# BPSU

## 25th Anniversary Report 2010-2011


RCPCH
Royal College of Paediatrics and Child Health
Leading the way in Children's Health

British Paediatric Surveillance Unit
Royal College of Paediatrics and Child Health

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# 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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# Foreword

Prof Alan Emond
Chair, BPSU Executive Committee

The British Paediatric Surveillance Unit (BPSU) was established in 1986 by a group of clinicians and epidemiologists who understood the importance of collecting information about rare conditions affecting children, with the objective of improving clinical care. The original aims- 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- are just as relevant 25 years later.

The BPSU has allowed paediatricians to participate in surveillance of uncommon disorders and lessened the burden on reporting doctors of such requests arising from numerous different sources, and increased awareness within the medical profession of the less common disorders studied. Results of BPSU studies have had an impact on screening policy (e.g. MCAD), on vaccination programmes (e.g. MMR), on clinical practice (e.g. biliary atresia), on prevention of rare conditions (e.g. Reye's syndrome), on our understanding of emerging conditions (e.g. variant CJD), and responded to public health emergencies (e.g. Guillain Barré/Fisher syndromes following H1N1 influenza vaccination)

The unique point of the BPSU is its consistent high coverage- over 93% of paediatricians in the UK and Ireland- which permits estimates of incidence and complications of disease to be made with confidence. One limitation of the BPSU card methodology has been the number of case notifications a study can handle administratively (approx 300/yr), but in the last year the unit has piloted electronic notification of cases and online reporting of case details to a secure web-based database, which should ease data reporting and facilitate larger sample sizes and expand the range of conditions suitable for research.

Another feature of the BPSU to highlight has been the involvement of lay members on the executive committee, which has led to an improvement in the quality and accessibility of written material associated with research projects using the BPSU, and increasing consultation by researchers with patient groups and support groups.

During the 25th year celebrations, presentations and symposia about the BPSU have been given in England (Excellence in Paediatrics and RCPCH Annual meeting), Scotland (Scottish Paediatric Society) and Ireland (Irish Paediatric Society) and we will be at the HPA annual conference and the International Network of Paediatric Surveillance Units meeting in Montreux, Switzerland in September.

Although the financial landscape ahead is very rocky, the need for good quality national surveillance of paediatric conditions will remain, and the BPSU aims to continue to support a high standard of scientific support for researchers and facilitate projects relevant to public health policy, commissioning and clinical practice.

With a big 'thank you' to all the clinicians who continue to voluntarily participate in BPSU surveillance.

Alan Emond
June 2011

# Past Reflections

In February 1986 I passed my MRCP examination, as it was in the days before the MRCPCH, and in July 1986 the first orange cards of the BPSU surveillance scheme were sent out. So I have been assiduously returning orange cards all my professional life as a paediatrician. That first card covered seven conditions including Kawasaki disease, neonatal herpes, haemolytic uraemic syndrome and AIDS. AIDS had first been described as a condition while I was a medical student. These 25 years have seen the emergence of new diseases – in addition to HIV, these have included BSE, SARS, H5N1 Avian Flu and H1N1 Swine Flu. Fortunately the last 25 years has also seen the eradication or reduction of equally serious diseases such as Haemophilus epiglottitis and meningitis in the United Kingdom. Throughout this quarter of a century, I am proud to say that the BPSU has led the way in surveillance of rare disorders of great importance to children and their families. Since the success of the paradigm was demonstrated in 1978 with the National Childhood Encephalopathy study, through the lead given by Peter Tizard, David Baum, Euan Ross, Catherine Peckham and Sue Hall to its inception and the 85 studies and over 25,000 cases detected since, the BPSU has served as a model for numerous similar bodies in countries around the globe. A return rate of over 90% from my colleagues around the British Isles has held up and has enabled us to describe with confidence important conditions such as Reye's syndrome, MCAD deficiency (for which there is now neonatal screening), MMR for which there is now a safe vaccine and biliary atresia (for which services are now concentrated in a few centres with better results). As a former Vice-president for Science and Research and now as President of the Royal College of Paediatrics and Child Health, I am delighted that the collaboration with the Health Protection Agency and the Institute of Child Health has been such a wonderful success story.

Professor Terence Stephenson
President

Euan Ross -
BPSU Founder and chair 1991-93

1984 turned out to be a better year than George Orwell had predicted. One sunny day that year I accepted an invitation from Dr Spence Galbraith to take tea at the 'Cowshed' known now as the HPA. Not many paediatricians knew about this place. Spence was the leader and guiding light behind the Communicable Disease Surveillance Centre where he created a medical version of MI5. Dr Galbraith was the Q, the master detective of epidemics and outbreaks both due to infections but also toxic substances, inorganic and organic chemicals and radiation. He was concerned that time could easily be lost and that there was no ready means to 'only connect' those medics who saw child cases that did not fall in to the narrow group of statutorily notifiable disease. Spence knew me from work with Prof David Miller and the whooping cough vaccine scares of the early 1970's. We talked over the possibility of using similar methodology to create a scheme that could use the power of paediatricians to collect data in a systematic way in order to jump on the aetiology of newly emerging health problems in children.

Getting an idea from afternoon teacakes and jam to fruition is not easy. There are sociological laws, yet to be written that protect society from over rapid change. The key to change is to find and recruit the elders of the tribe. Fortunately the UK and Ireland contained a number of radically minded paediatric elders who could recognise a good idea when intelligently presented to them.

Good ideas need a little financial lubrication to pay for postage, telephones, paper but above all, people able to use them to effect. Sir Peter at the head of the oblong table (inset) of the BPA used his authority and charisma to outwit the doubters. His friend the blessed Sir Cyril Clarke knew a gentleman of substantial means who had a trust fund. The trustees donated enough seed corn money to get the BPSU germinating; and look how we have grown.

Euan Ross – 2nd right
BPSU Founder and Chair 1991-93

I have a vivid memory of giving a presentation describing the importance of a proposed new surveillance scheme for rare conditions in pregnancy to a group of bankers and city businessmen on the top floor of a grand building overlooking the Thames. The objective was to raise funds for a 2 year salary to support Sue Hall to set up the BPSU. I was subjected to a barrage of penetrating and intelligent questions. Why was this initiative important? What would it achieve? Was it sustainable in the long term? I left the room in a state of exhaustion but I also felt exhilarated since I could see that they were fascinated by the concept. A few hours later I received a telephone call saying that the funding had been agreed. How different from the usual applications to major grant-funding bodies and the long wait for a response. Without this initial and generous support which enabled Sue Hall to devote her energy, knowledge and time to the setting up of the BPSU, I wonder if it would ever have been achieved.

Professor Catherine Peckham
BPSU Founder and Chair 1993-95

In 1985, when the newly formed BPSU Scientific Advisory Committee was planning how the system would operate, it decided that we should have a pilot run. A "dummy" card would be sent to a random sample of paediatricians and their views would be sought on the acceptability of the scheme, how many conditions should be included and whether or not the card should be reply paid!

The composition of the list of conditions to be put on the pilot card was debated by the committee. Sir Peter Tizard was Chair. I was very much in awe of him and he could be quite intimidating. However, I soon learned that he had a wicked sense of humour and it was he who proposed that the list should include a disorder which didn't exist in order to check whether the respondents were thinking carefully about their task and not just ticking boxes at random. At the time I had a cat who had developed a rare, newly emerging and epidemiologically mysterious disease called Key Gaskell syndrome. It manifested as sudden onset of paralysis of the autonomic nervous system and if it had occurred in children would have been an ideal BPSU candidate. I told Sir Peter about this and much to my surprise he jumped at the idea so it was included!

As I recall, when the cards were returned, there was indeed one report of a case, but I think the clinician added in brackets (in my cat!). Most respondents wrote "what is this?" on their card. We did of course subsequently send an explanatory note to our respondents, who took it in good part, but one took great offence at such a frivolous inclusion -Sir Peter was unimpressed by this complaint! The pilot was deemed a success and the rest, as they say, is history!

Dr Susan Hall and kitty
Medical Coordinator 1986-93

Back to the future – or, what's in a name? The BPSU had many parents It was set up by the British Paediatric Association, the Institute of Child Health (London), the Public Health Laboratory Service and was supported by the Communicable Disease Surveillance Centre (Scotland) and the Faculty of Paediatrics of the Royal College of Physicians of Ireland.

In 1994 the name was changed to BPASU in recognition of the central role of paediatricians in the successful running of the Unit. This name worked well until 1996 when the BPA became the College. What about the acronym? BPSU was fine, so was BPASU. SUCPCH was not so good and would have led to things like "Chair of the SUCPCHEC". Also it was hoped that the CPCH would get an "R", necessitating further change and not making the acronym more euphonious.

After discussion, Roy Meadow - then the President - agreed that we should revert to the name BPSU, emphasising the continuity and the pioneering role of the Unit in paediatric surveillance. By then there were 8 paediatric surveillance units outside the UK, all modelled on the BPSU. In the British Isles the Welsh and Irish Paediatric Surveillance Units were developing and other specialties were following the BPSU model.

The future was indeed good, because the number of national units grew and in 1998 the International Network of Paediatric Surveillance Units (INoPSU) was formed. Euan Ross and David Baum were strongly supportive of this development and much of the success of INoPSU resulted from the energy of the BPSU Medical Advisor, Angus Nicoll, who became the first INoPSU Convener and the work of Richard Lynn, who has continued to act as "server" for the network. Angus handed over to Elizabeth Elliott of the Australian Paediatric Surveillance Unit, a co-founder of INoPSU, who has continued to be a staunch supporter of this international work.

So – the name matters. After all, you wouldn't want to change the name of Apple Inc. just now, would you?

Chris Verity
BPSU chair 1996-2002

## Picture Gallery

Spence Gailbraith & the "cowshed"

BPSU Executive circa1987

Orange card 1986


INOPSU conference 2004 - Lisbon

Sir Peter Tizard, Wellchild & staff - 1988

BPSU Executive 2010

David Baum - BPSU Founder

# 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 University College London - Institute of Child Health Centre for Epidemiology and Biostatistics, 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 ten 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 2010.

# 2 How the Surveillance System Works

## Selection of studies for inclusion in the scheme

A study is eligible for participation in the scheme if the subject is a rare childhood disorder (or rare complication of a commoner disease) of such low incidence as to require cases to be ascertained nationally in order to generate sufficient numbers for study.

The number of conditions under surveillance is usually limited to 12. The BPSU application procedure consists of two phases: a screening phase based on an outline of the study and a detailed consideration of the full application. Details about the BPSU application procedure can be downloaded from the website at http://www.bpsu.inopsu.com.

Factors that increase the likelihood of a study being accepted include scientific importance, clear objectives, a workable case definition and proposals with outcomes of clear importance to public health. Once approved by the BPSU Executive, studies require approval from the Research Ethics Committee (REC) and Ethics and Confidentiality Committee of the National Information Governance Board 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' in that 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 after two months. A set of instructions for completing the card, including case definition of the conditions listed on the card is also circulated. When a new study begins, the mailing also includes a specially produced study protocol card and other information about the study.

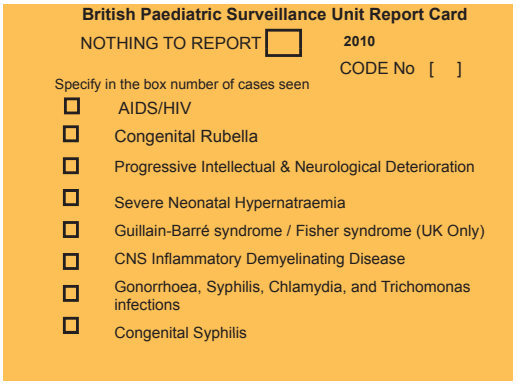


Figure 1: Orange Card Side A

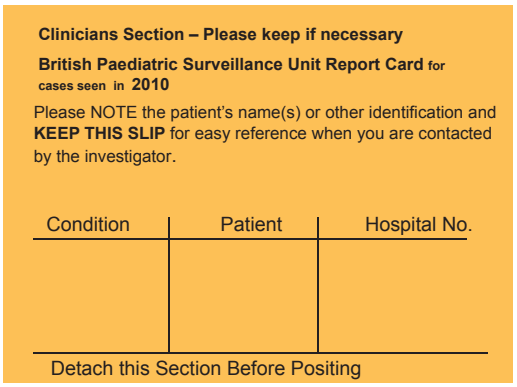


Figure 2: Orange Card Side B

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 allows us to measure compliance to the reporting system. The compliance rates are thus continually monitored 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. To gather further information the study team sends a short questionnaire to the reporting clinician. Particular care is taken

to ensure that questionnaires 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.

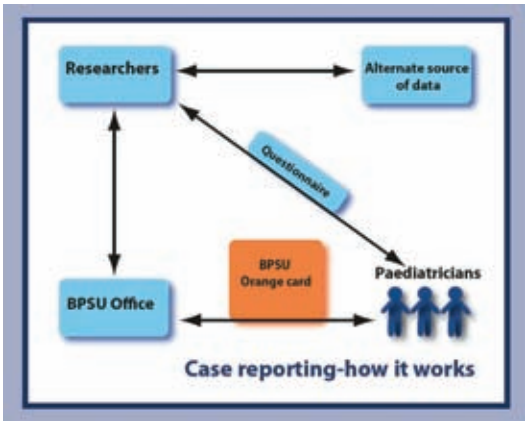


Figure 3: Surveillance mechanism

Table 2 (page 10) shows the number of cases reported to the BPSU from its inception until the end of 2010 for conditions under surveillance at December 2010. 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 May 2011, only 834 (7%) of the 13012 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 2010 and provides evidence for the level of accuracy of reporting by participating clinicians.

To improve case ascertainment for specific studies where a child may see specialist clinicians, consultants working in a number of other specialties have been invited to participate in the scheme. Pathologists have been included in the BPSU reporting scheme since 1992 and most studies of paediatric infections involve laboratory reporting by microbiologists. Paediatric surgeons (intussusception) and burns specialists (toxic shock syndrome) have recently been included in the reporting system. Apart from helping to improve ascertainment such complementary data sources help to validate the surveillance system.

## Funding

The BPSU continues to be in receipt of a grant from the Department of Health to cover the majority of the running costs of the unit. In addition, the BPSU asks surveillance teams to contribute a sum to cover specific administrative costs. These funds also permit us to undertake additional activities such as holding workshops to support current and potential investigators and conferences. The BPSU is also grateful for the ongoing support that it receives from the Royal College of Paediatrics and Child Health, the University College London - Institute of Child Health and the Health Protection Agency.

## Sir Peter Tizard Bursary

The bursary, named after one of the founders of the BPSU, is offered as a competitive award. With a value of upto to £15,000 it offers, each year, the opportunity for a junior doctor or newly appointed consultants to use the facilities to undertake their own surveillance study and to learn more about disease epidemiology. To date seven awards have been made. Details of the bursary are available on the BPSU website at www.bpsu.inopsu.com.

# 3 Scientific Coodinator's Yearly Review of Activities

This past year has seen the commencement of six new BPSU studies. January 2010 saw the commencement of studies on congenital syphilis (investigator Dr Ian Simms - HPA) and gonorrhoea, syphilis, chlamydia, and trichomonas infections in children aged one to thirteen years presenting to secondary care (investigator Dr Richard Reading – Norfolk and Norwich). June saw the commencement of three studies raised blood lead levels in children (investigator Ruth Ruggles – HPA), chylothorax (investigator Dr Peter Davis – Bristol), glutaric aciduria 1 (investigator Dr Beth Cheesebrough – London). Whilst a study on bacterial meningitis in babies <90 days of age (investigator - Dr Paul Heath, St Georges, London) commenced in July.

Three studies had their period of surveillance extended for a further year: HIV, congenital rubella, progressive intellectual and neurological deterioration (PIND).

May 2011 saw the commencement of a study into end stage renal failure (investigator Dr Karl McKeever – Belfast). This was followed in June 2011 by a study on primary congenital hypothyroidism in children aged five years and under (investigator Dr Rachel Knowles – UCL-ICH). July 2011 saw a Sir Peter Tizard bursary funded study on autoimmune Addison's disease (investigator Dr Hima Bindu Avatapalle – Manchester) commence.

Since its inception in 1986 the BPSU has completed 81 studies (Appendix A). During 2010/11, there were 14 publications and 40 presentations relating to BPSU studies (Appendix B).

