complications of varicella (chickenpox) in hospitalised children**

Surveillance Period: November 2002- November 2003

Investigator: Dr C Cameron

Published paper: 18<sup>th</sup> BPSU Annual Report 2003/04. BPSU London 2004

### **Invasive fungal infections in VLBW infants**

Surveillance Period: February 2003 – February 2004

Investigator: Dr L Clerihew, Dr T Lamagani, Dr W McGuire, Dr P Brocklehurst

Published paper: Invasive fungal infection in very low birthweight infants: national prospective surveillance study. Clerihew L, Lamagni T L, Brocklehurst P, McGuire W. *Arch Dis Child Fetal Neonatal Ed* 2006; **91**: F188-F192.

### **Symptomatic toxoplasmosis on childhood**

Surveillance Period: July 2002 – June 2004

Investigator: Dr R Gilbert, Mr M Stanford, Dr H Kuan Tan, Ms S Cliffe

Published paper: Symptomatic toxoplasma infection due to congenital and postnatally acquired infection. Gilbert R, Hooi HK, Cliffe S, Stanford M, Guy E. *Arch Dis Child* 2006; **91**(6): 495-8.

### **Severe hyperbilirubinaemia**

Surveillance Period: May 2003 – May 2005

Investigator: Dr D Manning

Published paper: Prospective surveillance study of severe hyperbilirubinaemia in the newborn in the United Kingdom and Ireland. Manning DJ, Maxwell MJ, Todd PJ, Platt MJ. *Arch Dis Child Fetal Neonatal Ed* 2006 Oct 30 doi:10.1136/adc.2006.105361.

### **Langerhans cell histiocytosis**

Surveillance Period:

Investigator: Professor L Parker, Ms J Salotti, Dr V Nanduri, Dr K Windebank, Dr J Pritchard, Mr R Lynn

Published paper: 20<sup>th</sup> BPSU Annual Report 2005/06. BPSU London 2006

### **Non-type 1 Diabetes**

Surveillance Period: October 2004 – October 2005

Investigator: Ms L Haines, Dr K C Wan, Mr R Lynn, Dr T Barrett, Dr J H Shields

Published paper: 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.

### **Thyrotoxicosis in children**

Surveillance Period: September 2004 – September 2005

Investigator: Dr Scott Williamson

Published paper: Thyrotoxicosis in childhood. 20<sup>th</sup> BPSU Annual Report 2005/06. BPSU London 2006

