BPSU

20th Annual Report 2005-2006

British Paediatric Surveillance Unit
Royal College of Paediatrics and Child Health

Supported by the Department of Health

DH 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

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British Paediatric Surveillance Unit 20th Anniversary Annual Report 2005/2006

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

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Foreword

Prof A Colver
Chair, BPSU Executive Committee

I took over from Mike Preece the chairmanship of the BPSU Executive in March this year. I am fortunate as Mike left the Unit with funding from the Department of Health (England and Wales) to 2009, the content in place for a prestigious 20th BPSU Anniversary Conference which took place in May, and discussions moving forward with the Patient Information Advisory Group (PIAG) about identifiable data being reported via the orange card system without parental consent.

Each BPSU study has either been submitted individually for consideration for exemption by PIAG under the Health and Social Care Act or, if the study is co-ordinated by the Health Protection Agency (HPA), there is a "Class" exemption. The HPA's exemption is reconsidered annually; and the BPSU is actively responding to PIAG's expectation that we explore whether it would be feasible to obtain parental permission in future.

I can therefore now assure paediatricians that, following notification of a condition on the orange card, you have authority to supply identifier data of the child without the need for parental permission. The identifiers we seek are minimal and identifier data are now separated from clinical information as soon as practically possible. We are working closely with investigators to ensure their data are held securely.

A very successful 20th anniversary conference was held in London this May attended by 150 delegates. It highlighted the work and achievements of the BPSU putting into context the work of the Unit on national and international fronts. In the evening there was a celebratory dinner at which Sue Hall, one of the founders of the BPSU and its first medical adviser (1986-1992) talked about and toasted the achievements of the BPSU. Angus Nicoll, also a former medical adviser (1992-2002), talked about and honoured Richard Lynn - scientific coordinator. Anyone who has contacted the BPSU will have experienced Richard's friendly and helpful manner. But for over 15 years he has also been the driving force behind the BPSU. He is more knowledgeable than anyone else about the Unit and he has dealt understandingly with the succession of committee members and chairpersons. I am the latest to come along with my ideas and suggestions and he is as tolerant as ever. I would like to thank him on behalf of all paediatricians for the work he has done and will hopefully continue to do for many years.

The orange card is not as full as it could be and a number of studies on it are atypical, long running ones such as HIV, Congenital Rubella and Progressive Intellectual and Neurological Deterioration. Some studies rightly come from our parent bodies the Institute of Child Health (London), the Health Protection Agency and the RCPCH Research Division but I would like more of the spaces available to be filled by studies co-ordinated by general or specialty paediatricians. I realise that the research environment is more difficult because of bureaucracy and consultant work being tightly tied to job plans. However the BPSU now has resources which should make the development of an application easier for you. Based on experience over the last few years, the BPSU can now give authoritative advice on how to complete ethics and PIAG applications. Further it can provide pre formatted questionnaires, faster processing of enquiries and applications; and advice on study design in the first instance from Richard Lynn or one of the medical advisers, Rachel Knowles and Chikwe Ihekweazu. One area I would like to encourage is surveillance of "circumstances" which are not diseases or which have a social as well as medical dimension or are infrequent complications of a common disease. Examples might be Failure to get funding for a drug for a specific child or HIV in children for adoption. Another possibility would be to include an occasional question just for that month which might relate to a practice or audit topic; however such a "survey" type of question would depart from the original intention of the BPSU and might confuse. I would welcome opinion on whether the orange card could be used more imaginatively.

Some paediatric conditions need active surveillance from more than one source. A few years ago a study of cataracts was undertaken in collaboration with the British Ophthalmology Surveillance Unit. Recently we have been undertaking a survey into early onset eating disorders with members of the Royal College of Psychiatrists. In the last year, the UK Obstetric Surveillance System has started work and we hope to collaborate with it over the coming years.

Results from BPSU studies continue to have a high chance of being published, reflecting the importance of the conditions surveyed and the diligence of the investigators. In the last year there were 17 publications; and at the RCPCH meeting in York a record 7 plenary and 9 group presentations.

Along with Mike Preece stepping down as chair several other members of the Executive Committee ended their term in office. Gabrielle Laing, Bill McGuire, Martin Richardson, Alun Elias Jones, Stuart Tanner, Hugh Davies and Carol Youngs and I thank them for their contribution to its deliberations. Richard Reading, Shankar Kanumakala, Donal Manning, Sue Hobbins, Adam Finn, Colin Michie, Simon Mitchell and Sue Banton have joined the committee and I welcome them.

I would like to thank our research administrator, Jennifer Ellinghaus, without whom the delivery of BPSU office functions and administration of the 20th anniversary conference and dinner would have been impossible. I also thank Linda Haines whose calm leadership of the research division of the RCPCH facilitates so well the work of the BPSU.

Finally, on behalf of all the investigators over the past 20 years I would like to thank all the clinicians who have diligently returned the orange card and when required completed the appropriate questionnaire. Here's to the next 20 successful years!

A Special Message on the Occasion of our 20th Anniversary

"As a Paediatrician myself, I have been proud to participate in the BPSU for 20 years, returning my orange card and case information for important studies enabling me to participate in national research into uncommon childhood conditions from a district base. As the national Clinical Director for Children, Young People and Maternity, it was an honour to chair a session at the recent academic day, appropriately celebrating the BPSU's 20th Anniversary. The Department of Health is pleased to provide core funding for this unit and to see that the BPSU is being emulated in places throughout the world. The founders were inspired, the work has been nurtured well over the years by dedicated, hardworking people and I am sure the unit will continue to prosper."

Dr Sheila Shribman
National Clinical Director for Children

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 2005. Reference is also made to studies and activities which commenced in the year 2006.

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 more common 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 now 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 Socal Care Bill (2000) before commencement.

The reporting system

Those participating in the reporting system include consultant paediatricians who are either members of the RCPCH 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 card for two consecutive months. A

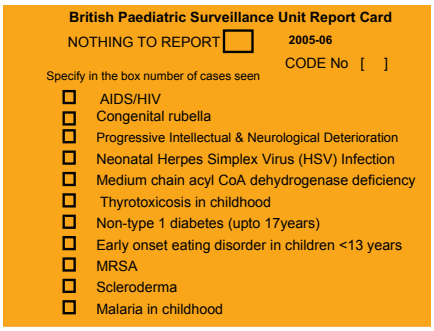

Figure 1:Orange Card Side A

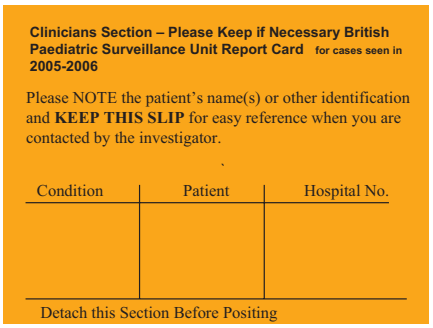

Figure 2: Orange Card Side B

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 is an important feature of the surveillance scheme as it confirms whether other clinicians have seen cases but not reported them and ensures that the number of cases found reflects the true incidence in the population. 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 written 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.

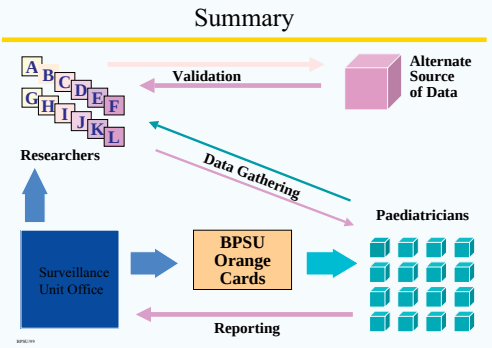

Figure 3: Surveillance Mechanism

Table 2 (page 10) shows the number of cases reported to the BPSU from its inception until the end of year 2005 for conditions under surveillance at October 2005. 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 2006, only 344 (4%) of the 8501 case reports had yet to be followed-up. The final completion rate normally averages between 90-95% for a study undertaken through the BPSU.

Table 3 (page 11) summarises the outcome of the follow-up of all cases reported to the BPSU by the end of year 2005 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. In 2005, child psychiatrists were involved in a parallel reporting system for the study of early onset eating disorders. Pathologists have been included in the BPSU reporting scheme since 1992 and most studies of paediatric infections involve laboratory reporting by microbiologists. 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 have recently been examined and the finding published. (Using multiple sources to improve and measure case ascertainment in surveillance studies: Knowles RL, Smith A, Lynn R, Rahi JS. 20 years of the British Paediatric Surveillance Unit J Public Health 2006 Jun;28(2):157-65. Epub 2006 Apr 26).

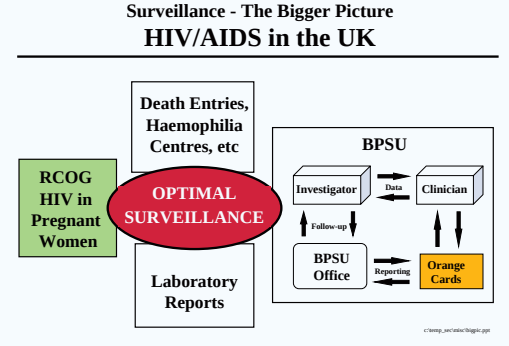

Figure 4: Surveillance- the bigger picture

Funding

In 2004, the BPSU received a five year funding 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 the study. These funds permitted the BPSU to hold a workshop to support current and potential investigators in 2005 and to plan two conferences for 2006: a conference to mark the 20th anniversary of the BPSU and an international network of paediatric surveillance units (INoPSU) conference. 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), the Health Protection Agency (Communicable Disease Surveillance Unit) and Health Protection Scotland.

3 Scientific Coodinator's Yearly Review of Activities

This past year has seen the commencement of three new BPSU studies: the early onset eating disorder survey in March 2005, the study of Methicillin-resistant Staphylococcus aureus (MRSA) bacterciemia in children in June 2005 and the study of childhood scleroderma in July 2005.

Also in 2005, five studies were extended for a further year: HIV, congenital rubella, progressive intellectual and neurological deterioration (PIND), medium chain acyl CoA dehydrogenase deficiency (MCADD) and herpes simplex virus. The five studies which ended in 2005 were of childhood tuberculosis (January), severe hyperbilirubinaemia in the newborn (May), Langerhans cell histiocytosis (June), childhood thyrotoxicosis (September) and non-type 1 diabetes (October). Between the inception of the BPSU in 1986 and December 2005, 64 studies have been completed (Appendix A). During 2005/2006, there were 59 publications and presentations relating to BPSU studies (Appendices B and C).

One study has so far commenced in 2006, malaria in childhood (January), the principal investigator, Dr Shamez Ladhani, being the recipient of the second Sir Peter Tizard research bursary. The third Sir Peter Tizard Bursary was awarded to Dr Yim Yee Matthews, for her proposed study of Idiopathic Intracranial Hypertension (IIH).

From July 2005 all BPSU facilitated studies now have to apply for approval under Section 60 from the Patient Information Advisory Group (PIAG) to allow the collection of minimal identifier data without consent. All our current studies have now received such approval and the BPSU has agreed a short application form with PIAG which will minimise the work involved in gaining such approval. As yet, no extra delays have been experienced and the BPSU and PIAG are working together to ensure that this remains the case.

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 and recent PowerPoint presentations. There is also information on patient support groups as the BPSU is working hard to make the information it produces more accessible to the public.

(Photo by Joe Spinoza, aged 9)

Richard Lynn
Scientific coordinator

The BPSU continues to contribute to the work of the International Network of Paediatric Surveillance Units (INoPSU). As INoPSU liaison officer it is my job to keep all the units in contact, informing them of each other's work and putting investigators in different countries in touch with each other in order to facilitate collaboration. In the past year, over 70 different conditions have been investigated across the 15 member surveillance units. The BPSU office also manages the INoPSU website http://www.inopsu.com where information on INoPSU's work is available. A short report of the 4th INoPSU conference, held in London in May 2006 can be read on page 61.

Participation in the scheme during the year 2005

The BPSU ascertains the names of new consultants primarily through the RCPCH advisory appointment committee, membership office, through personal communication and with the ongoing College workforce census. During the year, 271 consultants were placed on the BPSU mailing list whilst 124 were removed ostensibly following retirement. The number of consultant paediatricians participating in the scheme during the year 2005 therefore rose to 2,663, an increase of 5.6% on the previous year. The mailing list also includes selected groups of consultants other than paediatricians i.e. 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.

Reporting rates for returning the orange cards remains high - the overall card return compliance rate for the year 2005, calculated as a proportion of orange cards returned, was 93.6% (30,843/28,853), an increase of 2.4% from 2004. Monthly response rates ranged from 90.2% in December to 95.2% in April, with a median of 93.5%. 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 14 page 61).

Wales has once again achieved the highest average yearly response rate – 96.7%, with Northern Ireland ranked second with 95.5% and South Scotland ranked third with 94.7%. The Thames area showed a cumulative response rate of 92.1%, which is a rise of 4% on 2004. 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.

Table 1 Regional response rate 2004 and 2005

Region	Rank 2005	Rank 2004
Northern	5	10
Yorkshire	8	4
Trent	12	16
East Anglia	10	14
NWT	16	19
NET	19	20
SET	8	17
SWT	15	15
Wessex	9	6
Oxford	3	7
South Western	11	12
West Midlands	13	11
Mersey	17	8
North Western	7	5
Wales	1	1
North Scotland	4	9
South Scotland	14	2
West Scotland	15	13
Northern Ireland	2	3
Republic of Ireland	20	18

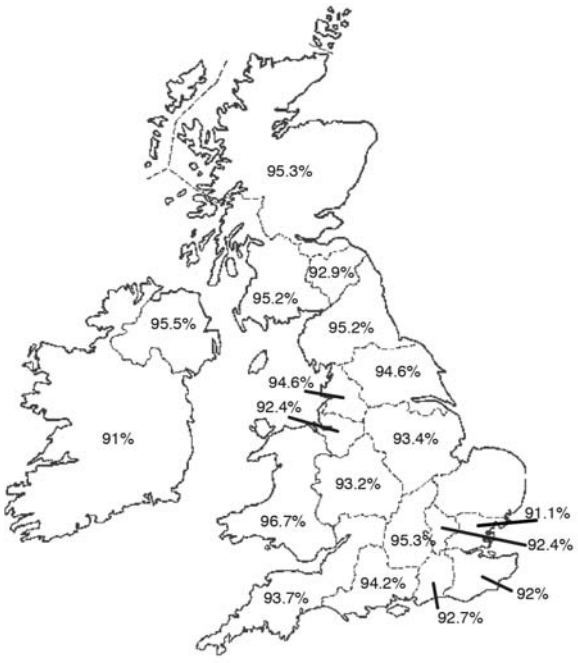

Figure 5: Average orange card return rate (%) by area, 2005

Workload of those reporting in the scheme

The BPSU continually monitors the workload of participants in the scheme in terms of the number of cases reported. 73% (1954) of participants reported no cases in 2005, 24.4% (649) reported between one and four cases and only 2.3% (60) reported five or more cases. The greatest numbers of cases reported were by HIV specialists, one of whom reported 52 cases and another 106. Specialties that had a particularly high level of reporting were paediatric neurologists (PIND), endocrinologists (thyrotoxicosis) and neonatologists (HIV, tuberculosis in childhood and hyperbilirubinaemia in the newborn.) Community paediatricians continue to make a significant contribution to the reporting, particularly to the PIND and HIV studies and their continued involvement in the scheme is very much welcomed.

