Royal College of Paediatrics and Child Health

British Paediatric Surveillance Unit

15th Annual Report 2000-2001

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British Paediatric Surveillance Unit – Annual Report 2000-2001

Compiled and edited by Richard Lynn, Hilary Kirkbride, Jugnoo Rahi and Chris Verity, September 2001

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"A Special message" from the CMO on the occasion of our 15th anniversary

The BPSU has a long established and admirable track record in the study of uncommon childhood health problems. Its strengths lie in its ability to deliver population based studies with very high levels of reporting from nearly all paediatricians in the British Isles. In doing so the information provided offers virtually unique insights into disorders and also offers opportunities for monitoring changes in health. The BPSU was developed by a number of key agencies (including the PHLS, RCPCH - former British Paediatric Association - and the Institute of Child Health London). Researchers use the system devised by the BPSU to conduct their studies. Several important studies have been commissioned by the Department of Health itself which now provides core funding to the Unit.

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

Professor Liam J Donaldson
Chief Medical Officer

Foreword

Fifteen Years of Protecting Child Health

The British Paediatric Surveillance Unit (BPSU) was set up in 1986. The founders of the BPSU scheme and all those who have contributed to it can congratulate themselves on producing a body of work that has significantly contributed to the health of children. The BPSU was set up jointly by the British Paediatric Association, the Institute of Child Health (London), the Public Health Laboratory Service, the Communicable Disease Surveillance Centre (Scotland) and the Faculty of Paediatrics of the Royal College of Physicians (Ireland). It partly resulted from the experience that Professor Euan Ross acquired whilst planning and performing the National Encephalopathy Study. He and others saw that a Unit which co-ordinated national studies of childhood disorders would be able to channel the accumulated experience of all the consultant paediatricians in the UK. Professor Ross retired from clinical work this year and so it is particularly relevant to mark his important contribution to the BPSU as a co-founder, past member and chair of the BPSU Executive Committee.

The BPSU Executive Committee has considered many proposals for surveillance studies over the years. Each study has to fulfill a number of criteria for acceptance. Perhaps the two most important criteria are a) that the study attempts to answer a question of scientific importance and b) that the outcome is of clear relevance to public health. It is interesting to review the studies that have been performed over the years in the light of these criteria. At present 47 have been completed and 9 are under way.

The studies fall into a number of distinct groups, although some do not fit neatly into one or other category. Those of infectious diseases in children form a big group –14 in all. One of the first was of haemolytic uraemic syndrome (HUS). This remains a topical subject – a further BPSU study of the same condition has just been completed. The recent study showed that most cases of HUS in the UK are due to verocytotoxin-producing *E.coli* O157 and in spite of the impression given by the newspapers most cases are sporadic – outbreaks are uncommon. As HUS surveillance has been undertaken by several other national surveillance units it has been possible to make international comparisons.

Surveillance of congenital infections by the BPSU has helped to provide a basis for deciding whether or not to perform national screening programmes. For instance it was found that there were sufficient cases of transmissible syphilis and of congenital rubella to justify continued screening. In contrast other BPSU studies have demonstrated that there are not enough cases of congenital toxoplasmosis and of neonatal herpes to make national screening worthwhile. More recently clinician reporting by obstetricians through the Royal College of Obstetricians and Gynaecologists, supplemented by paediatric reporting via the BPSU and unlinked anonymous HIV surveillance, has demonstrated that HIV is prevalent throughout the UK. It is estimated that routine universal voluntary antenatal HIV testing would be cost effective for London and possibly elsewhere.

The next largest group of BPSU studies is of non-infectious conditions that are rare but nevertheless important. Surveillance of Kawasaki disease raised the profile of the disorder amongst paediatricians with the result that the incidence apparently rose. This was probably because a greater number of cases were diagnosed due to increased awareness rather than because there was an epidemic! Surveillance of Rett syndrome and juvenile dermatomyositis also brought these important disorders to the attention of practising clinicians. A study of a relatively rare condition that had more general importance was that of medium chain acyl co-enzyme A dehydrogenase (MCAD) deficiency, in which susceptible children may have a severe encephalopathy. This condition might cause death after an apparently minor illness and this could be wrongly classified as sudden infant death syndrome. The MCAD study also complemented the BPSU study of Reye Syndrome which is a rare non-inflammatory encephalopathy associated with hepatic dysfunction. National surveillance for Reye Syndrome was transferred to the BPSU in 1986. This surveillance documented the dramatic reduction in the incidence of “classic” Reye Syndrome after the Committee on Safety of Medicines issued warnings about the use of aspirin in children. The BPSU study of MCAD deficiency served to highlight the fact that a number of metabolic disorders may present with a “Reye-like” illness which is clinically and pathologically similar to Reye Syndrome. Thus two BPSU studies have shed light on each other and both have helped to illuminate an important public health issue – the use of aspirin in young children.

The BPSU is not able to survey common conditions, because big numbers (in this context, more than about 300 cases a year) overload the reporting system for the paediatricians who fill in the questionnaires, the BPSU office and the surveillance groups who gather the data. However it has been possible to answer important questions about some disorders that are relatively common in the general population but uncommon in childhood. Thus there have been two studies of diabetes in children and more recently there have been studies of inflammatory bowel disease, blindness and (currently) stroke. Investigators have focused on questions about these conditions that are peculiar to childhood.

Children are susceptible to their physical and social surroundings. There have been studies of drowning and of fatal or severe reactions to food ingestion. There have also been three studies of

various aspects of child abuse – Munchausen's syndrome by proxy/non accidental poisoning and suffocation, sub-dural haemorrhage and more recently acute abdominal injury in the context of suspected child abuse. The BPSU has provided a means of concentrating and correlating clinical experience of these sometimes controversial areas of child care.

