BPSU

23rd Annual Report 2008-2009

British Paediatric Surveillance Unit
Royal College of Paediatrics and Child Health

Supported by the Department of Health

DH Department of Health

Aims of the British Paediatric Surveillance Unit

To:

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

British Paediatric Surveillance Unit
23rd Annual Report
2008-09

Royal College of Paediatrics and Child Health
Science and Research Department

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Foreword

Prof Allan Colver
Chair, BPSU Executive Committee

Following a concerted effort by the BPSU Executive, I am pleased to report that we were successful last year in obtaining a further three years funding from the Policy Research Programme of the Department of Health (DH). The grant covers a three year period to March 2012 during which we will:

Continue to deliver the core aims of the Unit which are to: facilitate research into uncommon childhood disorders, improve their prevention, treatment and service planning, provide timely epidemiological data in response to public health or policy concerns, enable paediatricians to participate in surveillance, build research capacity, increase awareness amongst health professionals and public of uncommon disorders.

And over the period 2009-12 to:

- improve quality and efficiency of BPSU system
- promote further public involvement, especially of young people
- enhance interchange with Government departments and pilot fast-track procedures for studies of emerging public health and policy concerns
- address inequalities by monitoring ethnic variation
- pilot electronic reporting and longer term follow-up using electronic record linkage.

I have completed three and a half years as chair and decided to step down to allow my successor full engagement in the programme of work funded by the new grant. My successor was appointed in June 2009 and is Professor Allan Emond.

Our internal evaluation went well; it contributed to our DH application, has given us clear areas where we need to improve and develop our processes and has been presented at the College meeting in York. A copy of the full report can be found on our website at www.bpsu.inopsu.com/about/Evaluation_20Full_20Report.pdf. We now move to the second part concerning evaluation of public engagement in the work of BPSU.

Following interest in the BPSU studies on early onset eating disorder and conversion disorder, we were delighted that May this year saw the launch of the Child and Adolescent Psychiatry Surveillance System (CAPSS) after much planning and advice from Richard Lynn. The new Unit is formally recognised and supported by the Royal College of Psychiatrists and is based in their research unit. Richard Lynn and Richard Reading from BPSU are members of its Executive Committee. The Unit's first study is bipolar disorder in children and youth. Information is available at www.rcpsych.ac.uk/capss

One of the pleasures of my position has been to represent the BPSU overseas. Last October I attended the 5th INoPSU conference in Munich, Germany. The meeting coincided with the German Paediatric Society annual scientific meeting and so there were German paediatricians as well as representatives from the national surveillance units. We heard presentations on prevention of paraffin aspiration (Germany); rapid response to flu complications (Australia); 'mad cow' disease (UK); seatbelt injuries, fetal alcohol syndrome (Australia); and cerebral palsy (Portugal). At the business meeting, the future direction of INoPSU was considered. Concern was raised over the apparent lack of EU interest in funding paediatric rare disease surveillance, our grant application once again being rejected. On the positive side there continues to be strengthening of links between national units and their researchers, with more joint presentations at international conferences.

March 2009 saw us hold our 6th scientific conference at the Royal Institute of British Architects. Like many meetings in these difficult economic times, there were fewer delegates than we had hoped but nevertheless ninety attended. All presentations were of high quality and positively evaluated by the delegates. Sheila Shribman, in the key note address, introduced us to the key elements of the Children's Plan "Healthy lives, brighter futures". Other presentations were on MRSA, HIV, herpes, emerging infections, varicella, neonatal hyperbilirubinaemia, vitamin K prophylaxis, feto-maternal alloimmune thrombocytopenia, and early onset eating disorders. Abstracts and the slide presentations are available from the BPSU office (bpsu@rcpch.ac.uk).

As always Richard Lynn our scientific coordinator has been the driving force behind the BPSU and I would like to thank him once again for all the help he has given me. Also Helen Friend, research facilitator, has been very helpful to me. Helen is now very familiar with BPSU processes; and undertook and reported the aspect of our internal evaluation concerning the survey of a sample of paediatricians and the survey of paediatric investigators.

It has been a privilege to have been on the BPSU Executive Committee for five years and then its chair for three. I would like to thank members of the Executive Committee for all the work they do; and to thank all paediatricians for your continuing commitment to this most important enterprise.

Allan Colver

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 the BPSU; the Royal College of Paediatrics and Child Health (RCPCH); the Health Protection Agency (HPA); the University College London-Institute of Child Health. Health Protection Scotland (HPS) and the Faculty of Paediatrics of the Royal College of Physicians (Ireland) also collaborate and support BPSU work. As the BPSU monitors conditions of public health importance, an observer from the Department of Health attends the BPSU's Executive Committee, which meets every eight weeks to consider individual applications and the progress of studies.

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

This report mainly focuses on activities undertaken during the year 2008.

2 Main findings of studies undertaken in 2008

September 2008 saw the commencement of s study looking into **anaphylaxis following immunisation.** In the seven months to March 2009 we have received nine reports of which four have been confirmed, one has been reported as error and four for which we await data. The number of cases reported is less than expected extending surveillance for a further year is currently under consideration.

Principal investigator: Dr M Erlewyn-Lajeunesse – Southampton University Hospital.

Congenital adrenal hyperplasia (CAH) surveillance commenced in August 2007 and is due to end in August 2009. In the first 18 months 214 notifications have been received from which 93 children have been confirmed with CAH suggesting a birth prevalence of 1 per 17,000 live births, with boys and girls equally affected. The majority of children present clinically in the first month of life with adrenal insufficiency or crisis, or virilisation of female genitalia. CAH mortality appears low, consistent with recent estimates from other countries, however deaths may be under-ascertained if based on BPSU methodology alone.

Principal investigators: Dr R Knowles, Dr J Oerton, Ms Javaria Khalid – ICH London.

Surveillance for **congenital rubella** (page 11) has been underway in the UK continuously since 1971. 17 infants have been reported from the British Isles in the last 10 years, and ten of their mothers caught rubella abroad. In almost all recent cases, maternal rubella infection was not diagnosed in pregnancy, and the diagnosis of congenital rubella infection in the newborn baby was unexpected.

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

The surveillance of **conversion disorder** is the first BPSU study undertaken in conjunction with all consultant child and adolescent psychiatrists. The first study of its kind undertaken in Europe aims to estimate incidence; describe presentation, management and outcome. During the first five months 181 cases have been reported 88 by paediatricians and 93 by psychiatrists. Confirmation of reports will be reported once the questionnaires have been returned.

Principal investigators: Dr C Ani, Professor E Garralda, Imperial College, London.

Undertaken in collaboration with the UK obstetric surveillance system a study on **feto-maternal alloimmune thrombocytopenia** (FMAIT**)** (page 16) commenced in October 2006. Data suggest that the incidence of clinically detected FMAIT is less than one third of that estimated from prospective screening studies. The information collected will be used to help reassess the case for antenatal screening.

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

Surveillance of **genital herpes in children under 11 years of age (**Page 19**)** commenced in April 2007. The study was extended to a second year to allow further case ascertainment which will permit meaningful analysis. By February 2009 just 19 cases had been confirmed. The rarity of the condition and potential implications mean that all suspected cases should be investigated with virological tests.

Principal investigator: Dr R Reading – Norfolk and Norwich University Hospital.

The BPSU survey of **HIV infection in children** (page 21) is the cornerstone of paediatric HIV surveillance in the UK and Ireland. Findings from this study have had a substantial impact on current UK antenatal screening policy and clinical practice. Less than half of all new reports now come from the London area, and cases are being notified from all parts of the country. Reported births to HIV infected women have increased substantially year on year since 2000 but the proportion of infants who are actually infected has declined, thanks to greatly improved antenatal detection rates and high uptake of interventions to prevent transmission. Nevertheless, infected infants born to both diagnosed and undiagnosed women in the UK and Ireland are still being reported. Finally, the proportion of newly reported infected children who were born abroad has increased in recent years; these children tend to be older at diagnosis than those born in the UK and Ireland.

Principal investigators: Dr P Tookey, Dr Cortina-Borja – ICH London.

The third Sir Peter Tizard bursary study, on **idiopathic intracranial hypertension** (IIH) (page 25), commenced in July 2007**.** In the first 18 months 269 cases were reported of which 88 probable or confirmed. The low number of newly diagnosed cases suggests that IIH in children might be rarer than previously estimated. It is for this reason that an extension to the surveillance period was granted.

Principal investigator: Dr Y-Y Mathews – Wrexham Maelor Hospital.

For the first time members of the British Association of Paediatric Surgeons are reporting on a monthly basis for a project on **Intussusception** (IS) (page 28) in children aged less than 12 months. Surveillance commenced in March 2008 for a 13 month period with the aim of describing the epidemiology of the condition. The study findings should inform on rotavirus vaccine policy by providing pre-exposure data on IS, which can be used to evaluate any changes in incidence following vaccine introduction.

Principal investigator: Professor B Taylor, Dr H El-Bashir, Dr L Samad, Mr R Lynn, Mr S Marven, Dr C Cameron – ICH London, Sheffield Children's Hospital, HPS.

Surveillance of **medium chain acyl CoA dehydrogenase deficiency** (MCADD) (page 30) commenced in June 2004 and ended in June 2008. The study has shown that newborn screening reliably identifies affected children before they are likely to develop symptoms, enabling parents to use simple measures to avoid fasting and thereby reduce the chances of severe illness or death.

The Department of Health announced a ministerial decision to introduce universal screening for MCADD in England by April 2009 (Gateway number 7801). This has now been fully implemented.

Principal investigators: Professor C Dezateux, Ms J Oerton, Ms J Khalid – ICH London.

Despite the complexity of the conditions involved the survey of **progressive intellectual and neurological deterioration in children** (PIND) (page 33) has proved successful. A primary objective of the study is to identify new cases of variant Creutzfeldt-Jakob disease (vCJD) in UK children. Over 2600 cases of suspected PIND have been reported. Among them 1095 cases have confirmed diagnoses, comprising 120 known neuro-degenerative conditions. Six cases of vCJD have been identified, but none since 2000; all have now died. Active surveillance will continue to at least 2010.

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

Sudden unexpected collapse (page 36) of a healthy term infant in the early postnatal period is rare but 50% of infants die and the majority of survivors suffer severe neurological damage. Surveillance commenced in November 2008 and in the first three months 24 reports have been received. It is hoped that the findings will help to establish guidelines for the optimal early postnatal care of all infants.

Principal investigators: Dr J-C Becher, Dr A Lyon, Dr S Bhushan – Royal Infirmary of Edinburgh.

The fourth Sir Peter Tizard funded bursary, on **Toxic shock syndrome** (page 38)**,** commenced in November 2008. This is the first BPSU study to also use case ascertainment from the national burns units. In the first three months there have been 24 reports of which 13 have so far been confirmed. Interestingly burns cases do not constitute a significant proportion of cases, in contradiction to previous published reports.

Principal investigators: Dr S Adalat, Dr T Dawson – Evelina Children's Hospital, London and Russell's Hall Hospital, West Midlands.

October 2008 saw the completion of the fourth BPSU survey of **vitamin K deficiency bleeding (**page 41**).** The reason for repeating this study is that since the withdrawal of Konakion Neonatal, the only product now licensed for intramuscular (IM) prophylaxis is Konakion MM. Published data about the long-term protection conferred by a single IM dose of this preparation, which has a completely different formulation from Konakion Neonatal, is very limited. This study will look for any change in incidence; assess the effectiveness of prophylactic regimens in use, particularly Konakion MM 1mg IM as a single dose at birth, to examine treatment and outcome. Over the period of this survey 46 cases have been reported.

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

3 Surveillance Studies Undertaken in 2008

Anaphylaxis following immunisation

Key points

- Anaphylaxis following immunisation is rare but has far reaching consequences for public confidence in vaccine safety.
- Surveillance commenced in September 2008 for 13 months.
- To date seven cases have been reported.
- For the first time BPSU data collection is being undertaken through a secure on-line website interface.

Background

Anaphylaxis following immunisation (AEFI) is a potentially life threatening adverse event. It is estimated incidence is one in every million doses of vaccine. All primary immunisers should be able to recognise and treat anaphylaxis and are asked to maintain training and facilities in order to do so. Despite this investment in training by front line staff, very little is known about this rare condition. Although rare adverse events following immunisation are difficult to study, improved knowledge about AEFI will be important for vaccine safety and public confidence.

Previous studies have been performed but interpretation has been hampered by retrospective data collection and differences in case definitions between studies have made comparisons problematic. This study uses the international consensus case definition created by the Brighton Collaboration in order to ensure that the results of this study can be compared to other similar studies of AEFI rates across the world.

Objectives

Specific aims of the project are to:

- define the incidence of anaphylaxis as an AEFI and the vaccines implicated in its onset
- estimate the level of under reporting of anaphylaxis as an AEFI by the 'yellow card' passive reporting system by prospective active surveillance through the BPSU

Dr Mich Erlewyn-Lajeunesse,

- describe the clinical presentation and, in particular, the clinical pathway taken by children experiencing a reaction and the time from immunisation to the onset of symptoms. The clinical management of cases including the initial resuscitation, requirement for adrenaline, use of serum mast cell tryptase as a marker for anaphylaxis, admission to hospital
- provide further validation of the Brighton Collaboration case definition for anaphylaxis as an AEFI in the context of a prospective reporting scheme
- contribute national incidence data to a multinational prospective study of anaphylaxis as an AEFI.

Study duration

Surveillance period: September 2008 – September 2009 (inclusive).

Methodology

We will use prospective data from BPSU reporters to obtain clinical data on the presentation and management of this rare adverse event.

For the first time a BPSU facilitated study will collect clinical data using a secure on-line web based interface. This is being facilitated through Bristol University.

Case definition

Any child under 16 years old who in the opinion of the notifying paediatrician may have experienced anaphylaxis following the administration of an immunisation.

Paediatricians are being asked to report cases where the diagnosis of anaphylaxis is only suspected but where it is felt that further doses of vaccine are contraindicated. Cases where the child received an immunisation in the 48 hours prior to the onset of anaphylaxis where no other precipitant has been identified are also being sought. We will consider cases that occur after this cut off where there is a strong clinical suspicion that a vaccine was implicated in the reaction. The BPSU surveillance **does not** replace other forms of adverse event reporting such as the MHRA yellow card scheme.

Additional sources of data

The study will also attempt to collect data from other data sources such as the MHRA yellow card system during the study period.

Analysis

In the seven months to March 2009 we have received nine reports of which four have been confirmed, one has been reported in error and four for which we await data. Further information will be presented once data analysis commences.

The number of cases reported is less than expected and an extension of surveillance for a further year is currently under consideration.

Discussion

The number of reports received has been slightly lower than expected; currently we do not know if this is because the condition is rarer than first thought. A clearer picture will emerge once we have compared the data collected through the BPSU with other sources.

A study of anaphylaxis is currently recruiting through the Swiss Paediatric Surveillance Unit (PSU) and we hope the German PSU will approve a similar study in the near future. The application of the Brighton definition will ensure that the results of this study can be compared with these units and any other similar studies that may be taking place across the world.

This study introduces the BPSU to on-line data collection; this method will be discussed fully at the completion of the survey. So far, however, receipt of data from the online questionnaire has been slower than expected and paper questionnaires were requested in two cases.

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

Funding

Sanofi Pasteur MSD.

Ethics approval

This study has been approved by the North Somerset and South Bristol NRES (Ref: 07/H0106/119) and has been granted PIAG Section 60 Support (Ref: PIAG/BPSU 3-05(FT1)/2008).

References

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Congenital Adrenal Hyperplasia

Dr Rachel Knowles

Key points

- Congenital Adrenal Hyperplasia (CAH) is due to recessively inherited enzyme deficiencies in cortisol production; children may present at any age with a life-threatening adrenal or salt wasting crisis, incorrect sex assignment, hypertension, short stature or precocious puberty.
- Preliminary results from the first 18 months of surveillance, suggest a birth prevalence of 1 per 17,000 live births, with boys and girls equally affected.
- The majority of children present clinically in the first month of life with adrenal insufficiency or crisis, or virilisation of the female genitalia.
- CAH mortality appears low, consistent with recent estimates from other countries, however deaths may be under-ascertained if based on BPSU methodology alone.