The 2010/11 Sir Peter Tizard bursary was awarded to Dr Emre Basatemur to undertake a study on Hypocalcaemic Seizures due to Vitamin D Deficiency, and this is due to start in Autumn 2011.

The BPSU continues to disseminate information on its activities to clinicians and the public alike. This is achieved mainly through this report, the BPSU bulletin and the recently re-launched BPSU website (http://www.bpsu.inopsu.com).

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

(Photo by Joe Spinoza, aged 13)

Richard Lynn
Scientific coordinator

we have developed a database of all the condition studied by each unit, publications and research contacts. To date we have over 220 conditions logged. We hope to make this data resources accessible as an aid to link researchers. INoPSU held its 6th conference in Dublin in October 2010 to continue the exchange of information, the 7th conference will be held in Montreux Switzerland in September 2011. Details on the international activities are available at INoPSU website (www.inopsu.com).

## Participation in the scheme during the year 2010

During 2010 215 clinicians were placed on the mailing list whilst 171 were removed, mainly following retirement or relocation overseas.

Reporting rates for returning the orange cards remain high - the overall card return compliance rate for the year 2009, calculated as a proportion of orange cards returned, was 93.2% (38034/35434) a fall of 0.6% from 2009. Monthly response rates ranged from 94.3% in March to 90.7% in December with a median of 93.5%. To maintain this compliance rate respondents who have not returned card are sent a monthly email reminder. This return rate remains higher than any equivalent UK scheme and ranks highly against other national paediatric surveillance units (Table 1 page 10).

Wales has topped the average yearly response rate ranking – 98.9%. The Thames area showed a cumulative response rate of 90.5%, a fall of 0.6% on 2009. Full details of regional response rates are provided in Table 2 page 10. Overall the response rate is still exceptional and is a testament to the willingness of clinicians to support the BPSU reporting scheme.

## Workload of those reporting in the scheme

79% (2690) of participants reported no cases in 2010, 14% (471) reported a single case, 5.0% (170) reported between two and four cases and 2.0% (51) reported five or more cases. The greatest number of cases reported was by HIV/AIDS specialists, one of whom reported 116 cases. Specialties that had a particularly high level of reporting were paediatric neurologists (PIND), neonatologists and infectious disease specialists and community paediatricians (HIV/AIDS).

### Table 1 Regional response rate 2009 and 2010

| Region | Rank 2010 | Rank 2009 |
|---|---|---|
| Northern | 13 | 7 |
| Yorkshire | 11 | 9 |
| Trent | 14 | 17 |
| East Anglia | 4 | 8 |
| NWT | 15 | 16 |
| NET | 20 | 20 |
| SET | 16 | 11 |
| SWT | 17 | 15 |
| Wessex | 6 | 5 |
| Oxford | 8 | 3 |
| South Western | 9 | 12 |
| West Midlands | 12 | 10 |
| Mersey | 7 | 18 |
| North Western | 10 | 4 |
| Wales | 1 | 2 |
| North Scotland | 2 | 13 |
| South Scotland | 3 | 1 |
| West Scotland | 18 | 14 |
| Northern Ireland | 5 | 6 |
| Republic of Ireland | 19 | 19 |


Figure 4. Average orange card return rate (%) by area, 2010

### Table 2 Cases reported from June 1986 - December 2010 for conditions under surveillance at May 2011

| Reports (confirmed cases) | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Date when reporting began | June 1986-Dec-95 | Jan-96 Dec-00 | Jan-01 Dec-03 | Jan-04 Dec-06 | Jan-07 Dec-09 | Jan-10 Dec-10 |
| Conditions under Surveillance | | | | | | | |
| HIV/AIDS | Jun-86 | 991 (691) | 1017 (705) | 1774 (1430) | 2172 (1856) | 2106 (1697) | 647 (365) |
| Con rubella | Jun-91 | 72 (39) | 49 (25) | 26 (6) | 13 (7) | 16(5) | 6 (3) |
| PIND | May-97 | | 1067 (629) | 612(318) | 518 (298) | 632 (420) | 175 (107) |
| CD | Oct-08 | | | | | 254 (125) | |
| SUPC | Nov-08 | | | | | 91 (45) | |
| CNS | Jul-09 | | | | | 67 (46) | 130 (68) |
| GBS/FS | Sept-09 | | | | | 44 (23) | 95 (56) |
| Con. syphillis | Jan-10 | | | | | | 40 (24) |
| GSCT | Jan-10 | | | | | | 31 (7) |
| Chylothorax | Jun-10 | | | | | | 109 (57) |
| GA1 | Jun-10 | | | | | | 17 (9) |
| Lead | Jun-10 | | | | | | 21 (7) |
| Bact Men | Jul-10 | | | | | | 220 (108) |
| | | | | | | | |
| **Total** | | **1063 (730)** | **2133 (1359)** | **2412 (1754)** | **2703(2161)** | **3210 (2361)** | **1491 (811)** |

## Table 3 Outcome of follow-up of the cases reported in 2010 for conditions under surveillance at May 2011

| | Date when reporting began | Valid reports | % | Duplicates | Errors | (D&E) % | Not yet known | % | Total |
|---|---|---|---|---|---|---|---|---|---|
| Condition under surveillance | | | | | | | | | |
| HIV/AIDS | Jun-86 | 6,744 | 77 | 757 | 692 | 17 | 514 | 6 | 8707 |
| Con. rubella | Jun-91 | 85 | 47 | 35 | 56 | 50 | 6 | 3 | 182 |
| PIND | May-97 | 1772 | 59 | 372 | 824 | 40 | 36 | 1 | 3004 |
| CD | Oct-08 | 125 | 49 | 15 | 44 | 23 | 70 | 28 | 254 |
| SUPC | Nov-08 | 45 | 49 | 7 | 25 | 35 | 14 | 15 | 91 |
| GBS/FS | Jul-09 | 79 | 58 | 19 | 6 | 27 | 35 | 15 | 139 |
| CNS | Sept-09 | 114 | 57 | 28 | 25 | 18 | 30 | 25 | 197 |
| Con. syphilis | Jan-10 | 24 | 60 | 5 | 6 | 28 | 5 | 13 | 40 |
| GSCT | Jan-10 | 7 | 23 | 2 | 18 | 65 | 4 | 13 | 31 |
| Chylo | Jun-10 | 57 | 52 | 6 | 8 | 13 | 38 | 35 | 109 |
| GA1 | Jun-10 | 9 | 53 | 3 | 3 | 35 | 2 | 12 | 17 |
| Lead | Jun-10 | 7 | 33 | 2 | 9 | 52 | 3 | 14 | 21 |
| Bact Men | Jul-10 | 108 | 49 | 14 | 21 | 16 | 77 | 35 | 220 |
| **Total** | | **9176** | **72** | **1265** | **1737** | **24** | **834** | **7** | **13012** |

| | |
|---|---|
| HIV | Human immunodeficiency virus: reports of AIDS in June 1986 include cases previously seen; case definition extended to include HIV infection in January 1990 |
| Con. rubella | Congenital rubella |
| PIND | Progressive intellectual and neurological deterioration |
| CD | Conversion disorder – excludes cases seen by psychiatrists |
| SUPC | Sudden unexpected postnatal collapse |
| GBS/FS | Guillain Barré/Fisher syndromes |
| CNS | CNS inflammatory demyelinating diseases |
| Con. syphilis | Congenital syphilis |
| GSCT | Gonorrhoea, Syphilis, Chlamydia, and Trichomonas |
| Chylo | Chylothorax |
| GA1 | Glutaric aciduria 1 |
| Lead | Raised blood lead levels in children |
| Bact Men | Bacterial meningitis in babies <90 days of age |

## 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 investigators 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 May 2011).

# 4 Surveillance Studies Undertaken in 2010

## Bacterial meningitis in babies 0-90 days of age

### Key points

- Paediatrician - reported cases via the BPSU are the major source of reports.
- Group B Streptococcus (GBS) remains the leading cause of bacterial meningitis in babies 0-90 days of age in the UK and Ireland.
- The number of reported cases suggests a burden of meningitis similar to or greater than in previous national studies.

### Summary

Meningitis in the first three months of life is associated with significant mortality and long term disability. In comparison with previous studies it appears that the death rate has fallen but the proportion of cases with long term disability has changed very little. The aim is to find out how much of a public health issue meningitis in this age group now is, how it is currently being managed and to identify any opportunities for improving the diagnosis and management. This is to be achieved through a comprehensive study of all cases of meningitis under 90 days of age that occur over a 13 month period throughout the UK and Ireland. In addition to reports from paediatricians through the BPSU we will identify cases through routine laboratory reports as well as reports from parents via relevant charities (Meningitis Research Foundation, Meningitis Trust UK, Group B Strep Support Group and Meningitis UK). Paediatricians are asked to complete a questionnaire about each case.

### Objectives

The primary objective of this study is to define the minimum incidence of meningitis in the UK and Ireland in infants aged less than 90 days.

The secondary objectives are to:

- define the bacterial pathogens that causes meningitis in this age group (and the antibiotic resistance profiles of these pathogens)
- describe the clinical presentation of cases of meningitis in this age group

Dr I Okike

Dr Paul Heath

- describe the mortality and short-term complication rates of meningitis in this age group
- describe the current management of meningitis in this age group.

### Study duration

Surveillance period: July 2010 - July 2011 (inclusive).

### Methodology

*Case Definition*

Any case where the clinician has made a clinical diagnosis of bacterial meningitis in babies less than 90 days of age.

*Additional sources of data*

To ensure as complete ascertainment as possible we are seeking additional cases by reviewing routine laboratory reports to the Health Protection Agency (HPA). Any case is then verified by contact with the local paediatrician. We are also obtaining information about possible cases from parents who report via the Meningitis Research Foundation, Group B Strep Support, the Meningitis Trust and Meningitis UK. Again, possible cases are verified by contact with the local paediatrician.

### Analysis

In the eight months to the end of March 2011 we have received a total of 396 reports from various sources (Figure 5 - see overleaf). Of the cases reported 70% (282) have been reported solely by the BPSU. Of the total reports 165 have so far been confirmed; 148 by the BPSU.

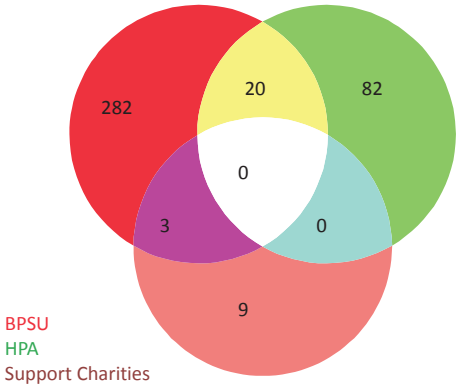


Figure 5: Sources of reports

## Discussion

The high number of cases reported suggest that, in comparison with previous studies, the ascertainment rate is likely to be as high or higher (1996-97 BPSU study reported ~200 cases of bacterial meningitis <2 months of age / year, compared with 165 confirmed cases in this study so far).

There are concerns about the number of reports in Scotland as they are less than we would have predicted and this is something that is being followed-up. Although paediatricians have reported the great majority of cases it is also clear that the other sources are vital in ensuring completeness. The pathogen distribution is similar to previous studies with GBS remaining the leading bacterial cause of meningitis in this age group.

Please also note that the data presented are preliminary and has not yet been peer reviewed and accordingly definitive conclusions should not be drawn

## Funding

Meningitis Research Foundation (MRF).

## Ethics approval

Cambridgeshire 2 REC (Ref: 10/H0308/45) and has been granted NIGB Section 251 Support (Ref: PIAG/ BPSU 6-06(FT1)/2008).

## Support groups

Meningitis Research Foundation - http://www.meningitis.org/
Meningitis UK - http://www.meningitisuk.org/
MeningitisTrust. - http://www.meningitis-trust.org/
Group B Strep Support (GBSS) - http://www.gbss.org.uk/

## Acknowledgements

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# Chylothorax in Infants and Children

## Key points

- Chylothorax is a rare cause of pleural effusion in childhood which can be difficult to diagnose and manage.
- Surveillance for this study commenced in June 2010 and will continue for 13 months.
- To date, the number of reported cases are greater than predicted whilst the infants and children have presented and been treated in 53 different hospitals across the UK and Republic of Ireland.

## Summary

A chylothorax develops when chyle, which is normally transported in lymph vessels throughout the body, builds up around the lungs and exerts pressure on them, making it difficult to breathe. Initial treatment usually requires drainage of the chyle by inserting a chest tube placed into the pleural space around the lungs.

Although the development of a chylothorax is relatively uncommon, it does result in significant risks and complications for particular groups of infants and children. Hospital stay can be extended by weeks; there is the risk of a surgical procedure, an increased risk of infection and the potential for a substantial impact on both the child and their family's quality of life.

Almost all previous research into chylothorax has been retrospective, and has relied on the review and interpretation of case notes for information. Those most commonly reported are in infants and children post cardiac surgery. Very little is known about the situation in the UK or Ireland, either the number of children affected, or how they are treated and what happens to them.

The evidence base therefore remains poor and the extent of the condition, both severity and numbers of children affected, difficult to quantify. Until we understand the scale and nature of the problem better, we are hampered in determining targets for prevention and how best to treat these infants and children and therefore reduce further complications, length of stay in hospital and improve their outcome.

Ms Caroline Haines and Dr Peter Davis

## Objectives

The study aims to identify the:

- incidence of chylothorax in infants and children from 24 weeks gestational to age – 16 years in the UK
- distribution by age, sex and underlying condition of infants and children who develop a chylothorax
- factors that predispose infants and children to develop a chylothorax
- presenting clinical features in infants and children who develop a chylothorax
- clinical management or therapeutic approaches used to treat this condition
- outcome of infants and children who develop a chylothorax.

## Study duration

Surveillance period: June 2010 – June 2011 (inclusive).
Follow-up period: One year outcome follow-up data to be sought until June 2012.

## Methodology

### *Case definition*

Any infant or child under the age of 16 years, including neonates ≥24 weeks gestation presenting for the first time with one of the following should be reported on the BPSU orange card system.

### *Inclusion criteria*

- A suspected clinical diagnosis of chylothorax, without pleural drainage.
- Where pleural drainage is cloudy / opaque fluid is obtained consistent with chylothorax, but no laboratory confirmation of the diagnosis has been sought.

**Or**

An accumulation of lymphatic fluid in the pleural space with:

- Triglyceride content >1.1 mmol/litre
- Total cell count >1000 cells / microlitre

## Table 4: Chylothorax data June 2010-April 2011

| | |
|---|---|
| Total Number of reported cases | 145 |
| Number of confirmed cases | 61 = 42% response rate |
| Number of duplicate questionnaires | 6 = 4% |
| Number of error questionnaires | 9 = 6% |
| Awaiting returned questionnaires | 84 = 58% |
| Number of Hospitals reporting cases | 53 |
| Gender of infants and children | Male – 47.5%, Female – 47.5%, Not Known – 5% |
| Ethnicity | White – 84%, Asian-Asian-British -11%, Mixed – 2%, Other – 3% |
| Weight range | 1.5kg – 51.4kgs -90% of cases <10kgs |
| Side of chylothorax | Bilateral – 48%; Right – 21%; Left – 26%; Not Known – 5% |
| Presumed cause of chylothorax | Neonatal (Congenital) – 16%<br>Neonatal (Other) -18%<br>Cardiac (Surgical) – 46%<br>Surgical Non-Cardiac -10% |
| Outcome of children | Discharged – 61%<br>Remained in Hospital – 20%<br>Died – 11%<br>Not Known – 8% |

*Additional sources of data*

Data collected by the BPSU will be supported and cross referenced with data obtained through the Paediatric Intensive Care Audit Network (PICANet), Hospital Episode Statistics (HES), and the Central Cardiac Audit Database (CCAD).

## Analysis

(See Table 4).

## Discussion

Surveillance of new diagnoses of chylothorax in infants and children has now been undertaken for almost one year. We have demonstrated that the BPSU surveillance methodology can successfully ascertain cases for a condition that predominantly seems to present to neonatal and paediatric intensive care units, to the extent that the number of reported cases is greater than predicted. However, the response rate is currently only 42%, with results awaited from two centres which account for a further 27% of reported cases. Within these two centres there may be some element of duplication, duplication being a possible issue for conditions that present to intensive care units but are then discharged elsewhere.