## APPENDIX B - Published Papers 2006-2007

1. British Paediatric Surveillance Unit – 20 years of surveillance. Lynn RM, Ross ER. *Arch Dis Child* – 2007- in press.
2. Vitamin K deficiency bleeding in infants in the Great Britain and Ireland: British Paediatric Unit Surveys 1993-94 and 2001-02. McNinch AW, Busfield A and Tripp JH. *Arch Dis Child*. 2007 - in press.
3. Neonatal vitamin K prophylaxis in the UK: efficacy and the impact of perceived risks and availability of licensed preparations on effectiveness. Busfield A, McNinch AW and Tripp JH. *Arch Dis Child* 2007 – in press.
4. Monitoring death and cancer in children born to HIV-infected women in England and Wales: use of HIV surveillance and national routine data. Hankin C, Lyall H, Peckham C, Tookey P. *AIDS* 2007 - in press.
5. Antiretroviral therapy and premature delivery in diagnosed HIV-infected women in the United Kingdom and Ireland. Townsend C, Cortina-Borja M, Peckham CS, Tookey PA. *AIDS* 2007;**21**:1019-26.
6. The long-term follow-up of antiretroviral therapy-exposed uninfected children born to HIV-infected women: parents' and health professionals' views. Hankin C, Newell M, Tookey P. *AIDS Care* 2007;**19**(4):482-86.
7. 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.
8. Beyond Counting Numbers – Public Health Impact of Studies Conducted through National Paediatric Surveillance Units. Grenier D, Elliott EJ, Zurynski Y, Pereira R Rodrigues, Reece M, Lynn R, Kries R von. *Arch Dis Child* 2007; **97**:527-533
9. The UK Collaborative Group for HIV and STI Surveillance. A Complex Picture. HIV and other Sexually Transmitted Infections in the United Kingdom: 2006. London: Health Protection Agency Centre for Infections, November 2006.
10. Uptake of antenatal HIV testing in the United Kingdom: 2000-2003. Townsend CL, Cliffe S, Tookey PA. *J Public Health* 2006; **28**: 248-52.
11. Prospective surveillance study of severe hyperbilirubinaemia in the newborn in the United Kingdom and Ireland. Manning DJ, Maxwell MJ, Todd PJ, Platt M. *Arch Dis Child Fetal Neonatal Ed*. 2006 Oct 30 doi:10.1136/adc.2006.105361.
12. Toxoplasmic retinochoroiditis presenting in childhood: clinical findings in a UK survey. Stanford MR, Tan HK, Gilbert RE. *Br J Ophthalmol* 2006 Dec;**90**(12):1464-7.
13. HIV Paediatric Prognostic Markers Collaborative Study. Predictive value of absolute CD4 count for disease progression in untreated HIV-1-infected children. *AIDS* 2006, **20**:1289-94.
14. Antiretroviral therapy and congenital abnormalities in infants born to HIV-1 infected women in the United Kingdom and Ireland, 1990-2003. Townsend CL, Tookey PA, Cortina-Borja M, Peckham CS. *JAIDS* 2006; **42**(1): 91-94.
15. Outcomes for HIV-1-infected infants in the UK and Republic of Ireland in the era of effective antiretroviral therapy. Doerholt K, Duong T, Tookey P, Butler K, Lyall H, Sharland M, Novelli V, Riordan A, Dunn D, Walker AS, Gibb DM. *Pediatr Infect Dis J* 2006; **25**(5):420-6.
16. The UK case-control study of cerebral oedema complication diabetic ketoacidosis in children. Edge JA Jakes RW, Roy Y, Hawkins M, Winter D, Ford-Adams ME, Murphy NP, Bergomi A, Widmer B, Dunger DB. *Diabetologia* **49**: 2006; 2002-09.
17. Twenty years of active paediatric surveillance in the the UK and Republic of Ireland. Lynn RM, Pebody R, Knowles R. *Euro Surveill*. 2006 Jul 20;**11**(7):E060720.4.
18. No clinical evidence of hidden vCJD in UK Children. Verity C, Winstone AM, Stellitano L, Nicoll A, Will RG. *Arch Dis Child* July 2006; **91**: 608 – 609.

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19. Invasive fungal infection in very low birthweight infants: national prospective surveillance study  
Clerihew L, Lamagni T L, Brocklehurst P, McGuire W. *Arch Dis Child Fetal Neonatal Ed.* 2006; **91**: F188-F192.
20. Using multiple sources to improve and measure case ascertainment in surveillance studies: 20 years of the British Paediatric Surveillance Unit. Knowles R L, Smith A, Lynn R, Rahi JS on behalf of the British Paediatric Surveillance Unit (BPSU). *Journal of Public Health* 2006 Jun; **28(2)**:157-65.
21. Symptomatic toxoplasma infection due to congenital and postnatally acquired infection. Gilbert R, Hooi HK, Cliffe S, Stanford M, Guy E. *Arch Dis Child* June 2006; **91(6)**:495-8.
22. Monitoring the effectiveness of HIV and STI prevention initiatives in England, Wales and Northern Ireland: where are we now? Brown AE, Tomkins SE, Logan LE, LaMontagne DS, Munro HL, Hope VD, Righarts A, Blackham JE, Rice BD, Chadborn TR, Tookey PA, Parry JV, Delpech V, Gill ON, Fenton KA. *Sex Transm Infect* 2006; Feb; **82(1)**:4-10.

## APPENDIX C - Presentations 2006-2007

### RCPCH Annual Scientific Meetings 2006 and 2007

The BPSU study of Biliary Atresia: Outcome 13 years. McKiernan, Baker A, Lloy C, Mieli-Vergani G, Kelly D. *Arch Dis Child* 2007; **92** (Suppl):A4-A5.

Enhanced surveillance of Meticillin-Resistant Staphylococcus aureus bacteraemia in children less than 16 years in the UK and Ireland. June 2006 – November 2007 Goodall C, Johnson A, Sharland M. *Arch Dis Child* 2007; **92** (Suppl 1): A75-79.

Morbidity, mortality and response to treatment in perinatally HIV-infected children in the UK and Ireland, 1996-2006: A prospective cohort study. Doerholt K, Judd A, Sharland M, Tookey P et al *Arch Dis Child* 2007; **92** (Suppl 1): A80-87.