Some surveillance work has provided information about treatment. For instance there have been three studies of haemolytic disease of the newborn. These have been important because of the changing use of vitamin K prophylaxis in neonates. Because of the concern that injected vitamin K might predispose children to later malignancy, the routine parenteral use this vitamin has changed and there are now several schedules for oral administration. The most recent study of vitamin K deficiency bleeding will be able to chart the effects of changes in management. Another example is the survey of cerebral oedema and death in diabetic ketoacidosis which provided information about the possible relationship between these outcomes and the treatment of children in diabetic coma.

In view of the high level of public concern about the use of some vaccines in children, it is perhaps surprising that there have only been a couple of studies directly related to vaccination. One surveyed meningo-encephalitis associated with MMR vaccine and the other surveyed acute flaccid paralysis in order to ascertain whether or not polio had been eradicated from the UK. Both of these surveys were complemented by data from laboratories to maximise ascertainment, which is the case for many BPSU studies. Because vaccinations are given to whole populations the study of possible vaccine side effects may involve numbers that are too large for the BPSU system. Also any such problems may be remote from the time of vaccination and the children with symptoms that are raising concern may not come to the attention of the consultant paediatricians who fill in the BPSU surveillance card. Despite these constraints the BPSU has had meetings with the Medicines Control Agency, the proposal being that the BPSU system could be used for targeted surveillance of drug and possibly vaccine side effects. We hope that this will be an area of future development.

This brief review is not able to give more than a flavour of all the studies that have been carried out by the BPSU. Each year the Annual Report has summarised the findings and there have been many publications in peer – reviewed journals (more than 150 at the last count).

At present the level of support for the work of the Unit is high. There is still an excellent response from all the paediatricians in the country who fill in the monthly orange surveillance card and who respond to questionnaires from the various surveillance groups. There is also tremendous support from the units that continue to have an active role in the organisation and management of the BPSU. These are the Royal College of Paediatrics and Child Health, the Communicable Disease Surveillance Centre of the Public Health Laboratory Service, the Institute of Child Health in London and the Scottish Centre for Infection and Environmental Health. The Department of Health continues to make a very significant financial contribution to the funding of the BPSU.

Each time that I write or talk about the BPSU I emphasise the key importance of the paediatricians who return the orange card. Certain guidelines that have been produced recently with regard to patient confidentiality have caused some concern amongst paediatricians. These issues were discussed in the foreword of the BPSU Annual Report last year. A paper about the issues of confidentiality and consent was prepared by the BPSU Executive Committee and has been discussed by the Executive Committee of the RCPCH. Professor Liam Donaldson, the CMO, made time at the end of last year to discuss these issues in some detail and he was both helpful and supportive. I am therefore particularly pleased that he has contributed to this Annual Report. Dr. Sheila Adam, the Deputy CMO, is leading on confidentiality issues and is also aware that strict interpretations of the guidelines on confidentiality might have the effect of stopping some child and public health surveillance. I hope that the information which is produced by the BPSU Executive Committee has the effect of reassuring paediatricians about their continued involvement with the surveillance unit studies. Any interested paediatrician is welcome to obtain a copy of the BPSU paper on confidentiality from Richard Lynn the Scientific Co-ordinator of the BPSU. A summary of the BPSU position on confidentiality can be seen on the College website.

Support for the BPSU has come from organisations that represent the parents of children with rare disorders, as was shown at a meeting last December entitled "Rare Disorders – the Need for A New Approach". This was the first national conference of the UK Rare Disease Alliance and took place at the Institute of Child Health in London. I was asked to outline the work of the BPSU and mentioned the issues of consent and confidentiality. Those attending the conference voiced tremendous support for the BPSU. They represented a large number of parent support groups and many of them reported the frustrations that parents feel when they are trying to understand the rare disorders that affect their children. The organisation "Contact-a-Family" has helped very many of them by setting up networks to provide information. The delegates at the meeting seemed all too aware of the need to pool resources and information in order to help children whose lives are so seriously affected by rare disorders. Because of this I am pleased that the BPSU Executive Committee

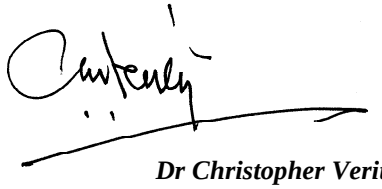
now includes a lay member, Mrs Carol Youngs, who is a representative of the Parent and Carers Group of the RCPCH. Carol is the Assistant Director of "Contact-a-Family" and is therefore ideally placed to improve communication between the BPSU and those who represent families afflicted by rare disorders of childhood.

One person who has worked extremely hard to ensure that patient confidentiality is compatible with continued public health surveillance is Dr. Angus Nicoll. Angus became Medical Advisor to the BPSU in 1994 and has just retired from that post, having given much more than the nominal two sessions that were generously provided by his employer, the Public Health Laboratory Service. He has been tireless in his support for the work of the BPSU and indeed all aspects of paediatric surveillance in the UK and abroad. He led the development of the International Network of Paediatric Surveillance Units. He has combined a clear strategic overview of the need for rational child health surveillance with the energy and drive to study in detail the projects and proposals that are put to the BPSU. He has now taken over as Director of the Communicable Disease Surveillance Centre (CDSC). Fortunately the BPSU Executive Committee will not lose him - he will remain on the Committee as the PHLS representative. All those who have worked with him are grateful for the effort that he has put into his role as Medical Advisor.

Angus Nicoll has been replaced as Medical Advisor by Dr. Hilary Kirkbride, a specialist registrar who works at CDSC. Two sessions of her time are given by the PHLS to support the BPSU. She will be working with the other Medical Advisor, Dr. Jugnoo Rahi, the ophthalmological epidemiologist, who is supported by the Institute of Child Health (London). The two Medical Advisors have a most important role in supporting and advising the Executive Committee and the individual surveillance groups who are planning and carrying out surveillance studies.