Infants and children reported to the study have so far been managed in 53 different hospitals across the UK and Republic of Ireland. Interim findings from completed questionnaires indicate a third of cases had a neonatal focus whilst approximately half occurred following cardiac surgery; 90% of cases occurred in infants and children of less than 10kg body weight. Given the large number of cases reported still awaiting returned questionnaires, these figures may change somewhat by the time the study is completed, although the much greater incidence in neonates and infants is likely to persist given the distribution of aetiologies noted so far.

Please also note that the data presented are preliminary and has not yet been peer reviewed and accordingly definitive conclusions should not be drawn.


## Funding

This study has been part funded by a non-medical research grant from UHBristol NHS Foundation Trust and the Variety Club Children's Charity, London.


## Ethics approval

Institute of Child Health / Great Ormond Street Hospital REC (Ref:10/H0713/27) and has been granted NIGB ECC for Section 251 Support (Ref: ECC/BPSU 3-02(FTI).

## References


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3 Paediatric Intensive Care Audit Network National Report 2004 – 2006 (published June 2007) Universities of Leeds and Leicester. ISBN 978 0 85316 264 3

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# CNS Inflammatory Demyelination


Dr Michael Absoud

## Key points

- CNS inflammatory demyelinating diseases (CIDDs) are rare neurological disorders in childhood but may culminate in physical and cognitive disability, or ultimately be diagnosed as Multiple Sclerosis (MS).
- Surveillance commenced in September 2009 for 13 months via the British Paediatric and Ophthalmological Surveillance Units. Outcomes (relapse and MS diagnosis) will be determined at one and two years.
- For the 13 months a total of 223 cases have been reported (197 BPSU, 26 BOSU). Clinical and MRI images are analysed and cases classified on a three monthly basis by an expert panel comprised of Paediatric Neurologists and Neuroradiologists. Information is available for 190 cases, and 125 cases have been included.

## Summary

CNS inflammatory demyelinating diseases (CIDDs) are rare disorders in childhood but may culminate in physical and cognitive disability, or ultimately be diagnosed as Multiple Sclerosis (MS). Children with MS present with a demyelinating episode involving single or multiple symptoms prior to developing a second event (majority usually within two years) to then meet criteria for MS diagnosis. At first presentation, children are diagnosed with an acute disseminated encephalomyelitis (ADEM), optic neuritis, transverse myelitis, neuromyelitis optica, or another clinically isolated syndrome (CIS [Figure 6 - 7]). It is not clear at the onset of symptoms which of these children will go on to develop MS.

There is evidence that 5% of MS cases manifest in childhood. The available literature, however, is limited to small series or retrospective reviews of established adult MS populations. The true incidence of childhood CIDDs is unknown, and the subject of recent international interest (International Paediatric MS Study Group 2007). This group recently published consensus definitions of paediatric CIDDs to facilitate uniformity in future research.

Unravelling the epidemiology, natural history, radiological features of paediatric CIDDs is crucial as there is currently no available biomarker for ADEM, CIS or MS diagnosis. For acute demyelinating illnesses, or relapses of MS, corticosteroids are the mainstay of treatment. Important newer weapons against MS are “disease modifying agents” that decrease relapses by modifying the immune system. There appears to be benefit in the early initiation of these therapies in adults, however, little is published on their use in children. This study is an essential pre-requisite for the design of any prevention or treatment trials and planning service provisions.

The study aims to determine the incidence of childhood CIDDs and establish one and two year outcomes of recurrence (and progression to MS).

## Objectives

The specific aims of the project are, within the UK and Ireland, to:

- determine the incidence of childhood acquired demyelinating disease and MS
- report clinical features, and distribution by age, sex and ethnic group
- identify the frequency of proposed predictors (clinical and radiological) for MS in children
- establish short term outcomes and recurrence after a first demyelinating event in children

- determine whether these children can be classified according to the new international classification and characterise those that cannot
- increase awareness amongst Paediatricians and describe current practices and treatments offered.

## Study duration

Surveillance: September 2009 – September 2010 (inclusive).
Follow up: one and two year questionnaires (September 2010-September 2012).

## Methodology

Cases are being ascertained through the British Paediatric Surveillance Unit (BPSU) and British Ophthalmological Surveillance Unit (BOSU). British Paediatric Neurology Association members, who are consultants and who do not receive the 'orange card' have been added to the mailing list for the duration of the study. Monthly notification cards will be sent to all registered Consultant Paediatricians, Paediatric Neurologists, and Ophthalmologists. Clinicians who notify a case will be asked to complete a brief questionnaire seeking information on diagnosis, clinical features, and also to provide a copy of the MRI. An expert panel is meeting on a quarterly basis to review all cases reported. Clinicians will be asked to report outcomes using questionnaires sent at one and two years following diagnosis, and information on the recurrence of the demyelinating event (if this occurred), death, current functional status and treatment will be sought.

### *Case definition*

Children under 16 years experiencing clinical neurological events consistent with site specific inflammatory CNS demyelination and confirmed with *white matter changes on MRI* (except in optic neuritis) as defined in Table 5.

**Excluding:**
Children presenting with their **second or subsequent** demyelinating episode.

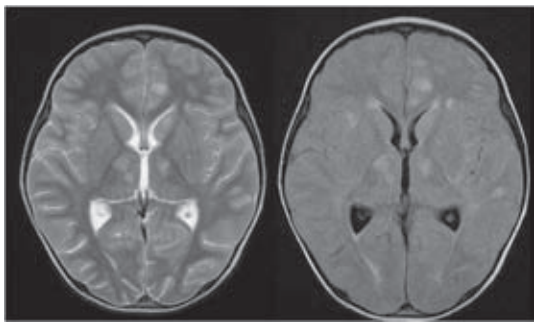

Figure 6: MRI in patient with pneumococcal meningitis demonstrating multiple vasculitic lesions (case was excluded).

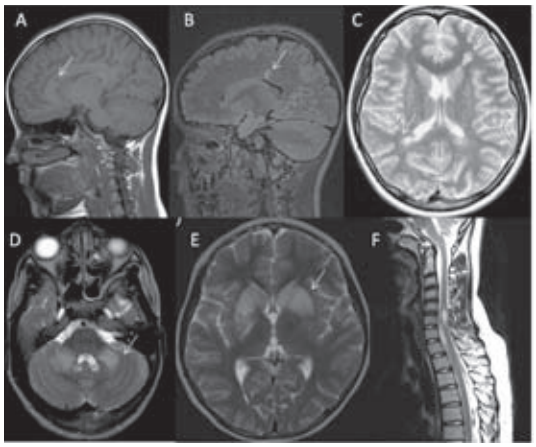


Figure 7: MRI in patient with polyfocal CIS (A,B,C) demonstrating black hole, corpus callosum and periventricular lesions. MRI in patient with ADEM (D,E,F) demonstrating diffuse bilateral cerebellar, basal ganglia lesions and a spinal lesion.

### *Additional sources of data*

Consultant Ophthalmologists via the British Ophthalmological Surveillance Unit (BOSU).

## Analysis

Information was available for 190/223 (85%). After removal of duplicates and cases not fitting inclusion criteria (n=16: vasculitis, infectious and autoimmune encephalitis, hyper-eosinophilic syndrome, tumour related events, peripheral nervous system demyelination and known MS relapses), 125 were included (median age 10.9 years [IQR 11.4-14.1 years], F: M ratio 1.12). Ethnicity comprised 100 white; 12 South Asian; 7 black; 5 mixed. The CIS: ADEM ratio was 2.24; 85 had CIS (34 optic

## Table 5

| | |
|---|---|
| Acute Disseminated Encephalomyelitis (ADEM) | A clinical event (subacute or acute, poly-symptomatic, must include encephalopathy) due to a presumed inflammatory or demyelinating cause affecting multifocal areas of the CNS, and MRI white matter changes. |
| Clinically Isolated Syndrome (CIS) | A first acute clinical episode of CNS inflammatory demyelination (monofocal or multifocal but does not include encephalopathy) and MRI white matter changes. |
| Transverse Myelitis | Weakness and/or numbness of both legs (with or without involvement of arms) and supported by demyelination on MRI of spine. |
| Optic Neuritis | Subacute/acute loss of vision with a presumed demyelinating origin. |
| Neuromyelitis Optica (NMO) | Optic neuritis and associated myelitis. |

neuritis, 26 transverse myelitis, 25 other monofocal or multifocal) and two NMO (aquaporin-4 antibody positive). Median age of onset was 5.8 years for ADEM and 12.8 years for CIS cases ($p<0.001$). The CIS F: M sex ratio was 1.36 ($p=0.12$). Using McDonald 2010 MS diagnostic criteria on CIS cases; 34/85 (40%) satisfied dissemination in space and eight (9.4%) both in time and space criteria.

## Discussion

Most reported cases were CIS (68%), followed by ADEM (18%) and two NMO patients. The expert reclassified several cases reported as ADEM to CIS as these cases did not have encephalopathy (behavioural change or altered consciousness) as a presenting feature. This is important as there is evidence from the literature that children with CIS are more likely to have relapses. Incidence figures will be calculated once the outcomes of all cases are known. Over the next year we will follow up cases of childhood CNS Inflammatory diseases, report clinical and radiological features and identify frequency of proposed predictors.

Please not that data presented here is provisional, not peer reviewed, and limited to these initial findings.


## Funding

UK Multiple Sclerosis Society and Action Medical Research Charities.


## Ethics approval

The study has Black Country Research Ethics Committee (Ref: 09/H1202/92) and NIGB Ethics and Confidentiality Committee approvals (Ref: ECC/BPSU 4-03 [FT1] /2009).

## Support groups

MS Society (www.mssociety.org.uk).

Young MS team, 372 Edgware Road, London NW2 6ND. Tel: 020 8438 0799 Monday to Friday 9-4pm. E-mail: youngms@mssociety.org.uk.

National MS Helpline, Freephone 0808 800 8000 (Monday to Friday, 9am-9pm).


## Acknowledgements

We are very grateful to all paediatricians who have completed monthly cards, particularly those who have notified cases and returned completed questionnaires and MRI copies to us. We also wish to thank all the secretaries and radiology departments who have assisted with administrative procedures such as posting case report forms and anonymised copies of MRIs.


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# Congenital Rubella

## Key points

- Congenital rubella continues to be extremely rare in the UK and Ireland; with only one or two births being reported each year.
- Among 19 infants with congenital rubella born and reported in the UK or Ireland since 2000, 12 had mothers who acquired infection abroad.

## Summary

The National Congenital Rubella Surveillance Programme (NCRSP), set up to monitor the impact of rubella vaccination, has been in existence for 40 years, with active surveillance through the BPSU for the last 20 years.

The World Health Organisation Regional Office set a target for Europe 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. Long-standing vaccination programmes have already led to the virtual elimination of congenital rubella in the British Isles, with only 12 cases diagnosed and reported in the last 10 years. However, sub-optimal uptake of the MMR (Measles, Mumps, Rubella) vaccine over a long period, and the absence of circulating rubella infection, means there are likely to be substantial numbers of susceptible children in parts of the UK and Ireland. In addition, inward migration from countries without long-standing effective rubella vaccination programmes has led to greater concentrations of susceptible individuals in some areas, often the very places where MMR uptake has been low (e.g. parts of London). Measles and mumps have reappeared, and under these circumstances it is possible that rubella, which is still endemic in many parts of the world, could also be re-introduced, putting susceptible pregnant women at risk.

Comprehensive national surveillance through the BPSU therefore remains extremely valuable, to provide a mechanism for timely reporting of any cases which do occur, to monitor whether maternal infections were acquired abroad or at home, and to maintain awareness of this now rare but potentially devastating infection. Congenitally infected infants can excrete rubella virus for an extended period of time, and every infected infant must be diagnosed and managed appropriately to avoid the risk of contributing to further community transmission.

Dr Pat Tookey

## Objectives

The study aims are

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

## Study duration

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

## 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 (Figure 8). This includes “imported cases”, i.e. children born in the British Isles where the maternal infection occurred abroad, AND children who were born abroad, as well as British-born infants whose mothers acquired infection in the British Isles.

### *Additional sources of data*

There is close collaboration with the HPA with respect to laboratory reports of infection.

CDC-Public Health Image Library

Figure 8: Cataracts due to congenital rubella syndrome

## Analysis

There were six reports to the BPSU in 2010. Two were confirmed cases, one born in 2009 and the other in 2010; both mothers were born abroad and one acquired infection in her country of origin while the other was infected in England. Two older children, both born abroad, were reported: one had confirmed and the other had possible infection. One report was made in error, and the other was a duplicate report of one of the confirmed cases.

The number of reported congenital rubella births and rubella associated terminations declined from about 50 births and 740 terminations in 1971-75 to 22 births and 54 terminations a year in 1986-90. Since active surveillance began in 1990, 178 reports have been made through the BPSU (Table 6).

Since the reporting definition was extended in 2005, ten reports have related to nine children who were born abroad. In previous years reports of foreign-born children were not requested, and any such reports were categorised as errors. These children are not included in Table 6 since the main aim of the surveillance is to monitor births in the UK or Ireland. However, in order to make sure cases are not missed, we request reports of all newly diagnosed cases and collect minimal data on these children born abroad.

*Congenital rubella births in the UK or Ireland 1990-2010*: Sixty-three children and four stillborn infants with confirmed or compatible congenital rubella have been born and reported since the beginning of active surveillance in 1990; 50 of these (75%) were first reported through the BPSU (Table 7). Nineteen infants were born since 2000, including one born in Ireland, and two who were stillborn. Although 12 were imported cases with maternal infection acquired abroad (seven in Southern or South Eastern Asia, five in Africa), seven infants were born to women whose infection occurred in the UK.

At least 80 terminations for rubella disease or contact in pregnancy have been recorded by the Office for National Statistics in England and Wales since 1990, but annual data are no longer published since the numbers are so low.

## Discussion

The number of reported cases of congenital rubella remains at a very low level, but virtually all reports concern infants with serious rubella-associated defects present at birth. It is possible that some infants with less obvious 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.[2] Women originating 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. Health professionals, particularly paediatricians and those working in primary care and antenatal care, must continue to be aware of the potential serious implications of rash illness in early pregnancy, the guidelines for the management of rash illness in pregnancy[3], and also of the early signs of congenital rubella.

Please continue to look out for and notify all infants with suspected congenital rubella, whether or not they have the associated typical defects, and regardless of country of birth.

## Funding

The Health Protection Agency makes a contribution towards the costs of the surveillance. Additional support comes from the MRC Centre of Epidemiology for Child Health at the UCL Institute of Child Health.

### Table 6: Congenital rubella reports to BPSU 1990-2010 (includes births occurring in earlier years)

| | Confirmed or compatible | Possible cases | Cases already reported | Duplicate, error or lost | Total |
|---|---|---|---|---|---|
| Place of birth | | | | | |
| Engalnd, Scotland and Wales | 54 | 4 | 14 | 80 | 152 |
| NI and Ireland | 4 | 1 | 2 | 9 | 16 |
| Born abroad (reports 2005-2010 only) | 7 | 2 | 0 | 1 | 10 |

## Table 7: Confirmed and compatible congenital rubella births in the UK and Ireland 1990-2010

| Year of birth | Primary source of notification | | |
|---|---|---|---|
| | BPSU | Other | Total |
| 1990-94*^ | 22 | 10 | 32 |
| 1995-99 | 12 | 4 | 16 |
| 2000-04* | 10 | 1 | 11 |
| 2005-10 | 6 | 2 | 8 |
| **Total** | **50** | **17** | **67** |

* Includes a stillborn infant
^ Includes a set of triplets, one of whom was stillborn

## Ethics approval

The London Multicentre Research Ethics Committee reaffirmed approval in 2005 (Ref: 05/MRE02/2); PIAG (now NIGB Ethics and Confidentiality Committee) approval (PIAG/BPSU 2-10(f)/2005).

## Support groups

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

## Acknowledgements

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3. HPA Rash Guidance Working Group. Guidance on viral rash in pregnancy. Available at http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1294740918985.

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# Congenital syphilis in children under 2 years of age

Dr Ian Simms

## Key points

- The study has just completed the first of its three years.
- Nine confirmed positives were found with a further 14 suspected cases are under investigation.
- An analysis of the first year's data is to be undertaken this summer with a view to publication in autumn 2011.