Vertically acquired HIV infection in the UK and Ireland in the era of routine antenatal testing (2000-5) Townsend J, Masters C, Peckham C, Tookey P. *Arch Dis Child* 2007; **92** (Suppl 1): A80-87.

Active surveillance of early onset eating disorders: potential for a child psychiatric surveillance system. Lynn R, Nicholls D, Viner R. *Arch Dis Child* 2007; **92** (Suppl 1): A50-A52.

Eating disorders in children under 13: clinical profiles from a British national surveillance scheme. *Arch Dis Child* 2007; **92** (Suppl 1): A50-A52.

Newborn screening for medium chain acyl co-a dehydrogenase deficiency: preliminary findings from the UK Collaborative study. Oerton J, Downing M et al. *Arch Dis Child* 2006; **91** (Suppl 1): A1-A7.

British Paediatric Surveillance Unit Childhood Tuberculosis Study. Teo SS, Alfaham M, Clark J et al. *Arch Dis Child* 2006; **91** (Suppl 1): A1-A7.

Bilirubin encephalopathy in the newborn: incidence, associations and outcome. Manning D, Platt M, Maxwell E, Todd P. *Arch Dis Child* 2006; **91** (Suppl 1): A1-A7.

Incidence and characteristics of Thyrotoxicosis in childhood: UK and Ireland BPSU Surveillance Study 2004 – 2005. Williamson S, Greene SA. *Arch Dis Child* 2006; **91** (Suppl 1): A1-A7.

Vitamin K prophylaxis and vitamin K deficiency bleeding in the UK: What progress in 15 years. Busfield A, McNinch A, Tripp J. *Arch Dis Child* 2006; **91** (Suppl 1): A1-A7.

National Childhood Stroke Study: Survival and recurrence. Williams A, Kirkham F. *Arch Dis Child* 2006; **91** (Suppl 1): A1-A7.

Rising Prevalence of Obesity related Type 2 diabetes in the British Isles. Haines L, Wan K, Barrett T, Shield J. *Arch Dis Child* 2006; **91** (Suppl 1): A20.

Children with mitochondrial cytopathies in a national prospective surveillance study". Krishnakumar D et al. *Arch Dis Child* 2006; **91** (Suppl 1): A43.

The Epidemiology of neonatal herpes simplex virus infection in the UK and Ireland: Surveillance through the BPSU 2004-05. Tookey P, Peckham C. *Arch Dis Child* 2006; **91** (Suppl 1): A70.

The historical development of the British Paediatric Surveillance Unit. Hall S, Lynn R. *Arch Dis Child* 2006; **91** (Suppl 1): A78.

What is the contribution of notification by specialists to the ascertainment of rare childhood conditions through the British Paediatric Surveillance Unit? Knowles R, Smith A, Lynn R, Preece M et al. *Arch Dis Child* 2006; **91** (Suppl 1): A87.

Surveillance of Medium Chain Acyl CoA dehydrogenase deficiency in the UK: Experience with combining multiple sources of ascertainment. Phillips P, Oerton J et al. *Arch Dis Child* 2006; **91** (Suppl 1): A90.

Trends in reporting of paediatric HIV infection and infants born to HIV women, United Kingdom and Ireland 1990-2004. RCPCH, York, April 2006 (poster). C.Townsend, J.Masters, P.Tooley. *Arch Dis Child* 2006; **91** (Suppl 1): G188.

Parents' views on long term follow up of uninfected children born to HIV infected women and exposed to antiretroviral therapy. RCPCH, York, April 2006 (poster). C.Hankin, R.Cross, P.Seery, D.Gurtin. *Arch Dis Child* 2006; **91** (Suppl 1): G187.

## International Network of Paediatric Surveillance Units: 4th Conference, London 2006

Fetal Alcohol Syndrome in Australia and New Zealand. Elliott E on behalf of Bower, Payne, Haan, Morris, Bucens, Leversha, Marks, Rowley; APSU, NZPSU Contributors. London May 2006.

International Comparison of Quality Assurance Criteria for Acute Flaccid Paralysis Surveillance: Grenier D, Macey J, Doherty J, Brussen K, Dickson N, Zimmermann HP. London May 2006.

Increase of incidence of NIDDM and MODY in paediatric endocrinology practice in Latvia during last 5 years. Dzivite I, Lauge U, Bikis E. London May 2006.

Invasive group B Streptococcal disease in infants – comparison of four Paediatric Surveillance Units data. Neto MT. London May 2006.