The BPSU Executive Committee is some other members who will be greatly missed. Angus Clarke, Chris Kelnar and Brent Taylor have all been on the Committee for more than 5 years and they are therefore retiring. The Committee meets monthly, so they and the other members have put in a lot of work for which they deserve grateful thanks. Many thanks also to Richard Lynn, the Scientific Co-ordinator, and his assistant Myra Schehtman. Without their continuing hard work the BPSU system would not function and paediatric surveillance would not have developed so well – at home or abroad! The BPSU is part of the Research Division of the College and thus receives valuable support from Linda Haines the Principal Research Officer and Professor Richard Cooke, the College Vice-President – they were both instrumental in helping the BPSU to obtain continued funding from the Department of Health.

It can be seen from the above that the work of the BPSU is multi-faceted. It relies on a complex interaction of activity in a lot of different areas. It will only continue to function if paediatricians support it. At present the signs are good. There is an excellent response rate to the monthly orange card and to the surveillance questionnaires. International links have been strengthened by the formation of the International Network of Paediatric Surveillance Units (INoPSU). Following the excellent INoPSU meeting in Ottawa last year we are planning with Professor Ian Booth and the Academic Board a further meeting which will take place in conjunction with the College Annual Meeting in York next spring. This is one example of the fruitful interactions that occur within the RCPCH and in this respect the BPSU is grateful for the support it receives from the President David Hall, the Hon Secretary Patricia Hamilton and many others. Organisations that support parent and carers value the work of the BPSU and understand the need to study rare but important disorders of childhood. With all this enthusiastic help I am sure that the BPSU will continue to thrive for the next 15 years – and longer!



Dr Christopher Verity
Chairman, BPSU Executive Committee

1 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 and by high rates of disabling sequelae or death. Most pose a large financial and emotional burden for affected children, their families and health systems.

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

The Unit's main concern is that of epidemiological surveillance. This is 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 collaborate in the BPSU: the Royal College of Paediatrics and Child Health (RCPCH), Public Health Laboratory Service (PHLS), PHLS Communicable Disease Surveillance Centre (CDSC), Department of Epidemiology at the Institute of Child Health, University of London (ICH), Scottish Centre for Infection and Environmental Health (SCIEH) which administers the scheme in Scotland and the Faculty of Paediatrics of the Royal College of Physicians of Ireland. As the BPSU monitors conditions of public health importance, an observer from the Department of Health also attends the BPSU's Executive Committee which meets 4-6 weekly to consider individual applications and the progress of studies.

The aims and key challenges of the Unit are summarised in the boxes below.

This report mainly focuses on activities undertaken during the year 2000. Reference is also made to studies and activities which have commenced in the year 2001.

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
- respond rapidly to public health emergencies.

June 1995 - adapted from prior documentation

Key challenges – 2000/2001

The BPSU's key challenges are to:

- facilitate research and provide expert advice to members of the RCPCH and other investigators using the BPSU
- continue to disseminate information about the BPSU to the wider scientific community
- respond rapidly to challenges and public health emergencies
- ensure future funding for the BPSU
- critically evaluate and validate the reporting system
- further develop links with other national and international units involved in the surveillance of rare conditions
- educate professionals concerning the value and mechanisms of epidemiological surveillance.

2 How the surveillance system works

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

The number of conditions under surveillance is usually limited to 12 and there is keen competition for places on the BPSU card.

Selection of studies for inclusion in the scheme

The BPSU application procedure consists of two phases: in phase one, a short study protocol is requested covering no more than two sides of A4 paper. This should include the background to the proposed study, a case definition, likely number of reports per month, the questions which the study aims to answer and details of financial and academic support. At this stage the Scientific Coordinator and Medical Advisers can offer guidance on the application before it is submitted to the BPSU Executive Committee (BEC). The BEC, which meets every 4-6 weeks, comprises of consultant paediatricians (general and specialist), epidemiologists and specialists in public health.

If the BEC agrees that the protocol is eventually suitable, a phase two application is requested. This should provide full details of the methodology; aims of the study; the practicalities of how the study is to be administered and funding source. Factors that increase the likelihood of a study being accepted are listed in the box. The BPSU will always help investigators to develop potentially valuable studies, especially those with less experience in surveillance methods.

For a number of reasons it may be considered that the BPSU system is not best suited for answering the objectives of a proposed study. The condition may be too common and therefore may place too great a burden on paediatricians for reporting or follow-up; there may be no suitable case definition; the aim of the study may constitute audit rather than surveillance; or data may be obtainable more easily elsewhere. If a study is not accepted, the committee always tries to advise the applicant on alternative means of undertaking the work.

Though considered stringent, the advantages of this procedure are two-fold. Firstly, respondents know that a study must be methodologically sound for it to appear on the orange card, and are thus more likely to contribute data. Secondly, prospective investigators know that if their study is placed on the card they are assured of a high level of involvement from clinicians.

Finally, all studies must have the approval of the appropriate Multi Ethics Research Committee. Though this is the responsibility of the investigators, the BPSU insists that there is compliance with the principles of the Caldicott Report (Report on the Review of Patient-Identifiable Information, NHSE, December 1997) on data confidentiality and information flow and procedures that come from it. The BPSU Executive Committee has produced a document that outlines its position on ethics and confidentiality in relation to surveillance and this is available from the BPSU office or can be viewed within the library section of the RCPCH web site (www.rcpch.ac.uk).

Factors that favour acceptance by the British Paediatric Surveillance Unit

- Scientific importance.
- Proposals with outcomes of clear importance to public health.
- Rarity of the condition, though short-term or geographically limited studies of commoner disorders are considered.
- Uniqueness, priority will not be given if similar studies have recently been undertaken or if other data sources are readily available (although the BPSU encourages the use of alternative data sources for validation and completeness of reporting).
- Attention to detail, in terms of clear achievable objectives, practicability, patient confidentiality and resources.
- Practicality and limited workload placed on the reporting paediatricians.
- Ethics approval.

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. Mailing lists are regularly updated by the BPSU office by monitoring new consultant appointments, retirements etc.