Table 2 Cases reported from June 1986 - December 2005 for conditions under surveillance at June 2006

		Reports (confirmed cases)				
	Date when reporting began	June 1986-Dec-96	Jan-96 Dec-00	Jan-01 Dec-03	2004	2005
Conditions under serveillance						
HIV	Jun-86	991 (691)	1017(705)	1823 (1382)	696(595)	730(556)
Congenital rubella	Jun-91	72(39)	49 (25)	26 (6)	2 (1)	7(0)
PIND	May-97		1066 (633)	610(339)	177 (122)	172(115)
Langerhans cell histiocytosis	Jun-03			46 (15)	68 (47)	46 (27)
Neonatal Herpes Simplex	Feb-04				61 (31)	57 (31)
MCADD	Jun-04				65 (47)	102 (69)
Thyrotoxicosis	Sep-04				76 (45)	175 (125)
Non-type 1 diabetes	Oct-04				82 (48)	164 (84)
EOED*	Mar-05					43 (177)
MRSA	Jun-05					52 (23)
Scleroderma	Jun-05					33(8)
Total		**1063 (730)**	**2132 (1363)**	**1505 (1742)**	**1227 (836)**	**1623 (994)**

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*

Table 3 Outcome of follow-up of the cases reported in 2005 for conditions under surveillance at June 2005

Condition under surveillance	Date when reporting began	Valid reports	(%)	Invalid reports: Duplication	Invalid reports: Errors	Total (%)	Not yet known	(%)	Total
HIV/AIDS	Jun-86	3,948	76	524	553	21	183	4	5208
Congenital rubella	Jun-91	71	46	28	52	51	5	3	156
PIND	May-97	1209	60	236	552	39	28	1	2025
Langerhans cell histiocytosis	Jun-03	89	56	27	36	39	8	5	160
Neonatal Herpes Simplex	Feb-04	62	53	22	20	36	14	12	118
MCADD	Jun-04	116	69	27	821	16	10	167	
Thyrotoxicosis	Sep-04	170	68	10	35	18	36	14	251
Non-type 1 diabetes	Oct-04	132	54	9	80	36	25	10	246
EOED	Mar-05	177	52	41	73	33	52	15	85
MRSA	Jun-05	23	44	2	13	29	14	27	52
Scleroderma	Jun-05	8	24	2	11	39	12	36	33
All		6005	69	928	1433	27	393	4	8759

Table 4 Case report table classification of case reports

Valid reports:

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.

Invalid reports:

These include:

duplicate reports of cases already reported to the BPSU,

and

reporting errors 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.

Outcome not yet known:

Outcome of follow-up not yet received by BPSU (by June 2006).

4 Main Findings of Studies Undertaken in 2005

Surveillance for **congenital rubella** (page 14) has been underway in the UK continuously since 1971 and importantly is the only source of surveillance for this condition in the UK. Thirteen 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 (EOED)** (page 18) aged between 5 and 12 inclusive commenced in March 2005. This is the first BPSU study that has involved members of the Royal College of Psychiatrists in the ascertainment of cases. After thirteen months of surveillance 430 suspected cases have been reported; 322 (75%) reported by psychiatrists and 108 (25%) by paediatricians. Details on 337 cases have been collected of which 190 have fitted the case criteria, 138 (73%) by psychiatrists and 52 (27%) by paediatricians. 151 (79%) of the cases are female and 39 (21%) are male. A one-year follow-up will be undertaken to confirm the outcome of the reported cases. However, this study has already demonstrated that rare childhood psychiatric conditions can be surveyed for using a monthly report card surveillance system.

Principal Investigators: Dr D Nicholls, Mr R Lynn, Dr R Viner, Professor P Lelliott - ICH/GOSH, RCPCH, The Middlesex Hospital, RCPsychs.

The BPSU survey of **HIV infection in children** (page 22) 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 British Isles 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 two-year surveillance of **Langerhans Cell Histiocytosis (LCH)** (page 27) came to an end In June 2005. LCH is a rare multi-system disorder with a wide range of clinical presentations such as skin rash, bony lesions, hormone deficiencies or vital organ involvement. The course of the disease is unpredictable, varying from spontaneous regression and resolution to rapid progression and death, or repeated recurrence with risk of irreversible long-term disabilities. There have been 84 confirmed cases to date, 54 boys and 30 girls. Children presented clinically with varying features such as head swelling, rashes or skin lesions. Three children have died.

Principal Investigators: Professor L Parker, Mrs J Salotti, Dr K Windebank, Dr V Nanduri, Dr J Pritchard, Mr R Lynn – RVI Newcastle, GOS, Edinburgh, RCPCH.

Surveillance of **Medium chain acyl CoA dehydrogenase deficiency (MCADD)** (page 31) 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, 182 cases have been reported to the BPSU, of which 111 cases have been confirmed.

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

Surveillance of **Neonatal herpes simplex virus (HSV)** (page 39) infection commenced in February 2004 for a period of three years. Virus has been typed in almost all cases reported to date, and about 45% 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.

There is a growing body of evidence that the epidemic of obesity in UK children has resulted in a rising incidence of type 2 diabetes (page 42). Surveillance of **non-type 1 diabetes** commenced in October 2004 to establish the clinical features that distinguish it from other forms of diabetes. In the first six months of surveillance 169 cases of non-type 1 diabetes have been reported; these include case of type 2, non-type 1 secondary to another condition and syndromic type 2 diabetes. Type 2 diabetes was the most commonly reported with 91/169 (54%) cases. Although the data are still being analysed, they suggest that cases of type 2 diabetes in children are more common than previously supposed. Nearly all type 2 cases are associated with being overweight or obese together with a positive family history. The results suggest that obesity-related type 2 diabetes is a growing problem, not only in ethnic minority groups, but now also in white children.

Principal Investigators: Mrs L Haines, Dr K Chong Wan, Mr R Lynn, Dr J Shields, Dr T Barrett – RCPCH, Bristol Royal Hospital for Sick Children, Birmingham Children's Hospital.

Despite the complexity of the conditions involved, the survey of **progressive intellectual and neurological deterioration in children (PIND)** (page 45) has proved successful. A primary objective is to identify new cases of variant Creutzfeldt-Jakob disease (vCJD) in UK children. Over 2000 cases of suspected PIND have been reported. Among them 862 cases are confirmed diagnoses, comprising of 114 known degenerative conditions. Six cases of vCJD have been identified. Active surveillance continues into 2006.

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

October 2004 saw the commencement of the first study funded by the Sir Peter Tizard Research bursary. A 13-month surveillance of **thyrotoxicosis in childhood** (page 52) was undertaken to ascertain incidence, examine presenting features and examine how children are being managed. To date 35 cases have been confirmed: 74% were Graves' Disease, 11% Hashimoto's thyroiditis and 3% congenital thyrotoxicosis.

Principal Investigators: Dr S Williamson, and Dr S Greene – University of Dundee.

Surveillance of **Methicillin-resistant Staphylococcus aureus (MRSA)** (page 35) commenced in June 2005 for an initial 13-month period. The study aims to document the incidence in children and the clinical features and patterns of presentation. To April 2006 72 cases have been notified, and so far 32 have been confirmed. Cases are also being reported through the HPA and voluntary reporting of isolates from hospital microbiologists to Labbase2.

Principal Investigators: Ms C Goodall, Dr A Johnson, HPA Centre for Infections. Dr M Sharland, St George's Hospital.

Commencing in July 2005 the study on **scleroderma in childhood** (page 49) 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. In the first 9 months, 49 cases have been notified though only 13 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, Dr AL Herrick, Professor AJ Silman, Ms D Taylor-Fesler, Liverpool Children's Hospital, University of Manchester, Hope Hospital.

5 Surveillance Studies Undertaken in 2005

Congenital Rubella

Key Points

- Since 1997 12 congenital rubella births have been reported in the UK, and one in Ireland.
- Only four of the 13 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.
- Although there is no evidence of rubella circulating at present, the uptake of MMR continues to be too low to maintain this situation indefinitely.
- 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.

Background

Rubella vaccination was introduced for schoolgirls in 1970 in the UK, and subsequently for susceptible women post-partum. The congenital rubella surveillance programme was established in Scotland, Wales and England in 1971 to monitor the effect of the vaccination strategy, and initially relied on passive reporting mainly from audiologists, paediatricians and microbiologists. 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. Active surveillance through the BPSU started in 1990, and since then reports have also been received from Ireland and Northern Ireland.

Since 1988 the combined Measles, Mumps and Rubella vaccine (MMR) has been offered to all children in the second year of life; in 1996 a second dose of MMR was introduced for four year olds, and schoolgirl vaccination was discontinued. The circulation of wild rubella virus has been at extremely low levels in the UK in recent years, and an increasing proportion of individuals are

Dr P Tookey

protected by vaccine-induced immunity. However, adverse publicity about unproven associations between MMR, bowel disease and autism led to a decline in MMR uptake from about 92% in 1997 to about 80% in 2003. Since then there have been some signs of improvement, with about 81% uptake in 2004, and about 82% in the first half of 2005. Because of problems relating to the implementation of new IT systems in London, UK-wide data are not yet available for the second half of 2005[1]. The situation has been similar in Ireland where MMR uptake dipped as low as 69% at the end of 2001, but recovered to 84% by the third quarter of 2005[2]. However, years of low vaccine uptake with no wild virus circulating mean that there must be a substantial number of susceptible individuals in the community; if vaccine coverage does not improve considerably 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.

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[3], sub-optimal MMR coverage and migration within Europe have been identified as major challenges to this target[4].

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.

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 sources of data

No active additional sources, but reports occasionally made direct to investigator (e.g. from virologists, audiologists).

Number of cases expected

Currently less than five a year, but could increase if there were renewed circulation of rubella infection in the community.

Denominator source

The total number of live and still births in the UK over the study period, obtained from the Office for National Statistics (ONS). Irish birth rate obtained from the Irish census 2002 (Central statistics office, Ireland).

Analysis

There were seven reports through the BPSU in 2005. Only one of these related to an infant born in the UK in 2005, and this was an imported case since the baby’s mother acquired infection in Southern Asia. Three young children were reported who had been born abroad; one of these cases was reported by two respondents. The other two reports were of older children who had already been notified to the NCRSP (one duplicate BPSU report and the other reported from another source).

Since the beginning of active surveillance in 1990, 152 reports have been made through the BPSU (Table 5). Of the 132 from England, Scotland and Wales, 49 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 (21), reporting errors (40) and five where further information could not be obtained. Sixteen reports were from Northern Ireland or Ireland, and included 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). The remaining four reports were of three young children (all under the age of three years at notification) who were born abroad. These cases now fall within the reporting definition; in previous years reports of children who were born abroad were not requested, and any such reports were categorised as errors.

Table 5. Confirmed and compatible congenital rubella births reported in the UK and Ireland 1990-2005

	Confirmed or compatible	Possible case	Cases already reported	Duplicate	Total error or lost
Place of birth					
Engalnd, Scotland and Wales	49	4	13	66	132
NI and Ireland	4	1	2	9	16
Elsewhere (2005 reports only)	2	1	0	1	4

Congenital rubella 1990-2005: Fifty-seven children and three stillborn infants with confirmed or compatible congenital rubella have been born and reported in the British Isles since the beginning of active surveillance in 1990; 45 of these (75%) were first reported through the BPSU (Table 6). 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[5,6]. 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[7]; the annual number of rubella-associated terminations is no longer published because there are so few cases.

Recent reports

Thirteen infants with congenital rubella were born and reported between 1999 and 2005, including one born in Ireland, and one stillborn infant. Although nine (including the Irish case) were imported cases with maternal infection acquired abroad (five in Southern or South Eastern Asia, four in Africa), four infants were born to women

CDC-Public Health Image Library

Figure 6: Cataracts due to congenital rubella syndrome

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[8]. Three maternal infections were acquired in England, one by a British-born woman, and the other two by women from Sri Lanka, both of whom had been in the UK for several years[9].

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 non-specific signs of congenital rubella 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[10]. 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, and continued surveillance of congenital rubella is vital.

It is essential that case ascertainment is as rapid and complete as possible, both for imported cases and those where infection was acquired in the UK or Ireland. Please continue to notify to the BPSU all infants with suspected congenital rubella, whether or not they have the associated typical defects, and regardless of country of birth.

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

Table 6. Congenital rubella reports to BPSU 1990-2005 *(Includes births occurring in earlier years)*

	Primary source of notification		
year of birth	BPSU	Other	Total
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
Total	45	15	60

* Includes a stillborn infant

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 Patient Information Advisory Group approval (PIAG/BPSU 2-10(f)/2005).

Support group

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Web: http://www.sense.org.uk.

Acknowledgements

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Early Onset Eating Disorders in Children Under 13 Years

Dr D Nicholls

Key Points

- This is the first prospective surveillance of preadolescent eating disorders presenting to secondary care in the British Isles.
- This is also the first joint paediatric/psychiatric surveillance study of eating disorders to be undertaken.
- In the first thirteen months 175 cases were reported; 51 have been classified with anorexia nervosa, five with bulimia nervosa, three with binge eating disorder, and 72 with 'eating disorder not otherwise specified'.
- Determined food avoidance was the most common presenting feature.

Background

Early-onset eating disorders (EOED: defined as onset before 13 years of age) are equally as likely to present to paediatricians as child psychiatrists in the UK[1]. 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[2] 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 (AN), has been increasing in adolescents over the last 50 years[3]: Work has focused on the peak ages of onset (15 years for AN and older for bulimia nervosa). Specialist services have recognised they are seeing increasing numbers of EOED cases, 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 AN was estimated as 17.5/100,000 in 10-19 year olds, and 0.3/100,000 in 0-9 year olds. For BN the rates are 20.5/100,000 and 0/100,000 respectively[4]. 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[5;6].

Eating disorders in prepubertal and peripubertal children frequently require paediatric admission and long-term medical monitoring as well as psychiatric management. This study, which is supported by the Royal College of Psychiatrists, will quantify the problem but will also examine the circumstances surrounding onset and examine 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 British Isles.
- 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.

"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.) This definition has been included in the questionnaire.

Reporting instructions

Please 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 and the Central Statistics Office in Ireland.

Number of expected cases

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

Alternative data sources

As it is known that cases would be 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 first 13 months of the study the return rates for the card was 80%, which is comparable to other 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 was first reported.

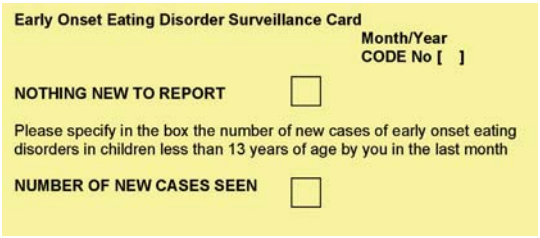

Figure 7: Early Onset Eating Disorders Surveillance Card

Analysis

After thirteen months of surveillance 430 suspected cases have been reported; 322 (75%) reported by psychiatrists and 108 (25%) by paediatricians. Details on 337 cases have been collected of which 190 have fitted the case criteria, 138 (73%) by psychiatrists and 52 (27%) by paediatricians. Both groups reported 24 cases (Figure 8). There have been 67 duplicate reports and 68 error reports, mainly due to diagnosis being made before the reporting period.