Public Health Impact of INoPSU studies. Zurynski Y, Elliott E on behalf of D Grenier, R Rodrigues Pereira, Preece M, Lynn R, Kries R von. London May 2006.

International Comparison of Severe Neonatal Hyperbilirubinemia and Herpes Simplex Virus Infection: Grenier D. London May 2006.

One-Time Surveys–CPSP Added Value: Grenier D, Doherty J, Srikanthan S. London May 2006.

Active surveillance of Vitamin K deficiency bleeding (VKDB) in infants by the Dutch Paediatric Surveillance Unit. Ijland M. London May 2006.

Breast-feeding associated hypernatremia and silent malnutrition of the breast. Pelleboer R Pereira RR. London May 2006.

The Importance of specialists in reporting cases. Knowles R, Lynn R, Smith A. London May 2006.

Early-onset eating disorders in young children: First report from the APSU and CPSP studies Morris A, Madden S, et al. (APSU) Katzman D, Pinhas L. London May 2006.

## Other Conferences & Meetings

An audit of laboratory diagnosis of HIV-1 infection in infants (oral). Tosswill J, Pillay D, Zuckermann M, Masters J, Tookey P, Parry J. BHIVA 2007.

Vertically acquired HIV infection in the UK and Ireland in the era of routine antenatal testing (2000-2005). Townsend CL, Masters J, Peckham CS, Tookey PA. RCPCH, York, March 2007.

Mother-to-child transmission of HIV in the UK and Ireland: 1990-2004. Townsend CL, Cortina-Borja M, Peckham CS, Tookey PA. CROI, Los Angeles, February 2007.

Langerhans Cell Histiocytosis (LCH) In Children in the UK and Ireland: An Epidemiological Survey. Salott I J, Nanduri V, Pritchard J, Windebank K, Lynn R, Parker L. *In: Twenty-Second Annual Meeting of the Histiocyte Society*, Buenos Aires, Brazil October 2006.

Prematurity and antiretroviral therapy: population-based HIV surveillance in the UK and Ireland, 1990-2005. Townsend CL, Tookey PA, Cortina-Borja M, Peckham CS. 16<sup>th</sup> International AIDS Conference, Toronto 2006. Abstract MOPE0532.

Feasibility of clinic-based follow-up of uninfected children born to HIV-infected women in the UK: The children exposed to ART study (CHART). Hankin CD, Lyall EGH, Masters JI, Peckham CS, Tookey PA. 16<sup>th</sup> International AIDS Conference, Toronto, Canada 2006. Abstract TUPE0328.

Universal antenatal HIV testing in Scotland and its effectiveness in detecting previously undiagnosed infection. Codere G, Roy K, Shaw L, Goldberg DJ Townsend C, Tookey P. 16<sup>th</sup> International AIDS Conference, Toronto 2006. Abstract THPE0576.

Exposure and response to highly active antiretroviral therapy (HAART) in ART naive children in the UK and Ireland. Judd A, Lee KJ, Duong T, Walker AS, Butler K, Donaghy S, Lyall H, Masters J, Menson E, Novelli V, Peckham C, Riordan A, Sharland M, Tookey P, Tudor-Williams G, Gibb D. 16<sup>th</sup> International AIDS Conference, Toronto 2006. Abstract THPE0106.

Should we be screening newborn infants for medium chain acyl CoA deficiency in the United Kingdom. Dezateux C. Wolfson Institute, London. November 2006.

Current newborn screening in the United Kingdom and future needs. Dezateux C. Copenhagen. October 2006.

Undertaking a national surveillance study. Lynn R. BACCH conference September 2006.

Premature delivery in women receiving HAART: data from national HIV surveillance in the UK and Ireland, 1990-2005 (oral presentation). Townsend C, Cortina-Borja M, Peckham C, Tookey P. HPA Conference, Warwick. 11<sup>th</sup>-13<sup>th</sup> September 2006.

The contribution of the British Paediatric Surveillance Unit to health protection in the UK. R Pebody, Dezateux C, Smith A, Knowles R, Ihekweazu C, Cameron C, Lynn R, Colver A. HPA Health Protection Conference. Warwick. 11<sup>th</sup>-13<sup>th</sup> Sept 2006.

Newborn Screening for Medium Chain Acyl CoA Dehydrogenase Deficiency: Preliminary Findings from the UK Collaborative Study. Shortland G. BIMDG, July 2006 and ICIEM, Japan. September 2006.