Where necessary to improve case ascertainment consultants working in a number of other specialties have been invited to participate in the scheme. For example, since 1992 pathologists who are not members of the RCPCH have also been included in the reporting scheme. In addition, most studies of infections also use laboratory reports to microbiologists. Current studies that are benefiting from such multiple ascertainment include HIV/AIDS, congenital rubella, Group b streptococcus disease and most recently the cerebral vascular disease and thrombosis studies who are also ascertaining cases through members of the British Society of Haematologists.

Surveillance is 'active' in that the stimulus to report the orange card comes from the Unit (Figure 1). Each month, all those participating in the scheme are sent an orange card listing the conditions currently under surveillance. A set of instructions for completing the card, including case definitions 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.

Respondents are asked to return the card to the BPSU office, indicating the number of cases of each condition on the card, which they have seen during the preceding calendar month. Scottish paediatricians return their completed cards via the Scottish Centre for Infection and Environmental Health. When reporting a positive case, respondents are also asked to complete the clinicians tear-off section making a note of the case and **keeping** the details for future reference (Figure 2). This is required, as there have been occasions when clinicians have been contacted and they have been unable to recall the case.

Participants are expected to return cards even if they have no cases to report - there is a 'nothing to report' box on the card for them to tick. This is an important feature of an active scheme as it allows potential under ascertainment to be identified. Follow-up reminders are sent to all participants in the scheme who have not returned their card for two consecutive months. Overall compliance rates are continually monitored. During this whole process, the BPSU office never receives or processes patient details.

Figure 1 *BPSU orange card*

British Paediatric Surveillance Unit Report Card

June 2001 [2106]

NOTHING TO REPORT **CODE No [ ]**

If case(s) seen, identify how many

1. HIV & AIDS ☐
2. Progressive intellectual & neurological deterioration ☐
3. Vitamin K deficiency bleeding ☐
4. Cerebrovascular disease/stroke or like illness ☐
5. Congental Cytomegalovirus ☐
6. Thrombosis I mth – 16 years ☐
7. Encephalitis in children 2 mths – 3 years 20 7679 9134 ☐
8. Internal abdominal injury due to child abuse in children under 14 years ☐

9. Congenital Rubella ☐ 10. SSPE ☐

Figure 2 *Clinicians section - BPSU orange card*

Clinicians Section **- Please keep if necessary**

British Paediatric Surveillance Unit Report Card
for cases seen in June 2001

Please note a patient identifier and KEEP THIS SLIP for easy reference when the investigator contacts you.

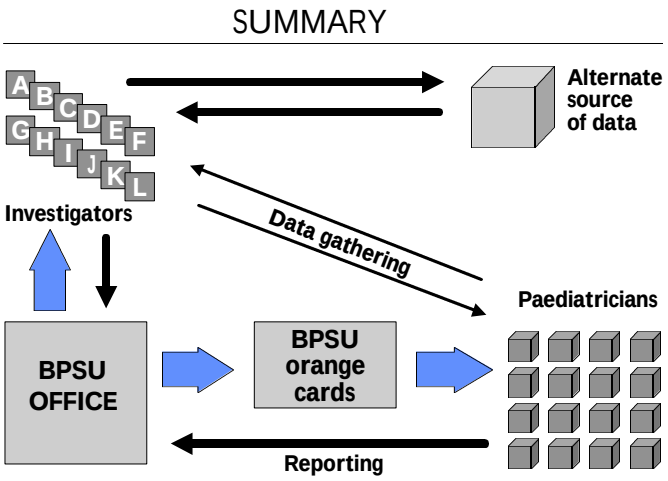
CONDITION	PATIENT	HOSPITAL NO

Detach this section before posting

Follow-up and confirmation of case reports

On receiving a case report the BPSU informs the relevant investigating team who contact the reporting clinician for further information about the case, in accordance with the agreed protocol for the particular study. Particular care is taken to ensure that questionnaires sent to reporting clinicians are as short as possible, clear, straightforward and not excessive in their demands. The amount a patient identifiable data collected is strictly limited, though not to an extent that would compromise study aims. In 2000 the Unit undertook a review of long-standing surveys of the Unit to ensure their data-collection procedures confirm to these principles. The investigators subsequently report back to the BPSU on the outcome of each case follow-up, indicating when cases have been confirmed as meeting the case definition and identifying duplicate case reports. Duplication of reporting is most likely to occur when the condition requires referral to a tertiary unit, but this is encouraged, as it is better to receive duplication than miss the chance of receiving a report.

Figure 3



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'**. Table 2 (page 11) shows the number of cases reported to the BPSU from its inception until the end of year 2000 for all the conditions under surveillance during year 2000. 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, of the conditions under surveillance at the end of year 2000, only 332 (5%) of the 6386 case reports had yet to be followed-up. As a study draws to a close this completion rate figure will rise. The final completion rate normally averages average between 85-98%. In the past, studies requesting pathological specimens have had a lower completion rate, though this has not been the case during the current encephalitis and *Haemophilius influenzae* surveys.

Table 3 (page 11) summarises the outcome of the follow-up of all cases reported to the BPSU by the end of year 2000 and provides evidence for the high level of accuracy of reporting by participating clinicians. By June 2001, 80 (13%) of the cases reported had been classified as reporting errors - details of the system used to classify case reports are set out in the box below.

Classification of case reports

Valid reports:

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

Invalid reports:

These include:

- **duplicate reports** of cases already reported to the BPSU,

  and

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

Outcome not yet known:

Outcome of follow-up not yet received by BPSU (by July 2001).

Difficulties in case reporting

Though the BPSU has much strength its Executive Committee is aware that reporting is never complete, and like any reporting or surveillance system some under-reporting always occurs, reasons for which are listed in the box below. The likelihood of under-reporting can usually be reduced by careful design and scrupulous attention to detail during the running of the study.

However, it always has to be borne in mind that complete reporting is rarely achievable and it is not always necessary; excessive 'hounding' of respondents can be counter productive.