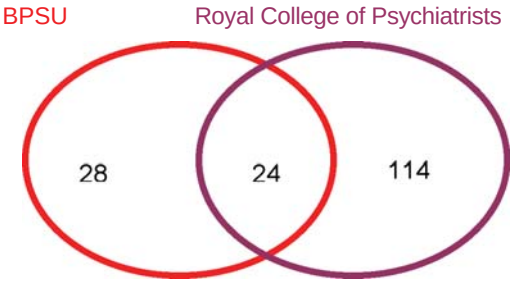

Figure 8: Muliple source case ascertainment

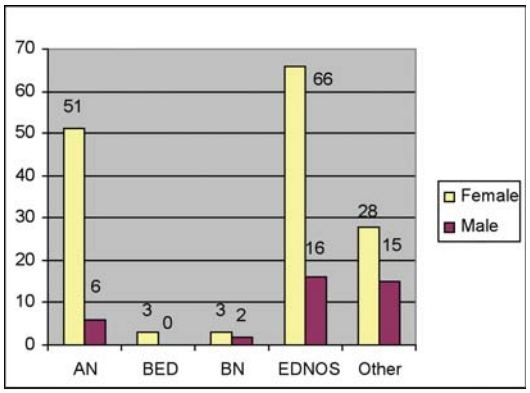

Figure 9: Classification of EOED cases by sex

Of the 190 cases 151 (79%) are female and 39 (21%) are male. From initial categorisation, 57 fit criteria for anorexia nervosa (AN), five for bulimia nervosa (BN), three for binge eating disorder (BED), 82 for eating disorder not specified (EDNOS) and 43 other eating difficulties that would not meet current criteria for an eating disorder. (Figure 9)

Categorisation of eating disorders was made on the basis of clinician report of weight &height, eating behaviour and attitudes, operationalised to fit with DSMIV diagnostic criteria

The median age of reported cases is 141 months (11.75 years), the youngest being a male of 69 months (5.75 years). All but six cases are ethnically white.

On presentation food avoidance was seen in 95% of cases, 65% showed a fear of weight gain and 79% had a pre-occupation with food. 64% were either preoccupied by their weight or shape. Nearly 40% excessively exercised as a means of controlling weight whilst 16% self-induced vomiting.

The standard deviation score for BMI ranged between – 4.3 and 7.8 with a median of –1.33.

Ninety seven (52%) children were admitted to hospital, 67 to a paediatric ward, 23 to an eating disorder unit and 25 to a psychiatric ward. 18 children were fed via a naso-gastric tube and 22 were treated with psychotropic medication. Where initial outcome is known, 89 children showed improvement with 75 unchanged, 13 deteriorating and unfortunately there has been one death due to renal failure.

A more extensive report will be made available once the follow-up data has been collected and analysed. 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.

Discussion

This is the first prospective study, involving a unique collaboration between members of the Royal College of Paediatrics and Child Health and 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 higher than expected. The proportion of cases reported in boys (21%) is higher than the literature for adolescent populations would predict (around 10%), but is consistent with previous clinical data from this age group. Puberty is a recognised trigger for the onset of eating disorders in girls, and the same degree of sexual dimorphism is not seen in this largely pre or peripubertal sample.

Underweight is a key component of AN, defined as below 85% of ideal body weight for height. 57 cases fitted categorisation for AN, while those above 85% weight for height were categorised as EDNOS. However the dynamic nature of weight loss and gain mean that some children categorised as EDNOS will go onto to develop AN, and some may have met full criteria for AN 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.

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. We intend to seek the views of child psychiatrists on their experience of the study, and to explore interest in similar studies and/or development of their own surveillance system.

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.

Ethics approval

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

Support group

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Acknowledgements

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

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HIV Infection in Childhood

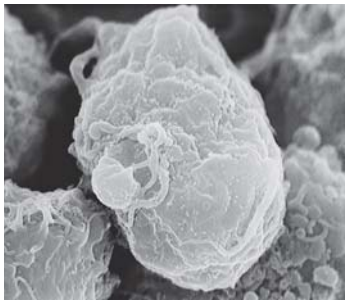
Key points

- Reports of HIV in childhood from all regions of the UK and Ireland have increased in recent years.
- 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 British Isles to both diagnosed and undiagnosed women are still being reported.
- 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.

Background

National surveillance of paediatric HIV infection and AIDS began in 1986 and is based on independent but overlapping paediatric, obstetric and laboratory reporting schemes. All 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[1].

Most children currently living with HIV in the UK and Ireland, whether born here or abroad, acquired their infection through mother to child transmission. Unlinked anonymous survey data[2] indicate that the number of births in the UK to HIV infected women (both diagnosed and undiagnosed) increased substantially from about 300 in 1997 to about 900 in 2004. Antiretroviral treatment, delivery by



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

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. In order for women to be able to access these interventions, the routine offer and recommendation of antenatal HIV testing to all pregnant women has been implemented throughout the UK and Ireland[3]. In the UK the proportion of women diagnosed before delivery increased from an estimated 32% in 1997 to over 90% in 2004[3].

Children with confirmed HIV infection who were born abroad are generally diagnosed in the British Isles either 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 instruction

Clinicians are asked to report any child with AIDS or who is HIV seropositive with or without symptoms, which they have seen for the first time.

Additional data sources

Additional data sources include 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 cases reported through the UK Haemophilia Centre.

Expected number of cases

The number of children born to HIV infected women in the UK and Ireland is continuing to rise, and exceeded 1000 in 2005; most of these infants are not infected. About 150 infected children (of all ages) are currently being reported each year, many of whom were born abroad. Direct reporting arrangements have been established with some centres caring for large numbers of exposed infants and/or infected children, in order to simplify reporting and reduce the burden on individual paediatricians. However, about half of all cases continue to be reported through the BPSU.

Denominator source

The total number of live births in the UK over the study period, obtained from the Office for National Statistics. Irish birth rate obtained from the Irish census 2002 (Central statistics office, Ireland).

Follow up

Follow up information is sought for all infants born to infected women to establish infection status. All infected children are followed up annually to monitor clinical and immunological status. Enhanced follow-up information for approximately 90% of infected children is collected through the Collaborative HIV Paediatric Study (CHIPS), a collaboration between the NSHPC, the MRC Clinical Trials Unit and participating clinics. Follow up of the surviving young adults infected in childhood through treatment for haemophilia (all born before 1984) is undertaken by the UK Haemophilia Centre and the HPA Centre for Infections.

Routine use of data

NSHPC data contribute to the overall national surveillance of HIV infection. UK summary tables appear quarterly in the Communicable Disease Report (England, Wales and Northern Ireland) (available at http:// www.hpa.org.uk) and the HPS Weekly Report (available at http://www.hps.scot.nhs.uk).

Table 7: HIV infection and infants born to HIV infected women *(all reporting sources) (notified by 31 December 2005)*

Exposure / likely source of infection	BPSU reports	Reports from other sources	Total
Children born to HIV infected women	3564	3661	7225*
Likely source of infection for other infected children			
Haemophilia treatment	48	219	267
Blood transfusion/products	34	20	54
Other/not yet established	18	41	59
Total	3664	3941	7605

*1412 known to be infected (see table 8)

Table 8: Infection status of children born to HIV infected women *(including children born abroad) (notified by 31 December 2005)*

Region of first report	Infected	Indeterminate	Not infected	**Total**
London	856	617	2399	3872
Rest of England	401	612	1101	2114
Wales & NI	18	18	41	77
Scotland	63	58	238	359
Ireland	74	147	582	803
Total	1412	1452	4361	7225

Analysis

Number and geographical distribution of reports: By the end of December 2005 there had been 4972 reports through the BPSU, of which 3664 were confirmed cases of HIV infection or infants at risk of vertical transmission, 584 were duplicates and 531 were reporting errors; the remaining 193 reports are still being investigated. A further 3941 confirmed cases were reported through other sources (see methods). Table 7 shows the likely source of infection or exposure risk for all confirmed reports.

Over the last ten years, the number of reports from every region of the UK and Ireland has increased. Before 2000, reports from paediatricians came from less than 50 units each year, this rose to over 140 units in 2005. In England, the proportion of cases reported from outside London increased from 20% before 2000, to almost 40% between 2000 and 2005.

Children born to infected women: The majority of reports (7225/7605 95%) were of children born to infected women. By the end of 2005, 1412 (20%) of these children were known to be infected, and 4361 (60%) uninfected; the infection status of the remaining 1452 (20%) children had not been reported (Table 8). While only 10% were born outside the British Isles, they accounted for over a third of confirmed vertical infections.

Almost three-quarters of the 6521 children born to infected women in the British Isles (Table 9) were born between 2000 and 2005. Although the infection status of many of these children has yet to be reported, the majority were born to diagnosed women and will themselves be uninfected.

Table 9: Year of birth and infection status of children born in the UK and Ireland to HIV infected women *(notified by 31 December 2005)*

Year of Birth	Infected	Indeterminate	Not infected	**Total**
1982-1999	585	191	1003	1779
2000	48	35	346	429
2001	31	68	491	590
2002	33	76	649	758
2003	28	130	878	1036
2004	19	318	752	1089
2005*	6	623	211	840
Total	750	1441	4330	6521

**reports for 2005 expected to rise substantially*

Transmission rates cannot be estimated from these data because of reporting bias; children born to undiagnosed women are only likely to be reported if they are infected.

Infected children: Altogether 1792 children with HIV infection have been reported (1412 born to infected women and 380 infected through other modes of transmission, see tables 7 and 8). Overall, nearly 40% of infected children were born outside the British Isles: the proportion has changed over time from about 23% of reports made before 2000 to about 60% made between 2000 and 2005. In a small proportion of cases it is not possible to ascertain the route of transmission as the HIV status of the mother at the time of the child's birth is unknown.

Thirty two percent of the infected children have had an AIDS diagnosis at some time and 68% have had symptoms reported. Three hundred and twenty four (18%) infected children are known to have died, 67 have gone abroad and 55 are lost to follow-up. Sixty young people, the majority of whom were born in Africa (83%), were diagnosed after their 13th birthday: 49 of the 60 were diagnosed since 2000.

Of the 750 children known to have been infected through mother to child transmission in the British Isles, the majority (79%) were born to undiagnosed women. In spite of generally high uptake of antenatal testing and of interventions to prevent transmission, 96 infants born between 2002 and 2005 are known to be infected (Table 9).

Discussion

Reports of infants born to HIV infected women in the UK and Ireland have increased substantially each year since 2000. This increase reflects both the growing prevalence of HIV infection in pregnant women and the dramatic improvement in diagnosis rates following the implementation of routine antenatal screening throughout the British Isles. The majority of these infants were born to diagnosed women and are not themselves infected: while the number of diagnosed infected infants born in the British Isles each year has remained fairly constant, since 2001 the proportion has substantially declined. However, in spite of improved antenatal detection rates, infants born in the British Isles to undiagnosed women continue to present with symptomatic HIV infection and often an AIDS diagnosis. An audit is currently underway to investigate the circumstances surrounding recent cases of vertical transmission in England.

A higher proportion of recently reported infected children were born abroad. The majority came from high prevalence countries and most were diagnosed in the British Isles because they were symptomatic. It is not always possible to ascertain how they acquired HIV infection as in some cases neither the child's medical history nor the mother's infection status is known. An increasing number of young people are being diagnosed in adolescence: the majority of these were born abroad and late diagnosis may be related to the age at which they arrived here.

Reports to the NSHPC from all areas of the UK and Ireland have increased in recent years. The large number of units now reporting cases, and their geographical distribution, is largely due to the dispersal of families recently arrived from sub Saharan Africa. It also highlights the important role of the BPSU in capturing cases diagnosed outside of the main centres caring for HIV infected pregnant women and children.

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 and the Department of Health; additional support is received 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 Patient Information Advisory Group approval (Ref: PIAG/BPSU 2-10(a/2005).

Support groups

Barnardos Positive Options, William Morris Hall, 6 Somers Road, Walthamstow, London E17 6RX.
Web: www.barnardos.org.uk
Positively Women, 347-349 City Road, London EC1V 1LR.
Tel: 020 7713 0444
Web: http://www.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.

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Langerhans Cell Histiocytosis

Key Points

- 63% of cases of Langerhans Cell Histiocytosis (LCH) had single system bone disease.
- 10% of cases had multi-system LCH with risk organ involvement.
- Mean interval time from first symptoms to diagnosis was 21 weeks.
- Confirmation of cases has been slower than expected.

Background

Langerhans Cell Histiocytosis (LCH) is a multisystem disorder that affects children and adults and may present as skin rash, (Figure 11 & 12) bony lesions, (Figure 13) hormone deficiencies or vital organ involvement (Figure 14 & 15). Little or no treatment may be required if only one system is affected and usually the disease regresses with time although this may take years. However, children under two years may have the most serious form of LCH with lung, liver, bone marrow or spleen involvement and are managed using the UK Children's Cancer Study Group (UKCCSG) international protocol. Children who survive severe LCH are often left with long-term sequelae which may have a significant impact on their health and quality of life.

LCH can present at any age ranging from the neonatal period to old age with a peak in diagnosis in children aged 1-3 years. A predominance of boys has been reported ranging from 1.2-2:1. LCH is usually considered a non-familial disease. However, at least 1% of LCH paediatric patients have another familial case which may involve siblings, cousins or two generations[1]. There have been few large multi-centre studies of LCH and the epidemiology of the disease is poorly documented. There are no well-accepted environmental risk factors for the disease. However, in one study in the US there was an association with infections in the neonatal period and with thyroid disease, and a protective correlation with childhood vaccinations prior to LCH[2].

Reliable data on the annual incidence are difficult to gather and until recently only one national incidence estimate (5.4 per million per year) had been reported, for Denmark, during the 1980's[3].

Dr V Nanduri,
Mrs J Salotti
Dr K Windebank

Objectives

The aims of the study are to

- describe the epidemiology of LCH in the UK and Ireland by age and gender.
- study variation in ethnic groups and regional differences.
- assess the presenting features, the interval between the onset of symptoms and diagnosis, referral patterns and outcome for the disease.

Surveillance period

1st June 2003 to 31st May 2005 (with one year follow-up to 31st May 2006).

Methodology

Clinicians were asked to report children of any age newly diagnosed with LCH during the study period. Details of cases were sought using a questionnaire and a follow up questionnaire was sent one year after diagnosis.

Case definition

Children of any age newly diagnosed in the past month with either (a) or (b)

(a) biopsy-proven LCH; lesional cells (LCH cells) must contain Birbeck granules or be CD1a positive or S100 positive with characteristic H&E morphology.

(b) Lytic bone lesion or pituitary/hypothalamic abnormality with the characteristics of LCH but not biopsied either because

1. clinical features suggest spontaneous resolution **or**

2. the risk of the biopsy procedure in view of the location of the lesion (e.g. cervical vertebra, pituitary mass) was considered too great.

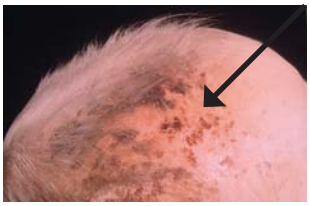

Figure 11: Scalp rash, resembling seborrhoeic dermatitis

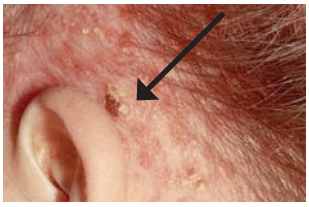

Figure 12: Post Auricular rash

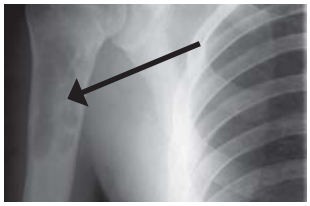

Figure 13: Lytic lesion of the humerus

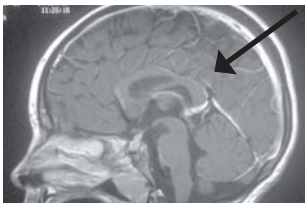

Figure 14: MRI showing pituitary involvement

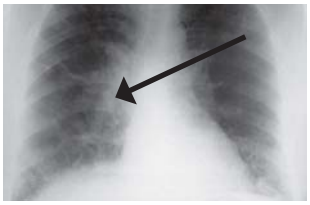

Figure 15: Interstitial shadowing in the acute phase of LCH

Reporting instructions

Clinicians were asked to report any new or suspected case seen during the surveillance period irrespective of whether or not they were the main clinician responsible for the patient.