Background

Congenital adrenal hyperplasia (CAH) is a recessively inherited deficiency of cortisol production with an estimated birth prevalence of 1 in 10,000 to 20,000. Just over half of those affected have a salt wasting form which can present in newborns with an acute life threatening adrenal crisis.[1] Excess androgen production can result in girls being incorrectly assigned as boys at birth or, in boys, accelerated growth and virilisation during the early years of childhood. Early detection by newborn screening combined with cortisol and mineralocorticoid replacement can prevent life-threatening episodes, and ensure normal growth and sexual development. Newborn screening for CAH is undertaken in most US states and many European countries, but has not been introduced in the UK[2] reflecting inconsistent information about disease burden. It is now timely to obtain better epidemiological data on CAH in the UK. The BPSU study of CAH will estimate incidence and short term outcome to inform future UK newborn screening policy.

The BPSU study of CAH was extended in August 2008 to undertake a further 12 months of surveillance, thus will remain on the orange card until August 2009, with one-year follow-up continuing until August 2010.

Objectives

The objectives of this study are to:

- determine the incidence of clinically presenting CAH in children under the age of 16 years in the UK (excluding Northern Ireland), and to report its distribution by age, sex and ethnic group
- report the clinical features at presentation
- report the proportion of cases who become clinically unwell by 5-8 days of life
- report early clinical management and morbidity and mortality to one year post diagnosis, including the proportion of girls with initially incorrect sex or sex reassignment.

Study duration

Surveillance period: August 2007 - August 2009 (inclusive).
Follow-up: One year outcome follow-up data sought to August 2010.

Methodology

Reporting paediatricians are asked to complete an initial case notification questionnaire and a further follow-up questionnaire after 12 months.

Case definition

A child will be considered to have a diagnosis of CAH:

IF AT LEAST ONE of the following clinical features is found:

- Adrenal crisis or adrenal insufficiency
- Virilisation of female genitalia
- Precocious puberty
- Accelerated skeletal age
- Short stature
- Hypertension
- Incomplete masculinisation of male genitalia
- Positive family history in first degree relative

AND AT LEAST ONE of the following criteria are met:

- Elevated 17 OHP in blood test
- Positive synacthen stimulation test
- Test result diagnostic of rarer form of CAH, e.g. 3β-hydroxysteroid dehydrogenase (3β-HSD) deficiency or 11β-hydroxylase (11β-OH) deficiency

The diagnosis of CAH may be made following clinical presentation, investigation of a sudden unexpected death, or diagnosis in a sibling or other affected family member.

All notifications are reviewed by an expert diagnostic review panel.

Additional sources of data

A Biochemical Surveillance System for CAH (BioCAHSS) with direct reporting of cases to the study investigators was established with 15 UK laboratories that provide diagnostic testing for CAH using 17-hydroxyprogesterone. During the period from 1st August 2007 until 31st January 2008, participating laboratories retrospectively reported new cases to the investigators. Between 1st February 2008 and 31st January 2009, laboratories received the BioCAHSS monthly reporting card and prospectively reported new cases.

Analysis

BPSU case notifications: During the first 18 completed months of surveillance, there were 214 case notifications received through the BPSU; 33 were duplicate notifications and 23 were excluded as the diagnosis was made before August 2007 or in error. We are awaiting further information for 51 notifications. After review of 107 potential cases by the expert Diagnostic Review Panel, 93 cases were confirmed as CAH, three cases were not CAH and seven cases were 'not yet determined' pending further details.

The 93 confirmed cases were of the following subtypes: 21-hydroxylase deficiency (n=86), 11α-hydroxylase deficiency (n=5), 3β-hydroxysteroid dehydrogenase deficiency (n=1) and lipoid hyperplasia (n=1).

There were 42 boys and 51 girls, thus boys were not significantly under-represented and comprised 45% of the study population (95% confidence interval [CI] 35 to 58). Using UK Census ethnic classifications, 26/93 (28%) of cases were Asian compared with 7% of England's child population.[3] (Figure 1).

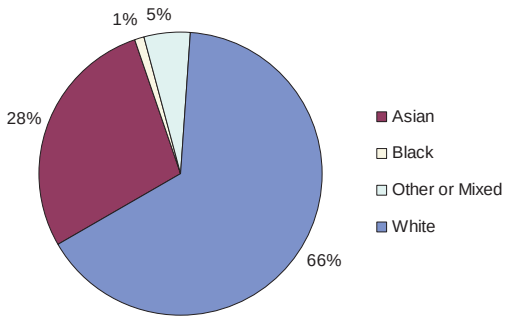

Figure 1: Ethnicity of children with CAH (interim results from 18 months of surveillance)

Adrenal insufficiency or crisis was reported in 32 children, and virilisation of the genitalia was present in 22 (43%) girls.

The majority [51/93 (55%; 25 boys)] of children with CAH presented in the first year of life (Figure 2).

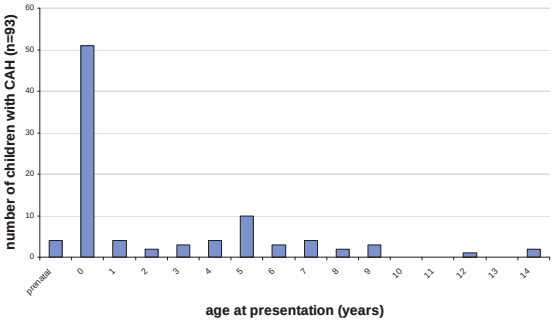

Figure 2: Children with CAH by age (years) at clinical presentation (interim results from 18 months of surveillance)

and the estimated birth prevalence was 5.9 (95% CI 4.3 – 7.9) per 100,000 live births (excluding those diagnosed prenatally [n=4]). 45 (88%; 22 boys) children diagnosed in the first year of life had presented by 30 days, with a further six presenting between one month and one year. There was one death, occuring in a child less than two months of age, however this appears unrelated to CAH.

One year outcome data are not yet available.

BioCAHSS Laboratory Reporting Scheme: Thus far 46 cases have been notified through the BioCAHSS laboratory reporting scheme, of which 33 (72%) have been matched to cases reported through the BPSU.

Discussion

CAH is of similar birth prevalence to other conditions for which newborn screening is

currently offered. Our findings suggest boys and girls are equally affected but that boys present with more severe manifestations in infancy. While CAH mortality is consistent with recent estimates from other countries, deaths may be under-ascertained if based on BPSU methodology alone.

Please note that the data presented here are provisional, not peer reviewed and limited to the first 18 months of surveillance.

Funding

The Department of Health.

Ethics approval

This study has been approved by the Thames Valley MREC (Ref: 07/MRE12/25) and has been granted PIAG Section 60 Support (Ref: PIAG/BPSU 1-05(FT4)/2007).

Support groups

CLIMB-CAH UK Support group is a sub-group of Climb (Children Living with Inherited Metabolic Disorders). Tel: 0800 652 3181.

CAH Support Group, 2 Windrush Close, Flitwick, Bedfordshire, MK45 1PX.
CAH support helpline: Tel: 01525 717536.
Web: http://www.livingwithcah.com (previous web address http://www.cah.org.uk also links into this site).

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Congenital Rubella

Key points

- Congenital rubella continues to be extremely rare in the UK and Ireland, with two confirmed births in 2008.
- Among the 17 infants with congenital rubella born and reported in the UK or Ireland since 1997, ten had mothers who acquired their infection abroad.
- In most recent cases, maternal rubella infection was not diagnosed in pregnancy, and the diagnosis of congenital rubella infection in the newborn baby was unexpected.

Background

The National Congenital Rubella Surveillance Programme (NCRSP) was established in 1971 to monitor congenital rubella births in England, Scotland and Wales. Active surveillance through the BPSU started in 1990, and since then reports have also been received from Ireland and Northern Ireland. Diagnosed rubella infection in pregnancy is monitored through laboratory reports to the Health Protection Agency (HPA) or Health Protection Scotland (HPS), and has remained at low levels in recent years (<10 a year). Women with diagnosed first trimester infection usually opt for termination of pregnancy in the UK; most mothers of congenitally infected infants are unaware of their infection until their baby is diagnosed.

The World Health Organisation Regional Office for Europe set a target for 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 UK and Ireland.[1] Nevertheless, sub-optimal MMR (Measles, Mumps, Rubella vaccine) coverage, and migration within Europe present major challenges to reaching this target, and maintaining control in the long term. As a result of over 10 years of inadequate vaccine uptake with little or no wild virus circulating, there are substantial pockets of susceptible children in parts of the UK and Ireland. In addition, inward migration from countries without long-standing high uptake rubella vaccination programmes has lead to greater concentrations of susceptible individuals in some areas, often the very places where MMR uptake has been low (e.g. parts of London). Under these circumstances it is possible that rubella could once again start to circulate in the British Isles, as it still does in many parts of the world.

Dr Pat Tookey

Comprehensive national surveillance through the BPSU therefore remains extremely valuable. Timely reporting by paediatricians will help us to recognise any resurgence in numbers at an early stage, and assist in the implementation of appropriate control measures. Congenitally infected infants can excrete rubella virus for an extended period of time, and they must be diagnosed and managed appropriately to avoid the risk of contributing to further community transmission.

Objectives

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

Study duration

Surveillance period: 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 (Figure 3) with or without defects, based on history, clinical, and/or laboratory findings. This includes “imported cases”, i.e. children born in the British Isles where the maternal infection occurred abroad, AND children who were born abroad, as well as British-born infants whose mothers acquired infection in the British Isles.

CDC-Public Health Image Library

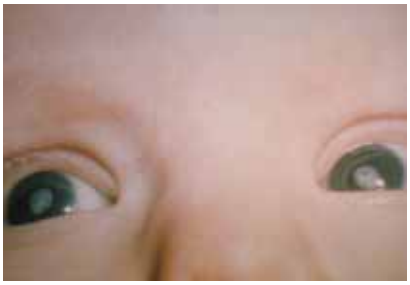

Figure 3: Cataracts due to congenital rubella syndrome

Additional sources of data

The BPSU system is the mainstay of congenital rubella reporting, but about a quarter of reports are made direct to the NCRSP, and there is close liaison with the HPA, HPS and the Health Protection Surveillance Centre in Ireland.

Analysis

There were only two reports to the BPSU in 2008. One was a duplicate report of the infant with congenital rubella born and reported in 2007; the other concerned an infant with congenital rubella who was born abroad, but diagnosed in the UK.

Two infants born late in 2008 with confirmed congenital rubella have been reported directly to the NCRSP; both mothers are believed to have acquired infection in the UK.

The number of reported congenital rubella births and rubella associated terminations declined from, on average, 50 births and 740 terminations a year in 1971-75 to 22 births and 54 terminations a year in 1986-90. Since the beginning of active surveillance in 1990, 167 reports have been made through the BPSU (Table 1). Of the 145 reports from England, Scotland and Wales, 51 are confirmed or compatible, previously unreported cases of congenital rubella, four are possible cases, and 13 had already been reported from another source; the remaining reports were: duplicates (26), reporting errors (46), and five where further information could not be obtained. Sixteen reports were from Northern Ireland or Ireland, and included four children with confirmed congenital rubella (one born in 1989, two in 1996 and one in 2004), and a fifth possible case (born in 1983); the other eleven Irish reports were duplicates, errors or previously reported.

Since the reporting definition was extended in 2005, six reports have related to five 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 five children are not included in Table 2 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 1990-2008: Sixty-one children and three stillborn infants with confirmed or compatible congenital rubella have been born and reported since the beginning of active surveillance in 1990; 47 of these (73%) were first reported through the BPSU (Table 2). Seventeen of these infants were born in the last 10 years, including one born in Ireland, and one stillborn infant. Seven of their mothers acquired infection in the UK (two British-born women and five women who were born abroad). The other ten infants were born to women who acquired abroad (five in Southern or South Eastern Asia, five in Africa).

There were at least 80 terminations for rubella disease or contact in pregnancy 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 has remained at a very low level since the last upswing in 1996, 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

Table 1: Congenital rubella reports to BPSU 1990-2008 (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	51	4	13	77	145
NI and Ireland	4	1	2	9	16
Born abroad (reports 2005-2008 only)	3	2	0	1	6

Table 2: Confirmed and compatible congenital rubella births repoted in the UK and Ireland 1990-2008

	Primary source of notification		
Year of birth	BPSU	Other	Total
1990-94*^	22	10	32
1995-99	12	4	16
2000-04*	10	1	11
2005-08	3	2	5
Total	**47**	**17**	**64**

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

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, and the management guidelines[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.

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

Funding

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

Ethics approval

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

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Acknowledgements

We are extremely grateful to all participating paediatricians, especially those who have notified cases and completed questionnaires.

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Conversion Disorder in Childhood

Dr Corenlius Ani

Key points

- Conversion disorder is an uncommon but highly disabling condition and affected children may experience paralysis, blindness, deafness or other sensory losses without any identifiable physical cause.
- Affected children are at risk of serious long-term physical, educational and psychosocial complications and the condition can be associated with extensive use of health resources.
- This is the first study of the incidence of conversion disorder in childhood in Europe.
- The study is being undertaken as a joint surveillance study involving BPSU and the Child and Adolescent Psychiatry Surveillance System (CAPSS).

Background

Conversion Disorder is an uncommon but highly disabling condition in childhood. Affected children may experience paralysis, blindness, deafness or other sensory losses without any medical explanation. 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 therefore conducting the first study to describe the frequency, pattern and short-term outcomes of Conversion Disorder in children in United Kingdom and Ireland. The study involves joint surveillance by the BPSU, involving paediatricians, and Child and Adolescent Psychiatry Surveillance System (CAPSS), involving child and adolescent psychiatrists. Findings from this study could help to inform health service planning for children with this rare but serious 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 outcome.

Study duration

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

Methodology

The study design is based on an active surveillance methodology. As cases may present to both paediatricians and child and adolescent psychiatrists, we are conducting a dual surveillance, involving BPSU and CAPSS, in order to capture the full spectrum of cases. Reporting by more than one clinician is being encouraged to maximise case ascertainment.

An initial questionnaire is sent to all clinicians reporting cases to gather both demographic and clinical information. A panel of experts are reviewing all reported cases to confirm whether or not they meet the case definition. For all confirmed cases, a second questionnaire will be sent to the reporting clinician a year after the case was first reported. This follow-up questionnaire will collect information on the treatment received by the child, the duration of the disorder and the outcome after one year.

Case definition

Any child younger than 16 years newly diagnosed with Conversion Disorder during the previous month in the UK 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 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 seven days or longer, **and**
- are accompanied by psychological factors that are judged to be associated with or have contributed to the presentation.

EXCLUSION CRITERIA
Certain cases are excluded, as follows:

- Cases where the clinical picture is predominantly or exclusively pain or fatigue, and/ or
- Cases where the dominant picture is another psychiatric disorder, such as depression or psychosis diagnosed by a child and adolescent psychiatrist, or tic disorder.

Additional sources of data

Additional cases are being ascertained from Child and Adolescent Psychiatrists through CAPSS.

Analysis

During the first five months of surveillance we have received 181 case reports; 88 by paediatricians and 93 by psychiatrists. Of these, 16 are confirmed cases, 26 have been reported in error and for 139 we await data for further clarification. Further information will be presented once data analysis commences.

Discussion

The numbers of case reports received are higher than expected, however many of the early reports were not newly diagnosed cases and were therefore excluded. Active surveillance of psychiatric conditions is a relatively new activity for psychiatrists and it has been necessary to continuously monitor the CAPSS mailing list during the surveillance period. There is evidence of improved reporting by participating psychiatrists over time and the response rate is now 60% per month and rising. However, it may be necessary to extend the study for some months in order to ensure that a 12 month period of adequate case ascertainment is achieved.

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

Funding

We are grateful to the BUPA Foundation for funding this study.

Ethics approval

This study has been approved by the 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.

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Feto-maternal Alloimmune Thrombocytopenia (FMAIT)

Dr Marian Knight

Key points

- Fetomaternal Alloimmune Thrombocytopenia (FMAIT) is the most common cause of severe neonatal thrombocytopenia in otherwise well term infants, and results from a fetomaternal incompatibility in platelet alloantigen that can lead to serious bleeding, intracranial haemorrhage and sometimes death of the unborn child.

- FMAIT is associated with significant fetal and infant morbidity and mortality; first pregnancies are often severely affected and the diagnosis is usually made with the birth of a first affected infant.