## Summary

Congenital syphilis occurs when syphilis is transmitted from a woman to her unborn baby during pregnancy. This can lead to miscarriage, stillbirth, neonatal death, or disorders such as deafness and bone deformities. As such, congenital syphilis is a distressing and costly condition. Cases can be prevented through antenatal screening and treatment. In recent years, cases of congenital syphilis have emerged as cases of syphilis in women have increased. There are thought to be around 20 cases of congenital syphilis each year but there was no national surveillance on which to base this estimate. This project will undertake detailed surveillance of congenital syphilis to accurately estimate the number of cases of congenital syphilis that occur each year. This information will be used to suggest improvements to health care systems so infected women can be appropriately managed.

## Objectives

The objectives of this study are to

- determine the incidence of congenital syphilis in children under two years of age over a three year period
- compare the incidence, management and presentation of cases with that observed in the similar UK study carried out in the 1990s which used a similar methodology
- compare the coverage of the available routine surveillance systems
- assess the proportion of congenital cases identified/not identified through antenatal screening, and identify factors associated with failure to identify maternal infection, or prevent congenital infection.

## Study duration

Surveillance period: January; 2010 – December; 2012 (inclusive).
Follow-up period: For a twelve month period ending in 2014.

## Methodology

### *Case definition*

Reporting case definition (surveillance) to be used by paediatricians for initial identification of cases.

Any child under the age of 24 months with a confirmed or presumptive diagnosis of congenital syphilis or acquired syphilis will be reported on the BPSU orange card. The study epidemiologist and medical advisor will then identify the reported congenital cases. Only the congenital cases will be included in further investigations.

(a) Confirmed case of congenital syphilis: any infant with a laboratory confirmed diagnosis of congenital syphilis.

(b) Presumptive case of congenital syphilis: any infant or child under 24 months in whom congenital syphilis is suspected but not yet laboratory confirmed, for example.

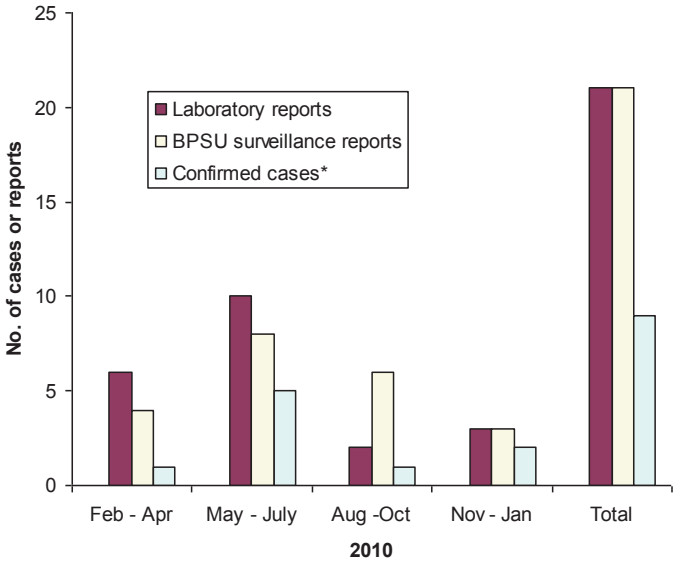
(i) with clinical signs consistent with congenital sypyhilis (snuffles, condyloma lata, osteitis, periostitis or osteochondritis, ascites, skin and mucous membrane lesions, hepatitis, hepatomegaly, splenomegaly, nephrosis, nephritis, or hemolytic anemia), **OR**

(ii) whose mother had untreated or inadequately treated* syphilis at the time of delivery.
*Those treated using suboptimal dose or duration in relation to the BASHH guidelines for treatment of infectious syphilis.

## Analysis

The study has completed its first year of operation. Three surveillance datasets were sourced. Twenty one suspected cases were detected through laboratory reports and the same number were reported through the BPSU (Figure 9). No cases were reported from genitourinary medicine clinics during the same period. Although the same number of reports was received through the laboratory report and BPSU surveillance systems, only five were reported by both. Suspected cases were seen in all English health service regions.

Follow-up of suspected cases continues and as at April 2011, nine cases had been confirmed.




* Confirmed cases were derived from both the lab report & BPSU surveillance systems

Figure 9: Congenital syphilis: cases or reports of suspected cases, 2010-2011

The remaining suspected cases continue to be investigated. Information on gender is not available for all the cases reported through the BPSU system, but laboratory report data indicate that 62% of cases were seen in males.

## Discussion

The first year of the study has focused on establishing the surveillance technique and investigating cases detected through the different surveillance systems. The dataset is not yet finalised so unfortunately it is not possible to summarise the findings here and disease incidence cannot be estimated. However, from the number of confirmed cases seen it would appear that the number of confirmed cases is similar to that anticipated at the start of the study. An analysis of the first year's data is planned for the summer/autumn 2011 with a view to publication later in the year.

Please also note that the data presented are preliminary and has not yet been peer reviewed and accordingly definitive conclusions should not be drawn.

## Funding

Health Protection Agency.

## Ethics approval

Central London REC (Ref: 09/H0714/44) and has Section 251 NIGB permission under HPA reference (PIAG 03-(c)/2001).

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# Conversion Disorder

## Key points

- Of 465 notifications, 214 cases were confirmed as true cases and 147 one year follow-up questionnaires have been received.
- Paediatricians reported 59% of confirmed cases while Child Psychiatrists reported 37%; only 4% of cases were reported through both systems.
- Motor weakness, abnormal movements and pseudo-seizures were the most frequent clinical manifestations.
- Most cases had no premorbid or concurrent psychiatric disorders.
- Majority of symptoms had improved by 12 months.

## Summary

Conversion Disorder is an uncommon but highly disabling condition in childhood. Affected children may manifest physical symptoms and signs, such as paralysis, blindness, deafness or other sensory losses, without any medical cause being found. These children are often severely impaired and at risk of serious long-term physical and psychosocial complications, including educational failure, social isolation and psychiatric morbidity. The condition can be associated with extensive use of paediatric and allied health resources. Despite the huge personal suffering and health resource implications of Conversion Disorder, the epidemiology and clinical burden in children has not been documented in the UK. We are conducting the first study to describe the frequency, pattern and short-term outcomes of Conversion Disorder in children in the United Kingdom and Ireland. The study involves joint surveillance by the BPSU (for paediatricians) and Child and Adolescent Psychiatry Surveillance System (CAPSS) involving Child and Adolescent Psychiatrists. The study's findings could help to inform service planning for children with this seriously impairing condition.

## Objectives

The study aims to

- estimate the incidence of Conversion Disorder in children in the UK and Ireland
- describe the clinical features of Conversion Disorder at presentation
- describe associated co-morbid psychiatric or medical illness and family history of psychiatric illness
- describe current management of children with Conversion Disorder, including investigations
- determine the duration of illness and the short term outcomes at one year after diagnosis.

Dr Corenlius Ani

## Study duration

Surveillance period: October 2008 – December 2009 (inclusive).
Follow-up period: One year outcome follow-up data was sought to December 2010.

## Methodology

As children affected by Conversion Disorder may present to both paediatricians and child and adolescent psychiatrists, we conducted a dual surveillance involving BPSU and CAPSS – in order to capture the full spectrum of cases. Reporting by more than one clinician was encouraged to maximise case ascertainment and clinical details. Duplicate reporting was identified by case matching. A questionnaire was sent to clinicians reporting a case to gather demographic and relevant clinical information. For all valid cases, a second 'follow-up' questionnaire was sent to the reporting clinician a year after the case was first reported. This provided information on treatment received, duration of the disorder and outcome. A panel of experts reviewed the reported cases to confirm whether or not they met the case definition.

### *Case definition*

Any child younger than 16 years newly diagnosed with Conversion Disorder during the previous month in Britain and Ireland.

Conversion disorder is DEFINED as:

The presence of one or more symptoms and or signs affecting motor function (e.g. weakness, abnormal gait or movements, difficulty with swallowing, or loss of speech), and or sensory function (e.g. loss or diminished sensation of touch, sight, or hearing), and or non-epileptic seizures (also known as pseudo seizures).

**AND**

The following symptoms and or signs:

- cannot be adequately explained by a medical condition after full investigation (according to the judgement of the treating clinician), **and**

- have no evidence that they have been intentionally produced, **and**
- cause significant distress and or interference in daily activities such as with self care, school attendance, play, or family activities for up to 7 days or longer, **and**
- are accompanied by psychological factors that are judged to be associated with or have contributed to the presentation.

EXCLUSION CRITERIA

1. cases where the clinical picture is predominantly or exclusively pain or fatigue, and or
2. cases where the dominant picture is another psychiatric disorder such as depression or psychosis diagnosed by a child and adolescent psychiatrist, and or Tic disorder.

*Additional sources of data*

CAPSS generated additional case ascertainment from Child and Adolescent Psychiatrists.

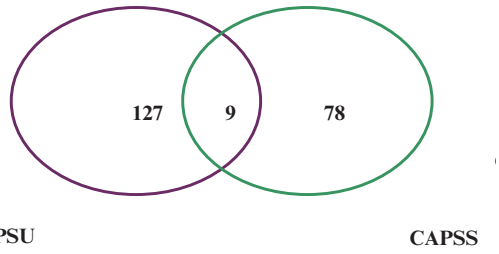


Figure 10: Reporting source of confirmed cases

## Analysis

A total of 214 cases have so far been confirmed from 465 notifications. 129 (28%) questionnaires have as yet not been returned. To date we have received one year follow-up details on 147 cases. Child psychiatrists and paediatricians reported 37% and 59% of cases respectively; there was limited overlap (Figure 10). A further 4% were reported jointly.

Interim analysis of the data collected by March 2011, showed that females (161 cases) were affected 2½ times more frequently than males. Most cases (75%) were aged 12-15 years (Mean age = 12.5, SD = 1.8, Range 7-15 years). The most frequent core symptoms were motor weakness (68%), abnormal movements (43%), pseudo-seizures (36%), and paralysis (23%). The associated stressors included bullying (24%), bereavement (18%), exam pressure (15%), and parental separation (13%). Twenty-three percent had a pre-morbid psychiatric history, most commonly, anxiety disorder (12%). A higher proportion (30%) had a concurrent psychiatric disorder, most commonly, anxiety disorder (25%). Most cases required in-patient admission (80%) for an average of 17 days (range 1-147 days). The children were extensively investigated including with MRI (59%), EEG (52%) and CT Scan (28%). Each child required an average of 4.3 professionals including paediatricians (91%), child and adolescent psychiatrists (71%).

Between 55% and 78% of symptoms had improved at 12 months follow up. Ninety-four percent of clinicians offered a non-organic explanation to families and this was accepted to a limited degree by 36% of families while 51% appeared to accept this well.

## Discussion

The limited overlap of cases reported through BPSU and CAPSS demonstrates the importance of dual surveillance strategy to ensure maximum case ascertainment for conditions at the interface of paediatrics and child psychiatry. Though this has helped in maximising ascertainment, given the high level of non questionnaire completion, the eventual incidence figure should be considered as a minimum.

Conversion disorder was associated with a range of stresses and anxiety disorder; hence addressing these stresses and anxiety disorder may be helpful in preventing onset of conversion disorder. The finding that 90% of families appeared to accept non-medical explanation to some extent, and that most cases had shown some improvement at 12 months should give clinicians confidence in discussing both the formulation and prognosis of this disorder with young people and their families.

## Funding

BUPA Foundation.

## Ethics approval

Charing Cross Hospital MREC (Ref: 08/H0711/30) and has been granted PIAG Section 60 Support (Ref: PIAG/BPSU 3-06(FT1)/2008).

## Acknowledgements

We are grateful to all the participating paediatricians and psychiatrists, especially those who have notified cases and completed questionnaires. We thank the BPSU and CAPSS for facilitating the methodology and BUPA Foundation for funding.

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# Glutaric Aciduria 1

## Key points

- The number of cases we have identified appears to be compatible with our lower estimate of incidence of approx 1:100,000.
- So far, the presenting features have been varied and usually distinct from classical presentations of non-accidental injury.
- Our one-year follow up questionnaires will begin to go out in August 2011.

## Summary


Glutaric Aciduria 1 (GA 1) is a rare inborn error of metabolism caused by a deficiency of the enzyme glutaryl-CoA dehydrogenase. Children who have GA 1 cannot break down glutaric acid, so harmful substances build up in the blood. Affected children are usually asymptomatic at birth but symptoms start in infancy or early childhood with episodes of illness. Symptoms may include loss of consciousness, loss of muscle tone and impaired brain function. Early treatment, including medication and special diet as well as careful management of childhood illnesses is important to prevent further deterioration.

The aim is to find out how many children are being diagnosed with GA1 in the UK and the Republic of Ireland and to find out more about the early signs and symptoms with the aim of helping doctors to make the diagnosis more quickly in the future. We will also send a follow up questionnaire to reporting paediatricians after one year to find out how the children progressed during this time.



Dr Beth Cheesebrough

## Objectives

The objectives of this study are to:

- estimate the incidence of GA 1 in children in the UK and Ireland and its distribution by age and ethnic group
- study the patterns of clinical presentation and neuro-imaging findings including incidence of subdural or retinal haemorrhage at diagnosis
- assess morbidity at mortality up to one year post diagnosis.

## Study duration

Surveillance period: July 2011 – July 2012 (inclusive).

Follow-up period: For a twelve month period ending in July 2014.

## Methodology

Standard BPSU methodology of reporting via the 'orange card' system is being used as well as cross referencing confirmed cases with positive enzyme assay results and DNA mutation analysis results at Sheffield Children's Hospital.

### *Case definition*

Any child under the age of 16 years with a confirmed or suspected diagnosis of GA 1
The child will be considered to have a proven diagnosis of GA 1 if at least one of the following criteria is met:

- two known pathogenic mutations on mutation analysis.
- reduced or absent glutaryl-CoA dehydrogenase activity in cultured fibroblasts or leukocytes.

The child will be considered to have suspected GA 1 if at least one of the following criteria is met:

- isolated elevation of glutarylcarnitine on blood spot analysis.
- elevated urinary excretion of glutaric acid and/or 3-hydroxyglutaric acid.

### *Additional sources of data*

Sheffield Children's Hospital enzyme laboratory and DNA laboratory.

## Analysis

The incidence over the past 10 months appears to be approximating our lower estimate of 1:100,000. The cases that have been reported have presented in a variety of ways and, so far, have presented in a way that is distinct form classical presentations of non accidental injury.

One-year follow up has not yet commenced so we do not have any information on short term morbidity and mortality yet.

Two cases have been confirmed by laboratory reporting and no additional cases have been identified through laboratory reporting which have not been reported via the BPSU.

## Discussion

Data analysis is in its early stages. Cases are being reported predominantly at early stages of diagnosis i.e. as suspected rather than confirmed GA 1. It is then taking some time for definitive laboratory testing to confirm or refute the cases. Ongoing e-mail contact with reporting clinicians has been undertaken to ascertain case outcomes. However estimates of the incidence of GA 1 that have been made by Pollitt et al 1997 (1:50,000) and Lindner et al 2004 (1:100,000) would give us approximately 8-17 cases per year in the UK and Ireland. So far case numbers are equivalent to the lower figure above although confirmatory tests are not yet available for all of our probable cases.


## Acknowledgements

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## Funding

Sir Peter Tizard Bursary.


## Ethics approval

Institute of Child Health/Great Ormond Street Hospital MREC (Ref: 10/H0713/10);
NIGB Ethics and Confidentiality Committee approvals (Ref: 38998/86476/4/1000).

## Support groups

Climb: www.climb.org.uk. Tel: 0800 652 3181.

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# Gonorrhoea, Syphilis, Chlamydia, and Trichomonas

## Key points

- Cases are rare – few confirmed reports have so far been received.
- A number of neonatal eye infections have been reported, but these are not included in the study (>1year of age).

## Summary

Infections which are sexually transmitted in adults are rare in childhood. They may be identified as the result of screening investigations after sexual assault or abuse, or they may present with symptoms or as a result of investigations for another apparently unrelated medical cause. We know very little data about these infections in childhood, information which are needed to guide treatment and for legal evidence in the case of child protection cases. We do not know how commonly these infections occur, how often they are thought to be associated with sexual transmission, whether there are characteristic symptoms or reasons for presentation, nor how frequently child protection investigations are initiated and their resulting outcome.