Additional data sources

Two additional methods of case ascertainment were used. A mailing to approximately 1600 clinicians who were not members of the RCPCH but who may see children with LCH was sent out every six months from Newcastle University. The Newcastle mailing list included pathologists, radiologists, dermatologists, orthopaedic surgeons and endocrinologists. In addition, cases were cross-referenced with those registered by the UKCCSG who register 90-95% of all cases of childhood cancers and LCH in the UK and Ireland.

Number of cases expected

Since LCH was thought to affect approximately 1 in 200,000 children per year, approximately 70 cases per year were expected.

Denominator source

Population data for the UK was obtained from the Office for National Statistics (Mid-2003 Population Estimates) and for Ireland from Census 2002. The total population aged 0-17 years was 13,823 831.

Analysis

Over 330 cases were notified, and of 330 questionnaires mailed to clinicians, 263 (78%) were returned. There were 84 confirmed cases up to September 2005. The BPSU identified 81% of cases, 26% uniquely. The additional methods of ascertainment (Newcastle mailing and UKCCSG reconciliation) identified another 16 (19%) cases (Figure 16).

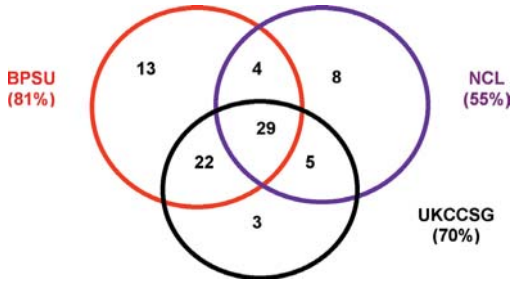

Figure 16: Case Ascertainment by source - confirmed cases

BPSU	Surveillance by BPSU
NCL	Mailing to specialists via Newcastle Study Team
UKCCSG	United Kingdom Children's Cancer Study Group Register

Over 70% of notifications were from paediatricians and oncologists, 20% from orthopaedic surgeons and pathologists and 6% from other specialists (Table 10).

Table 10: Notifications by Specialty

Specialty	% of notifications
Oncology	45
Paediatrics	29
Pathology	12
Orthopaedic Surgery	8
Dermatology	2
Paediatric Surgery	2
A&E	1
Gastroenterology	1

Of the 84 confirmed cases, there were 54 boys and 30 girls - a male to female ratio of 1.8:1. 86% of children were white and 14% were of mixed or other ethnicity. The median age at diagnosis was 5.7 years and was not significantly different for boys and girls, being 6.1 years for boys (age 32 days - 15 years) and 5.4 years for girls (age 43 days -13 years). 39% of cases were 0-3 years of age at diagnosis and there were none over 15 years.

70% of cases had single system disease (bone, skin, pituitary or lymph node), 90% of which were of bone. Over 60% of children with multi-system disease were aged under three years; eight cases had risk organ involvement (liver, spleen, bone marrow or lung) and three children died. The ratio of boys to girls with multi-system disease was 2:1.

The interval from the first symptoms to diagnosis was examined; 10% of cases were diagnosed in under three weeks and 40% of cases were diagnosed in 3-12 weeks. A further 40% were diagnosed between 12-48 weeks and 10% were diagnosed more than 48 weeks after the first symptoms. The mean interval from symptoms to diagnosis was 21 weeks. Four children had congenital LCH - two with multi-system disease, one with proptosis and another with Hashimoto-Pritzker Disease (skin). Three children were one of pairs of twins aged 11 months, 20 months and 12 years. Nine mothers had health problems during pregnancy, including hypertension (4), skin problems (3), hypothyroid (1) and cholestasis (1). Two children had medulloblastoma, one had partial Trisomy 3, one had pneumothorax and necrotising enterocolitis and one had had a seizure disorder since birth and developmental delay.

Discussion

The male predominance was similar to previous studies of single system involvement, however no difference between the sexes has previously been reported for multi-system involvement. The majority of single system disease cases involved bone. The other single system cases were of skin, pituitary and lymph node and it is notable that organs associated with multi-system were not affected in cases of single system LCH in this study. No familial cases of LCH were reported and only one mother was reported to have a thyroid problem.

The 84 cases reported to September 2005 give an incidence rate of 3 per million per year (CI 2.4 - 3.8) for children in the UK and Ireland aged 0-17 years. A recent study in the Northwest of England published an incidence rate of 2.55 per million per year[4].

Surveillance ended in June 2005 and the data presented is based on questionnaires returned up to September 2005. However at that time there were over 70 outstanding questionnaires. Since September 2005, 11 more cases have been confirmed bringing the current total to 95. Further eligible cases have been identified via the UKCCSG but they do not register all cases. We are grateful to all those who have returned questionnaires and would urge clinicians to return any outstanding questionnaires.

Conclusions

In a multi-centre study in France, an incidence rate of 4.5 per million per year aged 0-15 years was reported[5]. In comparison, for this age range, the BPSU study has so far identified 95 cases, the incidence rate for children aged 0-15 years in the UK and Ireland is estimated to be similar at 3.8 per million per year with several additional cases still expected to be confirmed. However, it is possible that there has been under-ascertainment of cases in patients in whom the symptoms were very mild and transient so that they never came to medical attention or were never investigated. Efforts are being made to collect the remaining questionnaires and one-year follow up questionnaires (which focus on treatment and outcome) will continue to be mailed until the end of May 2006. In addition, mortality data is being sought from the Office for National Statistics.

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

Final results are expected by the end of 2006.

Funding

The study has been funded by the Histiocytosis Research Trust.

Ethics approval

Ethical approval was given by the London Multi-centre Research Ethics Committee.

Support group

Although the main aim of the Histiocytosis Research Trust is to raise money for research, they are doing as much as possible to help connect families to information and to others with experience of similar problems and anxieties about Histiocytosis. Please contact for more information about this service.

18 Western Road, Wylde Green, Sutton Coldfield, West Midlands. B73 5SP.
Tel: 0121-355-5137. E-mail: info@hrtrust.org. Web: http://www.hrtrust.org.

Acknowledgements

We are grateful to the BPSU and all members of the RCPCH, as well as those clinicians on our alternate mailing list for their continued support. In particular we thank all clinicians who reported cases and completed questionnaires.

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Medium Chain Acyl CoA Dehydrogenase Deficiency


Prof C Dezateux

Key Points

- Medium chain acyl CoA Dehydrogenase Deficiency (MCADD) is an inherited metabolic disorder that may cause hypoglycaemia, encephalopathy and sudden death. 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 [1].

- The Department of Health and the National Screening Committee have funded a two year pilot newborn screening service for MCADD with a concurrent research evaluation. Screening commenced in March 2004, in six laboratories covering half of all UK births each year.

- The study 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 findings of this study will be used to inform newborn screening policy in the UK.

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[2,3,4]. 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[5,6,7,8,9], important questions remain unanswered[10]. 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.

A pilot screening service is being delivered from six newborn screening laboratories in England. This service started in March 2004, and continued for 24 months. The concurrent research study will estimate screening test performance, prevalence of MCADD in a screened population and clinical outcome to two years of age in the first instance in affected children diagnosed through screening, clinical presentation or sibling diagnosis.

Objectives

Primary: To ascertain all cases of MCADD diagnosed during the study period in order to determine clinical outcomes to two years of age.

Secondary: To determine the detection rate of screening for MCADD in a UK setting.

Surveillance period

Currently April 2004 – April 2008.

Methodology

Case definition

MCADD results from the lack of an enzyme required to convert fat stores into energy. During an intercurrent illness, particularly gastroenteritis, there may be progressive encephalopathy with hypoglycaemia, lethargy and hypotonia progressing to coma.

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[1].

Treatment entails avoidance of fasting, and use of an emergency dietary regime or admission to hospital during intercurrent illness.

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.
- Notified cases are reviewed by an independent diagnostic review panel.

Reporting instructions

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

Additional sources of data

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 undertaking MCADD screening.

Number of cases expected

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

The following will be reported:

- 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: By the end of February 2006, one hundred and eighty-two notifications of MCADD had been received by the BPSU. Of these, 36 were confirmed clinically diagnosed cases of MCADD, 75 were detected by newborn screening, three were old cases (diagnosed before April 2004), 35 were duplicates, six were notifications made in error, and 27 are as yet unknown, pending return of follow-up questionnaires.

Number of cases by source of data

The three sources of data are:

a) British Paediatric Surveillance Unit

b) Newborn screening laboratories currently undertaking MCADD screening, which notify screened cases

c) Biochemical Surveillance Scheme for MCADD (BioSS – MCADD)

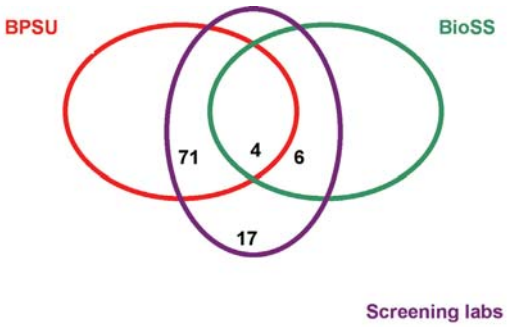

Figure 17: Number of Screen positive confired cases, N=98

Of the 36 diagnosed clinically, 19 presented clinically (including five deaths), one was investigated due to behavioural problems, and 16 were investigated because of affected siblings.

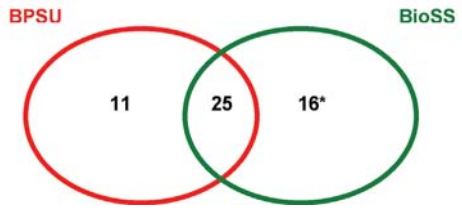

Figure 18: Number of clinically diagnosed cases, N=52

* Possible clinically diagnosed cases requiring further follow-up

Thirty-eight follow-up forms have been sent to clinicians in respect of infants diagnosed over one year ago. Thirty-four of these have been returned; the results are being collated and will be reported in next year's Annual Report.

Conclusions

As the second year of surveillance draws to a close, 182 notifications have been received through the BPSU. The data are consistent with reports of a higher frequency of MCADD diagnoses in screened compared to unscreened populations. BioSS appears to have received a substantial number of notifications for children not reported to the BPSU, however further follow-up is needed to confirm that these notifications represent genuine diagnoses of MCADD. 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, irrespective of whether they have been notified through the other schemes as it is only through the BPSU that clinical outcome can be ascertained. 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. Clinicians have also been encouraged to return any outstanding questionnaires.

Interim results from this study together with international evidence from other screening programmes will be considered by the National Screening Committee in 2006.

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

Funding

The Department of Health and the National Screening Committee.

Ethics approval

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

Support group

Children Living with Inherited Metabolic Disease (CLIMB). Climb Building, 176 Nantwich Road, Crewe, CW2 6BG. Tel: 0800 652 3181.
Web: http://www.climb.org.uk/Climb

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 support. We are also grateful to Professor Anne Green, Birmingham Children's Hospital and Dr Jim Bonham, Sheffield Children's Hospital, collaborators in the UKCSNS MCADD, who also helped set up the Biochemical Surveillance Scheme for MCADD. We also thank Professor James Leonard (Chair), Dr Jacqui Calvin, Dr Morteza Pourfarzam, Dr Johannes Zschocke and Dr Graham Shortland, members of the International Expert Diagnostic Review Panel.

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Methicillin-Resistant *Staphylococcus aureus* (MRSA) Bacteraemia

Dr A Johnson

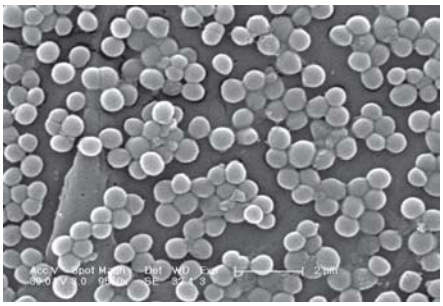
Ms C Goodall

Key Points

- 70 notifications of MRSA have been received from the BPSU, of which 32 have currently been confirmed as meeting the case definition.
- The majority of confirmed BPSU case notifications (68.75%) concern infants less than one year old.
- 27 of the isolates (79.4%) referred to the HPA Staphylococcal Reference Unit were characterised as healthcare-associated strains.

Background

Reports of bacteraemia in children due to methicillin-resistant *Staphylococcus aureus* (MRSA) have increased in recent years (Figure 19). 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. Isolates of MRSA from children will be 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 will be investigated.



Janice Carr

Figure 19: Scanning EM numerous clumps of MRSA: x9560.

Routine national surveillance has identified a worrying increase in MRSA bacteraemia, with the number of reported cases rising from four in 1990 to 77 in 2000[1]. Over half 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.

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 infections in children that have been acquired in the community with no demonstrable links to the hospital setting[2-5]. 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.

Surveillance period

June 2005 – June 2006 (inclusive).

Objectives

The study aims to determine

- the incidence of Methicillin-resistant *Staphylococcus aureus* (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.

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?

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

Additional sources of data

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 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 the 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).

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.

Number of cases expected

Approximately 100-120 per year.

Denominator sources

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

MRSA continued on page 37

Table 11: Reports made to the BPSU between June 2005 and March 2006

	Confirmed	Duplicates/or errors	Outstanding	Total
England	25	17	16	58
Wales	1	1	0	2
Scotland	3	0	1	4
Northern Ireland	2	0	0	2
Ireland	1	0	5	6
Total	32	18	22	72

Founded London 1986

BPSU TIMES 1986 -2006

http://bpsu.inopsu.com

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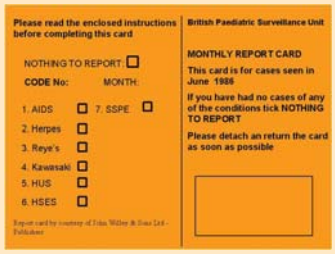
BPSU Celebrates 20 years of disease surveillance Page IV

Conditions on first card (July 1986)

The first mailing of the orange card in July 1986 surveyed 8 conditions; AIDS, XALED, Reye's syndrome, HUS, HSES, neonatal herpes, Kawasaki disease and SSPE. Paediatricians took to the new card reporting system quickly.



The response rate hit 85% within 6 months. By 1993 there were 14 studies on the card and the response rate had reached 95%. 20 years on it is still at 94%, 70 conditions have been studied and over 20,000 cases reported.

These have led to over 300 national and international presentations and publications.

1st BPSU Annual Report Published (1987)

20 years on the annual report and the quarterly newsletter has a worldwide circulation of 10,000, reaching many more via the web http://bpsu.inopsu.com

"Child disease aid for paediatricians" – BPSU birth announced in The Times (Feb 10th 1986)

A collaborative partnership was launched by the then British Paediatric Association, Public Health Laboratory Service and the Institute of Child Health (London) in February 1986 in collaboration with the Royal College of Physicians Ireland and the Scottish Centre for Infection and Environmental Health. The Unit aims to facilitate research into uncommon childhood conditions, increase awareness of such conditions within the medical profession and respond to public health emergencies. By 1993 such had been the success of the Unit, Sir Cyril Clarke was led to say "British and Irish paediatricians can feel justly proud of themselves as pioneers and key enactors of this unique system".

Professor Euan Ross (centre) celebrates his retirement with the rest of the BPSU Executive. Euan was the third BPSU chairman, the seventh and current being Professor Allan Colver.