- Parallel descriptive studies using the UK Obstetric Surveillance System (UKOSS) and the National Blood Service database, as well as the BPSU, suggest that the incidence of clinically detected FMAIT is less than one third of that estimated from prospective screening studies.

- There is currently a debate about the utility of antenatal screening for the condition and this study will inform ongoing review of the case for antenatal screening

Background

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

Additionally, there are considerable controversies in the optimal management of FMAIT-affected pregnancies.[3] There is no clear approach to the antenatal management of first affected pregnancies, and several questions remain in the approaches to managing second and subsequent affected pregnancies. This is the first study to be

conducted simultaneously through the BPSU and the UK Obstetric Surveillance System (UKOSS). The combined use of both obstetric and paediatric reporting systems will help to ensure identification of cases is as complete as possible and will allow collection of comprehensive antenatal and postnatal information. We will also be able to assess the outcomes following different antenatal management strategies. The study results will be used to inform ongoing review of the case for antenatal screening for this condition.

Objectives

The study aims are to:

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

Study duration

Surveillance period: October 2006 – September 2008 (inclusive).
Follow-up: One year outcome follow-up data sought to September 2009.

Methodology

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

Case definition

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

i Cord platelet count at birth <50 x 10^9/l

ii Haemorrhagic complications before or after birth (e.g. intraventricular haemorrhage, gastrointestinal bleed, bruising or petechiae)

iii Antenatal therapy with maternal steroids, intravenous immunoglobulin or fetal platelet transfusion.

Additional sources of data

Cases were also sought in a parallel study conducted through UKOSS. In addition, cases reported through the surveillance studies were compared with cases referred for investigation to the NBS or Welsh Blood Service (WBS).

Analysis

There were 174 cases reported through the three reporting systems over the period October 2006 to September 2008 in an estimated 1.5 million births. Capture-recapture analysis suggests a possible additional six cases not notified, giving an adjusted incidence of 1.2 cases per 10,000 births (95% CI 1.0-1.4). Reporting overlap (England and part Wales only) is illustrated in Figure 4.

We are currently still collecting clinical information about the cases identified through the NBS laboratories and data collection should be complete by the end of May 2009.

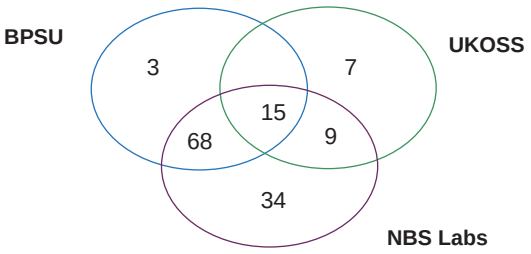

Figure 4: Reporting overlap for areas where information can be obtained from all three sources (England and part Wales). 37% of cases diagnosed antenatally, 63% postnatally.

We have received further information on 135 confirmed cases. Forty-three women (32%) were diagnosed antenatally; 33 (77%) of these women had previous affected pregnancies. Forty-five percent of women were delivered by caesarean section; 85% of antenatal cases and 29% of postnatal cases. There are 136 infants with known outcomes. For infants in whom the diagnosis was made antenatally, the median platelet count at birth was 129x10^9/L. In those diagnosed postnatally, the median platelet count at birth was 17x10^9/L. Sixty-two percent required a platelet transfusion at birth.

There were two intrauterine deaths, one infant death and nineteen infants had an intracranial haemorrhage. Twenty of these 22 cases with serious clinical problems occurred in women without a history of FMAIT.

Discussion

The incidence of clinically detected FMAIT estimated from this national study is less than one third of that estimated from prospective screening studies.[2] Our additional case ascertainment demonstrated that this was not simply due to under-reporting and we therefore extended the reporting period in order to collect sufficient cases to allow us to generate robust results. More than 90% of cases with serious clinical problems were diagnosed postnatally, highlighting the importance of appropriate assessment of the case for antenatal screening.

Results from this study will contribute to the assessment of the case for antenatal screening.

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

Funding

Wellbeing of Women.

Ethics approval

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

Acknowledgements

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Genital Herpes in children under 11 years of age

Dr Richard Reading

Key points

- Suspected genital herpes in children should always be confirmed by virological methods
- Few cases so far reported have resulted in child protection investigations

Background

Genital herpes in prepubertal children is rare, and when it occurs, raises the question of possible sexual abuse. Paediatricians currently have very little evidence on which to base an opinion on possible mode of transmission, yet their advice is key to whether or not a child protection investigation proceeds. A recently published literature review highlights both the inconsistency in current guidelines and the weakness of epidemiological data on this condition.[3]

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

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

Objectives

The study aims to:

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

Study duration

Surveillance period: April 2007 – April 2009 (inclusive).
Follow-up period: At one year to end April 2010.

Methodology

Case definition

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

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

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

Additional sources of data

Reported cases will be cross-referenced with laboratory reports from the Health Protection Agency (HPA) to ensure cases are not being missed. Laboratories notifying virological diagnoses on cases to the HPA which do not correspond with the partial identification information available to the BPSU study will be contacted by the HPA and requested to liaise with their local paediatrician, genito-urinary physician or dermatologist to report the case directly to the BPSU. This maintains confidentiality and at least enables the study to be aware of the number of possible unascertained cases. Members of the British Association for Sexual Health and HIV/

AIDS, and of the British Paediatric Dermatology Society have been circulated with details of the study and updated through their newsletters asking for notification of any cases known to them.

Analysis

Surveillance is not yet complete so interim analyses only have been completed. As of February 2009, 33 cases reports have been received of which 19 have been confirmed; 11 are error reports or duplicates and data for the remaining three are still outstanding.

The paucity of cases reported, even before the end of the surveillance period means that incidence will be lower than anticipated. So far, among cases reported, few have led to child protection investigations.

Discussion

We expected this to be a rare condition, and estimated around 20-30 cases per year. We have had between 15-20 cases per year reported (final figures not yet available).

In cross checking paediatrician's reports with laboratory data, there is evidence that some cases have not been reported, albeit low numbers. This will need to be confirmed and the implications fully considered in the final analysis.

The rarity of the condition and potential implications mean that all suspected cases should be investigated with virological tests – ideally either viral culture from vesicle fluid or by PCR. Serology in healing cases may help if active viral secretion has stopped. Other diagnoses in cases initially thought to be herpes simplex include herpes zoster, and various possible autoimmune blistering lesions of the genitalia. The low rate of child protection investigations probably reflects the lack of any evidence about the likelihood or otherwise of sexual transmission in children.

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

Funding

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Ethics approval

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

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HIV infection in childhood

Key points

- 1350 children born in 2007 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%.
- Of the 195 infected children born in the UK and Ireland since 2002 and reported by the end of 2008, two-thirds had mothers who had not been diagnosed prior to delivery.

Background

National surveillance of paediatric HIV infection and AIDS began in 1986 and is based on complementary paediatric, obstetric and laboratory reporting schemes. Reporting is voluntary and confidential and data from all sources are combined as the National Study of HIV in Pregnancy and Childhood (NSHPC) at the UCL Institute of Child Health (www.nshpc.ucl.ac.uk).

Most children currently living with HIV in the UK and Ireland, whether born here or abroad, acquired their infection through mother-to-child transmission. Combining NSHPC with unlinked anonymous survey data shows that in the UK the number of exposed infants increased substantially from about 300 in 1997 to over 1300 in 2007 (www.hpa.org.uk, and NSHPC data). Antiretroviral treatment, delivery by elective caesarean section and the avoidance of breastfeeding reduce transmission rates in diagnosed women to around 1% in comparison with a likely transmission rate of about 25% without interventions. Women must be diagnosed in time to be able to access these interventions, and antenatal HIV testing has been routinely recommended to all pregnant women in England and Ireland since 2000 and

Dr Pat Tookey and team

throughout the rest of the UK subsequently. The proportion of women diagnosed before delivery in the UK increased from an estimated 32% in 1997 to over 90% since 2004, and remains high (www.hpa.org.uk).

Children with confirmed HIV (Figure 5) infection who were either born abroad or were born to undiagnosed women in the UK/Ireland are generally diagnosed when they present with symptoms or because a member of their family is diagnosed with HIV infection.

Objectives

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

Study duration

Surveillance period: June 1986 and is regularly reviewed.
Follow-up: 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 the clinicians.

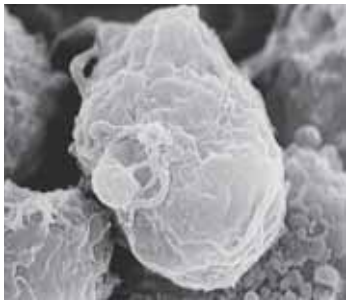
Methodology

Case definition

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

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.



C. Goldsmith

Figure 5: Scanning EM of HIV, grown in cultured lymphocytes. Virions are seen as small spheres on the surface of the cell

Table 3: 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 2008)*

Exposure / likely source of infection	BPSU reports	Reports from other sources	Total
Children born to HIV infected women	5333	6162	11495*
Likely source of infection for other infected children			
Haemophilia treatment	48	219	267
Blood transfusion/products	38	20	58
Other/not yet established	27	42	69
Total	5398	6491	11889

*1751 known to be infected

Analysis

Number and geographical distribution of reports: By the end of December 2008 there had been 7091 BPSU reports, of which 5398 were confirmed cases of HIV infection or exposed infants at risk of vertical transmission, 751 were duplicates and 639 reporting errors; the remaining 303 reports were still being investigated. A further 6491 confirmed cases were reported through other sources. Table 3 shows the likely source of infection or exposure risk for all confirmed cases.

Overall the majority of reports (83%) were made between 2000 and 2008 and this pattern was similar for all regions except Scotland (Table 4). In England before 2000, only 29% of reports were received from outside London compared with 46% of reports made between 2000 and 2008.

Children born to infected women: Most reported children (11495/11889; 97%) were born to infected women. By the end of 2008, 1751 (15%) of these children were known to be infected, and 8054 (70%) uninfected; infection status for the remaining 1690 (15%) had not yet been reported, but the majority were recent reports and very few are likely to be infected. While less than 8% were born abroad, they accounted for nearly half of all confirmed mother-to-child transmissions.

Between 2000 and 2008 there were over 8400 births to diagnosed women in the UK and Ireland, including 865 reported so far for 2008 (Table 5). 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 4: HIV infection and infants born to HIV infected women (all reporting sources) Region and time period report *(notified by 31 December 2008)*

Region of first report	1986-1999	2000-2008	Total
England Total	1575	8489	10064
London	*1122*	*4611*	*5733*
North	*181*	*1181*	*1362*
Midlands & East	*128*	*1650*	*1778*
South	*144*	*1047*	*1191*
Wales	26	110	136
Northern Ireland	4	43	47
Scotland	232	298	530
Ireland	170	942	1112
Total	2007	9882	11889

Table 5: Year of birth and infection status of children born in the UK and Ireland to women diagnosed by the time of delivery *(notified by 31 December 2008)*

Year of Birth	Infected	Indeterminate	Not infected	Total
1984-1999	110	146	896	1152
2000-2001	13	97	828	938
2002-2003	20	115	1598	1733
2004-2005	23	127	2164	2314
2006-2007	17	535	2075	2627
2008*	7	600	258	865
Total	190	1620	7819	9629

*reports for 2008 expected to rise substantially

Infected children: Since surveillance started in 1986, 2145 infected children have been reported, half of whom were born outside the UK and Ireland. A total of 345 (16%) are known to have died, 92 (4%) to have gone abroad and 142 (7%) to have transferred to adult services: a further 96 (4%) are either reported as lost to follow up or have had no follow up information reported since the end of 2005.

Of the 892 children known to have acquired infection from their mothers in the UK or Ireland, most (79%) were born to women who were not diagnosed by the time of delivery; 195 infants born since 2002 (128 to undiagnosed and 67 to diagnosed women) were confirmed infected by the end of 2008.

Discussion

The number of births to HIV infected women in the UK and Ireland has increased substantially each year since 2000, with reported births exceeding 1200 since 2005.[1] Most of these infants were born to diagnosed women who were able to take advantage of interventions to reduce the risk of transmission and are themselves uninfected. Overall mother-to-child transmission rates in diagnosed women in the UK and Ireland are now at around 1% with even lower rates among women who received appropriate treatment according to the British HIV Association guidelines (www.bhiva.org.uk).[2] However, despite high uptake of antenatal testing and interventions, some infants are still acquiring HIV infection from their mothers.

Changing trends in the demographic profile of HIV infected children and young people living in the UK and Ireland have implications for current and future health and social care provision. The availability of highly active antiretroviral therapy (HAART) since 1997 has substantially improved the prognosis for HIV infected children. A relatively small number of perinatally infected young people have already moved into transition or adult care services, but there are now several hundred young teenagers currently attending paediatric clinics who will need appropriate and specialised services to support their transition into adult care. A small number of women with perinatally acquired infection are also now being reported having babies of their own.[3]

Reports to the NSHPC from all areas of the UK and 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.

Please also note that the data presented are provisional, have not been peer reviewed and accordingly definitive conclusions should not be drawn.

Funding

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

Ethics approval

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

Support groups

Services Organised for Families Affected by HIV/AIDS (S.O.F.A.H.), 4th Floor, King Edward Building, 205 Corporation Street, Birmingham, B4 6SE.
Web: http://www.barnardos.org.uk/sofah.htm

Positively Women, 347-349 City Road, London, EC1V 1LR.
Web: http://www.positivelywomen.org.uk

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

Acknowledgements

Catherine Peckham, Claire Townsend, Barbara Willey, Hiwot Haile-Selassie, Icina Shakes, Kate Francis, UCL *Institute of Child Health.*

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

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Websites: www.nshpc.ucl.ac.uk; www.chipscohort.ac.uk; www.chiva.org.uk

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Idiopathic Intracranial Hypertension

Key points

- Idiopathic intracranial hypertension (IIH) is the rare condition of increased intracranial pressure without identifiable pathology. Despite intervention, the clinical course can be prolonged and recurring with the potential complications of distressing headache and blindness.
- Among the 269 notifications received over 18 months (from July 2007 to December 2008) of surveillance, there were 45 confirmed and 43 probable cases of childhood IIH identified.
- Notification of IIH cases through the BPSU ended in July 2009 and collection of one-year follow up data will be completed by August 2010.
- Of the 88 probable or confirmed cases of IIH, 58 cases (70%) were female; there was no difference between the sexes in the median age at diagnosis (12 years).

Background

Idiopathic intracranial hypertension (IIH), previously known as pseudotumour cerebri or benign intracranial hypertension, is the rare condition of increased intracranial pressure without identifiable pathology. In adulthood, IIH is most common in obese young women, however in childhood both genders have been reported to be equally affected. The clinical definition and association of this unique condition have evolved with time and the advances in neuroimaging making both the diagnosis and management challenging. Despite intervention, the clinical course of IIH can be prolonged and recurring with potential complications of distressing headache and blindness. The overall annual incidence of IIH (including child and adult cases) has previously been estimated to be 1-3 per 100,000 population, however epidemiological data on childhood IIH are lacking and limited to hospital-based retrospective case series.[1,2] Findings from this study will inform the diagnosis and management of future paediatric IIH cases.

Objectives

The study aims to determine the:

- annual incidence of IIH in children aged 1 to 16 years in the UK and Ireland

Dr Yim-Yee Matthews

- spectrum of clinical presentation of IIH in children by age
- national incidence of various established associations of IIH in children, in particular obesity at presentation
- frequency and spectrum of visual disturbances in children presenting with IIH
- current clinical management of children with IIH
- clinical course of headache and spectrum of the visual outcome one-year post diagnosis following various treatment modalities.

Study duration

Surveillance period: July 2007 to July 2009 (inclusive).
Follow-up: One year outcome follow-up data sought to July 2010.

Methodology

Reporting paediatricians are asked to complete an initial case notification questionnaire and a further follow-up questionnaire after 12 months.

Case definition

Any **newly presenting** child aged 1 to 16 years (not including 17th birthday) seen in the past month who fulfils at least two of the key features and all of the three essential criteria.

At least TWO Key Features:

- Symptoms of raised intracranial pressure (such as headache, nausea, vomiting or irritability) **and/or** visual symptoms of diplopia, blurring vision or transient visual loss
- Papilloedema, unilateral or bilateral
- Raised opening cerebrospinal fluid pressure above 20 cm by lumbar puncture.