This study of all cases of Gonorrhoea, Syphilis, Chlamydia and Trichomonas (the commonest bacterial and protozoal sexually transmitted infections in adults in the UK) among children under thirteen years in the UK and Ireland will gather epidemiological information to inform all these questions. Although we will not be able to answer the question of whether these infections are always contracted through sexual contact, or the factors which would indicate sexual transmission, it will provide much needed information on which to base recommendations about management and child protection implications. It will probably result in the largest reported series of such children in the world literature.

## Objectives

The objectives of this study are to identify:

- incidence of the four types of sexually transmitted infection in children aged one year to twelve years
- types of diagnostic test used
- mode of presentation

Dr Richard Reading

- associated clinical features
- features of the history, clinical findings or investigations which would indicate child sexual abuse
- outcome of any child protection procedures.

## Study duration

Surveillance period: January 2010 – January 2012 (inclusive).
Follow-up period: Six months to ensure completeness of data on initial questionnaire.

## Methodology

Paediatricians reporting a case through the orange card system will be asked to complete a questionnaire seeking demographic, clinical and relevant child protection information. The questionnaire is in two parts, one containing minimal identifier information, the other containing all other details, which are returned in separate envelopes to the investigators by the referring paediatrician in order to maintain confidentiality in the event of the post being misdirected, delivered to the wrong address or lost. If information is incomplete, for example child protection outcomes may not be known, the questionnaire will be sent out again at a time deemed appropriate by the reporting paediatrician.

### *Case definition*

Any child over the age of 12 months with a diagnosis of Gonorrhoea, Syphilis, Chlamydia or Trichomonas confirmed by laboratory tests. For syphilis we include infection at any site. For Gonorrhoea, Chlamydia and Trichomonas we include genito-urinary, rectal or oro-pharyngeal infections.

Laboratory tests may vary at different centres but include bacteriological isolation, nucleic acid amplification tests, enzyme linked immuno-assay and serology.[1,2]

## Analysis

By April 2011 there have been 30 reports, seven have been confirmed as eligible cases, two duplicate reports, 18 reported in error mainly either too young or too old, and three reports we await further details. There have been few confirmed cases. Of the seven cases six are female and there is one male. Six cases involved Chlamydia infection and one syphilis. Among those which were ineligible were several congenital eye infections presenting in the neonatal period.

Please also note that the data presented are preliminary and has not yet been peer reviewed and accordingly definitive conclusions should not be drawn.

## Discussion

An interim analysis has on the clinical information has yet to commence. The case reports are fewer than expected but probably this reflects the rarity of identifying these conditions in the childhood age range. We have been collaborating with the BPSU study investigators on congenital syphilis (Page 22) and have passed case details on to the investigators for this study in a very small number of cases which were reported to us but meet the criteria for possible congenital syphilis.


## Acknowledgements

Ms Julia Hill, Paediatric Research Nurse, Norfolk and Norwich University Hospital and Mr Tony Dyer, Database manager Norwich CRTU.

## Funding

WellChild.


## Ethics approval

London Research Ethics Committee (Ref: 09/H0718/56) and has been granted Section 251 Support by the Ethics and Confidentiality Committee of the National Information Governance Board (Ref: ECC/BPSU 1-03 (FT1)/2009.

## Support groups

The Survivors Trust. Tel: 01788 550554.
Website: www.thesurvivorstrust.org.

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# Guillain-Barré syndrome and Fisher syndrome

## Key points

- In 1976 a National Influenza Immunization Programme against swine influenza in the United States (US) was discontinued because of reports of Guillain-Barré syndrome (GBS) in some of those who were vaccinated.[1]
- It was therefore imperative to perform surveillance for Guillain-Barré syndrome (GBS) and Fisher syndrome (FS) in response to the planned introduction of the pandemic H1N1 (swine) influenza vaccine in the UK in October 2009. This study was fast-tracked through the BPSU system and was commenced in September 2009.
- Our results show that the majority of GBS or FS cases are temporally associated with a variety of previous infections whereas there is little association with H1N1 (swine) influenza vaccination or seasonal influenza vaccination.
- More GBS cases have been reported than were expected on the basis of a previous BPSU study.

## Background

Guillain-Barré syndrome (GBS) is an important cause of acute flaccid paralysis worldwide and it is believed that immune stimulation plays a central role in its pathogenesis. Fisher syndrome (FS) was described in 1956 and was hypothesised to be a form of GBS. As the clinical features of GBS and FS show similarities, both conditions were included in surveillance.

Because the 2009/2010 pandemic was caused by an H1N1 (swine) influenza virus, it was particularly important to start surveillance in UK children because of the association between the swine influenza vaccine and GBS that led to discontinuation of vaccine use in the US in 1976.[1] Since influenza-like illness has been shown to be associated with an increased risk of GBS[2], both influenza vaccination and illness needed to be evaluated as potential risk factors for GBS.

## Objectives

The study aims to identify

- all new cases of Guillain-Barré syndrome or Fisher syndrome
- the proportion of these that are temporally associated with recent infections or with H1N1 (swine) influenza vaccination or seasonal influenza vaccination.

Dr Chris Verity and team

## Study duration

Surveillance period: September 2009 to September 2011 (inclusive).

## Methodology

A questionnaire requesting clinical history, relevant physical findings and the results of investigations is sent to each paediatrician who reports a case through the BPSU. The team at the Health Protection Agency (HPA) then contact the GP or health clinic to obtain information about any vaccinations (for example, type and batch number) given to the child as information about vaccines is not always available within the child's hospital notes. Six months after initial notification, a brief follow-up questionnaire is sent to paediatricians to ask about clinical outcome and the results of any outstanding diagnostic tests.

Paediatricians have also been e-mailed to provide advice about the pathological specimens that can be collected for children presenting with features of GBS or FS – these samples are recommended for clinical and not research purposes. Current advice is to take blood samples to test for antibodies to H1N1 swine influenza from children with GBS or FS and send these to the HPA for analysis. The HPA provides further advice to paediatricians if necessary.

### *Case definitions*

The criteria below provide the highest level of diagnostic certainty for GBS or FS but the diagnosis can still be made if not all the criteria are met, so paediatricians are encouraged to report all suspected cases.

**Guillain-Barré syndrome (GBS)**

The presence of

- acute onset of bilateral and relatively symmetrical flaccid weakness/paralysis of the limbs with or without involvement of respiratory or cranial nerve-innervated muscles **AND**

- decreased or absent deep tendon reflexes at least in affected limbs **AND**
- monophasic illness pattern, with weakness nadir reached between 12 hours and 28 days, followed by clinical plateau and subsequent improvement, or death **AND**
- electrophysiological findings consistent with GBS **AND**
- presence of cytoalbuminologic dissociation (elevation of cerebrospinal fluid (CSF) protein level above laboratory normal value, and CSF total white cell count <50 cells/mm$^3$) **AND**
- absence of an alternative diagnosis for weakness.

**Fisher Syndrome (FS)**

- acute onset of all three of: bilateral ophthalmoparesis, bilateral reduced or absent tendon reflexes, and ataxia.

  Ophthalmoparesis, tendon reflexes, and ataxia are relatively symmetrical. Ptosis or pupillary abnormalities may be present in the setting of the ophthalmoplegia. The clinical severity of each component may vary from partial to complete. **AND**

- absence of limb weakness** **AND**
- monophasic illness pattern, with clinical nadir reached between 12 hours and 28 days, followed by clinical improvement, with or without treatment **AND**
- presence of cytoalbuminologic dissociation (elevation of cerebrospinal protein above the laboratory normal, with total CSF white cell count <50 cells/mm$^3$]) **AND**
- nerve conduction studies, if performed, are normal, or indicate involvement of sensory nerves only **AND**
- brain magnetic resonance imaging (MRI) normal, or if abnormal, absence of brainstem lesions consistent with encephalitis **AND**
- an alternative diagnosis is not evident.

**While the classic triad is often clinically recognized and occurs in the absence of limb weakness, in some cases there is clinical overlap with GBS, with limb weakness present.

## Analysis

Data collection remains incomplete and this is an interim analysis relating to the period September 2009 – January 2011.

In the first 17 months of the study there were 143 notifications, of which 81 cases met the criteria, seven were not true cases, 21 were duplicate reports and 34 cases were outstanding. There were 79 children who met the criteria for Guillain-Barré syndrome and two for Fisher syndrome. Of these 81 children, 61 had clinical or laboratory evidence of infections in the three months before their GBS or FS symptoms – 24 had upper respiratory tract infections, 17 gastroenteritis, six H1N1 influenza (two suspected, four laboratory confirmed), four pyrexias of unknown origin and two with "'flu-like symptoms". An additional eight children had laboratory evidence of other viral infections, including chicken pox (2), cytomegalovirus (2), Epstein-Barr virus (2) and influenza A (1) and B (1).

Four children (of 58 with vaccination details) had been given H1N1 vaccinations. One child was given H1N1 vaccinations (Celvapan, two doses) four weeks before the onset of GBS - the only child given H1N1 vaccine at a time interval that might indicate a causal relationship with GBS, on the basis of what is already known[1]. The three other children were given H1N1 vaccinations six months, seven months and 10 months before GBS symptoms, probably too distant to be causal.

Three children had been given seasonal influenza vaccines – two were probably too distant to have caused the neurological symptoms (four months and seven months before) and the third probably too close (three days before).

Nine children had received other vaccines in the three months before disease onset, according to the hospital notes, as follows: human papillomavirus (3), travel vaccines (3) MMR (1), DTP/polio/Hib/MenC/pneumococcal (1) and MenC followed by MMR/pneumococcal (1); seven of these children also had clinical or laboratory evidence of an infectious disease in the three months before symptoms started.

Please note that the data presented are preliminary and have not yet been peer reviewed. Accordingly definitive conclusions should not be drawn.

## Discussion

Findings from the first 17 months of surveillance show that the majority of GBS or FS cases are temporally associated with previous infections and that there is little evidence to suggest a link with H1N1 (swine) influenza vaccines or seasonal influenza vaccinations in children. We have already identified more GBS or FS cases than would have been predicted on the basis of the BPSU acute flaccid paralysis study performed from 1991 to 1994.[3]

To put these findings in context, the Department of Health reported[4] that, between October 1st 2009 and March 31st 2010, H1N1 (swine) influenza vaccine was given to an estimated 855,378 children in England (87.4% of GP practices yielded data). This vaccine was also given to children in the rest of the UK (the study covers all of the UK).

The study will continue until September 2011 and complements a surveillance study undertaken by the HPA and British Neurological Surveillance Unit to identify GBS cases in both older children and adults.

## Funding

Department of Health (England) Policy Research Programme (Ref: No: 0190047).

## Ethics approval

Trent Research Ethics Committee (Ref: 09/H0405/45) and the Ethics and Confidentiality Committee of the National Information Governance Board (Ref: ECC/BPSU 5-02 (FT1).

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# HIV/AIDS

## Key points

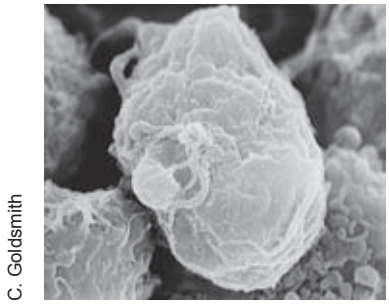
- More than 1300 children born in 2009 to women diagnosed with HIV by the time of delivery have been reported.
- Since 2000 the overall mother-to-child transmission rate from diagnosed women has been about 1%.
- Two thirds of infected children accessing paediatric or transition services are aged 11 years or older.

## Summary

National surveillance of paediatric AIDS began in 1986 and was extended to include HIV infection and perinatal HIV exposure in 1989; it is based on voluntary, active, non-selective, confidential paediatric and obstetric reporting schemes with some additional data from laboratory reports. Data from all sources are combined as the National Study of HIV in Pregnancy and Childhood (NSHPC) at the UCL Institute of Child Health.[1]

The majority of children diagnosed with HIV (Figure 11) infection in the UK and Ireland acquired their infection through mother-to-child transmission (MTCT). A number of young people with haemophilia were reported in the early years of the study, and some children acquired their infection through other routes e.g. blood transfusion abroad. The majority of recently diagnosed children were born abroad, mostly in sub-Saharan Africa.

Births to diagnosed HIV-positive women in the UK and Ireland have increased substantially from about 100 in 1997 to over 1300 each year since 2006. Antiretroviral treatment, appropriate mode of delivery (elective caesarean section, or planned vaginal delivery, depending on circumstances) and the avoidance of breastfeeding reduce transmission rates from diagnosed women to around 1% in comparison with a likely transmission



C. Goldsmith

Figure 11: Scanning EM of HIV, grown in cultured lymphocytes. Virions are seen as small spheres on the surface of the cell

Dr Pat Tookey and team

rate of about 25% without interventions.[2] The estimated proportion of HIV-positive women diagnosed before delivery in the UK increased from 32% in 1997 to over 90% since 2004, and remains high (www.hpa.org.uk ), but in spite of high diagnosis rates and high uptake of interventions to prevent MTCT, around 30 children a year are still acquiring HIV infection from their mothers.

## Objectives

The objective of this study is the surveillance of paediatric HIV infection and AIDS in the United Kingdom and the Republic of Ireland.

## Study duration

Surveillance period: Surveillance began in June 1986 and is continuing.

Follow-up period: Reported cases are followed up during the first year to establish infection status, and those who are infected remain in long-term follow up through the Collaborative HIV Paediatric Study (CHIPS), a collaboration between the NSHPC, the MRC Clinical Trials Unit, and clinicians.

## Methodology

### *Case definition*

Any child under 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.

### *Additional sources of data*

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

## Table 8: HIV infection and infants born to HIV infected women *(all reporting sources)* Source of report and exposure/likely source of infection *(notified by 31 December 2010)*

| Exposure / likely source of infection | BPSU reports | Reports from other sources | Total |
|---|---|---|---|
| **Children born to HIV infected women** | 6401 | 8043 | 14444* |
| **Likely source of infection for other infected children** | | | |
| Haemophilia treatment | 48 | 219 | 267 |
| Blood transfusion/products | 39 | 22 | 61 |
| Other/not yet established | 33 | 44 | 77 |
| **Total** | 6521 | 8328 | 14849 |

*1933 known to be infected

### Analysis

*Number and geographical distribution of reports:* By the end of December 2010 there had been 8586 BPSU reports, of which 6473 were confirmed cases of HIV infection or exposed infants at risk of vertical transmission: 580 reports were still being investigated. A further 8376 confirmed cases were reported through other sources (see methods). Table 8 shows the likely source of infection or exposure risk for all confirmed cases.

The majority of reports (86%) were made between 2000 and 2010 and this pattern was similar for all regions (Table 9). Only 29% of reports from English regions were received from outside London before 2000, compared with 52% of reports made between 2000 and 2010.

*Children born to HIV-positive women*: Most reported children (14444/14849 97%) were born to HIV-positive women. By the end of 2010, 1933 (13%) of these children were known to be infected, and 10322 (71%) uninfected; infection status for the remaining 2189 (15%) had not yet been reported, but the majority were recent reports and very few are likely to be infected. While only 7% were born abroad, they accounted for half (50%) of all confirmed mother-to-child transmissions.

Since 2006 the number of births each year to diagnosed women in the UK and Ireland has stabilized at about 1300 (reports for 2010 will increase substantially) (Table 10). Although the infection status of some of these children has yet to be reported, most will be uninfected. The overall transmission rate for births to diagnosed women between 2000 and 2006 was 1.2% (61/5151, 95% CI: 0.9-1.5%), and 0.8% (40/4864) for women who received at least two weeks of antiretroviral therapy prior to delivery.[2]

## Table 9: HIV infection and infants born to HIV positive women (all reporting sources) Region and time period report *(notified by 31 December 2010)*

| Region of first report | 1986-1999 | 2000-2010 | Total |
|---|---|---|---|
| **England Total** | 1575 | 11031 | 12607 |
| *London* | *1122 (71%)* | *5781 (52%)* | *6903* |
| *North* | *181 (11%)* | *1627 (15%)* | *1808* |
| *Midlands & East* | *129 (8%)* | *2262 (20%)* | *2391* |
| *South* | *144 (9%)* | *1361 (12%)* | *1505* |
| **Wales** | 26 | 150 | 176 |
| **Northern Ireland** | 4 | 62 | 66 |
| **Scotland** | 232 | 389 | 621 |
| **Ireland** | 170 | 1209 | 1379 |
| **Total** | 2008 | 12841 | 14849 |

**Table 10: Year of birth and infection status of children born in the UK and Ireland to women diagnosed with HIV by the time of delivery** *(notified by 31 December 2010)*

| Year of Birth | Infected | Indeterminate | Not infected | Total |
|---|---|---|---|---|
| **1984-1999** | 111 | 146 | 896 | 1153 |
| **2000-2002** | 25 | 147 | 1492 | 1664 |
| **2003-2005** | 35 | 173 | 3127 | 3335 |
| **2006-2008** | 26 | 567 | 3449 | 4042 |
| **2009** | 6 | 489 | 824 | 1319 |
| **2010*** | 4 | 593 | 284 | 881 |
| **Total** | 207 | 2115 | 10072 | 12394 |

*reports for 2010 expected to rise substantially

*Infected children:* Since surveillance started in 1986, 2071 infected children have been reported (excludes 267 young people with haemophilia reported early in the study period): 268 (13%) are known to have died, 109 (5%) to have gone abroad and 261 (13%) to have transferred to adult services: a further 121(6%) are either reported as lost to follow up or have had no follow up information reported since the end of 2007. Of the 1300 children and young people still being seen in paediatric or transition clinics nearly a quarter are aged 16 or over, and a further 42% are aged 11 to 15 years. Forty-two pregnancies have been reported in 33 young women who were previously notified as paediatric cases.