What are the phenotypes of Medium Chain Acyl Co-A Dehydrogenase Deficiency (MCADD) ascertained through newborn screening? Experience from the UK Collaborative Study. Oerton J. Genomics and public health, Montreal. June 2006.

The British Paediatric Surveillance Unit in Action. Lynn R. The Jack Rubie Lecture - Ealing Hospital. May 2006.

Poster - Older and wiser: continued improvements in clinical outcome and highly active antiretroviral therapy response in HIV infected children in the UK and Ireland, 1996-2004. A. Judd, T.Duong, S.Walker, P.Tooney, M.Sharland, A.Riordan, H.Lyall, J.Masters, E.Menson, G.Tudor-Williams, K.Butler, S.Donaghy, V.Novelli, C.Peckham, D.M.Gibb. RCPCH, York, April 2006 (poster). *Arch Dis Child* 2006; 91 (Suppl 1): G178. Also 12<sup>th</sup> Annual Conference of BHIVA, Brighton, April 2006, *HIV Medicine* 2006, 7(1): Abstract O8.

Poster - The Contribution of the British Paediatric Surveillance Unit to Public Health Intelligence in the UK. Knowles R, Smith A, Lynn R, Cameron JC, Pebody R, Dezateux C Faculty of Public Health Annual Scientific Meeting, Glasgow 2006.

Poster - Neonatal Herpes Simplex Virus (HSV) infection in the UK and Ireland: active surveillance through the BPSU 1986-1991 and 2004-2005, to monitor changes in prevalence, management and outcome over time. Tookey PA, Peckham CS, Brown D. HPA Conference, Warwick. 11<sup>th</sup>-13<sup>th</sup> September 2006.

Poster - Neonatal Herpes Simplex Virus (HSV) infection in the UK and Ireland: active surveillance through the BPSU 1986-1991 and 2004-2005, to monitor changes in prevalence, management and outcome over time. Tookey PA, Peckham CS, Brown D. HPA Conference, Warwick, UK 11<sup>th</sup>-13<sup>th</sup> September 2006.

Poster -. The epidemiology of neonatal Herpes Simplex Virus (HSV) infection in the UK and Ireland: surveillance through the BPSU 2004-2005. Tookey PA and Peckham CS. RCPCH, York, April 2006. *Arch Dis Child* 2006; 91(suppl1): Abstract G192.

Poster – Infantile Krabbes Disease in the UK. Characteristics of cases reported to the PIND study over 7 years. Winstone AM, Stellitano L, Verity C. British Paediatric Neurology Association Annual Meeting, Bristol, UK 18-20<sup>th</sup> January 2006.

Poster – National Surveillance for variant CJD – how useful is the PIND Expert Group? Winstone AM, Stellitano L, Verity C Winstone AM, Stellitano L British Paediatric Neurology Association Annual Meeting, Bristol, UK 18-20<sup>th</sup> January 2006.

## APPENDIX D - Membership of Executive Committee 2006/2007

Professor Allan Colver	Chair
Dr Claire Cameron	Health Protection Scotland
Professor Carol Dezateux	Institute of Child Health (London)
Professor Adam Finn	Consultant Paediatrician
Professor Denis Gill*	Royal College of Physicians (Ireland)
Dr Shankar Kanumukala	Consultant Paediatrician
Ms Linda Haines	Royal College of Paediatrics and Child Health Research Division
Dr Sue Hobbins	Royal College of Paediatrics and Child Health Treasurer
Dr Chikwe Ihekweazu	Medical Adviser (infectious disease)
Dr Rachel Knowles	Medical Adviser (non-infectious disease)
Mr Richard Lynn	Scientific Coordinator
Dr Donal Manning	Consultant Paediatrician
Professor Neil McIntosh*	Royal College of Paediatrics and Child Health Research Division
Dr Colin Michie	Consultant Paediatrician
Dr Simon Mitchell	Consultant Paediatrician
Dr Richard Pebody	Health Protection Agency
Dr Richard Reading	Consultant Paediatrician
Professor Terence Stephenson	Royal College of Paediatrics and Child Health Vice President for Science and Research
Dr Ted Wozniak	Department of Health (observer)
Dr Sandra Williams	Department of Health (observer)
Mrs Anne Seymour	Patient and Carers Advisory Group
Mrs Sue Banton	Patient and Carers Advisory Group

\* Stepped down in 2007