Warning on Aspirin to be monitored (1986)

The newly established BPSU is to monitor the impact of the new warnings for aspirin upon Reye's syndrome incidence. Lead investigator Dr Susan Hall states "we now expect to see a fall in the numbers of this distressing condition".

Aspirin warning extended to all children (2002)

After monitoring the fall in Reye's syndrome for 15 years BPSU data has led to the aspirin warning being extended to cover to all children.

BPSU Secures Funding (1988)

The Research Trust of Children Nationwide (now Wellchild) supported the BPSU from 1988-95. In 1998 the Department of Health agreed to fund a proportion of the running costs and in 2004 this was extended for a period of 5 years to cover the full costs.

Time line of survey success

1986 – HUS survey confirms link with E.coli O157.
Fall in Reye's syndrome monitored
1988 – Ongoing surveillance VKDB monitors impact of management changes.
1990 – MMR-M survey identifies problems with the Urabi strain of the mumps vaccine.
Rett Syndrome register set up AIDS Surveillance to include HIV.
1991- Chemistry set poisoning – data leads to change in legislation on packaging.
1992-97 - Hib vaccine efficacy monitored.
1993 – Biliary Atresia survey leads to concentration of surgical service in just 3 units.
1994 – Water birth survey demonstrates no additional risk to mother and child.
1995 - Congenital cataracts - first study to involve ophthalmologists.
1997 - PIND - national survey to identify paediatric vCJD.
1998 – Inflammatory bowel disease survey involves adult gastroenterologists, identifies difference in management.
2000 – Data from Group B streptococcal survey suggests screening is not cost effective.
2003 – The first Sir Peter Tizard Research bursary is awarded to Dr Scott Williamson for a study into thyrotoxicosis.
2004 – Concern over increase in obesity leads to type 2 diabetes study.
2005 – Early onset eating disorders becomes first BPSU study to involve child psychiatrists.
2006 – BPSU Celebrates 20 years of disease surveillance by hosting an international conference.

In memoriam

BPSU remembers its leading lights:
Professor June Lloyd
Professor Sir Peter Tizard
Professor Sir Cyril Clarke
Professor David Baum
Dr Ralph Counahan

Historical Development of the British
of the Royal College of Pa

What is the BPSU?

A standardised and reproducible system for mounting surveillance of rare childhood disorders of public health importance.

Main Aims

To encourage and facilitate:

- research into uncommon childhood infections and disorders
- paediatricians in surveillance of uncommon disorders
- an increase in awareness of uncommon disorders
- a rapid response to public health emergencies
- dissemination of information about uncommon disorders
- improvement in prevention, treatment and service planning for uncommon disorders.

Clinical reporting: The Beginning

- 1962: Congenital malformation notification post thalidomide disaster
- 1970's: Lead ingestion surveillance through members of the BPA by Prof Donald Barltrop
- 1976-78: National Childhood Encephalopathy Study
- 1977: Communicable Disease Surveillance Centre (CDSC) set up by PHLS. Dr Spence Galbraith was its first director
- 1977: Dr Bill Marshall and Dr Tony Jackson suggested a clinical reporting system of uncommon or unusual events. Professor June Lloyd suggests paediatricians contribute to the reporting of infectious disease to CDSC.

Next Steps

- 1979 – 1980: BAPP/CDSC surveillance of Neonatal necrotising enterocolitis
- 1981: Dr Martin Bellman persuades CDSC to undertake "passive" surveillance of Reye's syndrome in collaboration with the BPA; Dr Susan Hall assigned
- 1982: Dr David Harvey supports CDSC's proposal to add HUS and Kawasaki Disease, Haemorrhagic Shock Encephalopathy Syndrome to the report form
- 1984: BPA Executive supports papers by Dr Galbraith and Harvey to set up joint BPA/CDSC Surveillance Unit using " active" reporting system.

Some of t

Sir Cyril Clarke

Dr Spence Galbraith

Prof E

Prof Catherine Peckham

Dr Su

BPSU Executive circa 2006

n Paediatric Surveillance Unit (BPSU)
ediatrics and Child Health

the Players

Sir Peter Tizard

Euan Ross

Prof David Baum

usan Hall

Dr Chris Verity

Children Nationwide (Wellchild) et al

Next Steps

- 1984: BPA Winter newsletter announced the formation of the Steering group: Sir Cyril Clarke (chair), Sir Peter Tizard, Professor David Baum, Dr Tim Chambers, Dr Spence Gailbraith, Professor Euan Ross, Professor R Boyd, Dr Joan Davies, Dr Dan Reid and Dr J Smith
- 1985: appointment of medical coordinator Dr Susan Hall and administrator Myer Glickman; Professor Catherine Peckham joins the Steering Committee; formation of Scientific Advisory Committee
- October 1985 – March 1986: Pilot mailing of report cards
- 1986 – February: The birth of the BPSU was announced in The Times and on the Today programme
- 1985 – September: First BPSU Steering committee held
- 1986 – July: Surveillance of eight conditions begins.

As Time Goes By

- 1986-87: RCPI representative Dr Ralph Counahan joins the Steering Committee
- 1990: Richard Lynn joins as scientific coordinator
- 1991: First time card has 12 conditions under surveillance
- 1997: BPSU launches its website (http://bpsu.inopsu.com)
- 1998: International Network of Paediatric Surveillance Units formed
- 2001: Dr Chris Verity, after 5 years, steps down as BPSU Executive chair
- 2003: Sir Peter Tizard Research bursary introduced
- 2004: DH funding secured for 5 years
- 2006: 20 years of surveillance celebrated.

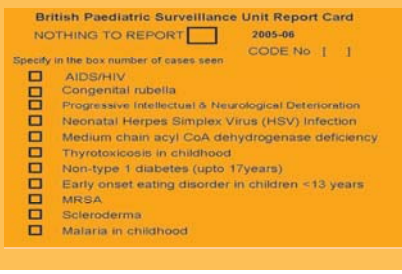
Achievements

Over 60 studies undertaken leading to over 300 papers and presentations and the BPSU methodology has been imitated across the world.

Acknowledgment

The success of the BPSU is wholly due to the contribution made by paediatricians. We thank all those who have returned cards and reported cases over the years. We also thank all our funders, in particular, WellChild and the Department of Health.

BPSU Celebrates 20th Surveillance Year



BPSU 20th Anniversary Conference (June 2006)

To celebrate the BPSU's 20th year of surveillance a conference highlighting the work of the unit was held at the Institute of Child Health (London). Over 140 delegates from around the world attended.

Presentations on topics such as inflammatory bowel disease by Professor Bhu Sandhu (below left), vaccine preventable disease, tuberculosis and biliary atresia were received, along with presentations from the first two Sir Peter Tizard bursary winners Dr Scott Williamson (thyrotoxicosis-below middle) and Dr Shamez Ladhani (malaria-below right).

Professor Angus Nicoll CBE (below left) was the guest speaker talking on pandemics and other emerging infections. The conference heard from Dr Sheila Shribman, the National Clinical Director for Children, who praised the work of the BPSU (below right).

BPSU bursary for young investigators launched (July 2003)

To encourage applications from junior doctors the BPSU introduced a bursary named after Sir Peter Tizard, one of the founders of the Unit. The bursary will be awarded each year to the deserving applicant. Three bursaries have been awarded, the latest, in 2005, to Dr Yim Yee Matthews to survey idiopathic intracranial hypertension.

BPSU duplicated across the globe (1992)

Such has been the success of the BPSU that paediatricians in Australia, Germany, Switzerland and the Netherlands have developed their own surveillance units. February 1992 saw the first meeting of the European Paediatric Surveillance Network. By 1998 there were 10 such national units, which joined to form the International Network of Paediatric Surveillance Units (INoPSU). By 2006 INoPSU had expanded to include15 units.

INOPSU

4th INoPSU Conference held in London (2006)

Following on from the successful conference in Lisbon in 2004, London hosted the 4th INoPSU conference. The meeting, attended by representatives from 12 of the 15 international units, heard presentations on conditions under surveillance in a various countries.

The Australian and New Zealand Units presented data on Fetal alcohol syndrome. The Canadian and British Units presented data on neonatal herpes and hyperbilirubinaemia. Talks on type 2 diabetes, vitamin k deficiency bleeding and acute flaccid paralysis were others that were received. A business meeting in the afternoon discussed potential joint studies for the future and the development of the INoPSU website (www.inopsu.com).

Surveillance of vCJD continues (May 2006)

Following the rise in cases of BSE in cattle during the 1990s and its subsequent association with vCJD, the BPSU thought it appropriate to commence surveillance for the condition. Dr Chris Verity, neurologist and then chair of the BPSU, leads the study. Since 1997, only 6 paediatric vCJD cases have been identified, whilst over 1500 cases of progressive intellectual neurological degenerative conditions have been identified.

"It is a matter of pride for this country that the innovative and scrupulous epidemiology of the BPSU has been emulated by several countries in Europe and beyond."

Professor Sir Liam Donaldson, Chief Medical Officer (Sept 2001)

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	22	7	2	1	0	32
Reference Laboratory Isolates	19	9	2	3	1	34
LabBase 2 reports	43	10	2	7	0	62

Analysis

By April 2006, 72 notifications of MRSA bacteraemia have been received (Table 11). However, 16 notifications were made in error (for example MRSA isolated from skin swabs not blood), and two duplicate notifications have been received.

At present there are 32 confirmed cases with 22 outstanding questionnaires yet to be returned. Of the 32 confirmed cases notified by paediatricians, 78% (25/32) were submitted by paediatricians in England, 9% (3/32) from Scotland, 6% from N. Ireland and 3% each from Wales and the Ireland (Table 11).

Of the notification source, reports were concentrated in children less than one year old (BPSU, 69%; Reference Laboratory, 56%; LabBase, 69%), although a substantial proportion of cases was reported in infants aged 1-4 years (BPSU, 22%; Reference Laboratory, 26%; LabBase, 16%) (Table 12).

Voluntary routine reporting to LabBase identified 62 cases while 23 cases were detected following referral of an isolate to the Reference Laboratory; nine cases were confirmed by all three reporting routes (Figure 20).

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)

Phage Type	Total
EMRSA-15	24
Distinct strain	4
Phage non-typable	2
EMRSA-15 positive variant	1
EMRSA 15 variant	1
EMRSA 16 variant	1
Irish	1
Total	34

Discussion

The results suggest that

1. MRSA bacteraemia in children remains rare in contrast to the situation in adults (where more than five thousand cases were reported in 2004).

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.

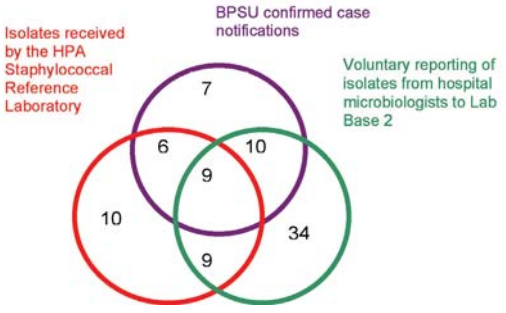


Figure 20: Muliple source case ascertainment

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 for their continued support, especially those who have notified cases and completed questionnaires.

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Neonatal Herpes Simplex Virus (HSV) Infection

Key points

- In the first two years of surveillance, 2004 2005, fifty-six infants were reported with confirmed neonatal HSV through the BPSU A further two confirmed cases were reported independently of the BPSU directly to the study investigators.
- Virus was typed in more than 95% of cases, and about 45% 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 this two-year period is suggestive of an increase in prevalence over the last 20 years.

Background

Neonatal herpes simplex virus (HSV) infection is a rare but potentially devastating condition. 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[1].

Surveillance of neonatal HSV was previously undertaken through the BPSU between 1986 and 1991[2]. Seventy-six cases were reported over the five and a half year period, and the estimated prevalence of neonatal infection was then 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[3]. 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 is to

- estimate the current prevalence of neonatal herpes 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 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 1st January 2004 and 31st December 2006 in the UK or Ireland with confirmed or suspected neonatal HSV infection.

Additional sources of data

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

Number of cases expected

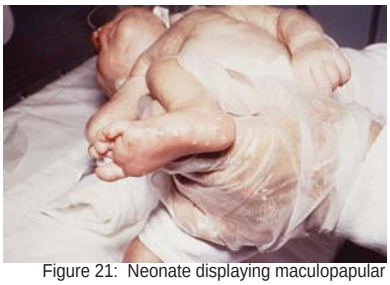
On the basis of the previous study, and allowing for a modest increase in prevalence, it was expected that there would be 10-25 confirmed cases a year.

Denominator source

The total number of live and still births in the UK over the study period, obtained from the Office for National Statistics (ONS). Irish birth rate obtained from the Irish census 2002 (Central statistics office, Ireland).

Analysis

Number of reports: By the end of December 2005 there had been 119 reports through the BPSU, of which 56 were confirmed cases of neonatal HSV infection, 10 were suspected, and 39 were duplicates or reporting errors. The remaining 14 reports were still being investigated. A further two confirmed cases were reported directly to the study investigators.



Judith Faulk

Figure 21: Neonate displaying maculopapular outbreak on feet due to congeuetally acquired HSV.

Confirmed and suspected cases: About 45% of the 58 infants with confirmed infection had HSV-1 infection. In just over a quarter of confirmed cases infection was localised to the skin, eye or oral mucosa (SEM); about 60% of those with disseminated and/or CNS infection had no SEM involvement. About a third of infants were born to young mothers (under 21 years at delivery), and almost 40% were premature. Diagnosis of maternal genital infection prior to delivery was extremely rare. 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 20% of cases a possible source of postnatal infection was identified, usually a close relative of the infant.

Follow up

Summary follow-up information is being sought in the second year of life.

Discussion

There have been more cases reported in each of these two years than in any single year in the previous study period[1]; these data are consistent with an approximate doubling of prevalence, although it is too early to make a robust estimate of prevalence since numbers are still relatively low, 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 2004 findings are similar to the previous survey. Data collection continues, and we have already started seeking follow-up information on outcome in the second year of life for children reported in the first year of surveillance.

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

Funding

The National Screening Committee is providing funding to keep neonatal HSV 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 18th December 2003 (London MREC/03/2/080). Patient Information Advisory Group 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.
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.

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Researchers

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Non-type 1 Diabetes

Key points

- Surveillance was undertaken to establish the incidence of non-type 1 diabetes in children in the UK and Ireland.
- A parallel reporting scheme was set up with diabetic nurse specialists to identify any cases referred straight to adult services.
- The majority of cases were obesity-related type 2 diabetes with a positive family history.
- Follow-up one year after diagnosis will report short-term morbidity and confirm diabetes status.

Background

The recent epidemic of childhood obesity has led to concerns that there may be a parallel increase in the number of children with type 2 diabetes given that type 2 is linked with obesity in adults. Although early reports of type 2 in children were in specific ethnic populations[1,2], four cases were recently reported in obese white adolescents in the UK[3] and a national survey of UK paediatric endocrinologists in 2000 identified 25 cases in children under 16 years of age[4]. If, as in the USA, the increasing incidence of childhood obesity in the UK is associated with an increase in the prevalence of type 2 diabetes[5] then there is likely to be a significant impact on health service resources.