Overall, about half (51%) of all infected children were born abroad, the majority in sub-Saharan Africa, but the proportion has changed over time from 33% of those diagnosed before 2000 to 62% of those diagnosed since. Median age at diagnosis for children diagnosed since the beginning of 2008 was eight years (IQR 3-11).

Of the 945 children known to have acquired infection through MTCT in the UK or Ireland, most (78%) were born to women who had not been diagnosed by the time of delivery. Eighty-six children born since 2006 were confirmed infected by the end of 2010 (36 born to diagnosed and 50 to undiagnosed women): the number of reports of children born to undiagnosed women during this period will increase as later diagnoses are made.

## Discussion

The number of births to HIV-positive women in the UK and Ireland has increased substantially each year since 2000, with reported births exceeding 1300 since 2006.[1] Most of these infants were born to diagnosed women who were able to take advantage of interventions to reduce the risk of transmission. Overall mother-to-child transmission rates from diagnosed women in the UK and Ireland are now at around 1% with even lower rates among women who received optimal treatment according to the British HIV Association guidelines (www.bhiva.org.uk).[3] However, despite high uptake of antenatal testing and interventions, some infants are still acquiring HIV infection perinatally or through breastfeeding.

Nearly two-thirds of infected children diagnosed between 2000 and 2010 in the UK or Ireland were born abroad, mostly in sub-Saharan Africa. A substantial number of young people who were diagnosed under the age of 16 are now adults: some have already transferred their care to adult services and in a few centres dedicated transition clinics help to facilitate this change. In coming years increasing numbers of pregnancies in perinatally infected young women are likely to be reported, and the median age of newly diagnosed children is likely to remain high.

Reports to the NSHPC from all areas of the UK, and from Ireland, have increased in recent years.[1] The wide geographical distribution of the newly reported cases highlights the valuable role of the BPSU in identifying infected children diagnosed outside the specialist paediatric HIV centres, as well as exposed infants born to infected women in lower prevalence areas throughout the British Isles.

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

## Funding

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

## Ethics approval

The London Multicentre Research Ethics Committee reviewed and approved the NSHPC and the associated CHIPS study on 28 January 2004 (Refs: London MREC/04/2/009; MREC/04/2/010). Paediatric surveillance of HIV through the BPSU also has PIAG (now NIGB) approval (Ref: PIAG/BPSU 2-10(a/2005).

## Support groups

Barnardo's Sofalli Service (Services organised for families affected by life long illness), 4th Floor, King Edward Building, 205 Corporation Street, Birmingham, B4 6SE.
Web: http://www.barnardos.org.uk/sofah.htm

Positively UK, 347-349 City Road, London, EC1V 1LR. Web: http://www.positivelyuk.org

Body and Soul, 99-119 Rosebery Avenue, London, EC1R 4RE.
Web: http://www.bodyandsoulcharity.org

## Acknowledgements

Catherine Peckham, Hiwot Haile-Selassie, Icina Shakes, Clare French, Claire Townsend, Claire Thorne UCL Institute of Child Health.

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# Progressive Intellectual and Neurological Deterioration in Children (Including Creutzfeldt - Jakob disease)

The PIND Expert Group

## Key points

- Continuing surveillance of UK children with progressive intellectual and neurological deterioration (PIND) is important to ensure that new cases of variant Creutzfeldt-Jakob disease (vCJD) are not being missed among the numerous rare neurodegenerative childhood disorders.
- Since May 1997, 3029 children have been notified; 1270 children have a known diagnosis other than vCJD, with 153 different neurodegenerative disorders in this diagnosed group.
- Six cases of vCJD have been reported to the study since December 1998; four have been classified as “definite” and two “probable”; all have now died.

## Summary

Active prospective surveillance of UK children with progressive intellectual and neurological deterioration (PIND) commenced in May 1997. Funded by the Department of Health (England) [121/6443], it is being carried out via the British Paediatric Surveillance Unit (BPSU) in conjunction with the National Creutzfeldt-Jakob Disease Surveillance Unit in Edinburgh (NCJDSU) and the Health Protection Agency (HPA). The study strategy is to look at a broad group of rare neurodegenerative disorders affecting children, and by carefully examining the clinical details, determine whether there are cases of vCJD amongst these PIND cases. This unique dataset provides the opportunity to detect vCJD cases and highlight the variety of PIND conditions in the UK[2] (Figure 12).

## Objectives

The study aims to:

- carry out active prospective surveillance of UK children with paediatric neurological conditions presenting as progressive intellectual and neurological deterioration (PIND) and to determine the incidence and distribution of these
- classify PIND cases by diagnosis
- investigate the possibility that new cases of vCJD are occurring in children.

## Study duration

Surveillance period: May 1997 - April 2012 (inclusive).
Follow-up: Regularly until case status determined.

## Methodology

Paediatricians reporting a child are contacted by the research nurse/co-ordinator to gather further information about the case by telephone, through a visit to review case notes or by postal questionnaire. An Expert Group, of nine paediatric neurologists, one geneticist and a NCJDSU representative, meets quarterly to review anonymised clinical information and classify cases. If a child with clinical features suggestive of vCJD is identified, the referring paediatrician is told and, if the parents agree, the child is notified to the NCJDSU.

### *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.

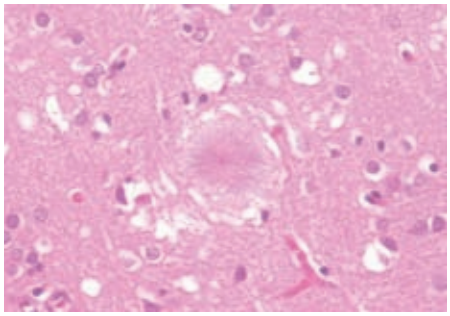

Figure 12: Florid plaque in vCJD x 400 haematoxylin/ eosin stain

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 who have confirmed neuro-degenerative conditions but who have not yet developed symptoms.

## Analysis

By March 2011, 3029 children had been notified (Figure 13); 179 are still "under investigation" by their paediatricians; 1225 did not meet the PIND definition, were duplicate or error notifications and 190 cases remain outstanding.

The remaining cases were classified as follows:

*Definite and probable cases of vCJD:* Six cases of vCJD (four definite and two probable) have been notified - the youngest was a girl aged 12 years at onset. There were three other girls (two aged 14 years and one aged 13 years at age of onset) and two boys aged 15 years at onset. The last child to present developed symptoms in 2000. All have now died and neuropathology has confirmed vCJD in four cases; a post-mortem was not carried out on the remaining two cases.

*Children with PIND who have definite diagnoses other than vCJD:* 153 different neurodegenerative conditions were diagnosed in these 1270 children. The five most commonly occurring diagnostic groups (Figure 14) are the neuronal ceroid lipofuscinoses (n=163), mitochondrial cytopathies (n=150), gangliosidoses (n=115), mucopolysaccharidoses (n=107), and peroxisomal disorders (n=79).

*Children with PIND and no underlying diagnosis (idiopathic group):* The Expert Group meet regularly to discuss this group of 159 children. If a "new" variant of vCJD should arise or if the paediatric presentation differed from the adult presentation, this group could possibly include such a phenotype. However, there is currently no evidence of a "new" unrecognised disorder in this group.

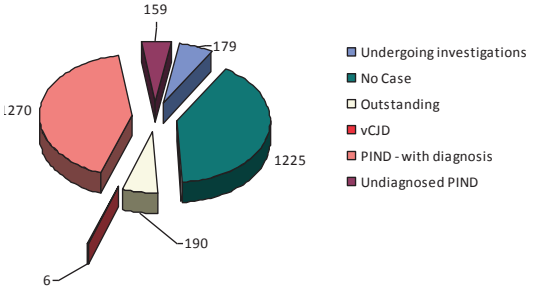


Figure 13: PIND study – current status March 2011

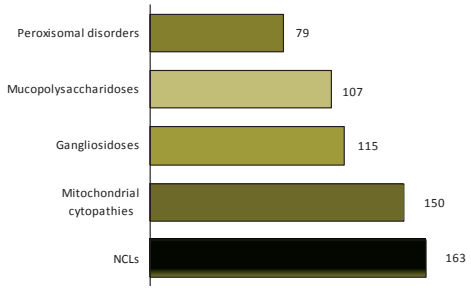


Figure 14: Five most commonly reported PIND diagnostic groups

## Discussion

During almost 14 years of surveillance, six children presenting with vCJD under 16 years of age have been notified to the study, including four with definite vCJD and two with probable vCJD. There remains concern that more childhood cases may appear, perhaps related to underlying genotype[3], and children within the 'idiopathic' PIND group are under regular review. Children are still at risk of vCJD infection by blood, plasma products, surgical and dental instruments and theoretically via vertical transmission. Continued surveillance is essential as there are still many unanswered questions about this relatively new disorder – in particular, the number of children who may be incubating vCJD, the length of the incubation period and the exact nature of transmission.

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

## Funding

Department of Health (Ref: 121-6443).

## Ethics approval

Approved by Cambridgeshire2 REC (Ref: 97/010), Public Health Laboratory Service Ethics Committee and the Patient Information Advisory Group (Ref: PIAG/BPSU 2-10(c) 2005).

## Support groups

Creutzfeldt-Jakob Disease Support Network. www.cjdsupport.net

Batten Disease Family Association. www.bdfa-uk.org.uk

Society for Mucopolysaccharide Diseases. www.mpssociety.co.uk

Climb (Children Living with an Inherited Metabolic Disease). www.climb.org.uk

ALDLife (Adrenoleukodystrophy). www.aldlife.org

## Acknowledgements

We are grateful to all clinicians who are still responding enthusiastically. The PIND surveillance team is very grateful to the members of the paediatric neurology Expert Group; Prof. J. Aicardi, Dr P. Baxter, Prof Y. Crow, Dr. C. de Sousa, Dr J. Livingston, Dr. M. Pike, Prof. R. Robinson, Dr E. Wassmer, Dr J. Wilson and Dr. S. Zuberi.

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# Raised Blood Lead Levels in Children

## Key points

- Of 22 case notifications of children with clinically diagnosed elevated blood lead concentrations, eight have been confirmed as meeting the case definition.
- Parallel reporting from Supra-Regional Assay Service (SAS) Trace Elements Laboratories has started, and will assist in developing sustainable systems for laboratory reporting of elevated blood lead concentrations and other environmental toxins.
- Resources for paediatricians, environmental health and health protection professionals, as well as the public, have been developed to generate awareness and provide guidance about the clinical presentation and management of lead exposure.

## Summary

Public health interventions have succeeded in removing most sources of lead from the environment. However, a small proportion of children continue to be exposed to harmful levels of lead, usually in the home. Exposure to lead in children is associated with a range of adverse health effects, from sub-clinical neurodevelopmental impairment to encephalitis.

Dr Ruth Ruggles

There are no reliable data on the incidence or prevalence of clinically significant lead toxicity or the prevalence of elevated blood lead concentrations in children in the UK. Currently, the UK has no formal monitoring for blood lead concentrations within laboratory or clinical systems and the public health response to such cases is likely to be sub-optimal.

The aim of this study is to estimate the incidence of elevated blood lead concentrations in children. The study will provide important information on the clinical management and public health response.

## Objectives

The aim of the study is to:

- report the incidence of clinically diagnosed blood lead concentrations greater than or equal to 10 micrograms per decilitre (≥ 10µg/dL) in children in the UK and Republic of Ireland, including distribution by sex, age, ethnicity and clinical presentation

- describe the management and short-term outcomes at one year after diagnosis
- report the proportion of cases in which a source of lead exposure was identified and to describe the main sources of exposure to lead
- raise awareness amongst paediatricians about the clinical presentation and management of lead exposure in children, including the involvement of clinical toxicologists, public health and environmental health professionals in contact tracing and exposure remediation.

## Study duration

Surveillance period: June 2010 – June 2012 (inclusive).
Follow-up period: For a twelve month period ending in June 2013.

## Methodology

The study has employed BPSU methodology to obtain case notifications of newly recognised cases of children aged under 16 years with blood lead concentrations ≥10µg/dL from paediatricians. A parallel reporting system, involving Supra-Regional Assay Service (SAS) Trace Elements Laboratories and using the same case definition as for the BPSU reporting, has been established to identify cases that may not be under the care of a paediatrician.

### *Case definition*

Any child under 16 years of age, with a blood lead concentration reported by the laboratory as ≥ 10µg/dL (or 0.48µmol/L), with or without any of the accepted clinical signs and symptoms of lead toxicity.

## Analysis

In the period 1st June 2010 to 31st March 2011, there were 22 case notifications reported via the BPSU, of which eight have been confirmed as meeting the case definition. Other case reports have been excluded from the study because the date of diagnosis is unknown or outside the study period. Questionnaires requesting clinical details have been returned in all except three cases.

SAS Laboratories have reported 24 cases, however, we are still investigating whether these are incident or prevalent cases. Three laboratory notifications have been matched to cases reported by paediatricians (Figure 15).

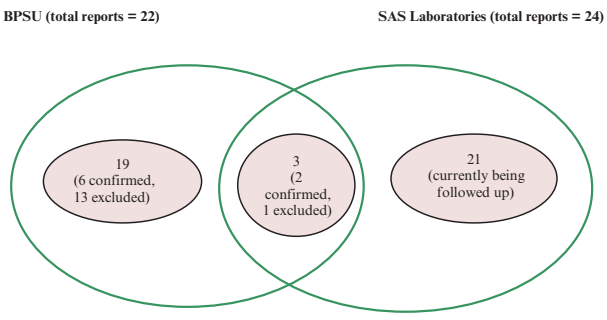


Figure 15: Sources of case ascertainment

## Discussion

Although the number of children reported to the study in the first ten months is lower than expected, it is greater than the number reported through existing surveillance systems which rely on ad hoc reporting to public health agencies, such as the Health Protection Agency (HPA).[1] Importantly, as children are not routinely screened for exposure to lead in the UK and the Republic of Ireland, our estimated incidence is based on children who were selected by a clinician for testing.

The parallel reporting system through SAS laboratories is an important source of additional case ascertainment and we hope to develop this methodology for the routine reporting of environmentally related diseases. Experience in the first year suggested that not all cases of raised blood lead levels in children were being managed by paediatricians or clinical toxicologists and some children appeared to remain under the care of General Practitioners. We are currently applying to the Regional Ethics Committee to allow the inclusion of additional reporting sources, specifically cases reported directly to the HPA and the National Poisons Information Service.

*Awareness-raising with professionals and the public:* A project webpage developed within the HPA website provides an overview of the study as well as resources for those involved in reporting or managing children with elevated blood lead levels.

During the first 10 months of the study, the HPA convened a focus group to establish what concerns parents about lead. This led to the development of 'Frequently Asked Questions' (FAQ) for members of the public. In addition, in response to enquiries received from health professionals, clinical guidance has been prepared as FAQs for paediatricians and health professionals. (www.hpa.org.uk/chemicals/lead)

Training events for health professionals have been organised in England and participants have included Environmental Health Officers and HPA staff working in local and regional teams. Training materials and resources are now available on the HPA website and include case studies, action cards, legislative options and links to remediation guidance.