Reasons for incomplete case reporting

- Cases not seen by paediatricians
- Condition is hard to define
- Condition not easily recognisable
- Condition diagnosed but not reported

As highlighted, some conditions under study may have necessarily complex case definitions, these can be off-putting to respondents and lead to under-ascertainment. Some investigators are coming up with a solution to this problem by devising two kinds of case definition. Firstly, a surveillance definition, concise and simple to use, sensitive but relatively non-specific (i.e. producing quite a few false positives). Secondly, an analytic

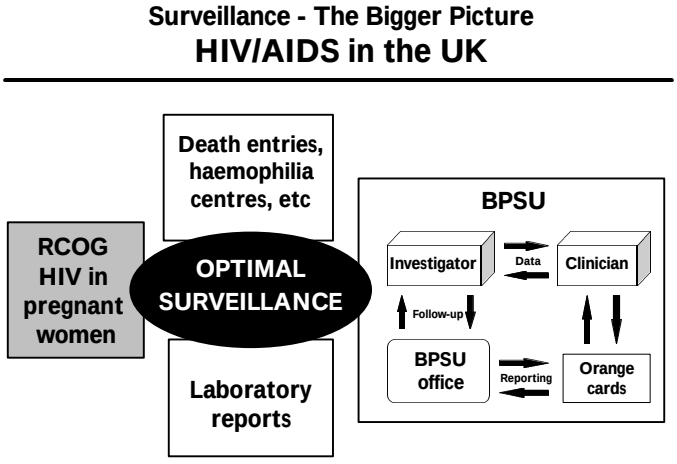
case definition that the researcher applied to the cases reported. This second definition can be as complex as the researcher requires, though the reporter is aware of this definition through the protocol card, they are not expected to use it in reporting. Paediatricians, however, often find these complex analytic definitions useful in diagnosing cases of very rare conditions.

The use of complementary data sources

A distinctive and powerful feature of the BPSU system is the ability to use data from complementary sources to validate the surveillance system, to increase case ascertainment and to increase the accuracy of data (Figure 4). The first complementary data sources to be used were laboratory reports to the PHLS of infectious disease. In the past year the *Haemophilus influenza*, Group b streptococcal disease, HIV/AIDS, haemolytic uraemic syndrome and SSPE studies have included this additional ascertainment. Other sources which have been used include death registration (Reye's syndrome), hospital episode data (congenital brachial palsy and fatal/severe allergic reactions to food ingestion) and in the past, birth registrations (higher order births). In order to increase ascertainment of subdural haematoma, forensic and paediatric pathologists were involved in surveillance. The use of multiple sources of data has shown to improve case ascertainment, demonstrated through the inflammatory bowel disease (IBD) study which identified cases through the BPSU, adult gastroenterologists and the IBD register. However, it is known that completeness varies between studies and conditions, according to the ease of case ascertainment and the availability of complementary data sources.

The use of alternate sources of ascertainment and capture-recapture techniques indicates that on average the BPSU ascertains 75-85% of expected cases. Applicants are made aware of these facts and are encouraged where possible to supplement BPSU data with data from appropriate alternate sources.

Figure 4



Funding

For the three-year period to September 2001 the BPSU has been in receipt of a grant from the Department of Health. The departments willingness to extend the grant for a further three years to September 2004 acknowlegdes that the BPSU's work is an effective way of contributing towards improved child health in the UK. This contribution will support a substantial percentage of the Unit's running costs. In addition, the BPSU asks surveillance teams to contribute a sum to cover the printing/ distribution of the orange cards, and where possible the administrative costs of coordinating the study. In the year 2001 this sum was £7,000 per annum. Between them these two funding sources manage to cover the day-to-day costs of running the Unit.

Further non-cost support is received from the Royal College of Pediatrics and Child Health, the Public Health Laboratory Service and its Communicable Disease Surveillance Unit, the Scottish Centre for Infection and Environmental Health, the Institute of Child Health (London) and Radcliffe online who helped to develop the web-site.

The Unit received a donation from Serono Laboratories towards the cost of holding the RCPCH/RCPE symposium. Finally the Sir Jules Thorn Charitable Trust recently made a small donation to the running of the Unit.

3 Surveillance activities in 2000

Of six studies approved in 2000, one, Group b streptococcal disease (GBS), has commenced. Its main aims are to determine incidence, mode of detection and causes. This will be the first prospective surveillance of GBS ever undertaken in the UK. Not only will the study be able to determine the incidence of GBS in infants less than 90 days old but it will also describe clinical presentation, determine mortality and assess short-term complication rates. To ensure ascertainment, microbiologists and Consultants in Communicable Disease Control are encouraged to report cases.

The year 2001 has seen the commencement of five new studies within the first three months. January saw the commencement of the cerebrovascular disease/stroke and stroke-like illness survey and the vitamin K deficiency bleeding study. February saw the start of the thrombosis in chldhood and congenital cytomegalovirus studies and March saw the start of a survey on internal abdominal injuries due to child abuse. Both the cerebrovascular disease and thrombosis studies are utilising the National Haematology Forum in order to ascertain cases likely to be seen by adult haematologists.

Two studies ended in the year 2000, the two-year study on fatal/ severe allergic reactions to food ingestion was completed in March 2000 and, after nine years, *haemophilus influenzae* infections (September). Several studies were given extensions, these being congenital rubella, sub-acute sclerosing panencephalitis (SSPE), progressive intellectual and neurological deterioration (PIND), encephalitis in under threes, haemolytic uraemic syndrome (HUS) and Reye's syndrome, the latter two ending in January and March 2001 respectively. By December 2000 forty-four studies had been completed since the BPSU began in June 1986 – those completed prior to the year 2000 are listed in Appendix A. Investigators are encouraged to inform the Unit when data gained through the BPSU is published or presented. Known publications and presentations in 2000/2001 relating to these studies and the Unit's work totaled 45 and are listed in Appendices B and C.