Table 6: Regional distributions of the 269 IIH notifications over 18 months of surveillance

	Confirmed/ Probable	Positive duplicate	Error	Negative duplicate	Excluded	Unable to follow up	Awaiting ascertainment	Awaiting reply
England	74	19	28	6	12	12	18	53
Scotland	3	1	2	0	1	0	0	5
Wales	6	1	3	1	0	0	1	6
NI	2	0	1	0	0	0	2	0
ROI	3	2	2	0	0	1	0	2
Total	**88**	**23**	**36**	**7**	**13**	**13**	**21**	**66**

AND all THREE Essential Criteria:

- Normal level of consciousness
- Cranial imaging (including CT or MRI and MR or CT venography) does not reveal a structural cause such as ventricular dilatation, cerebral mass, vascular lesion or sinus venous thrombosis*, to explain the presenting symptoms or signs of raised intracranial pressure
- Normal cerebrospinal fluid contents (for atraumatic tap, white cell count < 6 x 10^6 /L, protein < 0.4 g/L, ratio of cerebrospinal fluid glucose to blood glucose > 0.5 or cerebrospinal fluid glucose > 2.1 mmol/l).

Excluding

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

Analysis

A total of 269 IIH notifications were received over the first 18 months of surveillance (July 2007 to December 2008) and their regional distributions are as shown in Table 6. Among these 45 were confirmed and 43 were probable (without MR or CT venography) IIH cases. Two cases of sinus venous thrombosis were notified during this study period and excluded at review. There were 23 positive duplicates, 36 cases reported in error (either diagnosed outside the surveillance period or not IIH cases), 13 cases were excluded for not meeting the case definition, 13 cases could not be followed up, 21 cases are awaiting case ascertainment by the investigators team and the remaining 66 cases are pending return of a completed questionnaire.

Over the 18 months surveillance period, the distribution of the numbers of the confirmed or probable IIH cases and the outstanding notifications whose questionnaires are either not yet returned or incomplete for case ascertainment are shown in Figure 6.

Of the 88 confirmed/probable IIH cases, 58 cases (70%) were female. The median age at diagnosis was 12 years in both female (range 5 to 16) and male (range 3 to 16).

Discussion

Over the 18 months surveillance period, 88 cases of either confirmed or probable IIH have been identified. As the number of cases reported to the study was much lower than expected during the first six months of surveillance, the IIH study surveillance period was extended to 25 months and thus ended in July 2009. This longer period for case ascertainment has enabled us to achieve an adequate sample size to evaluate the contemporary national incidence of IIH in children. The follow up data collection at one-year post diagnosis, which started in July 2008, will continue until the end of July 2010.

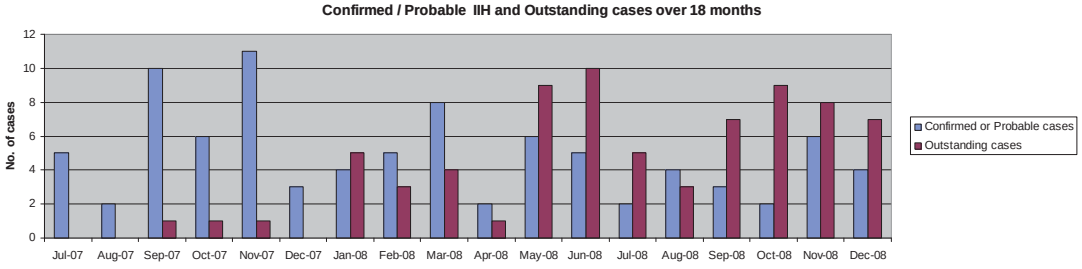

Figure 6: Monthly number of confirmed/probable IIH cases and outstanding notifications over 18 months

Significant number of notifications (66 out of 269 or 25%) are currently awaiting return of the completed questionnaire or a response from clinicians to clarify incomplete data on a returned questionnaire. Hence, the data presented is provisional and has not yet been peer reviewed and accordingly definitive conclusions should not be drawn.

After which we would hope to establish a consensus national guideline based on current best clinical practice.

Funding

Sir Peter Tizard Bursary.

Ethics approval

East London and the City Research Ethics Committee (Ref: 07/Q0603/47)
PIAG Section 60 Support [Ref: PIAG/BPSU 1-05(FT3)/2007].
NHS R&D Department at Wrexham Maelor Hospital.

Support groups

The Association for Spinal Bifida and Hydrocephalus, 42 Park Road, Peterborough, PE1 2UQ. Tel: 08454507755. Fax: (01733) 555985.
E-mail: helpline@asbah.org.
Web: www.asbah.org

Acknowledgements

We are very grateful to all the paediatricians who have notified cases of IIH and completed the questionnaires, and to the BPSU for their support. We would also very much like to thank the entire investigating team for their efforts and to Jayne Cooke for her able administrative assistance.

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Intussusception in children aged less than 12 months

Key Points

- Intussusception is a condition in which one portion of the bowel telescopes within another immediately downstream portion causing obstruction. It is a surgical emergency with the majority of children affected during the first year of life.
- This has been the first surveillance project that has ascertained cases through a separate paediatric surgeons reporting system.
- Active surveillance through the BPSU has recently ended with case notifications presently being followed-up.
- The study findings should inform rotavirus vaccine policy by providing pre−exposure data on intussusception, which can be used to evaluate any change in incidence following vaccine introduction.

Background

Intussusception (IS) is caused by a bowel section telescoping, causing obstruction (Figure 7). It is a surgical emergency, but most cases can be managed non-surgically with good outcome.

Availability of high quality (IS) epidemiological data at a national level is becoming a high priority due to the availability of new rotavirus vaccines. A previous oral rotavirus vaccine (RotaShield®; Wyeth Vaccines) was withdrawn from the United States in 1998, shortly after its introduction due to evidence for a causal association with IS. At present, two new rotavirus vaccines, have received European approval (Rotarix®; GSK Vaccines and Rotateq®, Sanofi Pasteur). However, the UK Joint Committee on Vaccination and Immunisation has yet to consider recommendations for their use.

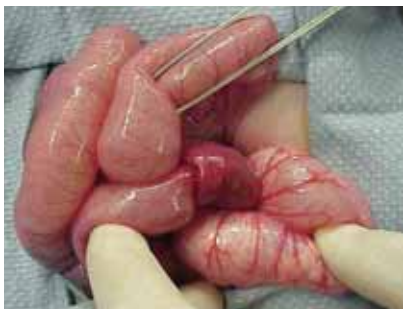

Figure 7: Intussusception identified at laparotomy

Prof Brent Taylor

The risk of IS has been a prime consideration throughout the development of these new rotavirus vaccines. Large clinical trials have been able to exclude any significant association with relatively high power,[1,2] but nevertheless many countries are implementing high quality IS surveillance studies to gain data on background incidence. This is in order to provide clear statements to the public and health professionals about the incidence of IS pre-vaccination, and to have a baseline against which to rapidly evaluate any post-vaccination adverse event reports that may be submitted. It is considered a high possibility that safety concerns will be raised, potentially causing controversy and adversely affecting uptake.

Objectives

The study aims to:

- estimate the incidence of IS in children aged less than 12 months
- describe the epidemiology of IS, including:
- age, gender, and ethnicity
- associated risk factors
- variation in management strategies (enema, surgical reduction, surgical resection spontaneous recovery)
- short-term outcomes (recovery, death).

Study duration

Surveillance period: March 2008 – March 2009 (inclusive).

Methodology

Case definition

Any child under 12 months of age, who in the opinion of the notifying paediatrician / surgeon, has suspected or confirmed intussusception based on clinical, radiological and/ or surgical findings. Reported cases have been classified by the investigators as definite, probable, possible, or suspected intussusception cases according to internationally agreed and the validated Brighton Collaboration criteria.[3]

Analysis

Although the active surveillance time-period has come to an end, follow-up of case notifications and tracking missing information is still in process. Provisional figures therefore are being continually updated.

As of May 2009 we have received 358 case notifications from paediatricians and paediatric surgeons. This is lower than expected and we are aware of some gaps in the national data. To address this we are contacting units direct to elicit further cases whilst taking the opportunity to audit the cases already received.

The overall questionnaire response rate from both paediatricians and paediatric surgeons has been 77% (275/358 case notifications) and we expect this to rise. So far, the response rate among paediatricians has been 79.6% (of 152 cases notified), whilst paediatric surgeons have returned 74% of questionnaires (of 206 cases notified).

Of 275 questionnaires received, 219 are confirmed IS cases, 36 are duplicates and the remaining 20 require follow-up for case ascertainment. Twenty-three cases did not meet study eligibility criteria i.e. were older than 12 months or had a diagnosis other than intussusception; 60 case notifications are currently being followed-up.

Discussion

The number of cases reported twice i.e. duplicates is likely to increase with further follow-up of cases that have been notified particularly towards the end of the study. Attention is being focussed on surgical units which had apparent low levels of case notifications – to ensure complete-as-possible case ascertainment.

The nomination of a 'study-lead' has proved successful in ensuring a complete response from the individual hospitals. A study-lead is either a consultant or trainee (registrar/SHO) representing his/her hospital and is the key point of contact between the hospital and study investigators.

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

Funding

Educational grant from GlaxoSmithKline Biologicals.

Ethics approval

Wandsworth Research Ethics Committee [Ref: 07/Q0803/62] and PIAG [Ref: 2-5(FT1)/2007].

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Medium-chain acyl-CoA dehydrogenase deficiency

Key points

- Medium-chain acyl-CoA dehydrogenase deficiency (MCADD) is an autosomal recessive disorder of fatty acid oxidation that may cause hypoglycaemia, encephalopathy, hepatic dysfunction and sudden death**.**
- Since 2004, approximately two million babies have been screened for MCADD in England as part of this study.
- This study has demonstrated that newborn screening reliably identifies affected children before they are likely to develop symptoms, enabling parents to use simple measures to avoid fasting and thereby reduce the chances of severe illness or death.
- Newborn screening for MCADD is now fully implemented throughout England and was celebrated on 23rd March 2009 with a formal reception at the Houses of Parliament.

Background

Medium-chain acyl-CoA dehydrogenase deficiency (MCADD) is a recessively inherited metabolic disorder that may cause hypoglycaemia, encephalopathy, hepatic dysfunction and sudden death.[1] MCADD has been identified as a candidate for newborn screening through three systematic reviews commissioned by the Health Technology Assessment Programme which concluded that more information was needed on test performance and clinical outcomes in a UK setting. Subsequently the Department of Health and the National Screening Committee funded a pilot newborn screening service for MCADD. They also commissioned a concurrent research study to evaluate the service. Although studies of MCADD screening in other countries have been carried out, important questions remain unanswered [2] and specifically uncertainty remained over the clinical outcome following detection through newborn screening. Furthermore, the findings of previous studies may not be generalisable to a UK setting; screening is carried out several days later in the UK and the population is ethnically more diverse than countries that have previously reported MCADD screening.[3]

Objectives

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

Prof Carol Dezateux

- To estimate test performance, predictive value, specificity and detection rate of screening for MCADD.

Study duration

Surveillance period: June 2004 – May 2008.
Follow-up: Two year outcome follow-up data sought to May 2010.

Methodology

Case definition

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

Diagnosis of MCADD was accepted if one or more of the following criteria were met:

- Elevated octanoyl carnitine in the presence of normal free carnitine levels on blood test using tandem mass spectrometry.
- Characteristic urine profile of organic acids with hexanoyl, suberyl and phenylpropionyl glycine.
- Molecular genetic studies confirming the presence of a mutation characteristic of MCADD.
- Enzyme studies based on skin fibroblasts showing reduced activity of MCAD.

Diagnosis of MCADD can be made through newborn screening, clinical presentation, investigation of children with an affected family member or through post mortem investigation.

All valid notifications reported were reviewed by an independent diagnostic review panel.

Additional sources of data

A Biochemical Surveillance Scheme for MCADD (BioSS–MCADD) was set up through UK laboratories providing diagnostic testing for MCADD, in order to increase ascertainment of cases. Presumptive positive cases were also (and continue to be) notified to the study through the laboratories currently undertaking MCADD screening.

Analysis

Numbers of cases notified to the BPSU: Between April 2004 and the end of June 2008, 377 notifications of MCADD had been received by the BPSU. We received completed questionnaires for 327 and 17 notifications were made in error (not MCADD or diagnosed outside surveillance period) – a return rate of 91%. Of these, 74 were duplicates (some multiply notified) bringing the case total to 236 cases of MCADD reported through the BPSU. 77 were clinically diagnosed cases of MCADD (clinical presentation including deaths, and affected siblings), 157 were detected by newborn screening, and two require further information on mode of presentation.

Of the 77 diagnosed clinically, 43 presented with clinical symptoms, nine (11%) died, one was investigated due to behavioural problems, and 24 were investigated because of affected siblings.

Of those who presented with clinical symptoms, 18 (42%) were female, with a median age at diagnosis of 12 months (range 0 to 213 months). Of those who died, two (22%) were female, with a median age of death at four days (range 2 days to 32 months). Of the 24 who were confirmed as having MCADD following diagnosis of an affected sibling, 12 (50%) were female, with a median age at diagnosis of 2.5 months (range 0 to 131 months).

200 follow-up forms have been sent to clinicians to ascertain clinical outcome of infants one year post-diagnosis. 191 (96%) of these have been returned. There were no MCADD related encephalopathic events or deaths reported in the first year following diagnosis.

162 two-year follow-up forms have been sent to clinicians. Of these 153 (94%) have been returned. There were no MCADD related deaths or major encephalopathic events reported through this follow-up.

Number of cases by source of data

The three sources of data are:

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

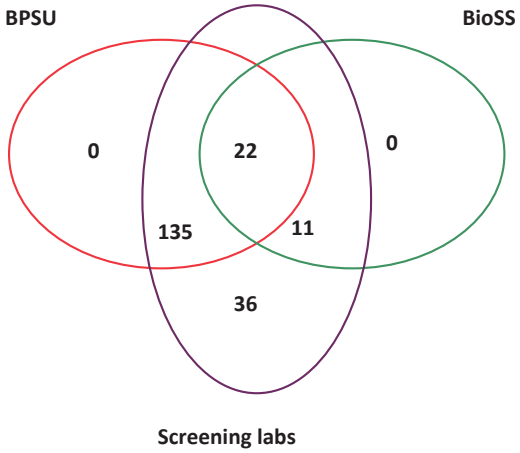

Figure 8: Number of confirmed cases by source of data.
Screened (presumptive) positives N=204

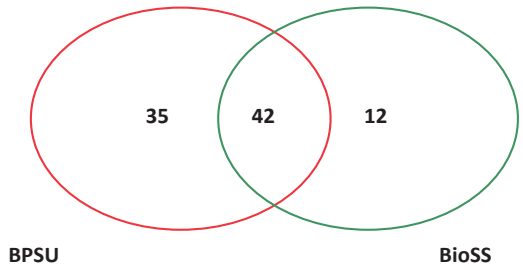

Figure 9: Confirmed clinical cases. Clinically diagnosed N=89

Discussion

From preliminary analyses comparing screened and unscreened populations in the UK, the estimated prevalence of MCADD identified after clinical diagnosis appears to be a half to two-thirds of that after newborn screening. This suggests under-diagnosis and/or variable penetrance – similar to that reported in other countries and screening programmes. Of those presenting with clinical symptoms for whom we have a DNA result, 78% are homozygous for common mutation 985A>G, whereas this falls to 44% for those notified as presumptive positive through newborn screening.

This study is one of the largest studies of newborn screening carried out worldwide, with approximately two million babies having been screened for MCADD in England to date. The study has shown that newborn screening reliably identifies affected children before they are likely to develop symptoms, enabling parents to use simple measures to avoid fasting and thereby reduce the chances of severe illness or death.

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

Implementation of screening for MCADD in England has been managed by the UK Newborn Screening Programme Centre. Details are available at http://www.newbornbloodspot.screening.nhs.uk

Research on the panel of mutations identified by screening through extended mutation DNA sequencing is underway, along with further refinements to the screening protocol for MCADD.

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

Funding

The Department of Health and the National Screening Committee.