## Funding

Health Protection Agency.

## Ethics approval

Riverside REC (Ref: 10/H0706/10) and has section 251 NIGB permission under HPA reference (PIAG 03-(c)/2001).

## Acknowledgements

Dr Rachel Knowles and Prof. Alan Emond, BPSU; Dr Ted Sheehan, Supra-Regional Assay Service Trace Elements Laboratories; Dr Sally Bradberry, National Poisons Information Service; Dr Ina Kelly and Dr Farhana Sharif, Health Service Executive; Dr Colin Ramsay, Health Protection Scotland; Dr Anne Wilson, Public Health Agency for Northern Ireland; Mr Huw Brunt, Public Health Wales.

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# Sudden Unexpected Postnatal Collapse

## Key points

- Data collection, including one year follow up, is now complete.
- There were 45 cases of sudden unexpected postnatal collapse reported.
- In over 50% of cases the presumed cause of collapse was accidental suffocation.

## Background

Sudden unexpected collapse of a healthy term infant in the early postnatal period is a rare and devastating scenario in which 50% of infants die and the majority of survivors suffer severe neurological damage. Although well recognised in individual centres, these infants fail to register nationally, a missing group of 'mortality and morbidity' who are currently under-investigated. This was the first national study which aimed to describe the incidence, presenting features, investigation and outcome of such infants.

## Objectives

The aims of this study are to:

- estimate the incidence of sudden early postnatal collapse in apparently healthy term infants
- describe the clinical presentation and associated factors of infants undergoing sudden early postnatal collapse
- describe current management of such infants including investigations
- determine the outcome at discharge and at 1 year of age.

## Study duration

Surveillance period: November 2008 - November 2009 (inclusive).
Follow-up period: For a twelve month period ending in November 2010.

## Methodology

Consultant paediatricians were asked to report all cases of sudden unexpected postnatal collapse every month and provide demographic and clinical data, including outcome at one year of age. Full data about the mother, her birth and the circumstances of collapse were collected.

### *Case definition*

Infants = or > 37 completed weeks of gestation with a 5 minute Apgar score of = or > 8 who have a sudden and unexpected collapse in hospital or 12 hours or less of birthing requiring resuscitation and who either die or go on to require intensive care.

Dr Julie-Clare Becher

**Definitions:**
'Resuscitation'- positive pressure ventilation by bag and mask or endotracheal tube,
'Intensive care'- requiring positive pressure ventilatory support following admission.

**Exclusions:**
1. Infants < 37 weeks
2. Infants with 5 min Apgar score of < 8
3. Infants who collapse outside of hospital
4. Infants who collapse > 12 hours of age
5. Infants who collapse who survive resuscitation but who do not require intensive care.

## Analysis

Forty-five cases of sudden unexpected postnatal collapse (SUPC) were reported, of whom 12 died and 33 infants survived to discharge. Outcome data were available for all infants. There were 22 (49%) male infants. The median gestational age was 40 weeks and the mean birthweight 3328g.

Fifteen infants were determined by pathologist or clinician to have an underlying condition responsible for their deterioration whilst in others no underlying condition was found.

*Characteristics of mother, labour and delivery*
*Infants with an underlying condition:* Ten (67%) mothers were primiparous and all were in good health during pregnancy. Six infants were born by spontaneous vertex delivery, three by instrumental vaginal delivery, and six by caesarean section. In six there was meconium staining of the liquor.

*Infants without an underlying condition:* Twenty-three (77%) mothers were primiparous and all mothers were in good health prior to pregnancy. Paediatric staff were present at over half of these deliveries and in four cases there was meconium-staining of the liquor.

*Circumstances of collapse:* The median age at collapse was shorter in infants with no specific cause for collapse compared to those with an underlying condition. Around 30% of infants were presumed to be feeding at the time of collapse. Two infants died immediately despite resuscitative efforts and 43 infants were subsequently admitted to a neonatal unit.

*Investigations:* Figure 16 shows the range of investigations undertaken to determine the cause of collapse in those infants where an underlying abnormality could not be found. Ten children who died underwent post mortem examination and an underlying diagnosis was found in five (50%).

## Discussion

This study is the first to investigate the population incidence in the United Kingdom of sudden unexpected postnatal collapse (SUPC) in infants who were assessed as being healthy at birth. One third of infants reported to the study had an underlying condition leading to collapse and around 30% of infants were presumed to be feeding at the time of collapse. The finding that the majority of mothers were primiparous (compared to around 50% of all deliveries) is consistent with previous literature.

This study established that few cases underwent systematic investigation. Where death occurs, post mortem was not universal despite the fact that these were sudden and unexpected deaths in hospital. Recently developed national guidelines specific to infants who collapse suddenly in the first week of life should improve diagnostic certainty as well as clarifying prognosis and ongoing management in those who survive (http://www.bapm.org/media/documents/SUPC%20Guidelines%20_2_.pdf).

This study will raise the profile of this group and help to establish guidelines for the optimal early postnatal care of all infants.

Please note these are preliminary data that have not been peer-reviewed and definitive conclusions should not be drawn.

## Funding

WellChild.

## Ethics approval

The London REC (Ref: 08/H0718/47) and has been granted PIAG Section 251 Support (Ref: PIAG 5-06(FT1)/2008).

## Support groups

1. Stillborn and neonatal deaths charity (SANDS) 28 Portland Place, London, W1B 1LY. Sands National Helpline: Tel: 020 7436 5881 Web: http://www.uk-sands.org.
2. Scottish Cot Death Trust. The Scottish Cot Death Trust, Royal Hospital for Sick Children, Yorkhill, Glasgow G3 8SJ. Tel: 0141 357 3946. Web: http://www.sidscotland.org.uk.
3. Foundation for the Study of Infant Death (FSID). 11 Belgrave Road, London SW1V 1RB.Tel (general enquiries): 020 7802 3200. Web: http:// www.fsid.org.uk.

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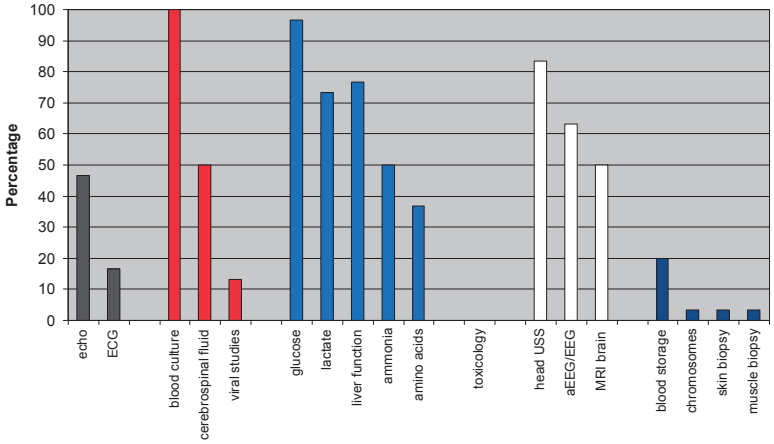


Abbreviations: ECG- electrocardiogram, EEG- electroencephalogram, MRI- magnetic resonance imaging, USS- ultrasound scan

Figure 16: Proportion of infants with no specified cause for collapse undergoing investigation (n=30)

# 5 New Studies 2011

## End-stage Renal Disease in Early Infancy

### Summary

End stage renal disease (ESRD) in early infancy is rare with an incidence quoted of 0.31 per million UK population per year but presents complex clinical and ethical problems. Controversy continues as to how best care for this population with reports of poor outcome and significant morbidity.

There is anecdotal evidence in the UK of increasing numbers of young infants being treated with dialysis but there is no data available on the outcome of ESRD during the first six months of life.

National ascertainment is required to establish a sufficient cohort, to provide accurate data on this rare but important condition.

It is now possible to support infants with ESRD through Renal replacement therapy (RRT). However, this population differs from older children receiving dialysis in terms of their primary renal diagnosis and are more likely to be diagnosed with renal dysplasia or obstructive uropathy and have more co-morbidities which impact upon long term outcome.

The provision of long term dialysis for neonates with ESRD presents major public health issues with complex clinical, ethical and health-care resource issues. Improvements in neonatal survival and advances in RRT have resulted in higher numbers of infants presenting with ESRD for whom a decision has to made to dialyse or treat palliatively, yet the experience of the infant population has not been reported.

### Objectives

The study aims to:

- identify the incidence in infants aged 4 weeks to 6 months (excluding patients with reversible acute renal failure)
- characterise incidence by primary renal pathology, age at presentation, gestational age at birth, sex, ethnic origin and region of birth
- describe the primary renal diagnosis
- record the complications and co-morbidities

Dr Karl McKeever

- characterise management
- describe morbidity and mortality outcomes at age 1 year.

### Study duration

Surveillance period: May 2011 – May 2012 (inclusive).
Follow-up: At 12 months to May 2013.

*Case definition*

Patients from age 4 weeks to 6 months with presumed end stage renal disease who have a serum creatinine of equal to, or greater than 120 micromols/l.

### Ethics approval

Belfast REC (Ref: 10/NIR03/32).

### Funding

The Children's' Renal Fund, Belfast

### Researchers

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# Primary Congenital Hypothyroidism in Children Aged Five Years and Under

Dr Rachel Knowles

## Summary

Primary congenital hypothyroidism (CHT) is a disorder involving reduced thyroxine production by the thyroid gland. This may be due to an abnormally sited or absent thyroid gland or a failure of hormone production within the gland. Babies with CHT may have feeding difficulties, sleepiness, constipation and jaundice. Infants, who do not start treatment with replacement oral thyroxine therapy soon after birth, may have problems with their mental development and growth. Around 200 babies with CHT are born in the UK each year and most are detected by newborn bloodspot (heel-prick) screening. Although newborn screening for CHT started in 1981, we do not know how successful it is in identifying babies who require lifelong therapy.

## Objectives

The study aims to:

- determine the incidence in the UK of confirmed diagnoses of primary CHT in children up to and including age five years and report the distribution by age, sex and ethnic group
- report the clinical features at presentation and describe variations in referral and clinical management including initiation of replacement therapy
- describe clinical outcomes at one and two years post-diagnosis, including the proportion of infants who are recognised to have transient hypothyroidism
- evaluate performance of the newborn screening test for CHT, including estimation of confirmed cases as a proportion of referrals for confirmatory tests following screening results suggestive of CHT and of late diagnoses up to five years of age.

## Study duration

Surveillance period: June 2011 – June 2012 (inclusive).
Follow-up: Until June 2014.

*Case definition*

Any child up to and including five years of age who, during the past month, has been referred **EITHER** for diagnostic confirmation following a newborn screening test result suggestive of primary CHT,

**OR** has been confirmed with a diagnosis of primary CHT (known or considered likely to be present from birth), based on a serum TSH ≥ 10mU/l.

## Ethics approval

Cambridge South REC (Ref: 11/EE/0152) and has been granted Section 251 NIGB support (Ref: ECC 3-04(k)/2011).

## Funding

UK NHS Newborn Screening Programme Centre (Department of Health).

## Researchers

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*Collaborators*
UK NHS Newborn Screening Programme, British Society of Paediatric Endocrinology and Diabetes (BSPED), UK Newborn Screening Laboratory Network (UKNSLN), British Thyroid Foundation (BTF).

# Autoimmune Addison's Disease in Children

Dr Hima Bindu Avatapalle

## Summary

The most common cause of severe adrenal insufficiency in children, now known as Addison's disease, is autoimmune. In this condition the body's own immune system attacks the adrenal glands and destroys them. People suffering from Addison's disease are also at increased risk of other organ-specific autoimmune diseases, e.g. of the thyroid gland.

If untreated the condition is life threatening and unfortunately it is not always spotted early enough. Though it is now more than 150 years since first described, the disease remains under diagnosed, leading to unnecessary morbidity and mortality. Autoimmune Addison's disease in children is an uncommon but potentially lethal condition.

## Objectives

The study aims to identify:

- the incidence in under the age of 16 years
- clinical patterns of presentation
- the variations in the emergency management of children with autoimmune Addison's disease.

## Study duration

Surveillance period: July 2011 – July 2012 (inclusive).

### *Case definition*

A child will be considered to have a diagnosis of autoimmune Addison's disease if the following criteria are met:

Presence of adrenal cortical antibodies at diagnosis or confirmed subsequently

**AND**
One or more of the following signs and symptoms

- Hyperpigmentation
- Poor growth in weight and height
- Electrolyte abnormalities (Hyperkalaemia, hyponaetremia, hypoglycaemia)
- Addisonian crisis

**AND**
Low cortisol levels with high ACTH levels

"Addisonian crisis" or "adrenal crisis" indicates severe adrenal insufficiency.

Characteristic symptoms are:

- Severe vomiting and diarrhea, resulting in dehydration
- Low blood pressure
- Syncope (loss of consciousness)
- Hypoglycemia, severe hyponatremia and hyperkalaemia
- Confusion, psychosis, slurred speech, convulsions

Exclusion Criteria: children on steroid medication for other causes.

## Ethics approval

West London REC 2 (Ref: 11/LO/0581) and ECC Section 251 NIGB support (Ref: ECC 6-02 FT4/ BPSU/2011).

## Funding

Sir Peter Tizard Bursary.

## Researchers

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# 6 International Network of Paediatric Surveillance Units (INoPSU)

Figure 17: International Network of Paediatric Surveillance Units (INoPSU)

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 initiative was also the stimulus for the development in 1992 of an Australian unit and later the Malaysian unit (1994) to be followed by units in Canada (1996), Papua New Guinea (1996), New Zealand and Latvia (1997), Portugal (2001) and Greece/Cyprus (2003). Wales (1994) and Republic of Ireland (1996) developed surveillance units using a similar methodology to the BPSU, but some include more common disorders in their surveillance. Recently a Belgian surveillance system has approached INoPSU to join; this will be considered at our meeting in Switzerland in September 2011. In 2010 a Scottish surveillance unit was established and is currently liaising with the BPSU.

INoPSU missions is to advance of knowledge of rare and uncommon childhood infections and disorders and enable the participation of paediatricians in surveillance on a national and international basis, in order to achieve a series of benefits to clinical practice and health policy.

Over the past 10 years, INoPSU countries have facilitated the surveillance of over 200 different rare conditions, covering a child population of over 50 million and involving over 10,000 clinicians.

Using similar research protocols, the units can provide an efficient, effective framework for case finding across national populations. Comparative papers on haemolytic uraemic syndrome, hyperbilirubinaemia, eating disorders and acute flaccid paralysis are under development.

October 2010 saw INoPSU hold its 6th conference in Dublin, Ireland. Fifteen representatives from eight different INoPSU units were present including: UK, Ireland, Canada, Australia, Netherlands, Switzerland and Portugal, with only representatives from New Zealand, Wales, Greece, Germany and Latvia unable to attend (Figure 17).

The meeting provided an excellent opportunity for representatives from each of the national units to meet and exchange views on rare disease surveillance and discuss issues that currently pose challenges to the units. Funding and the increasingly cumbersome processes for ethical approval of surveillance studies were a particular focus.

Dr Ana Rath of Orphanet (www.orphanet.org) – the EU funded web portal for Rare disease – presented the work of the network and discussions on how INoPSU could collaborative from the paediatric dimension was discussed.

The following day a business meeting was held to discuss recent developments, as well as the future direction of INoPSU.

Details on all the activities of each surveillance unit is available form their respective websites and also from the INoPSU website (www.inopsu.com), where the current annual report can be found.

# APPENDIX A - Completed Studies 1986-2010

By the end of 2010 the BPSU had facilitated surveillance for 81 studies. Information about these are included in previous annual reports of the BPSU, listed on the BPSU website.