If the number of children with type 2 diabetes is rising it will become increasingly important to classify the type of diabetes correctly as the appropriate treatment is often different. Although children with type 1 diabetes often present with an acute illness, such as diabetic ketoacidosis (DKA) while type 2 diabetes has a slower, more insidious onset, the clinical presentation of children with type 2 diabetes may be indistinguishable from type 1. Certain clinical features are highly suggestive of type 2 diabetes, including obesity, a family history of type 2 diabetes, acanthosis nigricans and polycystic ovarian syndrome. The presence of antibodies to glutamic acid decarboxylase-65 (GAD-65), tyrosine phosphatase (IA-2α), and islet cells (ICA) can confirm autoimmune diabetes in children where there is diagnostic doubt and the absence of autoantibodies in children with obesity-related diabetes strongly suggests type 2 diabetes. However, 10% of children with type 2 diabetes also have a positive antibody test.

Ms L Haines

Objectives

The survey will establish

- the UK and Ireland incidence of non-type 1 diabetes in children.
- and explore the early clinical features of type 2 diabetes and its association with obesity.

The follow-up questionnaire at one year, identifying clinical management, will help to confirm how many non-type 1 cases are type 2 and will also examine short-term morbidity.

Surveillance period

October 2004 – October 2005 (inclusive).

Methodology

Case definition

The case definition was any new diagnosis of non-type 1 diabetes (suspected or confirmed) in a patient 0-16 years of age. These were not necessarily new cases of diabetes, but newly recognised as atypical for type 1.

Paediatricians were asked to report all cases on the orange cards. 157 specialist diabetes nurses (SDNs) were identified as additional sources of cases and asked to report cases every two months. Paediatricians reporting a case were sent a clinical questionnaire and completed questionnaires were scrutinised to confirm that the cases met the study criteria and that cases were diabetic according to the American Diabetic Association (ADA) criteria. The physician diagnoses were also reviewed in the light of the information provided on the questionnaire. A case was only categorised as type 2 diabetes on the basis of the presence of one or more signs of insulin resistance (high insulin level, high C peptide levels or a report of acanthosis nigricans). For valid cases, a second questionnaire is being sent to the reporting paediatrician one year

after the case was first reported. On completion of the surveillance period, we will determine the incidence and presenting patterns of the various causes of non-type 1 diabetes (NT1D), as well as establishing management patterns and any associated morbidity.

Reporting instructions

Paediatricians and SDNs were asked to report any new cases seen for the first time during the surveillance period.

Additional sources of data

It was recognised that paediatricians may not see older teenagers, therefore to maximise ascertainment SDNs were included in the surveillance. A monthly parallel reporting system was therefore established. A card was sent each month to designated SDNs to report cases of NT1D. Those reporting cases were contacted in the same way as the paediatricians.

Number of cases expected

Approximately 100 confirmed cases were expected to be reported in the 13-month period.

Denominator source

The total number of births in the UK over the study period, obtained from the Office for National Statistics (ONS). Ireland: census 2002 (Central statistics office, Ireland).

Analysis

During the 13-month surveillance period, a total of 361 cases were notified; 248 (69%) of these cases through the BPSU and the other 113 (31%) were notified by nurses. To date clinical data has been retrieved for 338 (94%) cases.

168/361 (47%) cases have been confirmed as meeting the American Diabetic Association criteria for diabetes and having NT1D. Of these, 93 were girls and 75 boys. The overall mean age at diagnosis of NT1D was 12.6 years with the majority (82%) aged between 11 and 16 years. In 65% of cases of NT1D there was a family history of diabetes. 44% of cases had a history of diabetes in a parent or sibling, and a further 21% in other relatives. The majority (72%) of cases were in white children while 13% of cases were in Asians / Asian British and 8% in blacks / black British.

A distribution of the different types of NT1D reported is shown in Figure 22. Type 2 diabetes was the most commonly reported with 81/168 (48%) cases. Of these 81 type 2 cases, 69 have been confirmed and 12 are probables – confirmation will be obtained at follow-up. 13 cases were a revised diagnosis of type 1. There were also 11 cases, which were unclassified i.e. did not meet the criteria for type 2 but which also did not meet the criteria for type 1. Of the 81 type 2 cases, 44 (54%) were female, presenting mainly in puberty with ages ranging from 9.9 to 16.8 years. 85% of cases had a family history of diabetes, 67% of which were in a 1st degree relative. 75% of children were obese and all but three were overweight; the mean BMI SDS was 3.03 (girls) and 2.43 (boys). A higher proportion of white children (58%) were reported to have type 2 compared with those of ethnic minority origin (42%).

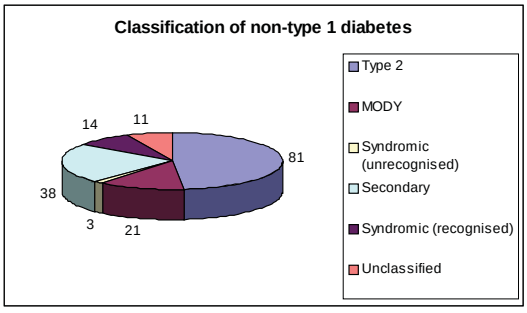

Figure 22: Types of non-type 1 diabetes reported (October 04-October 05)

Secondary diabetes made up 38/168 (23%) of reported cases. Of these, 22 cases were diabetes secondary to cystic fibrosis. Other diagnoses included steroid-induced diabetes and diabetes as a result of bone marrow transplantation. 21/168 (13%) were cases of confirmed or probable MODY (Maturity Onset of the Young). 14 cases were associated with a recognised syndrome of which nine (56%) were neonatal diabetes. The other four cases were associated with Alstroms, Turner, Mulivihill-Smith, DIDMOAD and Wolcott-Rallison syndrome. In addition, there were three cases reported as having diabetes as part of an unrecognised syndrome.

Further analysis of the clinical data is ongoing and a full report will be available at completion of the study. In this study, diabetic nurses appear to have reported many additional cases not reported by the paediatricians. However, as SDNs and paediatricians often work in teams, the reporting sources were not usually independent and joint reporting occurred in the majority of cases. In fact,

it emerged that all but three cases were diagnosed and treated by paediatricians; only three cases seen by adult endocrinologists/diabetologists. For this reason, capture-recapture analysis will not be used in this study [6].

Discussion

This study will provide the first estimates of incidence for non-type 1 diabetes in children under 17 in the UK and Ireland. Although the data are still being analysed, they suggest that cases of type 2 diabetes in children are more common than previously supposed and more common than MODY in white children. Nearly all type 2 cases are associated with being overweight or obese together with a positive family history. The results suggest that obesity-related type 2 diabetes is a growing problem across all ethnic groups.

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

Funding

The study has been partly funded by a grant from Diabetes UK.

Ethics approval

The South West MREC (ref 04/MREC06/39) and the Patient Information Advisory Group have approved this study (PIAG/BPSU 2- 10(b)/2005).

Support group

Diabetes UK, from whom patient information is available on request, can be contacted at 10 Parkway, London NW1 7AA. Tel: 020 7424 1000. Web: http://www.diabetes.org.uk.

Acknowledgements

We are grateful to the BPSU and all members of the RCPCH, as well as those DSN's on our alternate mailing list for their continued support. In particular we thank all clinicians and DSN's who reported cases and completed questionnaires.

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Progressive Intellectual and Neurological Deterioration in Children

Key Points

- After almost nine years of surveillance 2030 children have been notified. 1450 cases have been discussed by the Expert Group of six paediatric neurologists. 862 have a definite diagnosis which is not variant Creutzfeldt-Jakob disease (vCJD), and these comprise 114 known degenerative conditions.
- Six cases of vCJD 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 Surveillance Unit. All have now died.
- Further active surveillance is planned until January 2007.
- 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 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[1]. vCJD (Figure 23) has been described in patients as young as 12 years of age[2] and it could occur in younger children. It is possible that the clinical presentation of vCJD in young children might be different from that described in adults. The strategy is to detect suspected vCJD cases by looking at a broader group of conditions causing 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 affect children. An Expert Group of seven paediatric neurologists independently reviews the anonymised clinical details for all the PIND cases. In this way, not only is there

Mrs L Stellitano
Dr C Verity
Ms A M Winstone

the opportunity to detect vCJD cases, but also unique epidemiological data on a variety of PIND conditions are obtained[3].

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.

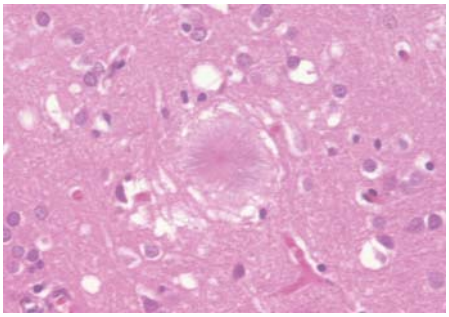

Figure 23: Florrid plaque in vCJD x 400 haematoxylin/ eosin stain

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 - 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.

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 will be used as the denominator. These will be obtained from the Office for National Statistics and in Ireland from the census 2002 (Central Statistics Office, Ireland).

Analysis

By the end of January 2006 a total of 2030 children had been reported via the BPSU (see Figure 24). There were 862 PIND children with a definite underlying diagnosis, 119 in whom no diagnosis had been made and 132 who were still under investigation. There were 829 "No Cases" including those who did not fulfil the criteria for PIND, reporting errors, duplicate notifications etc. The 82 outstanding cases include eight due for discussion at the April 2006 Expert Group meeting and 74 awaiting data collection. The six cases of definite/probable vCJD are discussed below.

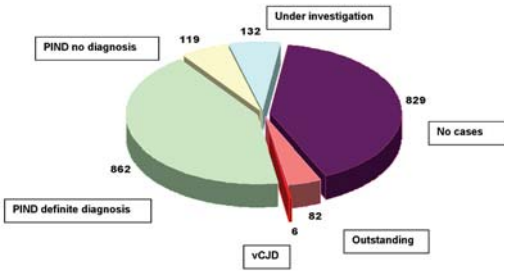

Figure 24: PIND study - current status

Definite/Probable cases of vCJD: Six cases of vCJD 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 died without neuropathological study (classified by the NCJDSU criteria as "probable" cases[4]).

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 862 children with a confirmed diagnosis other than vCJD there were 114 different neurodegenerative conditions. The eight most commonly occurring diagnoses are shown in Figure 25 (page 47).

Variation in reporting by district: Geographical analysis by hospital of reports 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 (242 cases) with North East Thames (217 cases) followed by West Midlands (216 cases).

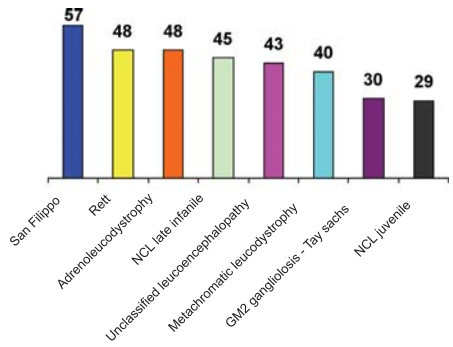

Figure 25:Eight most commonly reported PIND diagnoses

Variation in reporting by category of referring:
General paediatricians notified the largest number of children followed by paediatric neurologists then community paediatricians. (See Figure 26)

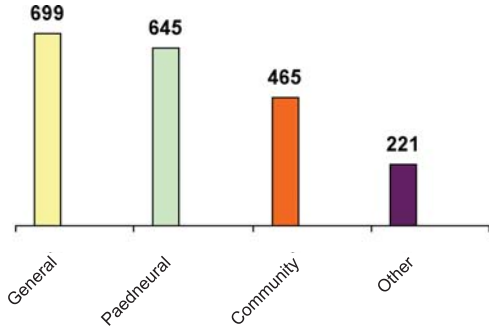

Figure 26: Category of referring paediatrician

Discussion

PIND surveillance has been running for almost nine 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. Nine 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. New cases are still appearing in older patients and there is now concern about possible transmission of vCJD by blood products.

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), the Public Health Laboratory Service Ethics Committee and the Patient Information Advisory Group (PIAG/BPSU 2-10(c)/2005).

Acknowledgements

PIND surveillance is working 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 18 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 S. Green, Dr. M. Pike, Prof. R. Robinson, Prof. R. Surtees and Dr J. Wilson) for all their work in classifying cases.

Support Groups

1. Creutzfeldt-Jakob Disease Support Network, CJD Support Network, P.O.Box 346, Market Drayton, Shropshire,TF9 4WN
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2. Batten Disease Family Association, c/o Heather House, Heather Drive, Tadley, Hampshire, RG26 4QR.
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3. The Society for Mucopolysaccharide Diseases, MPS House, Repton Place, White Lion Road, Amersham, Buckinghamshire, HP7 9LP, UK
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   Web: http://www.mpssociety.co.uk/

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://wwwclimb.org.uk

5. Adrenalleukodystrophy (ALD), ALD Family Support Trust,30-32 Morley House, 320 Regent Street, London, W1R 5AB.
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6. Niemann Pick Disease Group, 11 Greenwood Close, Fatfield, Washington,Tyne and Wear NE38 8LR
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Scleroderma in Childhood

Dr A Herrick

Key points

- Thirteen cases of childhood scleroderma (12 linear, one systemic sclerosis) have been notified since July 2005.
- Childhood scleroderma may be even more rare than previously thought.
- A period of surveillance longer than 13 months will be required to provide clinically meaningful data on secondary research questions including: presenting symptoms, delay in diagnosis, patterns of care, and age and gender of children affected.

Background

Scleroderma is well described in children as well as in adults, and is associated with significant morbidity and mortality[1-4]. While some children with scleroderma have systemic sclerosis (SSc), more commonly scleroderma in children is localised in that it is confined to the skin and underlying tissues.

Systemic Sclerosis. There are two main subtypes of SSc - limited cutaneous and diffuse cutaneous (Figures 27, 28 & 29). 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[5]. Even if rare, SSc in children is an important condition because its internal organ involvement can be life-threatening.

Localised scleroderma. Although localised scleroderma (as opposed to 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. If the affected area crosses a joint, for example knee or elbow, then contracture and growth retardation can occur (Figure 30) and skin lesions can also be very disfiguring, especially if the face is involved. As with SSc, little is known about the epidemiology of localised scleroderma in children. Applying the incidence obtained in the United States Rochester Epidemiology Project[6], we anticipated approximately 450 children per year to be diagnosed as having localised scleroderma, of whom around 40% (180) would have the linear form of the disease. The paucity of data on localised scleroderma incidence

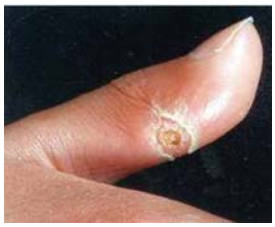

Figure 27: Limited cutaneous

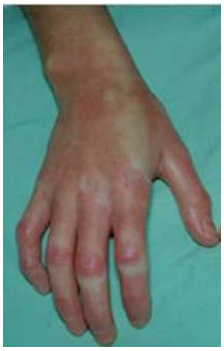

Figure 28: Diffuse cutaneous

Figure 29: Diffuse cutaneous

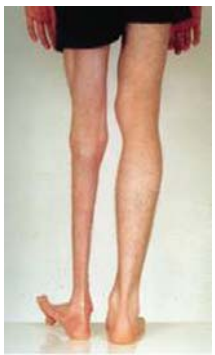

Figure 30: Localised

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 there is potential benefit from early diagnosis and intervention at this stage of the disease.

Objectives

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

- usual presenting symptoms.
- delay between symptom onset and diagnosis.
- pattern of care received by the affected children before and after diagnosis.
- age at which most children are affected.
- the male: female ratio of affected children and whether this varies with age.
- regional and ethnic variations.

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 a dermatologist or paediatric rheumatologist has confirmed the diagnosis.

Reporting instructions

Paediatricians were asked to report any new or possible cases meeting the surveillance definition during the period of surveillance, irrespective of whether it was felt that the case would be reported elsewhere.