Ethics approval

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

Support group

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

Acknowledgements

We are very grateful to the BPSU and all members of the RCPCH, particularly those paediatricians who have reported cases and completed questionnaires, for their support. We are also grateful to Professor Anne Green, Birmingham Children's Hospital and Dr Jim Bonham, Sheffield Children's Hospital, collaborators in the UKCSNS MCADD, who also helped set up the Biochemical Surveillance Scheme for MCADD. We also thank Professor James Leonard (Chair), Dr Jacqui Calvin, Dr Morteza Pourfarzam, Dr Johannes Zschocke and Dr Graham Shortland, members of the international expert Diagnostic Review Panel. Thanks are also due to the Department of Health and National Screening Committee for funding this study and to the UK Newborn Screening Programme Centre for overseeing implementation in England.

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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.

- Surveillance commenced in May 1997 and continues until at least April 2010. 2600 children have been notified to date**.** 1801 cases have been discussed by the Expert Group of seven paediatric neurologists and one geneticist. There have been 1095 children with a known diagnosis other than vCJD, and in the diagnosed group there are over 120 different neurodegenerative disorders.

- Six cases of variant Creutzfeldt-Jakob disease have been reported to the study since December 1998. Of these four have been classified as "definite" and two "probable" according to the National Creutzfeldt-Jakob Disease Surveillance Unit criteria. All have now died.

- Even if you have made a diagnosis we still want to hear about all children with progressive intellectual and neurological deterioration.

Background

Active prospective surveillance of UK children with progressive intellectual and neurological deterioration (PIND) commenced in May 1997. Funded by the Department of Health (121/6443), it is being carried out via the BPSU in conjunction with the National Creutzfeldt-Jakob Disease Surveillance Unit in Edinburgh (NCJDSU) and the Health Protection Agency (HPA).

The main aim is to determine whether or not any children in the UK have developed variant Creutzfeldt-Jakob disease (vCJD). This disease was initially reported by Will et al in 1996. vCJD (Figure 10) has been described in patients as young as 12 years of age[1] and it could occur in younger children. It is possible that the clinical presentation of vCJD in young children might differ from that described in adults. The strategy is to detect suspected vCJD cases by looking at a broader group of conditions causing progressive intellectual and neurological deterioration (PIND) in children. It is only by carefully examining the clinical details in all these PIND cases that we can be reasonably sure that vCJD is not being missed among the numerous rare neurodegenerative disorders that affect children. This unique dataset provides the opportunity to detect vCJD cases and highlight the variety of PIND conditions in the UK.[2]

Objectives

The study aims to:

- carry out active prospective surveillance of UK children with paediatric neurological conditions *(including those with specific diagnoses)* defined by their common presentation – progressive intellectual and neurological deterioration (PIND) - to determine the incidence and distribution of the diseases causing PIND

- evaluate cases presenting with PIND in order to classify them by diagnosis and investigate the possibility that vCJD is occurring in children.

Study duration

Surveillance period: May 1997 - April 2010.
Follow-up: Regularly until case status determined.

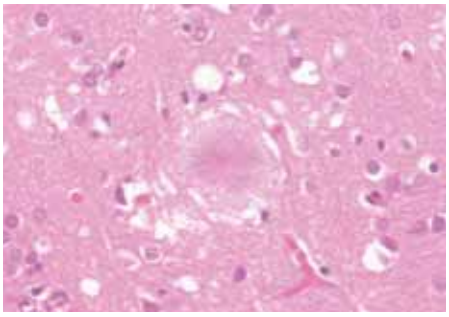

Figure 10: Florid plaque in vCJD x 400 haematoxylin/ eosin stain

Methodology

Paediatricians reporting a child with PIND are sent an initial contact form then contacted by the research nurse or research co-ordinator to arrange a detailed telephone discussion to gather further information about the case. Alternatively the surveillance team may arrange a visit to the reporting paediatrician to review the case notes or send a postal questionnaire. An Expert Group, comprising seven paediatric neurologists and one geneticist together with a representative from the NCJDSU, meet quarterly in London to review the anonymised clinical information and classify all PIND cases. If a child with clinical features suggestive of vCJD is identified, the referring paediatrician is made aware of this and, if the child's parents agree, the child with suspected vCJD will be 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.

Including:

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

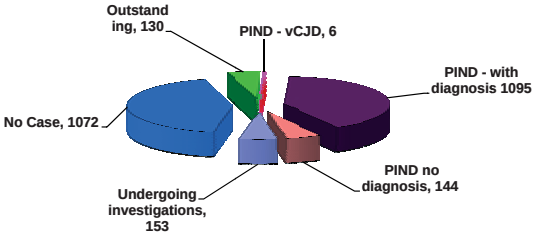

Figure 11: PIND study – current status March 2009

Analysis

By the beginning of March 2009, a total of 2600 children had been notified (Figure 11). 1072 are "No Cases" (not meeting PIND definition, duplicate notifications, reported in error, no traceable clinical information) and 130 cases are outstanding. The rest 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. The other five were three 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: The majority of children with PIND have a confirmed or likely underlying diagnosis that is not vCJD. In the 1095 children with a confirmed diagnosis there were over 120 different neurodegenerative conditions. The five most commonly occurring diagnostic groups are shown in Figure 12. They are the neuronal ceroid lipofuscinoses (NCLs) (138 cases), the mitochondrial cytopathies (117 cases), the mucopolysaccharidoses (101 cases), the gangliosidoses (100 cases), and peroxisomal disorders (67 cases).

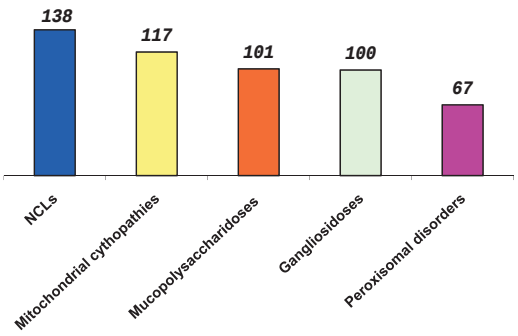

Figure 12: Five most commonly reported PIND diagnostic groups (NCLs: neuronal ceroid lipofuscinoses).

Children with PIND and no underlying diagnosis (idiopathic group): The Expert Group met specifically to discuss this group of children (n=144: 82 were male and 62 were female). This group gives cause for concern because if a "new" variant of vCJD should arise or if the paediatric presentation should differ from the adult presentation the idiopathic group could possibly include such a phenotype. However, after scrutinising all the available data the Expert Group was satisfied that all children had been fully investigated or had a sibling with similar disease pattern who had undergone extensive investigations. None of the 144 had a clinical presentation typical of vCJD and there was no evidence of a "new" unrecognised disorder in this group.

Discussion

PIND surveillance has continued for almost twelve years now. Six cases of vCJD in children under 16 years of age at first presentation have been notified to the study. There were four cases of definite vCJD and two cases of probable vCJD. One girl was age 12 years at onset, the youngest ever reported case of vCJD. There have been no other children with the clinical features of vCJD, particularly within the group of children with idiopathic PIND which was extensively reviewed in August 2008. However there remains concern that more childhood cases may appear, perhaps related to underlying genetic predispositions.[3] Surveillance is essential as there are still many unanswered questions about this relatively new disorder – for example, 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

Cambridgeshire2 Research Ethics Committee, (Ref: 97/010), the Public Health Laboratory Service Ethics Committee and PIAG section 251 support (PIAG/BPSU Ref: 2-10(c) 2005).

Support Groups

1. Creutzfeldt-Jakob Disease Support Network, PO Box 346, Market Drayton, Shropshire TF9 4WN. Web: http://www.cjdsupport.net

2. Batten Disease Family Association, c/o Heather House, Heather Drive, Tadley, Hampshire, RG26 4QR. Web. http://www.bdfa-uk.org.uk

3. The Society for Mucopolysaccharide Diseases, MPS House, Repton Place, White Lion Road, Amersham, Buckinghamshire, HP7 9LP. Tel: 0845 389 9901.
   E-mail: mps@mpssociety.co.uk
   Web: http://www.mpssociety.co.uk

4. Climb National Information and Advice Centre for Metabolic Diseases. 176 Nantwich Road, Crewe, CW2 6BG. Tel: 0800 652 3181 Freephone Family Service Helpline, 0870 770 0326. E-mail:info@climb.org.uk. Web: http://www.climb.org.uk

5. Ald Life, PO BOX 43642, London SE22 0XR Tel: 020 8473 7493. E-mail: info@aldlife.org Web: http://www.aldlife.org

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Sudden Unexpected Postnatal Collapse

Key points

- 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.
- Surveillance into 'Sudden Unexpected Postnatal Collapse' commenced in November 2008.
- In the first three months, 24 reports have been received.
- Data from the study will help in the establishment of clinical guidelines for the optimal early postnatal care of all infants.

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. A UK preliminary survey has shown that there is no consistent approach to investigation among clinicians and many cases remain unexplained. We propose the first national study aimed to describe the incidence, presenting features, investigation and outcome of such infants. Consultant paediatricians will be asked to report all cases of sudden unexpected postnatal collapse every month. A questionnaire seeking demographic and clinical data will be sent to reporting clinicians at the point of notification and again at 12 months

Dr Julie-Clare Becher

to determine outcome. The study's findings will raise the profile of this group and help to establish guidelines for the optimal early postnatal care of all infants. The study also expects to demonstrate the widely disparate approach to investigation of these infants and thus highlight the need for a consensus.

Objectives

Specific aims of the project 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 one year.

Study duration

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

Methodology

Paediatricians reporting a case through the orange card system will be asked to complete a questionnaire seeking demographic and relevant clinical information. A further follow-up questionnaire will be sent after one year to gather information on outcome.

Case definition

Infants ≥ 37 completed weeks of gestation with a five minute Apgar score of ≥ eight who have a sudden and unexpected collapse in hospital ≥ 12 hours of birth requiring resuscitation and who either die or go on to require intensive care.

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

Examples:

1. Male infant born at 41 weeks gestation by SVD, Apgar nine at five minutes. Placed skin to skin to establish breast feeding whilst mother having perineum sutured. At 50 minutes of age, found grey, apnoeic and very bradycardic prone on his mother's chest. Required cardiopulmonary resuscitation and was admitted to the neonatal unit ventilated where he suffered multiorgan failure. Survived neonatal period but was discharged home tube feeding.

2. Female infant at 37 weeks gestation born by forceps for failure to progress. Well at delivery, no resuscitation required. Had several breast feeds over the subsequent hours. Nappy change at 10 hours of age and appeared to be well. Found by parents at 11 hours of age in cot, lifeless. Resuscitation unsuccessful.

Exclude:

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

Additional sources of data

Contact with Information Services Division – Scotland, Northern Ireland Statistics Research Agency, Confidential Enquiry into Maternal and Child Health and Central Statistics Office - Ireland will be made to ensure case ascertainment and case de-duplication.

Analysis

As of February 2009, we have received 24 reports of which six have been confirmed, four have been reported in error and for 14 we await further data from questionnaires. Further information will be presented once data analysis commences.

Discussion

Notification of cases during this initial period of surveillance is encouraging.

We hope that the findings from this study will raise the profile of this condition and inform clinical guidelines for the optimal early postnatal care of all infants. A steering committee, supported and represented by relevant professional bodies, has been convened to examine the need for a standardised diagnostic protocol for infants suffering sudden unexpected postnatal collapse. Based on the results of this study, a research protocol will be developed to elucidate the various causes of early postnatal collapse.

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

Funding

We are grateful to WellChild for funding this study.

Ethics approval

This study has been approved by 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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3. Hays S, et al. Respiratory arrest in delivery room during skin to skin care in 11 full term healthy neonates. *Arch Ped* 2006; **13**: 1067–8

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Toxic shock syndrome in childhood

Key points

- Toxic shock syndrome (TSS) is a rare toxin related disease with potentially fatal or catastrophic consequences.
- There is little data on the incidence of TSS in children in the UK.
- This BPSU study will inform paediatricians about incidence and management of this potentially fatal condition.
- For the first time BPSU surveillance will ascertain cases from burns units.

Background

Staphylococcal toxic shock syndrome (TSS) was first described in children in 1978 and was later described in association with tampon use in young women. Subsequently burns have been recognised as a significant factor predisposing to TSS, but may be over-reported as part of burns sepsis.

In the 1980s streptococcal toxic shock syndrome was described and has subsequently been described to have a more variable presentation. It is much less frequent than staphylococcal TSS and may be clinically indistinguishable from it.

Dr Shazia Adalat

Dr Tom Dawson

Other bacteria such as clostridium have variant syndromes associated with toxin production which are even less common and a neonatal variant called neonatal toxic shock syndrome–like exanthematous disease (NTED) has also been described.

Many staphylococci have the genes for toxin production but only express these under certain conditions. It is not clear what triggers toxin production in these organisms but it seems to be multifactorial, dependent on environmental and host features. Several toxins have been identified but none has been linked to clinical symptoms.

TSS is thought to have a significant mortality and morbidity but there is very little data on outcome and mortality associated with TSS. A recent European enhanced surveillance study for Streptococcal TSS from the HPA reported only eight cases over the course of one year. This low figure is felt to be due to underreporting although there is little firm evidence for this.

There is no clear published recent epidemiological data and so the burden of disease is unknown although we estimate that there are fewer than 150 cases in total per year in the UK. It is hoped that this study will add to the understanding of the true incidence of TSS in the UK and clarify both the range of organisms and diverse clinical presentations.

Objectives

The study aims to idntify:

- the incidence of TSS due to staphylococcal or streptococcal organisms in children in the UK and identify any geographic variation.
- the presence of previously described associated factors with the development of TSS in children in the UK.
- the different forms of clinical presentation of TSS due to staphylococcal or streptococcal organisms in children in the UK, including relevant laboratory parameters.
- the key features of clinical management of TSS due to staphylococcal or streptococcal organisms in children in the UK.
- toxins and bacterial type causing TSS due to staphylococcal or streptococcal organisms in children in the UK.
- mortality and morbidity rates caused by TSS due to staphylococcal or streptococcal organisms in children in the UK.

Study duration

Surveillance period: November 2008-November 2009 (inclusive).

Methodology

Case definition

Any child under 16 years of age whom the attending paediatrician believes has toxic shock syndrome according to the following criteria:

- Fever
- Hypotension- systolic BP less than the 5th centile for age according to the following chart :
- Involvement of at least two other systems

Age (Years	5th Centile Systolic Blood Pressure (mmHg)
0-2	70
2-4	76
4-6	82
6-8	85
8-10	90
10-12	92
12-14	95
14-16	97

(derived from :-
Update on the 1987 Task Force Report on High Blood Pressure in Children and Adolescents**.** *Pediatrics*. 1996 Oct; **98(**4 Pt 1):649-58.

BP centiles in Great Britain. Jackson LV, Thalange NKS and Cole T J. *Arch. Dis. Child.* 2007; **92:298**-303.)

And either

- Rash (with or without desquamation)

Or

- No rash **BUT** isolation of Group A streptococcus

Analytic case definition: The definitions used for staphylococcal toxic shock syndrome will be those adopted by the Centre for Disease Control and Prevention in the United States and streptococcal toxic shock syndrome will be defined by the American Academy of Paediatrics definition (derived from the American working group on Streptococcal Toxic Shock Syndrome)**.** This can be viewed at http://bpsu.inopsu.com/studies/Toxic_Shock_Syndrome/protocol.html

Additional sources of data

Along with a monthly report card being sent to paediatricians a similar card is being dispatched to burns units (which are sometimes run by doctors e.g. anaesthetists or surgeons not covered by the mailing to paediatricians) on a monthly basis.

We are also liaising with the Health Protection Agency Staphylococcal and Streptococcal reference laboratories for the UK and Republic of Ireland. All cases of *staphylococcal* and Streptococcal toxin positive isolates in children (<16 years) will be kept on a data base. A regular provision of data from their existing database will be made available to us via E-mail. We will then try to cross reference this against our data from paediatricians.

If cases occur here that we are unable to match from other sources of reporting, a letter will be sent

to the local paediatricians, burn unit and paediatric intensive care units (PICU) explaining that a case has occurred and we are suspicious that it may have been missed and urging them to make enquires.

Finally we will also collaborate with the paediatric intensive care audit network (PICAnet – www.picanet.org.uk) to corroborate numbers seen. At present they hold some data on TSS in burns units in the UK. The main problem is the variable criteria used to identify these cases.