In promoting the work of the BPSU, representatives of the Unit have been invited to give talks at a variety of events and meetings. The BPSU was once again involved in the RCPCH research division session at the RCPCH scientific meeting. The BPSU was also the theme of two Royal Society of Medicine Paediatric & Public Health meetings in February and October 2000. December of that year also saw the BPSU in conjunction with Contact a Family, contributing to the first national UK Rare Disease Alliance conference, an umbrella organisation of UK support groups for those with a rare or debilitating disease.

Through the convening of an annual discussion forum the Unit has strengthened its links with other surveillance units in other specialities and national epidemiological institutions in the UK. At the most recent forum the matter of ethics and confidentiality was considered. It was agreed that the BPSU chairman Dr Chris Verity would represent the group in discussions with the Department of Health over this matter. The Unit continues to receive requests for information from parents with children with rare diseases and with the recent inclusion of the Assistant Director of Contact a Family we are now in an excellent position to deal with such enquiries. Invariably most requests have been related to immunisation. Much of the increase in enquiries is due to the interest generated by the BPSU web-site (http:// bpsu.rcpch.ac.uk). Developed in consultation with Radcliffe-online the site has recently been revamped and it is hoped that this site will grow to be a first stop for all those interested in paediatric rare disease, clinicians and public alike.

The Unit continues to liaise with the other national paediatric surveillance units. The International Network of Paediatric Survaillance Unit's (INoPSU) first official meeting was held in Ottawa, Canada, last June, attended by representatives of all the existing units. The meeting agreed the constitution of this organisation and plans are underway to hold the next conference in the UK in April 2002. Also last June, the BPSU scientific coordinator visited the Portuguese Paediatric Society, advising on the development of their unit. The international scene is described more fully in Chapter 8.

Participation in the scheme during the year 2000

The BPSU ascertains the names of new consultants primarily through the RCPCH advisory appointment committee's, membership office, BMJ adverts, through personal communication and this past year through the College 1999/ 2000 manpower census. During the year 165 new consultants were added to the reporting base, 83 were removed following retirement or emigration. The number of consultant paediatricians participating in the scheme during the year 2000 therefore rose to 2097, an increase of 8.5% on the previous year. It should, however, be noted that some paediatricians who hold consultant status are excluded, as they do not undertake relevant clinical work, or else colleagues report on their behalf. The BPSU mailing list also includes selected groups of consultants other than paediatricians i.e. cardiologists, clinical geneticists and pathologists. In order to help in the ascertainment of cases pathologists continue to be included in the surveillance system, and our thanks are extended to the Royal College of Pathologists for supporting this initiative.

Organge card return rates remains high – the overall response rate for the year 2000, calculated as a proportion of orange cards returned, was 92.7% (22,201/23,941), slightly down on 1999 (93.4%). Monthly response rates ranged from 90.4 % in January to 95.7% in April, with a median of 92.8**%.** Though the overall response rate remains above 90.0% there continues to be a downward trend in the response rate. No particular reason has been identified, it may just be part of the natural cycle of such a system. In order to address this, respondents who appear not to have returned cards for two consecutive months are sent letters,

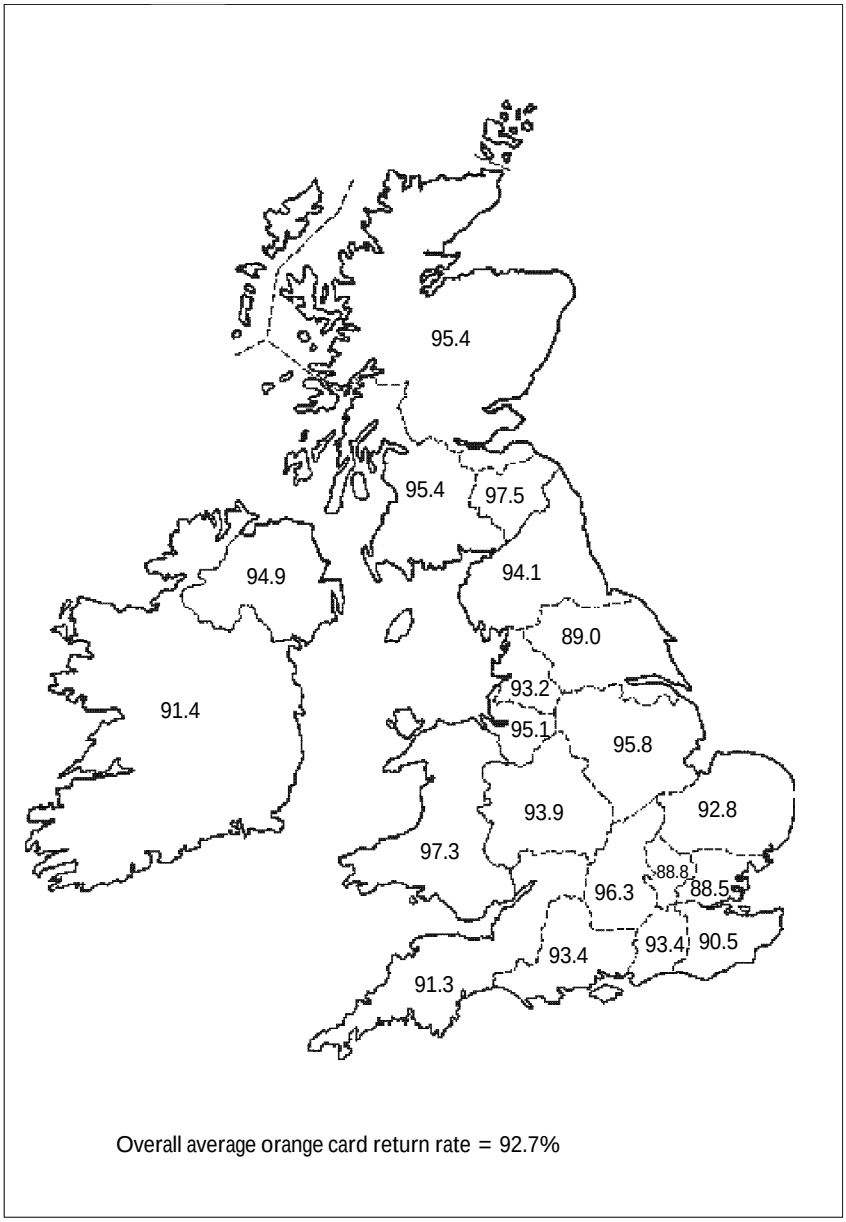
as much to verify postal address as to act as a reminder. Of those responders not returning cards less than 2% could be considered as persistent. Despite the slight downward trend, the return rate is higher than any equivalent UK scheme and ranks eight of the 13 other national paediatric units (Table 16 page 42).