Additional sources of data

Although it is anticipated that the BPSU will be the main source of case ascertainment, some children with scleroderma are referred directly to adult rheumatologists or dermatologists with an interest in scleroderma. Questionnaires are also being sent to members of the British Society for Paediatric and Adolescent Rheumatology, the British Association of Dermatologists, and the UK Scleroderma Study Group.

Number of cases expected

It is anticipated that in the order of 180 patients per year will be notified with localised scleroderma and approximately 20 with systemic sclerosis. However it already appears, as outlined below, that numbers may fall short of this.

Analysis

Until the end of March 2005, 49 cases were notified. Of these 49 cases notified, we received 24 questionnaires (25 questionnaires are awaited). Of the 24 notified only 13 have been valid (and one was a duplicate). Most of the invalid cases (9 out of 11) have been due to their referral prior to June 2005. The other two were not felt to be cases of scleroderma.

Of the 13 valid cases notified six were female and seven male. The median age was 7.5 years (range 4 to 14 years). Twelve had linear scleroderma and one had SSc.

Discussion

The small number of notifications may reflect both the rarity of childhood scleroderma as well as the difficulty with making this diagnosis at an early stage of the disease.

All efforts are being made to maximise recruitment during the forthcoming months. Awareness is being raised regarding the study, for example by discussion at professional meetings.

Conclusions

The study remains at an early stage but the main conclusions so far are as follows:

1. Childhood scleroderma (both localised and in association with systemic sclerosis) is rare.

2. Awareness of the spectrum of childhood scleroderma is being increased.

3. The surveillance period has been extended to allow a sufficient number of notifications to answer the secondary research questions.

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

Funding

The Raynaud's and Scleroderma Association are funding the study.

Ethics approval

The study has been approved by the South Manchester Research Ethics Committee and the Patient Information Advisory Group (PIAG/BPSU 4-059a)/2005).

Support Group

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Web: http://www.raynauds.org.uk.

Acknowledgements

We are extremely grateful to all paediatricians who have already notified cases and/or expressed interest in the study.

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Thyrotoxicosis in Childhood

Key Points

- To determine the incidence of thyrotoxicosis in childhood, clinicians are being asked to report all new cases of thyrotoxicosis seen in children under 16 years.
- Preliminary results are available for 12 months of the study while a small number of questionnaires are still awaited.

Background

The incidence of thyrotoxicosis in children in the UK and Ireland is not known. Graves' disease is known to be the commonest cause of thyrotoxicosis in the general population (60-90% of cases worldwide), followed by rarer causes such as solitary thyroid adenomas, multinodular goitre and, in neonates, congenital Graves' disease. Data from other countries in Europe report incidences of Graves' disease in childhood from 0.79/100,000 per year (Denmark[1]) to 8/100,000 per year (Iceland, 10-19 yr olds)[2]. The incidence in Hong Kong was recently reported as 6.5/100,000 per year[3]. The mean age of diagnosis there has been reported as 11.34 years with a female: male ratio of 5.5:1[4].

In some countries the incidence of Graves' disease is increasing and increased dietary intake of iodine has been implicated[4,5]. Other than this the aetiology of Graves' disease is unknown, but genetic susceptibility, puberty and emotional stress are known contributing factors[6]. The pattern of practice in investigating thyrotoxicosis is not clear. The gold standard for detecting primary hyperthyroidism is a suppressed thyroid stimulating hormone (TSH), but diagnosing the underlying condition may be more difficult. Clinicians may rely on history, clinical findings and basic thyroid function tests to diagnose Graves' disease, or they may wish to investigate further to distinguish it from the other rarer forms of thyrotoxicosis in childhood which may present with identical symptoms and signs. Treatment options for the child with Graves' disease are medical (antithyroid drugs), surgery and radioiodine. Worldwide debate over the safest and most effective use of these treatments in children continues, but historically in Europe antithyroid drugs have been favoured[7].

This study aims to be a comprehensive survey of childhood thyrotoxicosis in the UK and Ireland in order to make the best data available on the current incidence, patterns of presentation and management of this disease. As well as an increased understanding of this disease, the provision of this data is expected to direct future studies, and give clues to the best management of children with this condition.

Dr S Williamson

Objectives

The study aims to identify what

- the incidence of childhood Graves' disease in the UK and Ireland?
- are the incidences of the other causes of childhood thyrotoxicosis, in the UK and Ireland?
- are the presenting features of thyrotoxicosis in children?
- initial management is received by children in the UK and Ireland diagnosed with thyrotoxicosis?

Surveillance period

September 2004 - September 2005 (inclusive).

Methodology

Paediatricians are asked on a monthly basis to report all cases meeting the case definition through the orange card system. Paediatricians reporting a case are sent a questionnaire seeking demographic details and clinical features. On completion of the surveillance period, the incidence and presenting patterns of the various causes of thyrotoxicosis will be determined.

Case definition

Any child less than 16 years of age who in the opinion of the notifying paediatrician has thyrotoxicosis, based on history, clinical and laboratory findings.

Reporting instructions

Clinicians were asked to report any new cases that were seen for the first time during the surveillance period.

Additional sources of data

It is assumed that a small number of children with thyrotoxicosis presenting in the older age range covered by the study, i.e. 14-16 yr olds, would be treated as adults and would be referred for diagnosis and treatment to a general endocrinologist. These children would therefore not be notified via the orange card system. In order to include these children in the survey, as many of the general endocrinologists practising in the UK and Ireland as possible needed to be informed of the study. This was done by publicising the survey by e-mailing lists, newsletter and conference fliers through the following societies: *British Society for Paediatric Endocrinology and Diabetes, Society for Endocrinology, British Thyroid Association, The Irish Endocrine Society and British Endocrine Societies annual conference.*

Number of cases expected

Based on an incidence of 0.79/100,000 cases per year (Denmark[1]), the expected number of cases of Graves' disease in this study were 90 cases per year in the UK and seven cases per year in Ireland.

Denominator source

Population estimates are based on:
UK: Mid-2004 Population Estimates from Office for National Statistics (11,645,600 children <16ys)
Ireland: census 2002 data (888,310 children <16yrs) (Central statistics office, Ireland).

Analysis

Over the 12-month period there were 156 confirmed cases of childhood thyrotoxicosis in the UK and four confirmed cases in Ireland. Confirmation of a further 17 reports is awaited. The prevailing causes are: Graves' 74%; Hashimoto's 11%; Congenital 8%. Currently the annual incidence of acquired thyrotoxicosis is 1.14 per 100,000 (0-15 yr olds) for UK and Ireland, and the incidence of congenital thyrotoxicosis is 1 case per 59,830 live births based on confirmed cases. In Graves' disease the mean age at diagnosis is 12.4 yrs (range 3.3 - 16.0). In females there was a sharp rise in incidence after the onset of puberty. Prepubertally the Female : Male ratio was 1.25:1 and after the onset of puberty a Female : Male ratio of 4.6:1 was observed. A variety of presenting symptoms (all causes) were reported, with the commonest being weight loss (61%) and 'change in behaviour' (53%). The commonest signs were tachycardia (82%), goitre (72%) and tremor (65%). There was one case of thyroid storm. 10% of cases overall were asymptomatic when they were diagnosed.

Discussion

These findings show a similar incidence of Graves' disease to other countries in Europe. An increase in incidence cannot be suggested by these results alone, so we recommend that the study be repeated in 5 or 10 years time to establish this. The study has described the modern presenting features of this disease and report for the first time a substantial group of children diagnosed biochemically, before symptoms have been noted. The previously reported sharp increase in the incidence in girls after the onset of puberty is outlined by the data. The practice of managing thyrotoxicosis with drugs alone is confirmed by the preliminary results although this may be subject to change, once follow up data at one-year post diagnosis has been received.

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

Funding

RCPCH - Sir Peter Tizard Bursary.

Ethics approval

The Scottish MREC approved this study in July 2004.

Support Groups

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Web: http://www.btf-thyroid.org.

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6 New Studies 2006

Malaria in Children

The United Kingdom currently has the highest incidence of imported malaria cases among industrialised countries[1]. 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 [2]. The incidence of paediatric malaria in the UK has tripled over the past 30 years[3,4] and what is particularly concerning is that the proportion of cases due to Plasmodium falciparum, which is responsible for almost all the complications of malaria (shock, severe anaemia, acute renal failure, convulsions, coma, long-term neurological damage and death[5], has increased exponentially over the past three decades. Nationally, the proportion of P. falciparum cases reported to the MRL has increased from 17% in 1977 to 40% in 1987 and 77% in 2001 in both adults and children[2]. In children, one south London observational study reported that the proportion of cases due to P. falciparum in children rose from 50% in 1975-1979 to 82% in 1990-1999[4]. Many parents who have immigrated to industrialised countries continue to take their children back to their home countries, often with no prophylaxis[6]. In addition, because children with malaria often present with symptoms of common childhood illnesses, the diagnosis is often missed initially. A recently completed six-year retrospective study of children with malaria in East London found that only 15% took appropriate antimalarial prophylaxis[7]. The General Practitioner suspected malaria 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[7]. Previous studies have consistently shown that delay in diagnosis is the single most important determinant of an adverse outcome in imported malaria[8].

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

James Gathnay-CDC

Figure 31: Female *Anopheles freeborni* taking a blood meal from a human host.

Dr S Landhani

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 is based on laboratory notifications, current knowledge on the clinical features of imported malaria is limited to small retrospective case series. As a result, for example, there is no data on the incidence, risk factors, clinical features, management and outcome of severe malaria in children. 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. The BPSU 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.

Ojectives

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

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

Surveillance period

January 2006 – January 2007 (inclusive).

Methodology

Paediatricians will be asked on a monthly basis to report all cases meeting the case definition through the orange card system. Paediatricians reporting a case will be sent a questionnaire seeking information on travel history, antimalarial prophylaxis, presenting features, severity, diagnosis, laboratory investigations, management and outcome at hospital discharge.

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

Additional data sources

The first page of the questionnaire requests minimal information about the patient to allow cross-reference with the MRL database, which will be used as an additional alternative data source.

Expected numbers (per year)

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

Source of denominator data

The denominator used will be children under 16 years of age as identified by the Office of National Statistics.

Funding

Sir Peter Tizard Research Bursary provided by the RCPCH.

Ethics approval

This study has been approved by the Leicestershire, Northamptonshire, and Rutland MREC (Reference: 05/Q2502/120). Patient Information Advisory Group approval comes via the HPA.

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Vitamin K Deficiency Bleeding

Background

Vitamin K deficiency bleeding (VKDB) is a rare, potentially-handicapping or fatal condition of the early months of life (Figure 32). The latest BPSU study (2000-'02) demonstrated the lowest incidence of VKDB for 15 years with no mortality or long-term morbidity[1,2]

At the time of this study 60% of newborns received intramuscular (IM) VK prophylaxis, most of these receiving the cremophore preparation (Konakion Neonatal)[3]. A single IM 1mg dose of this preparation has been shown to protect almost every baby against VKDB for several months[4]. It is possible that this prolonged protection results from the formation of an 'intramuscular depot' at the injection site, from which the VK is only slowly absorbed[5].

The manufacturer has now withdrawn this preparation in the UK, as it has already done in the rest of Europe, and recommends that the micellar preparation (Konakion MM) be used for IM prophylaxis. Konakion MM has a very different formulation which enhances bioavailability when given orally - however there is little information about long term serum levels after a single IM dose (We understand a small number of infants underwent formal pharmacokinetic evaluation with blood levels but we are not aware of any published data) and its efficacy in protecting against late VKDB in large populations is unproven by epidemiological or survey data.

The Medicines and Healthcare Product Regulatory Agency advised the manufacturer to attempt a study to monitor the effects of withdrawing the cremophore preparation. Hoping that this could be achieved by another BPSU study of VKDB, the manufacturers delayed withdrawal of Konakion Neonatal to mid 2006.

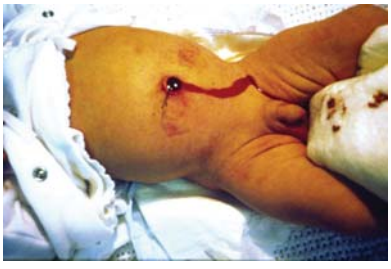

Figure 32: Bleeding from umbillicus due to VKDB

Dr A Busfield

Among other things this study aims to provide information, not currently available, about the efficacy of a single IM injection of Konakion MM 1mg in preventing late VKDB.

Objectives

The study aims to document

- incidence of VKDB and associated outcomes (death, intracranial bleed, significant sequelae) following the withdrawal of Konakion Neonatal.
- what prophylaxis failed to protect, or reason if none given.
- presence of risk factors such as breast feeding, liver disease or other causes of malabsorption.
- clinical presentation – timing, site of bleed, warning bleeds.
- treatment given to correct bleeding and its effectiveness.

Combining data from a contemporaneous survey of prophylaxis practice will allow determination and comparison of the efficacy and effectiveness of different prophylaxis regimens, including intramuscular Konakion MM, 1mg.

Surveillance period

Autumn 2006 – Autumn 2008.

Methodology

Notifying paediatricians will be asked to complete a questionnaire and cases will be classified as 'confirmed', 'possible' or 'no case' by the criteria used in the three previous studies, to document

trends in the British Isles; cases of late VKDB will also be classified by the more stringent international criteria [1,4] to allow international comparisons. No specimens are required to be collected.

A contemporaneous survey of maternity units in the study area will be undertaken to document the VK prophylaxis policies and annual delivery rate in each. This will provide the denominator data necessary to determine the efficacy and effectiveness of different prophylactic regimens in use

Case definition

The definition used in three previous BPSU studies of VKDB will be used to allow direct comparison:

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

Cases of late VKDB will also be classified in accordance with the more stringent criteria internationally agreed for this important sub-group, to allow international comparison:

Any infant 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 4 X control value (or INR greater than 4.0) 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 PIVKA proteins above normal controls.

Reporting instructions

Please report any new case, definite or doubtful.

Expected numbers (per year)

0-70 cases per year

Source of denominator data

If no vitamin K prophylaxis is given the incidence of VKDB is estimated at 1/10,000 births in the proposed study area[2]. This would result in 60-70 cases/year with current birth rates. There were only 8 confirmed cases during the 2-year BPSU study in 2001-2[1] when most of the 60% of units recommending IM prophylaxis used cremophore Konakion Neonatal, 24% used oral regimens and 16% offered both[3]. If Konakion MM does not provide equivalent protection the incidence of VKDB will rise but not exceed 1/10,000 births.

Funding

Roche pharmaceuticals.

Ethics approval

Has been obtained from Cornwall Research Ethics Committee (ref 06/Q2101/74). Site-specific approval for Trusts reporting cases is not required. Patient Information Advisory Group approval being sought.

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7 International Network of Paediatric Surveillance Units (INoPSU)

Figure 33: 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, in 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 more recently by units in Canada (1996), Papua New Guinea (1996), New Zealand and Latvia (1997), Portugal (2001), Greece/Cyprus (2003) and Trinidad and Tobago (2004). Wales (1994) and Republic of Ireland (1996) developed surveillance units using a similar methodology to the BPSU, but are including more common disorders in their surveillance (Table 15).

Through the use of active ascertainment, the fourteen 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 22nd International Congress of Paediatrics in Amsterdam, The Netherlands. The first INoPSU conference was held in June 2000 in Ottawa, Canada. At the second INoPSU meeting in York, UK, the British Ophthalmology Surveillance Unit was accepted as an affiliate member of the network. 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 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 at http://www.inopsu.com.