Analysis

In the first three months we have had 24 reports from paediatricians, 16 of the questionnaires sent out have been returned. Two replies were excluded as the case occurred outside the time frame of study. There was one duplicate report.

Nine of the thirteen confirmed cases were under five years of age. Seven were female. All were white caucasion.

Hypotension was present on arrival to hospital in 31%. 54% had a diffuse macular erythroderma, 62% reported a generalised erythematous macular rash. 31% reported both types of rash in the same patient. Desquamation has not been reported.

31% had GI involvement. Deranged renal function was present in over half. 15% had CNS involvement. 46% had soft tissue involvement. (one had soft tissue necrosis, five had mucous membrane involvement).

Sources of sepsis identified by the reporting paediatrician were: - chest (three), skin (five), tampon use (two), throat (one), unknown (one). Only one patient had a burn source of their condition.

Of positive isolates, 6/13 grew Staphylococcus aureus (from non-sterile sites) and 2/13 Group A Streptococcus. Other organisms isolated include pseudomonas and coliforms. No significant information on toxin isolation is available as yet.

With respect to place of management, five patients required a PICU admission. One patient was managed in an adult ITU, ten on a paediatric ward at some point during their admission, and one on a burns unit.

One patient required haemofiltration. Six patients required ventilation. All patients received antibiotics, however only six patients had been given potentially disease modifying antibiotics- all of these received clindamycin, none received linezolid.

Three patients required surgical debridement; one had a skin graft procedure.

Of the cases reported so far there were two deaths, three had residual morbidity at discharge, only one at follow-up.

Discussion

We are still relatively early into the study; therefore any lengthy analysis would be premature.

The number of cases being reported is in keeping with anticipated numbers. The ages of cases are in keeping with previous data. Interestingly, so far, burns cases do not constitute a significant proportion of cases, in contradiction to previous published reports.

A history of recent varicella infection is recognised as a risk factor for infection with group A streptococcal infection. We have had one confirmed case with varicella subsequently developing streptococcal toxic shock.

It is regrettable that the majority of units are not sending samples for toxin isolation enabling definitive identification of the responsible toxin.

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

Funding

RCPCH - Sir Peter Tizard Bursary.

Ethics approval

This study has been approved by the Lewisham MREC (Ref: 08/H0810/16) and has been granted PIAG Section 251 support (Ref: PIAG/BPSU 5-07 (FT2)/2008).

Acknowledgement(s)

Angela Kearnes, Staphylococcal laboratory of Health Protection Agency, England.
Androulla Efstratiou, Streptococcal laboratory of Health Protection Agency, England, Scotland and Northern Ireland.
Donald Morris, Staphylococcal laboratory, Health Protection Agency, Scotland.

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Vitamin K Deficiency Bleeding

Key points

- Forty-six reports of Vitamin K deficiency bleeding (VKDB) have been received and to date and 10 occurring during the reporting period have been confirmed.
- The majority of cases of VKDB occurred in infants who had received no vitamin K (VK), despite the recommendation by the National Institute for Clinical Excellence (NICE) that all newborns should receive prophylactic VK.
- Compared with the last BPSU study of VKDB in 2000-02 there has been a small increase in the number of confirmed cases of VKDB and some have suffered long term morbidity.
- As some important data are still outstanding it is too early to draw firm conclusions.

Background

Vitamin K Deficiency Bleeding (VKDB) is a rare, potentially-handicapping or fatal condition (Figure 13), preventable by a combination of vitamin K prophylaxis and surveillance for predisposing conditions, particularly liver disease.[1,2] Following

Figure 13: Bleeding from umbillicus due to VKDB

Dr Alison Busfield

three previous BPSU studies of VKDB, all UK units now offer prophylaxis[2] and there is greater awareness of the importance of investigating 'warning bleeds' and prolonged jaundice.

The third BPSU study (2000-02) found the incidence of VKDB in the UK/Ireland to be the lowest recorded with no death or long-term morbidity. Following 42 notifications there were only seven confirmed cases of VKDB; four had received no prophylaxis, in each case because parents refused consent for recommended intramuscular (IM) vitamin K and, probably, for an alternative oral regimen; one had received IM prophylaxis and two had received oral prophylaxis.[2]

At the time of the third study Konakion Neonatal was used by most of the 60% of units recommending IM prophylaxis. With exceedingly rare exceptions, a single 1mg IM dose of that preparation at birth was known to protect against VKDB for many weeks. Since then, however, there have been two important developments: first, Konakion Neonatal has been withdrawn (leaving Konakion MM as the only licensed preparation for IM or oral prophylaxis); second, guidelines from the National Institute for Health and Clinical Excellence have recommended IM in preference to oral prophylaxis. It is inevitable that the use of IM prophylaxis with Konakion MM will increase (there being no alternative preparation for IM administration) despite the paucity of published data about the duration of protection it confers.[3]

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

Objectives

The most recent study aims to document

- incidence of VKDB following the withdrawal of Konakion Neonatal
- effectiveness of current prophylactic regimens, including Konakion MM 1mg IM as a single dose at birth
- whether alternative routes of administration were offered to parents who withheld consent for IM vitamin K
- clinical presentation and management of bleeding
- risk factors
- outcomes following VKDB.

Study duration

Surveillance period: October 2006 – October 2008 (inclusive).

Methodology

Case definition

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

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

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

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

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

Analysis

The two year surveillance period is now complete. There were a total of 46 notifications, 44 via the BPSU and two reported directly to the investigators.

Further information is still awaited on three of the cases notified. The remaining 42 have been classified as follows: 10 confirmed cases of VKDB; 14 'no case', 11 were duplicate reports; two were lost to follow up without sufficient information being accrued to allow classification. Six notifications fell outside the study period and were therefore excluded.

The results so far available are similar in some respects to those of the 2000-02 BPSU survey - infants developing VKDB are still most likely to be solely breast fed and to have received no VK; parental refusal of prophylaxis remains a problem which deserves further study. Compared with the previous survey, however, there has been a small increase in the number of confirmed cases and at least two are expected to suffer long-term morbidity; these figures may rise if more data are received.

Discussion

As further information is still awaited on three possible cases and all the denominator data from the 2008 survey of VK prophylaxis policies are not yet available (replies from 18% of maternity units still outstanding), no firm conclusions can yet be drawn. We intend to publish all available data by the end of 2009.

Measurement of PIVKA-II and vitamin K levels

Measurement of serum PIVKA-II, using blood taken days (even weeks) after treatment and normalisation of clotting, can give retrospective confirmation of recent vitamin K deficiency. In VKDB intravenous vitamin K alone may improve clotting sufficiently to stop bleeding in just 20-30 minutes, but the raised serum PIVKA-II levels are unaffected by vitamin K (or blood products) and decline only slowly. Both vitamin K and PIVKA-II levels can be measured in just 0.5 ml of serum/ plasma, or PIVKA-II alone in 10 microlitres of

serum/plasma – samples should be protected from light from immediately after collection (light degrades vitamin K). Dr Martin Shearer is happy to carry out the assays; contact details are:

Dr Martin J Shearer, Consultant Clinical Scientist & Honorary Senior Lecturer, Centre for Haemostasis and Thrombosis, 1st Floor North Wing, St Thomas' Hospital, London SE1 7EH. Tel: 020 7188 2801 (office), 020 7188 6815 (lab). E mail: martin.shearer@gstt.nhs.uk
Website: http://keqas.com

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

Funding

Roche Pharmaceuticals Ltd.

Ethical approval

Cornwall Research Ethics Committee (Ref: 06/Q2101/74); PIAG approval (Ref: BPSU PIAG 03-04(FT5)/2006).

Acknowledgements

We thank Roche for funding the study and the BPSU for both allowing and facilitating it. Particular thanks are due to all paediatricians who have notified cases, completed questionnaires and often supplied further information to make the data as complete and accurate as possible.

References

1. McNinch AW, Busfield A and Tripp JH. Vitamin K deficiency bleeding in infants in the Great Britain and Ireland: British Paediatric Unit Surveys 1993-94 and 2001-02. *Arch Dis Child 2007*; **92**:*759-766*

2. Busfield A, McNinch AW and Tripp JH. Neonatal vitamin K prophylaxis in Great Britain and Ireland: the impact of perceived risk and product licensing on effectiveness. *Arch Dis Child 2007;* **92**:754-758

3. Joubert P, Bolton K, Shearer M, Kneer J. Comparison of the effects of a mixed micellar and cremophor formulation of vitamin K, given intramuscularly to healthy neonates. *J Clin Pharmacol* (thirty-third annual ACCP meeting abstracts). 2004:1195

Researcher(s)

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E-mail: John.Tripp@pms.ac.uk

4 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.

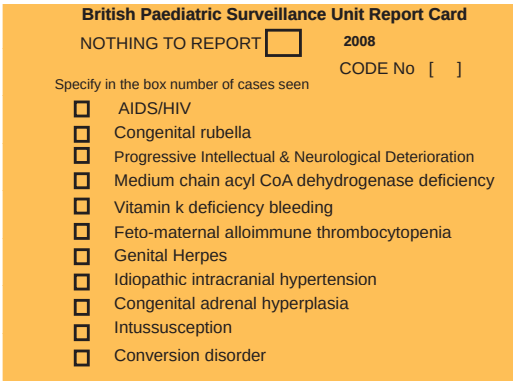
The number of conditions under surveillance is usually limited to 12. The BPSU application procedure consists of two phases: a screening phase based on an outline of the study and a detailed consideration of the full application. Details about the BPSU application procedure can be downloaded from the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

Factors that increase the likelihood of a study being accepted include scientific importance, 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 Governance Information Board, formerly (Patient Information Advisory Group (PIAG) 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 14) Each month, all clinicians participating in the surveillance scheme are sent the orange card listing the conditions currently under surveillance; follow-up reminders are sent to those who have not returned their card for two consecutive months. A 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.


British Paediatric Surveillance Unit Report Card

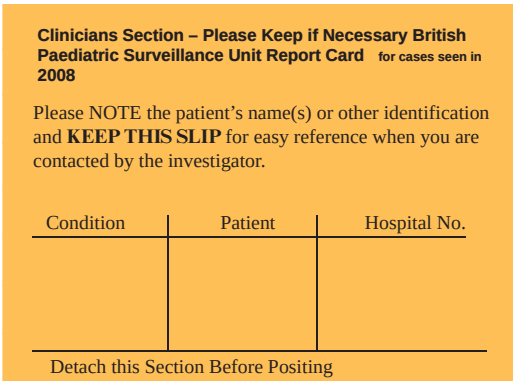
NOTHING TO REPORT ☐ 2008

CODE No [ ]

Specify in the box number of cases seen

- ☐ AIDS/HIV
- ☐ Congenital rubella
- ☐ Progressive Intellectual & Neurological Deterioration
- ☐ Medium chain acyl CoA dehydrogenase deficiency
- ☐ Vitamin k deficiency bleeding
- ☐ Feto-maternal alloimmune thrombocytopenia
- ☐ Genital Herpes
- ☐ Idiopathic intracranial hypertension
- ☐ Congenital adrenal hyperplasia
- ☐ Intussusception
- ☐ Conversion disorder

Figure 14: Orange Card Side A


Clinicians Section – Please Keep if Necessary British Paediatric Surveillance Unit Report Card for cases seen in 2008

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

Condition	Patient	Hospital No.

Detach this Section Before Positing

Figure 15: Orange Card Side B

When reporting a case, respondents are also asked to make a note of the case (Figure 15) 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 being 'nothing to report' box on the card for them to tick. This is an important feature of the surveillance scheme as itallows us to measure compliance to the system. The compliance rates are continually monitored, thus ensuring good coverage of the paediatric surveillance scheme across the whole of the UK and Ireland.

Follow-up and confirmation of case reports

On receiving a case report the BPSU informs the relevant study team. 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

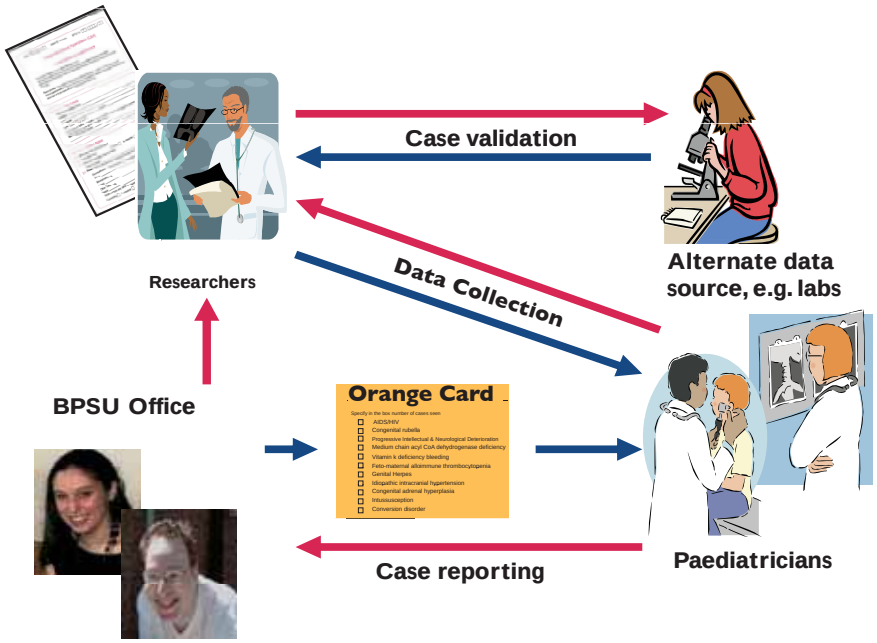


Figure 16: Surveillance mechanism

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 16). 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.

Table 8 (page 47) shows the number of cases reported to the BPSU from its inception until the end of year 2008 for conditions under surveillance at November 2008. 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 2009, only 587 (5%) of the 11424 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 9 (page 48) summarises the outcome of the follow-up of all cases reported to the BPSU by the end of year 2008 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. Currently, paediatric surgeons (intussusception) and burns specialists (toxic shock syndrome) are 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 the administrative costs of coordinating their study. These funds also permit us to undertake additional activities such as holding workshops to support current and potential investigators and conferences most recently in March 2009. The BPSU is also grateful for the ongoing support that it receives from the Royal College of Paediatrics and Child Health, the UCL Institute of Child Health and the Health Protection Agency.

5 Scientific Coodinator's Yearly Review of Activities

This past year has seen the commencement of three new BPSU studies. The first, anaphylaxis following immunisation (investigator Dr Mich Erlewyn-Lajeunesse) commenced in October 2008. November saw the commencement of two studies, toxic shock syndrome, the investigators Dr Tom Dawson and Dr Shazia Adalat being the Sir Peter Tizard bursary recipients for 2006 and sudden unexpected early postnatal collapse (investigator Dr Julie-Claire Becher).

Four studies had their period of surveillance extended for a further year: HIV, congenital rubella, progressive intellectual and neurological deterioration (PIND) and genital herpes in children under 11 years.

One study has so far commenced in 2009 – severe hypernatraemia in May 2009 (investigator Dr Sam Oddie). Several studies are currently in final preparation and are likely to start in the autumn. These include bacterial meningitis in infants less than 3 months of age; childhood inflammatory demyelinating disease and sexually transmitted infections in children under 11 years of age presenting to secondary care.

Since its inception in 1986 the BPSU has completed 71 studies (Appendix A). During 2008/2009, there were 20 publications and 42 presentations relating to BPSU studies (Appendices B).

The 2008-09 Sir Peter Tizard bursary, funded by the RCPCH, was awarded to Dr Lleona Lee (University Hospital Of North Staffordshire) for a study on surgical ligation of the patent ductus arteriosus (PDA) in premature infants.

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 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 INoPSU hold a bi-annual conference. In 2008 this was held in Germany. Here it was reported that over 90 different conditions have been investigated across the 13 member surveillance units. The BPSU office continues to manage the INoPSU website (http://www.inopsu.com) where information on INoPSU's work is available and produce the INoPSU e-newsletter.

(Photo by Joe Spinoza, aged 11)

Richard Lynn
Scientific coordinator

Participation in the scheme during the year 2008

One hundred and fifty eight consultants were placed on the mailing list whilst 146 were removed mainly following retirement or due to moving overseas. The BPSU mailing list continues to include selected groups of consultants other than paediatricians such as cardiologists, clinical geneticists and pathologists. Paediatric surgeons and child and adolescent psychiatrists and national burns units have also been receiving a report card in order to help with ascertainment of sudden unexpected early postnatal collapse, conversion disorder and toxic shock syndrome.