As in previous years, reporting rates varied considerably across the country, as is shown in Figure 5. Wales once more achieved the highest average yearly response rate – 97.3%. Once again the Thames area showed the lowest response rates, cumulatively just 88.2% for the North Thames regions. With so many teaching hospitals in London there is a concern that cases may be going unreported. However, it should be recognised that there are many paediatric specialists in London who receive the orange card but are never likely to see the conditions and thus may be less likely to return the cards on a regular basis. With regard to rank order over the year West Scotland rose by 11 places, while South West and Yorkshire fell by 12 and 10 places respectively (Table 1).

Table 1
Regional ranking 1999 and 2000

Region	Rank 2000	Rank 1999
Northern	9	11
Yorkshire	18	8
Trent	3	7
E Anglia	14	17
NWT	19	15
NET	20	20
SET	17	19
SWT	11	13
Wessex	12	18
Oxford	4	5
SWest	16	4
WMids	10	12
Mersey	7	10
NWest	13	9
Wales	1	1
NScot	5	6
SScot	2	2
WScot	5	16
NIre	8	3
RIre	15	14

Figure 5 *Average orange card return rate (%) by area 2000*



Workload of those participating in the scheme

The BPSU continually monitors the workload of participants in the scheme in terms of the number of cases reported. Fifty-eight percent (1206) of participants reported no cases in 2000, a similar level to 1999 (57%). Forty-percent (831) reported between one and four cases and only 3% (63) reported five or more cases. The greatest number of cases reported by a single paediatrician was 53. Specialties that had a particularly high level of reporting were paediatric nephrologists (HUS), paediatric neurologists (PIND, encephalitis, SSPE, Reye's syndrome) and neonatologists (severe visual impairment, GBS, HIV, encephalitis). In the past year community paediatricians have made a significant contribution to the reporting. One hundred and twenty two community paediatricians reported 235 cases, mainly for PIND, GBS, severe visual impairment and HIV. With the continuation of the PIND and HIV studies and the recent commencement of the severe internal abdominal injury study we would expect this important contribution to continue.

Table 2 *Cases reported from June 1986 – December 2000 of conditions under surveillance during the year 2000 (cases confirmed by July 2001 shown in brackets)*

		Reports (confirmed cases)					
Condition under surveillance	**Date when reporting began**	**June 1986 to Dec 1989**	**Jan 1990 to Dec 1992**	**Jan 1993 to Dec 1995**	**Jan 1996 to Dec 1998**	**1999**	**2000**
HIV/AIDS	Jun 86	137 (90)	495 (386)	359 (215)	488 (326)	202 (126)	327 (202)
Reye's syndrome	Jun 86	149 (76)	71 (31)	57 (21)	31 (21)	12 (5)	7 (3)
SSPE	Jun 86	84 (50)	55 (29)	28 (14)	27 (10)	9 (1)	9 (3)
Congenital rubella	Jun 91	– –	43 (27)	29 (12)	40 (18)	2 (2)	7 (5)
Hi infection	Sep 92	– –	25 (20)	146 (106)	200 (126)	69 (45)	97 (54)
HUS	Feb 97	– –	– –	– –	374 (223)	188 (114)	190 (112)
PIND	May 97	– –	– –	– –	617 (394)	218 (140)	226 (135)
Encephalitis (2-36 months)	Oct 98	– –	– –	– –	56 (31)	138 (64)	122 (34)
SV/Blind	Sept 99	– –	– –	– –	– –	210 (85)	435 (189)
GBS	Mar 00	– –	– –	– –	– –	– –	425 (280)
Total		**370 (216)**	**689 (493)**	**619 (368)**	**1833 (1149)**	**1048 (582)**	**1845 (1017)**

HIV/AIDS Acquired immune deficeiency syndrome/human immunodeficiency virus: reports of AIDS in June 1986 includes cases previously seen; case definition extended to include HIV infection in January 1990.

SSPE Subacute sclerosing panencephalitis:
a) reports of SSPE in June 1986 included all cases seen in the previous 12 months;
b) cases "not confirmed" include those outside of Engalnd and Wales which are not followed up by CDSC.

Hi infection Invasive *Haemophilus* influenzae infection, pre Oct 1995 Hib vaccine failures only.

HUS Haemolytic Uraemic syndrome. In January 2001 the last month of surveillance 6 cases were reported of which 3 were confirmed.

SV/Blind Severe visual impairment and blindness; many of the cases are still under review and may eventually be classified as a case.

GBS Group B streptococcal disease

Table 3 *Outcome of follow-up of the cases reported in 2000 of conditions under surveillance during the year 2000.*

	Valid reports (%)		**Invalid reports**			**Not yet**		**Total**
Condition under surveillance			**Duplicates**	**Errors**	**(Total %)**	**known (%)**		**reports**
HIV /AIDS	1,345	(67)	270	322	(29)	71	(4)	2008
Reye	157	(48)	51	115	(51)	4	(1)	327
SSPE	107	(50)	46	35	(38)	24	(11)	212
CR	64	(53)	24	32	(46)	1	(1)	121
Hi*	351	(65)	39	136	(33)	11	(2)	537
HUS*	449	(60)	249	44	(39)	10	(1)	752
PIND	669	(63)	113	260	(35)	19	(2)	1061
Enceph	129	(41)	27	122	(47)	38	(12)	316
SV/Blind	274	(42)	32	170	(31)	169	(26)	645
GBS*	280	(66)	56	59	(27)	30	(7)	425
All	**3825**	**(63)**	**907**	**1295**	**(34)**	**377**	**(6)**	**6404**

* Studies in which validation depends on microbiological/pathological details.