The 3rd INoPSU conference was held in Lisbon Portugal in April 2004. The meeting received reports from new and developing units, most notably Trinidad and Tobago, and Argentina, Poland and, more recently, India, expressed interest in establishing surveillance. This meeting led to the publication "Acknowledging contributions from surveillance units. Pereira-da-Silva L, Kries R von, Rose D, Elliott E. Arch Dis Child. 2005: 90: 768". The 4th INoPSU conference was held in London in May 2006 alongside the BPSU's 20th anniversary celebrations.

Over the past two years, INoPSU countries have facilitated the surveillance of 70 different rare conditions and have now undertaken over 150 studies (Table 15), 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 form their respective websites and also from the INoPSU website

Table 14: National paediatric surveillance units

Country	Child population (10^6- 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	E	93%
Canada	7.5	1996	2500	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%
Malaysia(1)	7.7	1994	395	C	75%
Netherlands	3.0	1992	640	C/E	100%
New Zealand	0.8	1997	208	C/E	94%
Papua New Guinea	2.0	1996	40	C	79%
Portugal	1.8	2001	1800	C/E	33%
Switzerland	1.3	1995	100	C	100%
Wales	0.65	1994	133	C	96%

1) Malaysian paediatric surveillance unit is temporarily closed.

INoPSU Conference 2006

Following on from the successful 3rd INoPSU meeting held in Lisbon Portugal during 2004, a fourth meeting was held in London to coincide with the BPSU's 20th anniversary conference. Representatives attended the meeting from 12 of the 15 national units; only representatives from New Zealand, Papua New Guinea and Malaysia were not able to attend.

The meeting allowed representatives from each of the national units to get and exchange views on rare disease surveillance and issues that affect each of the units, particularly funding and the increasing need for confidentiality and consent. The morning session consisted of presentations from individual units. The Australian unit presented data on behalf of New Zealand and itself on Fetal Alcohol Syndrome. There was much interest in replicating the study though concerns over case definition needed to be addressed. The Canadian unit presented data on neonatal herpes and hyperbilirubinaemia and talks on type 2 diabetes (Latvia), vitamin k deficiency bleeding (Netherlands) and acute flaccid paralysis (Switzerland) were also received. A business meeting in the afternoon discussed funding needs, the potential for international collaboration in undertaking studies and the development of the INoPSU website.

INoPSU Delegates

Table 15 Conditions under surveillance 2005-06

Condition	Country
Accidents with baby walkers	Portugal
Acquired demyelinating syndromes of the CNS	Canada
Acute flaccid paralysis	Australia, Canada, New Zealand, Switzerland
Acute rheumatic fever	Canada, Switzerland
Adverse drug reactions – serious and life-threatening	Canada
Acute Encehalitis & Encepholomyalitis	Portugal
Adverse Events from Complementary and Alternative Medicine	Wales
Alcohol & children	Ireland
Ambiguous genitalia	Netherlands
Anorexia	Netherlands
Atypical mycobacteriosis	Germany
CEMACH- Child Death Review Pilot	Wales
Child abuse	Netherlands
Childhood TB	British Isles
Chronic interstitial lung disease	Germany
Complicated Pneumonia including Empyema	Wales
Complications of measles	Germany
Complications of Varicella Zoster Virus or Herpes Zoster	Germany, Netherlands
Congenital Toxoplasmosis	Ireland, Greece/Cyprus
Congenital cytomegalovirus infection	Australia, Canada
Congenital malformation after maternal use of epileptica	Netherlands
Congenital myotonic dystrophy	Canada
Congenital rubella	Australia, British Isles, Netherlands, New Zealand, Switzerland
Diabetes Mellitus	Netherlands, Germany, Ireland, Portugal
DM type II and MODY in paediatric praxis	Canada, Latvia, Wales, British Isles
Down's syndrome	Netherlands
Early onset eating disorders	Australia, British Isles, Canada
Familial Epilepsy in children	Wales
Foregut and Hindgut Malformations	New Zealand
Fragile X	Ireland
Fungal infections in preterm infants	Latvia
Group B streptococcal infection	Portugal
Haemoglobinopathies	Australia, Netherlands
Haemolytic-Uraemic Syndrome	Greece/Cyprus, New Zealand, Switzerland, Portugal
Head injuries secondary to suspected child maltreatment	Canada
Henoch-Schönlein Purpura	Netherlands
Hepatitis C virus infection	Australia
Hereditary periodic fever syndrome	Germany
HIV/AIDS, Perinatal exposure to HIV	Australia, British Isles, New Zealand
Hyperbillirubinemia	British Isles, Netherlands, Germany, Canada, Switzerland
Hyperinsulinaemic hypoglycaemia of infancy	Australia, New Zealand
Hypernatraemia in Infancy	Wales
Immune Thrombocytopenia Purpura	Ireland
Inborn Errors of Metabolism	New Zealand
Influenza-associated intensive care and deaths cases among children and adolescents	Germany

Condition	Country
Ingestion of lamp oil (intoxications)	Germany
Inherited hypocalemic salt-losing tubulopathies / Bartter-like syndromes	Germany
Insufficient' breastfeeding	Netherlands
Intussusception	Latvia, Switzerland
Invagination in childhood	Germany
Invasive Haemophilus influenzae infections	Germany
Juvenile Idiopathic Arthritis	Wales
Kawasaki Disease	Portugal
Lap-belt syndrome	Canada
LCH	British Isles
Malaria in children	British Isles
Medium-chain acyl-coenzyme A dehydrogenase deficiency	Canada, British Isles, Netherlands
Morbide Obesitas	Netherlands
MRSA	British Isles
Neonatal herpes simplex virus	Australia, British Isles, Switzerland
Neonatal sinus venous thrombosis	Germany
Neonatal/ Infant Group B streptococcal sepsis	Australia
Nephrotic syndrome	Germany, Netherlands
Neural tube defects	Switzerland
Neuroborelliosis	Netherlands
Non CF bronchiectasis	Ireland
Non tuberculosis mycobacterial infection	Australia
Opsuclonnis mycoclonus synd	Ireland
Osteogenesis imperfecta	Canada
Peanut allergy	Ireland
Pertusis	Switzerland
PIND	British Isles
Pneumococcal sepsis / Meningitis	Germany, New Zealand
Pregnancy in adolescence	Latvia
Prolonged Infantile Cholestasis	New Zealand
Retinopathy of prematurity	Latvia
Rett syndrome	Australia
Scleroderma	British Isles
Serious seatbelt injuries (# & helmets)	Australia, Latvia#
Severe bronchiolitis requiring ICU/HDU care	Ireland
Severe combined immunodeficiency	Canada
Severe RSV infections	Switzerland
Shaken Baby Syndrome	Netherlands, Switzerland
Simple Vitamin D deficiency rickets	Australia, Ireland
Stroke and transient ischaemic attacks	Ireland
Systemic Lupus erythematosus	Germany
Thyrotoxicosis	British Isles
Transfusion-related acute lung injury	Canada
Vitamin K deficiency bleeding	Australia, British Isles, New Zealand, Netherlands, Switzerland

APPENDIX A - Completed Studies 1986-2005

By mid-2005 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 I

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

Lowe syndrome

Surveillance Period: June 1986 - February 1988
Investigator: Dr C McKeown
Published Paper: BPSU 2nd 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:** 443-7

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:** 3-5

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 5th 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: 10th 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: 11th 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

Published paper: 9th 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: The 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* 200; **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, Hernon 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 MacDougal

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 comjugate 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

Investigatosr: 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: 15th 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 and 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: 17th 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: 17th BPSU Annual Report 2002/03. BPSU London 2003

Congenital cytomegalovirus (cCMV)

Surveillance Period: February 2001 - February 2003
Investigators: Dr P Tookey, Professor M-Lnewell, Dr M Sharland
Published Paper: 17th 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: 17th 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: 17th BPSU Annual Report 2002/03. BPSU London 2003

Severe complications of varicella (chickenpox) in hospitalised children

Surveillance Period: November 2002- November 2003
Investigator: Dr C Cameron
Published Paper: 18th 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; **90.**

Severe hyperbilirubinaemia

Surveillance Period: May 2003 – May 2005
Investigator: Dr D Manning
Published Paper: 19TH BPSU Annual Report 2004/05. BPSU London 2005.

APPENDIX B - Published Papers 2005-2006

1. 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* 2006 in press.

2. Toxoplasmic retinochoroiditis presenting in childhood: clinical findings in a UK survey. Stanford MR, Tan HK, Gilbert RE. *BJO* 2006 in press.

3. 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 Journal of Public Health Advance Access published online on April 26, 2006 doi:10.1093/pubmed/fdl005

4. 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.

5. Symptomatic toxoplasma infection due to congenital and postnatally acquired infection. Gilbert R, Hooi HK, Cliffe S, Stanford M, Guy E. *Arch Dis Child*. Published Online First: 17 March 2006. doi:10.1136/adc.2005.088385 (published in print in Vol 9 issue 6 (June)).

6. 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; **11(4):** 590-6.

7. Human herpes viruses-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.

8. Subdural haematoma and effusion in infancy: An epidemiological study. Hobbs C J, Childs A, Wynne J, Livingston J, Seal A. *Arch Dis Child*. 2005 Sep; **90(9):** 952-5.

9. Unexpected Occasional Persistence of High levels of HHV-6 DNA in Sear: Detection of Variants A and B. Ward KN, Thiruchelvam AD, Couto-Parada X. *Journ Med Virol* 2005, **76:**563-570.

10. Severe food-allergic reactions in children across the UK and Ireland, 1998-2000. Colver AF, Nevantaus H, Macdougall CF Cant AJ. *Acta Paediatrica* 2005; **94:** 689-695.

11. 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.

12. No clinical evidence of hidden vCJD in UK children. Verity CM, Nicoll A, Will RG, Winstone AM, Stellitano L. Article to *Arch Dis Child:* published online 31 Oct 2005. doi:10.1136/adc.2004.071266.

13. Newborn screening for Medium Chain Acyl CoA Dehydrogenase Deficiency at one week of age: octanoyl carnitine distributions from a multicentre study using electrospray tandem mass spectrometry of underivatised blood spot samples. Phillips P et al, *J.Inherit.Metab.Dis*. 2005; **28,** Suppl.1; 17-P.

14. Predictive value, clinical status and genotype of Medium Chain Acyl CoA Dehydrogenase Deficiency (MCADD) ascertained by screening at one week of age using electrospray tandem mass spectrometry of underivatised blood spots: findings from a UK multicentre study. Oerton J et al. *J.Inherit.Metab.Dis*. 2005; **28,** Suppl.1; 18-P.

15. Quality Assuring a Multicentre Newborn Screening Programme for MCADD in the UK. Goddard et al *J.Inherit.Metab.*Dis 2005: **28**, Suppl.1; 236-P.

16. Newborn Screening for Medium Chain Acyl CoA Dehydrogenase Deficiency: acylcarnitine C8/C10 ratio at day 6 differentiates affected cases from carriers. Downing M et al, *J.Inherit. Metab.Dis*. 2005; **28**, Suppl.1; 19-P.

17. Acknowledging contributions from surveillance units. Pereira-da-Silva L, Kries R von, Rose D, Elliott E. *Arch Dis Child*. 2005: **90:** 768.

APPENDIX C - Presentations 2005-2006

RCPCH Annual Scientific Meetings 2005 and 2006

Severe complications of chickenpox in hospitalised children. Cameron JC, Allen G, Johnston F, Booy R, Heath PT, Finn A. York 2005. *Arch Dis Child* 2005; **90** (Suppl II): A1-A8.

Abdominal injury due to child abuse: Final results from the BPSU study. Sibert JR, Barnes PM, Norton C, Yates D, Dunstan FD, Kemp AM. York 2005. *Arch Dis Child* 2005; **90** (Suppl II): A1-A8.

The UK prospective study of cerebral oedema complicating diabetic ketoacidosis. Edge JA, Jakes R, Roy Y, Widmer B, Ford-Adams ME, Murphy NP, Bergomi A, Dunger DB. York 2005. *Arch Dis Child* 2005; **90** (Suppl II): A1-A8.

The essential role of all UK Paediatricians in performing surveillance for vCJD via the study of progressive intellectual and neurological deterioration (PIND). Verity CM, Stellitano L, Winstone AM, Nicoll A, Will RG. York 2005. *Arch Dis Child* 2005; **90** (Suppl II): A1-A8.

Severe hyperbilirubinaemia in the newborn: The first year of surveillance. Manning DJ, Todd PJ, Maxwell MJ. York 2005. *Arch Dis Child* 2005; **90** (Suppl II): A1-A8.

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 charahcteristics 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 prohpylaxis and vitamin K deficiency bleeding in the UK:What progess 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: Expereicnce with combining multiple sources of ascertainment. Phillips P, Oerton J et al. *Arch Dis Child* 2006; **91** (Suppl 1): A90.

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

Poster – Infantile Krabbes Disease in the UK. Characteristics of cases reported to the PIND study over 7 years. British Paediatric Neurology Association Annual Meeting, Bristol. 18-20th January 2006.

Poster – National Surveillance for variant CJD – how useful is the PIND Expert Group? British Paediatric Neurology Association Annual Meeting, Bristol. 18-20th January 2006.

Poster – Surveillance of Early onset eating disorders. Lynn RM, Nichol D, Vinner R, Lelliott P. British Association of Community Child Health. University of Reading, September 2005.

Prospective surveillance for all cases of progressive intellectual and neurological deterioration (PIND) occurring in children in the UK. Winstone AM. Health Protection Agency, University of Warwick, September 2005.

Langerhans Cell Histiocytosis in the UK and Ireland: preliminary Findings from a Two-year Epidemiological Study. Twenty-First Annual Meeting of the Histiocyte Society. Salotti J Vancouver, September 2005.

Poster - Experience in screening for MCADD. Dezateux C, Oerton J. Phillips, P. Euromedlab, May 2005.

UK Collaborative Study of Newborn Screening for MCADD. Dezateux C, Oerton J. Phillips P. UKNSLN Annual Meeting, Birmingham Feb 2005.

A national view of neurodegenerative disease: the PIND study after 7 years 6 months of surveillance. Verity CM. British Paediatric Neurology Association Annual Meeting. 19-21 January 2005.

Are UK children developing vCJD? Findings from the PIND Study Verity CM. UKOSS, Royal College of Obstetricians and Gynaecologists, London. 11th February 2005.

APPENDIX D - Membership of Executive Committee 2005/2006

Professor Mike Preece*	Chair
Professor Allan Colver+	Chair
Dr Claire Cameron	Health Protection Scotland
Dr Hugh Davies*	Co-opted
Professor Carol Dezateux	Institute of Child Health (London)
Professor Adam Finn	Co-opted
Professor Denis Gill	Royal College of Physicians (Ireland)
Dr Alun Elias-Jones#	Royal College of Paediatrics and Child Health Treasurer
Dr Shankar Kanumukala	Co-opted
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 Advisor (non-infectious disease)
Dr Gabrielle Laing*	Co-opted
Mr Richard Lynn	Scientific Co-ordinator
Dr Donal Manning	Co-opted
Dr William McGuire*	Co-opted
Professor Neil McIntosh	Royal College of Paediatrics and Child Health Research Division
Dr Colin Mitchie	Co-opted
Dr Simon Mitchell	Co-opted
Dr Richard Pebody	Health Protection Agency
Dr Richard Reading	Co-opted
Dr Martin Richardson*	Co-opted
Dr Alan Smith#	Medical Adviser (infectious disease)
Professor Stuart Tanner#	Department of Health (observer)
Mrs Carol Youngs*	Patient and Carers Committee representative
Mrs Susan Banton	Patient and Carers Committee representative

* Stepped down in 2005
\# Stepped down in 2006
\+ New BPSU Executive Chair


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