Reporting rates for returning the orange cards remain high - the overall card return compliance rate for the year 2008, calculated as a proportion of orange cards returned, was 94.1% (34,717/32,578), an increase of 0.3% from 2007. Monthly response rates ranged from 96.5% in February to 92.3% in October with a median of 94.6%. To maintain this compliance rate respondents who have not returned cards for two consecutive months are sent letters, as much to verify postal address as to act as a reminder. This return rate remains higher than any equivalent UK scheme and ranks highly against other national paediatric surveillance units (Table 7 page 47).

Wales continues to achieve the highest average yearly response rate – 98.3%. The Thames area showed a cumulative response rate of 91.8%, no change on 2007. North Scotland fell 15 places to rank 17. Full details of regional response rates are provided in Table 7. 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

77% (2315) of participants reported no cases in 2008, 14% (413) reported a single case, 7.5% (220) reported between two and four cases and 1.5% (42) reported five or more cases. The greatest numbers of cases reported were by HIV/AIDS specialists, one of whom reported 103 cases and another 45. Specialties that had a particularly high level of reporting were paediatric neurologists (PIND), neonatologists and infectious disease specialists (AIDS/HIV, MRSA). Community paediatricians continue to make a significant contribution to the reporting, particularly to the PIND and HIV/AIDS studies and their continued involvement in the scheme is very much welcomed.

Table 7: Regional response rate 2007 and 2008

Region	Rank 2008	Rank 2007
Northern	7	4
Yorkshire	5	11
Trent	13	8
East Anglia	15	5
NWT	18	18
NET	20	20
SET	8	15
SWT	17	19
Wessex	4	3
Oxford	6	9
South Western	11	10
West Midlands	16	12
Mersey	14	16
North Western	10	17
Wales	1	1
North Scotland	12	2
South Scotland	2	14
West Scotland	9	7
Northern Ireland	3	6
Republic of Ireland	19	13

Figure 17 : Average orange card return rate (%) by area, 2008

Table 8: Cases reported from June 1986 - December 2008 for conditions under surveillance at May 2009

Reports (confirmed cases)							
	Date when reporting began	June 1986-Dec-96	Jan-96 Dec-00	Jan-01 Dec-03	Jan-04 Dec-06	Jan-07 Dec-07	Jan-08 Dec-08
Conditions under Surveillance							
HIV/AIDS	Jun-86	991 (691)	1017 (705)	1774 (1430)	2172 (1852)	711 (577)	709(464)
Congenital rubella	Jun-91	72 (39)	49 (25)	26 (6)	13 (4)	9(1)	2(1)
PIND	May-97		1066 (628)	610(317)	505 (297)	212(142)	170(119)
MCADD	Jun-04				267 (181)	67 (33)	36 (21)
FMAIT	Oct-06				17(10)	85(57)	59(33)
VKDB	Oct-06				7(1)	21(4)	17(4)
Genital herpes	Jun-07					14(7)	19(10)
IIH	Jul-07					104(39)	172(49)
Congenital Adrenal Hyperplasia	Aug-07					74(36)	137(72)
Intussusception	Jun-08						118(50)
Anaphylaxis	Sep-08						4(3)
Conversion Disorder	Oct-08						59(17)
Toxic Shock Syndrome	Oct-08						23(14)
SUPC	Nov-08						16(5)
Total		**1063 (730)**	**2132 (1358)**	**2410 (1753)**	**2981(2345)**	**1297 (896)**	**1541 (862)**

Table 9: Outcome of follow-up of the cases reported in 2008 for conditions under surveillance at May 2009

	Date when reporting began	Valid reports	%	Duplicates	Errors	(D&E) %	Not yet known	%	Total
Condition under surveillance									
HIV/AIDS	Jun-86	5,719	78	684	662	18	309	4	7374
Congenital rubella	Jun-91	76	44	33	61	55	1	1	171
PIND	May-97	1503	59	327	719	41	14	1	2563
MCADD	Jun-04	135	64	60	75	36	0	0	370
FMAIT	Oct-06	100	62	16	17	20	28	17	161
VKDB	Oct-06	9	20	10	19	64	7	16	45
Genital Herpes	Jun-07	17	52	0	9	27	7	21	33
IIH	Jul-07	88	32	28	66	34	94	34	276
Congenital Adrenal Hyperplasia	Aug-07	108	51	41	27	32	35	17	211
IS	Jun-08	50	42	17	7	20	44	37	118
AP	Sep-08	3	75	0	1	25		0	4
Conversion disorder	Oct-08	17	29	0	2	3	40	68	59
Toxic Shock Syndrome	Oct-08	14	61	0	6	26	3	13	23
SUPC	Nov-08	5	31	1	5	38	5	31	16
Total		**8076**	**70**	**1217**	**1676**	**25**	**587**	**5**	**11424**

HIV	Human immunodeficiency virus: reports of AIDS in June 1986 include cases previously seen; case definition extended to include HIV infection in January 1990
PIND	Progressive intellectual and neurological deterioration
MCADD	Medium chain Acyl Co A dehydrogenase deficiency
MRSA	Methicillin-resistant *Staphylococcus aureus*
FMAIT	Feto-maternal alloimmune thrombocytopeania
VKDB	Vitamin K deficiency bleeding
IIH	Idiopathic intracranial hypertension
CAH	Congenital adrenal hyperplasia
IS	Intussusception – excludes cases seen by paediatric surgeons
AP	Anaphylaxis following immunisation
CD	Conversion disorder – excludes cases seen by psychiatrists
TSS	Toxic shock syndrome
SUPC	Sudden unexpected postnatal collapse

Valid reports:
Cases confirmed at follow-up as being both unique (i.e. not a duplicate) and satisfying the diagnostic criteria set out in the case definition. Confirmed cases reported to the BPSU but already known to the research worker from another source are included.

Invalid reports:
These include:

- duplicate reports of cases already reported to the BPSU, and
- reporting errors arising as a result of a misdiagnosis, the wrong box on the orange card being ticked, the case not meeting the diagnostic criteria set out in the case definition or an inability to follow-up a case.

Outcome not yet known:
Outcome of follow-up not yet received by BPSU (by May 2009).

6 International Network of Paediatric Surveillance Units (INoPSU)

Figure 18: International Network of Paediatric Surveillance Units (INoPSU)

Background

Following the success of the BPSU, the same methodology was adopted and adapted in the 1990s to other countries who wished to set up active paediatric surveillance systems. In 1992, surveillance units were established in the Netherlands and Germany and, in 1994, in Switzerland. The European initiative was also the stimulus for the development in 1992 of an Australian unit and later the Malaysian unit (1994) to be followed by units in Canada (1996), Papua New Guinea (1996), New Zealand and Latvia (1997), Portugal (2001) and Greece/Cyprus (2003). Wales (1994) and Republic of Ireland (1996) developed surveillance units using a similar methodology to the BPSU, but are including on more common disorders in their surveillance. Unfortunately the Papua New Guinea unit is currently not active. However, Argentina and Italy continue to show an interest in developing similar such units. More recently we have seen the establishment of a Scottish unit.

The mission of INoPSU is the advancement of knowledge of rare and uncommon childhood infections and disorders and the participation of paediatricians in surveillance on a national and international basis so as to achieve a series of benefits to clinical practice and health policy.

Using similar research protocols, the units can provide an efficient, effective framework for case finding across national populations. Comparison of hyperbilirubinaemia, eating disorders and congenital rubella cases has demonstrated this through recent presentations at international conferences. It also led in June 2007 to the publication of a joint paper entitled - Beyond counting cases: public health impacts of national paediatric surveillance units in ADC vol. 92 pg. 527-533.

Over the past 10 years, INoPSU countries have facilitated the surveillance of over 180 different rare conditions, covering a child population of over 50 million and involving over 10,000 clinicians. Details on all the activities of each surveillance unit is available form their respective websites and also from the INoPSU website, where the current annual report can be found.

To strengthen the links between units a bi-annual conference is held, the most recent being in Munich Germany in October 2008.

For further information on INoPSU visit www.inopsu.com.

APPENDIX A - Completed Studies 1986-2008

By mid-2009 the BPSU had completed 71 studies. Information about these studies has been included in previous annual reports of the BPSU, which are available from the BPSU office and are also listed on the BPSU website (http://bpsu.inopsu.com/studies/completed.html). Information on studies completed from 2005, principal investigators and definitive papers are listed on page 51.

X-linked anhydrotic ectodermal dysplasia

Haemorrhagic shock encephalopathy syndrome

Haemolytic uraemic syndrome I

Kawasaki disease

Lowe syndrome

Neonatal herpes

Insulin dependent diabetes in under fifteens

Drowning and near drowning

Haemorrhagic disease of the newborn

Galactosaemia

Congenital toxoplasmosis

Higher order births

Acute rheumatic fever

Rett syndrome

Measles, mumps, rubella-meningoencephalitis

Chemistry set poisoning

Acute flaccid paralysis

Androgen insensitivity syndrome

Long term parenteral nutrition

Insulin dependent diabetes in under fives

Juvenile dermatomyositis

Congenital dislocation of the hip

Haemophagocytic lymphohistiocytosis

Non-accidental poisoning/ Munchausen syndrome by proxy

Neonatal necrotising enterocolitis

Vitamin K deficiency bleeding II

Biliary Atresia

Transient and permanent neonatal diabetes

Adverse neonatal outcomes of delivery or labour in water

Congenital syphilis

Congenital cataract

Medium chain acyl-CoA dehydrogenase

Pyridoxine dependent seizures

Neonatal meningitis

Cerebral oedema and death following diabetic ketoacidosis

Hepatitis C virus infection

Congenital brachial palsy

Subdural haematoma and effusion

Inflammatory bowel disease in under 20 year olds

Fatal/Severe allergic reactions to food ingestion

Invasive *Haemophilus influenzae* infection

Severe visual impairment /Blindness

Haemolytic uraemic syndrome II

Group B *Streptococcal* disease

Reye's syndrome

Subacute sclerosing panencephalitis

Encephalitis in early childhood (2 months – 3 years)

Cerebrovascular disease, stroke and like illness

Vitamin K deficiency bleeding III

Congenital cytomegalovirus

Thrombosis in childhood

Internal abdominal injury due to child abuse

Suspected fatal adverse drug reaction in children

Severe complications of varicella (chickenpox) in hospitalised children

Invasive fungal infections in VLBW infants

Langerhans cell histiocytosis

Tuberculosis

Severe hyperbilirubinaemia
Surveillance Period: May 2003 – May 2005
Investigator: Dr Donal Manning
Published Paper: Prospective surveillance study of severe hyperbilirubinaemia in the newborn in the United Kingdom and Ireland. Manning DJ, Maxwell MJ, Todd PJ, Platt MJ *Arch. Dis. Child. Fetal Neonatal Ed. 2007;* ***92****: F342-F346*

Thyrotoxicosis in children
Surveillance Period: September 2004 – September 2005
Investigator: Dr Scott Williamson
Published Paper: Thyrotoxicosis in childhood. 20th BPSU Annual Report 2005/06. BPSU London 2006

Non-type 1 diabetes in children under 17 years
Surveillance Period: October 2004 – October 2005
Investigator: Ms Linda Haines, Dr Kay C Wan, Mr Richard Lynn, Dr Tim Barrett, Dr Julian H Shields
Published Paper: Rising incidence of type 2 diabetes in children in the United Kingdom. Haines L, Wan KC, Lynn R, Barrett TG, Shield JP *Diabetes Care*. 2007; **30(5)**: 1097-1101

Early onset eating disorders in children under 13 years
Surveillance Period: March 2005 – March 2006
Investigator: Dr Dasha Nicholls, Mr Richard Lynn, Dr Russell Viner
Published Paper: 21th BPSU Annual Report 2006/07. BPSU London 2007

Neonatal herpes simplex virus (HSV)
Surveillance Period: January 2004 – January 2007
Investigator: Dr Pat Tookey, Mr Richard Lynn, Professor Catherine Peckham
Published Paper: 21th BPSU Annual Report 2006/07. BPSU London 2007

Malaria
Surveillance Period: January 2006 – January 2007
Investigator: Dr Shamez Ladhani
Published Paper: 22nd BPSU Annual Report 2007/08. BPSU London 2008

Methicillin-Resistant Staphylococcus (MRSA)
Surveillance Period: June 2005 – June 2007
Investigator: Dr Alan Johnson, Dr Catherine Goodall, Dr Mike Sharland
Published Paper: 22nd BPSU Annual Report 2007/08. BPSU London 2008

Childhood scleroderma
Surveillance Period: July 2005 – July 2007
Investigator: Dr Anne Herrick, Dr Eileen Baildam
Published Paper: 22nd BPSU Annual Report 2007/08. BPSU London 2008

Feto-maternal alloimmune thrombocytopenia
Surveillance Period: October 2006 – October 2008
Investigator: Dr Marian Knight
Published Paper: 23rd BPSU Annual Report 2008/09. BPSU London 2009

Vitamin K deficiency bleeding
Surveillance Period: October 2006 – October 2008
Investigator: Dr Alison Busfield, Dr A McNinch
Published Paper: 23rd BPSU Annual Report 2008/09. BPSU London 2009

APPENDIX B - Publications and Presentations 2008-09

BPSU

Presentations

1. RL Knowles, R Lynn, H Friend, S Mitchell, C Michie, C Ihekweazu. The British Paediatric Surveillance Unit: A public health evaluation. Royal College of Paediatrics and Child Health 13th Spring Meeting, York, 2009. *Arch Dis Child 2009*; **94**(Suppl-1): Abstract G221
2. H Friend, C Ihekweazu, RL Knowles, S Mitchell, C Michie, R Lynn. Evaluating the British Paediatric Surveillance Unit: Views from users of the system. Royal College of Paediatrics and Child Health 13th Spring Meeting, York, 2009. *Arch Dis Child 2009*; **94**(Suppl-1): Abstract G246

Congenital adrenal hyperplasia

Presentations

3. JM Khalid, C Dezateux, J Oerton, C Kelnar, P Hindmarsh, RL Knowles. Prevalence and clinical features of newly diagnosed congenital adrenal hyperplasia in the UK. Royal College of Paediatrics and Child Health 13th Spring Meeting, York, 2009. *Arch Dis Child 2009;* **94**(Suppl-1): Abstract P6
4. RL Knowles, JM Khalid, J Oerton, P Hindmarsh, C Kelnar, C Dezateux. National surveillance of congenital adrenal hyperplasia in children. 36th Meeting of the British Society for Paediatric Endocrinology and Diabetes 2008. *Endocrine Abstracts* 2008;**17**(Nov):S1
5. RL Knowles, JM Khalid, J Oerton, P Hindmarsh, C Kelnar, C Dezateux. Prevalence and clinical features of congenital adrenal hyperplasia (CAH) in a multiethnic population without newborn screening. 6th ISNS European Regional Meeting, 27th April 2009, Prague, Czech Republic

Congenital cytomegalovirus

Presentations

6. CS Peckham, M Sharland, PA Tookey. National surveillance of symptomatic congenital CMV in the UK and Ireland, 2001-2002: confirmed cases: presentation and outcome. Congenital CMV Conference, Centers for Disease Control and Prevention, Atlanta, USA. November 2008 (*Poster*)

Early onset eating disorders

Presentations

7. D Nicholls. Early onset eating disorders – Developing a psychiatry reporting scheme. BPSU Conference March 2009, London, UK
8. D Nicholls, R Lynn, R Viner, L Phinas, S Madden. Eating Disorders in Children: are the numbers really increasing? Faculty of Child and Adolescent Psychiatry Conference. September 2008, Liverpool, UK

Emerging infections in children

Presentations

9. D Shingadia. Emerging infections in children. BPSU Conference March 2009. London, UK

Feto-maternal alloimmune thrombocytopenia

Presentations

10. M Knight**.** Feto-maternal alloimmune thrombocytopenia–Developing joint paediatric and obstetric reporting. BPSU Conference March 2009, London, UK