Acute flaccid paralysis

Acute rheumatic fever

Adverse neonatal outcomes of delivery or labour in water

Androgen insensitivity syndrome

Biliary atresia

Cerebral oedema and death following diabetic ketoacidosis

Cerebrovascular disease, stroke and like illness

Chemistry set poisoning

Congenital brachial palsy

Congenital cataract

Congenital cytomegalovirus

Congenital dislocation of the hip

Congenital syphilis

Congenital toxoplasmosis

Drowning and near drowning

Early onset eating disorders in children under 13 years

Encephalitis in early childhood (2 months – 3 years)

Fatal/Severe allergic reactions to food ingestion

Feto-maternal alloimmune thrombocytopenia

Galactosaemia

Genital Herpes In Children Under Eleven Years Of Age Presenting To Secondary Care

Group B *Streptococcal* disease

Haemolytic uraemic syndrome I-II

Haemophagocytic lymphohistiocytosis

Haemorrhagic shock encephalopathy syndrome

Hepatitis C virus infection

Higher order births

Inflammatory bowel disease in under 20 year olds

Insulin dependent diabetes in under fifteens

Insulin dependent diabetes in under fives

Internal abdominal injury due to child abuse

Intussusception in children aged less than 12 months

Invasive fungal infections in VLBW infants

Invasive *Haemophilus influenzae* infection

Juvenile dermatomyositis

Kawasaki disease

Langerhans cell histiocytosis

Long term parenteral nutrition

Lowe syndrome

Malaria

Measles, mumps, rubella-meningococcal meningitis

Medium chain acyl-CoA dehydrogenase I-II

Methicillin-Resistant Staphylococcus (MRSA)

Neonatal herpes

Neonatal herpes simplex virus (HSV)

Neonatal meningitis

Neonatal necrotising enterocolitis

Non-accidental poisoning/ Munchausen syndrome by proxy

Pyridoxine dependent seizures

Rett syndrome

Reye's syndrome

Scleroderma

Severe complications of varicella (chickenpox) in hospitalised children

Severe hyperbilirubinaemia

Severe Neonatal Hypernatraemia

Severe visual impairment /Blindness

Subacute sclerosing panencephalitis

Subdural haematoma and effusion

Suspected fatal adverse drug reaction in children

Thrombosis in childhood

Thyrotoxicosis in children

Transient and permanent neonatal diabetes

Tuberculosis

Vitamin K deficiency bleeding I-IV

X-linked anhydrotic ectodermal dysplasia

# APPENDIX B - Publications and Presentations 2010-11

**Clinically recognised elevated blood lead concentrations**

**Presentations**

1. S Saikat, R Kamanyire R. Lead in older residential homes in London: a potential risk to child health and the role of public health. 28th European Conference of the Society for Environmental Geochemistry and Health (SEGH). Edge Hill University, Lancashire. 13th April 2011
2. D Crowley, F Sharif. Lead poisoning in children. INoPSU 6th Scientific Meeting. Dublin, Ireland October 2010

**Congenital Cytomegalovirus**

**Presentations**

3. CL Townsend, CS Peckham, PA Tookey. Surveillance of congenital cytomegalovirus in the UK and Ireland. 15th Annual Meeting of the Royal College of Paediatrics and Child Health, Warwick, UK, April 2011 *Arch Dis Child* 2011;**96**(suppl-1):A46

**Publications**

4. C L Townsend, Catherine S Peckham, Pat A Tookey. Surveillance of congenital cytomegalovirus in the UK and Ireland. *Arch Dis Child* doi: 1136/adc.2010.199901.

**Congenital adrenal hyperplasia**

**Presentations**

5. RL Knowles, J Oerton, JM Khalid, P Hindmarsh, C Kelnar, C Dezateux. Clinical outcome of congenital adrenal hyperplasia (CAH) one year following diagnosis: A UK wide survey. 15th Annual Meeting of the Royal College of Paediatrics and Child Health, Warwick, UK, April 2011 *Arch Dis Child* 2011;**96**(suppl-1): G40
6. RL Knowles, JM Khalid, J Oerton, P Hindmarsh C, Kelnar, C Dezateux. Congenital adrenal hyperplasia. Workshop presentation, NSC Fetal, Maternal and Child Health Subgroup workshop on extended newborn screening, March 2010
7. RL Knowles, JM Khalid, J Oerton, P Hindmarsh C, Kelnar, C Dezateux. Congenital adrenal hyperplasia – the UK view. Workshop presentation, UK Newborn Screening Laboratories Network, March 2010

**CNS – Demyelination**

**Presentations**

8. E Wassmer. Demyelinating disease in childhood. Invited Lecture. 14th Annual Meeting of the Royal College of Paediatrics and Child Health, Warwick, UK, April 2010

**Conversion Disorder**

**Presentations**

9. C Ani, R Reading, R Lynn, V James, S Forlee, E Garralda, Child and Adolescent Psychiatry Surveillance System (CAPSS): Epidemiology of Childhood Conversion Disorder in UK and Ireland 15th Annual Meeting of the Royal College of Paediatrics and Child Health, Warwick, UK, 5th April 2011
10. C Ani, R Reading, R Lynn, V James, S Forlee, Garralda E. Findings from the joint CAPSS / BPSU conversion disorder study. Royal College of Psychiatrists Faculty of Child and Adolescent Psychiatry Annual Meeting 29th September – 1st October 2010, St Catherine's College, Oxford, UK
11. C Ani, R Reading, R Lynn, V James S, Forlee, E Garralda. Epidemiology and clinical features of childhood conversion disorder in United Kingdom and Ireland. World Congress of the International Association for Child and Adolescent Psychiatry and Allied Professions in Beijing June 2-6, 2010

**Congenital Herpes**

**Publication**

12. R Reading, G Hughes, J Hill, G Debelle. Genital Herpes in children under 11 years and investigations for sexual abuse. Arch Dis Child 2011. Online doi 10.1136/adc2010.205971.

**Early onset eating disorders**

**Presentations**

13. R Lynn, D Nicholls, R Viner, S Madden., L Pinhas. Eating disorders in children: are the numbers really increasing? International Network of Paediatric Surveillance Units 6th Conference, Dublin 7th October 2010

**Publications**

14. DE Nicholls, R, Lynn RM Viner. Childhood eating disorders: British national surveillance study. *British Journal of Psychiatry* Apr 1, 2011; **198 (4)** 295-301

**Feto-maternal alloimmune thrombocytopenia**

**Publications**

15. M Knight, M Pierce, D Allen, JJ Kurinczuk, P Spark, DJ Roberts, MF Murphy. The incidence and outcomes of fetomaternal alloimmune thrombocytopenia: a UK national study using three data sources. *Br J Haematol.* 2011 Feb;**152(4)**:460-8

**Guillain Barré syndrome/ Fisher syndrome**

**Presentations**

16. C Verity, AM Winstone. Can the BPSU respond to public health emergencies? Royal College of Paediatrics and Child Health - BPSU 25th Anniversary Symposium. Warwick April 2011
17. C Verity. Is Guillain Barré/Fisher syndrome associated with swine 'flu vaccination in children? Results from a UK-wide epidemiological study Royal College of Paediatrics and Child Health Annual Meeting, Warwick, UK, April 2011; *Arch Dis Child* 2011; **96**(suppl):A5
18. A M Winstone, C Verity. Fast track surveillance for public health emergencies – is it possible? International Network of Paediatric Surveillance Units 6th Conference, Dublin 7th October 2010

**HIV/AIDS**

**Publications**

19. H Haile-Selassie, CL Townsend, PA Tookey. Use of neonatal post-exposure prophylaxis for prevention of mother-to-child transmission of HIV infection in the UK and Ireland, 2001-2008. HIV Medicine 2011; doi:10.1111/j.1468-1293.2010.00902.x
20. CL Townsend, J Schulte C, Thorne, KL Dominguez, PA Tookey, M Cortina-Borja, CS Peckham, B Bohannon, ML Newell, for the Pediatric Spectrum of HIV Disease Consortium, the European Collaborative Study, and the National Study of HIV in Pregnancy and Childhood. Antiretroviral therapy and preterm delivery – a pooled analysis of data from the United States and Europe. *BJOG*. 2010 Oct; **117(11)**:1399-410
21. CL Townsend, PA Tookey, ML Newell, M Cortina-Borja. Antiretroviral therapy in pregnancy: balancing risk of preterm delivery with prevention of mother-to-child HIV transmission. *Antiviral Therapy* 2010; **15(5)**:775-783
22. HIV Paediatric Prognostic Markers Collaborative Study. Discordance between CD4 cell count and CD4 cell percentage: implications for when to start antiretroviral therapy in HIV-1 infected children. *AIDS* 2010; **24(8)**:1213-1217

**Presentations**

23. J Masters, C Peckham, P Tookey. Children born abroad and diagnosed with HIV-infection in the UK/Ireland, 2000-08. Royal College of Paediatrics and Child Health 14th Spring Meeting, Warwick 2010 (oral); *Arch Dis Child* 2010; **95**(suppl):A24
24. C French, C Thorne, M Cortina-Borja, P Tookey. Are sequential pregnancies in HIV-positive women associated with an increased risk of MTCT? (Poster 736) CROI Boston 2011
25. C French, C Thorne, M Cortina-Borja, Tookey PA. Increasing repeat pregnancies among HIV-infected women in the United Kingdom and Ireland (Poster). XVIII International AIDS Conference, Vienna 18-23 July 2010
26. H Haile-Selassie, J Masters, P Tookey. HIV-infected children diagnosed in the UK and Ireland, 2000-2009: country of birth, timing and reason for testing. 2nd International Workshop on HIV Pediatrics, 16-17 July 2010, Vienna (Poster P12), *Rev in Antiviral Therapy & Inf Dis* 2010; **8**:39
27. H Haile-Selassie, A de Ruiter, P Tookey. Duration of ruptured membranes and vertical transmission of HIV: data from national surveillance in the UK and Ireland. BHIVA Manchester 2010 (oral), *HIV Medicine*, 2010; **11**: 1
28. B Williams, J Kenny, P Tookey, C Foster. Pregnancy outcomes in women growing up with HIV acquired perinatally or in early childhood. BHIVA Manchester 2010 (poster), *HIV Medicine*, 2010; **11**:66
29. S Huntington, L Bansi ,C Thorne, P Tookey, C Sabin, on behalf of the UK Collaborative HIV Cohort (CHIC) Study and the National Study of HIV in Pregnancy and Childhood (NSHPC). Use of antiretroviral therapy during and after pregnancy among HIV-infected women already aware of their infection before conceiving. BHIVA Manchester 2010 (poster), HIV Medicine, 2010; **11**:69-70
30. K Doerholt, K Boyd,E Menson, A Riordan, G Tudor-Williams, J Masters, C Peckham, P Tookey, M Sharland, D Gibb. Paediatric HIV projection for the next 5 years – informing service planning and commissioning. Royal College of Paediatrics and Child Health 14th Spring Meeting, Warwick 2010 (oral); *Arch Dis Child* 2010; **95**:A23
31. S Tariq, C Thorne, CLTownsend, T Duong, J Elford, PA Tookey (on behalf of the European Collaborative Study and the National Study of HIV in Pregnancy and Childhood). Pregnancy Outcomes in HIV-infected Women Using Non-Zidovudine HAART in Europe: 2000-2009. (Poster 895) CROI San Francisco 2010

**Intussusception in children less than 12 months of age**

**Presentations**

32. L Samad, HE Bashir, S Marven, JC Cameron, R Lynn, A Sutcliffe, B Taylor. Intussusception In The First Year Of Life: A UK National Surveillance Study. 14th Annual Meeting of the Royal College of Paediatrics and Child Health, Warwick, UK, April 2010. *Arch Dis Child* 2010; **95**(suppl-1): A1–A7

**Lead poisoning in children**

**Presentations**

33. D Crowley, F Sharif. Lead poisoning in children International Network of Paediatric Surveillance Units 6th Conference, Dublin 7th October 2010

**Malaria**

**Publications**

34. S Ladhani, M Garbash, CJ Whitty, PL Chiodini, RJ Aibara, FA Riordan, D Shingadia. Prospective, national clinical and epidemiologic study on imported childhood malaria in the United Kingdom and the Republic of Ireland. *Pediatr Infect Dis J*. 2010 May; **29(5)**:434-8

**Medium chain acyl CoA dehydrogenase deficiency (MCADD)**

**Publications**

35. JM Khalid, J Oerton, G Besley, N Dalton, M Downing, A Green, M Henderson, S Krywawych, V Wiley, B Wilcken, C Dezateux on behalf of the UK Collaborative Study of Newborn Screening for MCADD. Relationship of Octanoylcarnitine Concentrations to Age at Sampling in Unaffected Newborns Screened for Medium-Chain Acyl-CoA Dehydrogenase Deficiency. *Clin Chem.* 2010 Jun;**56(6)**:1015-21

**Presentations**

36. J Oerton, JM Khalid, A Chakrapani, M Champion, M Cleary, M Sharland, J Walter, J Leonard, BS Andresen, C Dezateux. Clinical outcome at 2 years following diagnosis of medium chain acyl Coenzyme A dehydrogenase deficiency through newborn screening: findings from the prospective UK collaborative and British Paediatric Surveillance Unit Studies. Royal College of Paediatrics and Child Health, 14th Annual Meeting, April 2010, Warwick. *Arch Dis Child* 2010; **95**(suppl-1): A1–A7

**Progressive intellectual and neurological deterioration (PIND)**

**Publications**

37. CM Verity, AM Winstone, L Stellitano, D Krishnakumar, R Will, R McFarland. The clinical presentation of mitochondrial diseases in children with progressive intellectual and neurological deterioration: a national, prospective, population-based study. *Dev Med Child Neurol* 2010;**52(5)**: 434–440
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**Presentations**

39. CM Verity, AM Winstone. Can the BPSU respond to public health emergencies? Royal College of Paediatrics and Child Health, BPSU 25TH Anniversary Symposium, Warwick April 2011
40. CM Verity. The leucoencephalopathies of childhood: an evolving national picture. British Paediatric Neurology Association Meeting, Edinburgh. January 2011
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43. AM Winstone, CM Verity, L Stellitano *PIND Research Group,* The clinical presentation and diagnosis of juvenile neuronal ceroid lipofuscinosis: A prospective national study. Royal College of Paediatrics and Child Health Conference 22nd April 2010, Warwick. *Arch Dis Child* 2010; **95** (suppl–1):A8–A13
44. N Smith, AM. Winstone, L Stellitano, T Cox, C Verity Paediatric GM2 Gangliosidosis: the changing characteristics of disease in contemporary U.K. patients, British Paediatric Neurology Association Meeting, January 2010, Edinburgh, Scotland
45. AM Winstone. The clinical presentation and diagnosis of juvenile neuronal ceroid lipofuscinosis: a prospective national study. Royal College of Paediatrics and Child Health, 14th Annual Meeting, April 2010, Warwick, UK
46. N Smith, AM. Winstone, L. Stellitano, T. Cox, C. Verity. Paediatric GM2 Gangliosidosis: the changing characteristics of disease in contemporary U.K. patients. British Paediatric Neurology Association Meeting, Edinburgh. January 2010

**Scleroderma**

**Publications**

47. A Herrick, H Ennis, M Bhushan, A Silman, E Baildam. Incidence of childhood linear scleroderma and systemic sclerosis in the UK and Ireland. *Arthritis Care & Research* 2010; **62(2)**: 213–218

**Sudden unexpected postnatal collapse**

**Presentations**

48. J-C Becher. Sudden Unexpected Postnatal Collapse. Invited lecture. Reason meeting. July 2010, University of Warwick
49. J-C Becher. Early Postnatal Collapse in the Term Newborn. Invited lecture. Royal College of Paediatrics and Child Health 14th Annual Meeting, University of Warwick. April 21st 2010

**Thyrotoxicosis**

**Publications**

50. S Williamson, S A. Greene. Incidence of thyrotoxicosis in childhood: a national population based study in the UK and Ireland. *Clinical Endocrinology*. 2010; **72(3)**: 358- 363

**Toxic Shock Syndrome**

**Presentations**

51. S Adalat, T Dawson, S Hackett, J Clark. Surveillance of Toxic Shock Syndrome in the paediatric population in the UK. 15th Annual Meeting of the Royal College of Paediatrics and Child Health, Warwick, UK, April 2011 *Arch Dis Child* 2011;**96**(suppl-1):A5
52. T Dawson, S Adalat, S Hackett, J Clark. International Network of Paediatric Surveillance Units 6th Conference, Dublin 7th October 2010

**Tuberculosis**

**Presentations**

53. D Shingadia, Paediatric TB across Europe. International Network of Paediatric Surveillance Units 6th Conference, Dublin 7th October 2010

**Vitamin K prophylaxis**

**Presentations**

54. A Busfield1, R Samuel, A McNinch, J Tripp Vitamin K prophylaxis and vitamin k deficiency Bleeding in the UK. Royal College of Paediatrics and Child Health Conference 22nd April 2010 UK. *Arch Dis Child* 2010**; 95(**suppl -1): A65–A73

# With Thanks for 25 Years of Support

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