***Haemophilus influenzae* B vaccine failures**

Presentations

11. S Ladhani, P Heath, RJ Aibara, M Ramsay, M Slack, M Hibberd, A Pollard, R Moxon, R Booy. Long-term follow-up study of children with *Haemophilus influenzae* serotype B vaccine failure to determine long term complications and the risk of serious infections. *Arch Dis Child;* 2008; **93**(Suppl-1): Abstract 80

Herpes in children

Presentations

12. R Reading, P Tookey. Herpes in children. BPSU Conference March 2009, London, UK

HIV/AIDS

Papers

13. A Judd, R Ferrand, E Jungmann, C Foster, J Masters, B Rice, H Lyall, P Tookey, K Prime. Vertically acquired HIV diagnosed in adolescence and early adulthood in the United Kingdom and Ireland: findings from national surveillance. *HIV Medicine* 2009; **10**:253-256
14. CL Townsend, BA Willey, M Cortina-Borja, CS Peckham, PA Tookey. Antiretroviral therapy and congenital abnormalities in infants born to HIV-infected women in the UK and Ireland, 1990-2007. *AIDS* 2009; **23**:519-524

15. A Riordan, A Judd, K Boyd, D Cliff, K Doerholt, H Lyall, E Menson, K Butler, D Gibb; Collaborative HIV Paediatric Study. Tenofovir use in human immunodeficiency virus-1-infected children in the United Kingdom and Ireland. *Pediatr Infect Dis J* 2009; Mar;**28(3**):204-9

16. C Foster, A Judd, P Tookey, G Tudor-Williams, D Dunn, D Shingadia, K Butler, M Sharland, H Lyall, D Gibb. Young people in the UK and Ireland with perinatally acquired HIV: the paediatric legacy for adult services. *AIDS Patient Care STDS.* 2009 March 2009, **23(3)**: 159-166. doi:10.1089/apc.2008.0153

17. A De Ruiter,. D Mercey, J Anderson, R Chakraborty, P Clayden, G Foster, C Gilling-Smith, D Hawkins, N Low-Beer, H Lyall, S O'Shea, Z Penn, J Short, R Smith, S Sonecha, P Tookey, C Wood, G Taylor. British HIV Association and Children's HIV Association guidelines for the management of HIV infection in pregnant women 2008. *HIV Medicine* 2008; **9**:452-502

18. The Collaboration of Observational HIV Epidemiological Research Europe (COHERE) study group. Response to combination antiretroviral therapy: variation by age. *AIDS* 2008; **22**:1463-1473

19. A Kekitiinwa, KJ Lee, AS Walker, A Maganda, K Doerholt, SB Kitaka, A Asiimwe, A Judd, P Musoke, DM Gibb; Collaborative HIV Paediatric Study (CHIPS) Steering Committe; Mulago Cohort Team. Differences in factors associated with initial growth, CD4, and viral load responses to ART in HIV-infected children in Kampala, Uganda, and the United Kingdom/ Ireland. *J Acquir Immune Defic Syndr* 2008; Dec 1:**49(4)**:384-92

20. CL Townsend, M Cortina-Borja, CS Peckham, A de Ruiter, H Lyall, PA Tookey. Low rates of mother-to-child transmission of HIV following effective pregnancy interventions in the United Kingdom and Ireland, 2000-2006. *AIDS* 2008; **22(8)**:973-81

21. C Townsend, M Cortina-Borja, C Peckham, P Tookey. Trends in management and outcome of pregnancies in HIV infected women in the United Kingdom and Ireland, 1990-2006. *BJOG* 2008; **115**:1078-1086

22. R Chakraborty, CJ Smith, D Dunn, H Green, T Duong, K Doerholt, A Riordan, H Lyall, P Tookey, K Butler, CA Sabin. D Gibb, D Pillay. HIV-1 drug resistance in HIV-1 infected children in the UK from 1998 to 2004. *PIDJ* 2008; **27**:457-59

23. CD Hankin, EGH Lyall, CS Peckham, JI Masters, PA Tookey. In utero exposure to antiretroviral therapy; **21(7)**: 809-816

Presentations

24. H Lyall. The contribution of paediatric surveillance to HIV monitoring: The UK experience. BPSU Conference March 2009. London, UK

25. J Masters, CS Peckham, PA Tookey. Monitoring cancer and death in uninfected children born to HIV-infected women in England and Wales 1996-2006. Royal College of Paediatrics and Child Health 13th Spring Meeting, York, 2009. *Arch Dis Child* 2009; **94**(Suppl-1): Abstract G30

26. H Haile-Selassie, J Masters, CL Townsend, PA Tookey. HIV infection in Central and Eastern European pregnant women living in the UK/ Ireland: data from national Surveillance 1992-2007. BHIVA conference, Liverpool, UK. 2009 HIV Medicine 2009; **10**(Supp 1):42 *(Poster)*

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29. L Bansi, C Thorne, PA Tookey, C Sabin. Linkage of the UK Collaborative HIV Cohort (CHIC) study and National Study of HIV in Pregnancy and Childhood (NSHPC) to assess ART patterns in pregnant women. BHIVA conference, Liverpool, 2009 *HIV Medicine* 2009; **10**(Supp 1):27 (*Poster*)

30. CL Townsend, PA Tookey, M Cortina-Borja. Premature delivery and mother-to-child transmission: risks and benefits of HAART in pregnancy. 16th Conference on Retroviruses and Opportunistic Infections (CROI), Montreal, Canada. 8-11 February 2009

31. CL Townsend, M Cortina-Borja, CS Peckham, H Lyall, A de Ruiter, PA Tookey. Very Low Risk of Mother-to-Child Transmission (MTCT) in Women on HAART Who Achieve Viral Suppression: Data from the United Kingdom and Ireland, 2000-2006. Royal College of Paediatrics and Child Health 12th Spring Meeting, York, 2008. *Arch Dis Child* 2008; **93**(Suppl-1): Abstract P8

32. BA Willey, CL Townsend, M Cortina-Borja, CS Peckham, PA Tookey. Congenital abnormalities and in utero exposure to antiretroviral therapy in the UK and Ireland. Royal College of Paediatrics and Child Health 12th Spring Meeting, York, UK, 2008. *Arch Dis Child* 2008; **93**(Suppl-1)

33. CL Townsend, M Cortina-Borja, CS Peckham, H Lyall, A de Ruiter, PA Tookey. Very Low Risk of Mother-to-Child Transmission (MTCT) in Women on HAART Who Achieve Viral Suppression: Data from the United Kingdom and Ireland, 2000-2006. 15th Conference on Retroviruses and Opportunistic Infections (CROI), Boston, USA. 3-6 February 2008. Abstract S-108. Poster #653. (*Poster*)
34. K Prime, R Ferrand, C Foster, A Judd, J Masters, H Lyall, E Jugmann. First presentation of vertically acquired HIV infection in adolescence. BHIVA 2008. *HIV Medicine;* **9** (Supp 1):3
35. Townsend CL, Schulte J, Thorne C, Dominguez K, Cortina-Borja M, Peckham CS, Tookey PA, Bohannon B, Newell M-L. Differences in the association between HAART in pregnancy and premature delivery: a comparison of three studies in the United States and Europe. XVII International AIDS conference, Mexico City, Mexico. 3-8 August 2008 Abstract THPE0248 (*Poster*)
36. PA Tookey, J Masters, I Vaughan, F Lyons, S Farthing, A Namiba, M Dixon, H Lyall, G Tudor- Williams. NSHPC, AIAU and Children's HIV Association collaboration. Reasons for Perinatal HIV Transmissions in England, 2002-2005. XVII International AIDS conference, Mexico City, Mexico. 3-8 August 2008 Abstract MOPE0498 (*Poster*)
37. AS Walker, KL Boyd, K Doerholt, H Lyall, E Menson, K Butler, P Tookey, A Riordan, D Shingadia, A Judd, G Tudor-Williams, D Gibb. To overdose or under dose? The question of Kaltetra in children in the UK/Irish Collaborative HIV Study (CHIPS). Ninth International Congress on Drug Therapy in HIV Infection, Glasgow. UK November 2008 (Oral O123); *J International AIDS Society* 2008, **11**(Suppl 1):08
38. J Franklin, A Douglas, A Clarke, G Nartey, P Tookey, M Cortina-Borja, J Smith, G Taylor. Interpretation of Serum α-fetoprotein, Human Chorionic Gonadotrophin and the Risk of Down's Syndrome in Pregnant Women Infected with HIV. (Poster 655) CROI 2008, Boston, USA. (*Poster*)

Idiopathic intracranial hypotension

Presentations

39. YY Mathews. *Facelift on a 19th Century Mystery – IIH in Children.* Pop Watkins Lecture, Wales Paediatric Society Spring Meeting. May 2008

Intussusception in children less than 12months of age

Publications

40. L Samad, S Marven, H El Bashir, JC Cameron, R Lynn, B Taylor. Intussusception in children less than 12 months of age: a UK national surveillance study. *J Pediatr Surg* 2008; Nov; **43(11)**:2136.

Langerhans cell histiocytosis

Publications

41. J A Salotti, V Nanduri, M S Pearce, L Parker, R Lynn, K P Windebank. Incidence and clinical features of Langerhans cell histiocytosis in the UK and Ireland. *Arch Dis Child* 2009; **94**: 376 – 380

Malaria

Presentations

42. S Ladhani, M Garbash, A Riordan, P Chiodini, C Whitty, D Shingadia. The burden of imported childhood malaria in the UK and Ireland. *Arch Dis Child;* 2008; **93**((Suppl-1): Abstract 83

Medium chain acyl CoA dehydrogenase deficiency (MCADD)

Publications

43. JM Khalid, J Oerton, M Cortina-Borja, BS Andresen, et al. UK Collaborative Study of Newborn Screening for MCADD. Ethnicity of children with homozygous c.985A>G medium-chain acyl-CoA dehydrogenase deficiency: findings from screening approximately 1.1 million newborn infants. *J Med Screen* 2008;**15**:112-7
44. JV Leonard, C Dezateux. Newborn screening for medium chain acyl CoA dehydrogenase deficiency. *Arch Dis Child* 2009; **94(3)**:235-8. [Epub 2008 Oct 6]

Presentations

45. J Oerton, JM Khalid, BS Andresen, C Dezateux, et al. Spectrum of Medium Chain Acyl CoA Dehydrogenase (MCAD) mutations identified from newborn screening of 1.14 million ethnically diverse infants. 6th ISNS European Regional Meeting, 27th April 2009, Prague, Czech Republic

Methicillin-resistant Staphylococcus aureus (MRSA) in children

Presentations

46. A Johnston. The rise of Methicillin-resistant Staphylococcus aureus in children. BPSU Conference, March 2009, London, UK

Neonatal hyperbilirubinaemia

Presentations

47. D Manning. Neonatal hyperbilirubinaemia – Informing NICE guidelines. BPSU Conference March 2009, London, UK

Non-type 1 diabetes

Publications

48. JP Shield, R Lynn, KC Wan, L Haines, TG Barrett. Management and 1 year outcome for UK children with type 2 diabetes. *Arch Dis Child* 2009; **94(3)**:206-9

Progressive intellectual and neurological deterioration (PIND)

Publications

49. C Verity, AM Winstone, L Stellitano, D Krishnakumar, R McFarland, R Will. The clinical presentation of mitochondrial diseases in children with progressive intellectual and neurological deterioration (PIND): a national prospective population-based study. (In press)

Presentations

50. C Verity, L Stellitano, AM Winstone. Leigh syndrome – a familiar phenotype but a disappearing disease?" Royal College of Paediatrics and Child Health 13th Spring Meeting, York, 2009. *Arch Dis Child* 2009; **94**(Suppl-1): Abstract G182. (*Poster*)
51. C. Verity, L. Stellitano, AM Winstone, D. Krishnakumar. "Is it possible to diagnose mitochondrial disease on the basis of the clinical presentation?" British Paediatric Neurology Association Annual Meeting. January 2009. Birmingham, UK
52. A. Maw, L. Stellitano, AM Winstone, C. Verity. "The clinical features of children with unclassified leucoencephalopathy in a national prospective population study." British Paediatric Neurology Association Annual Meeting. January 2009. Birmingham, UK *(Poster)*
53. AM Winstone, C Verity, L. Stellitano, R. Will, A. Nicoll. "More than 10 years of national surveillance for variant CJD in children: The UK experience and its significance for Europe". 2nd European Congress of the Academy of Paediatrics. October 2008. Nice, France
54. C Verity, L. Stellitano, AM Winstone. A spectrum of neurodegenerative disease in UK children. Findings of a prospective national study after almost ten years of surveillance. *Arch Dis Child* 2008; **93**(Suppl-1): Abstract 41-42
55. C. Verity, L. Stellitano, AM Winstone. "Are UK children developing v CJD?" European and Associated Countries Collaborative CJD Surveillance Group. May 2008 Riga, Latvia
56. D Krishnakumar, C. Verity, L. Stellitano, AM Winstone. A national prospective population-based study of children with mitochondrial disease: clinical presentation and method of diagnosis in 101 cases. British Paediatric Neurology Association Annual Meeting, January 2008, Leeds, UK

Severe complications of varicella in hospitalised children

Presentations

57. JC Cameron. Varicella surveillance – Implications for immunisation policy. BPSU Conference March 2009, London, UK

Scleroderma

Presentations

58. A Herrick, H Ennis, E Baildam. Incidence of childhood scleroderma in the UK and Ireland. Royal College of Paediatrics and Child Health 13th Spring Meeting, York, 2009. *Arch Dis Child* 2009; **94**(Suppl-1): Abstract G206

Suspected fatal adverse drug reactions

Publications

59. K Cheng, S Masters, T Stephenson, R Cooke, R Ferner, M Ashworth, A J Nunn. Identification of suspected fatal adverse drug reactions by paediatricians: a UK surveillance study. *Arch Dis Child* 2008; **93**: 609 – 611

Tuberculosis

Publications

60. S S Teo, A Riordan, M Alfaham, J Clark, MR Evans, M Sharland, V Novelli, JM Watson, P Sonnenberg, A Hayward, J Moore-Gillon, D Shingadia for the British Paediatric Surveillance Unit Childhood Tuberculosis Study Group. Tuberculosis in the United Kingdom and Republic of Ireland. *Arch Dis Child* 2009; **94**: 263 - 267
61. S S Teo, A Riordan, M Alfaham, J Clark, MR Evans, JM Watson, A Riordan, P Sonnenberg, J Clark , A Hayward, M Sharland, J Moore-Gillon , V Novelli, D Quinn, D Shingadia for the British Paediatric Surveillance Unit Childhood Tuberculosis Study Group. An evaluation of the completeness of reporting of childhood tuberculosis. *Eur Respir J* 2009; **34**: 1–4 DOI: 10.1183/09031936.00031808

Vitamin K prophylaxis

Presentations

62. A McNinch. Vitamin K prophylaxis – A moving goalpost. BPSU Conference March 2009, London, UK
63. A Busfield A McNinch JH Tripp Vitamin K prophylaxis; recent trends in UK practice XIL Congresso Nationale della Societa Italiana di Neonatologia. Societa Italiana di Neonatologia. 13-16 May 2008 Torino, Italy

APPENDIX C - Membership of Executive Committee 2008- 2009

Professor Allan Colver*	Chair
Mrs Sue Banton	Patient and Carers Advisory Group
Dr Colin Campbell	Medical Adviser (infectious disease)
Dr Paul Daubeney	Co-opted
Professor Carol Dezateux	Institute of Child Health (London)
Dr Shankar Kanumakala	Co-opted
Ms Linda Haines	Royal College of Paediatrics and Child Health Science and Research Department
Dr Sue Hobbins	Royal College of Paediatrics and Child Health Treasurer
Dr Rachel Knowles	Medical Adviser (non-infectious disease)
Mr Richard Lynn	Scientific Coordinator
Dr Colin Michie	Co-opted
Dr Simon Mitchell	Co-opted
Professor Neena Modi	Royal College of Paediatrics and Child Health Science and Research Department
Dr Richard Pebody	Health Protection Agency
Dr Richard Reading	Co-opted
Professor Terence Stephenson*	Royal College of Paediatrics and Child Health Science and Research Department
Dr Delane Shingadia	Co-opted
Mrs Ann Seymour	Patient and Carers Advisory Group
Dr Katy Sinka	Health Protection Scotland
Dr Ted Wozniak	Department of Health (observer)
Mr Zoltan Bozoky	Department of Health (observer)

* Stepped down in 2009

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