4 Main findings of studies undertaken in 2000

Surveillance for **congenital rubella** (CRS) (page 13) in the UK has been underway continuously since 1971. Seven infants born since 1999 have been reported; in five of these cases the maternal infection was acquired abroad. The current level of MMR uptake gives cause for concern, as it may not be enough to prevent circulation of rubella infection in the long term.

Surveillance of **encephalitis in children two months to three years** has to date reported 244 children most of whom presented between 10 and 18 months of age. HHV-6 and HHV -7 infections were identified as commonly as herpes simplex and varicella zoster virus infections.

Group b streptococcal disease (GBS) (page 17). This recently completed one-year study is the first UK surveillance of culture-proven GBS in infants. 416 cases have been confirmed, two distinct groups are apparent, early onset and late onset, each with differing clinical presentations and apparent risk factors. Mortality was higher in those with early onset GBS. The study confirms that GBS is a significant cause of disease in UK infants.

The second survey of **haemolytic uraemic syndrome** (HUS) (page19) through the BPSU has so far confirmed that most HUS cases in the UK are due to *E. coli* O157 and that it is commoner in children under age 4 but rare beyond age 10. Most cases are sporadic but cases are reported associated with contaminated food and water and person to person transmissions. The survey reports eight deaths and significant long-term morbidity in some children.

The BPSU survey of **HIV and AIDS** (page 21) is the prime source of paediatric data about this condition in the UK. The findings suggest that almost all new infections are now acquired through mother to child transmission and that, although the greatest number of infections are in London, cases are occurring in all parts of the country. As a result of previous findings it is now a Department of Health policy to routinely offer and recommend HIV testing to all pregnant women. For several years it has been known that interventions such as antiretroviral therapy for the pregnant woman and newborn child, elective caesarean section, and avoidance of breast feeding substantially reduce mother to child transmission of infection. However, as many infected pregnant women were not aware of their HIV status, they could not take advantage of these interventions.

After seven years of BPSU surveillance the study of invasive ***Haemophilus influenzae*** **b infection** (Hib) (page 23) has ended, though surveillance will continue through the microbiology laboratories. Over this period it has been possible to confirm that Hib vaccination has dramatically reduced invasive disease in the UK and Eire. In 2000 there was an overall reduction of 94% compared to the pre vaccine era. Vaccination failures are occurring but many of these are in children with other conditions that prejudice their immune response. The UK and Eire are unusual world-wide in only giving a primary vaccine course and not using a booster. There is now some evidence of waning protection with age though the fall is small. There has been an increase in the incidence of Hib over the last two years and this trend needs to be monitored.

Despite the complexity of the conditions involved, the survey of **progressive intellectual and neurological deterioration in children** (PIND) (page 25) has proved successful. It is being undertaken to identify any cases of variant Creutzfeldt-Jakob disease in UK children. Over 1000 cases of suspected PIND have been reported. Among them 435 cases are due to confirmed diagnoses, consisting of 89 different conditions. Four cases of variant CJD have been identified.

This annual report is the last in a series on **Reye's syndrome** which started in 1981/82 (page 27). The total of cases in the last complete surveillance year is three and equals the lowest total recorded in 19 years. Results from long-term surveillance of Reye's syndrome suggest that children presenting with conditions that could be Reye's are not always being optimally investigated. Some cases are occurring in children over age 12 years who had taken aspirin. This is the upper age limit of the warning not to take aspirin and the investigators suggest that the age limit may need to be reviewed and raised. However the trends vindicate the public health action taken on the use of aspirin in children in 1986 which represents a triumph of primary prevention of a devastating childhood illness.

Surveillance of **severe visual impairment and blindness** (page 30) has collated data using reports to the BPSU and the British Ophthalmological Surveillance Unit. To date over 350 cases have been confirmed which is more than anticipated. Interesting emerging findings include that over half of all children have other, non-ophthalmic, impairments and about a quarter are of low birthweight. A one-year follow up is in progress and will be reported in a future report.

An important enhancement of the long-term survey of **Sub-acute sclerosing panencephalitis** (SSPE) (a condition which is a late complication of measles) (page 31) is that it is proving possible to distinguish between 'wild' measles virus and the measles virus used in vaccines. Analysis of the causative measles virus in SSPE cases so far investigated has not shown any to be related to the vaccine-like strain (genotype A).

5 Surveillance studies undertaken in 2000

During the year 2000, 10 conditions were the subject of surveillance. 3 studies were completed: fatal/severe allergic reactions in childhood, *haemophilus influenzae* infections, and severe visual blindness and one study Group b streptococcal disease commenced. All the studies undertaken in 2000 are listed in Table 3 and reported on except the fatal/severe allergic reactions in childhood survey, whose final report was contained in the 1999 BPSU annual report.

Five projects have so far commenced in 2001 these being vitamin K deficiency bleeding, congenital cytomegalovirus, cerebral vascular disease/stroke in childhood, severe internal abdominal injuries due to child abuse and venous/arterial thrombosis and are described in Chapter 6.

Table 4 *Studies underway in 2000*

Page	Study	Principal Investigators	Research Institutions
	Congenital rubella*	P Tookey, C Peckham	ICH (London)
	Encephalitis (2 months - 3 years)*	K Ward, E Ross	King's College Hospital, London
	Group b streptococcal disease	P Heath, A Nicoll	St George's Hospital, London, PHLS
	Haemolytic uraemic syndrome	M Taylor, GK Adak, R Lynn, S Locking	B'ham Children's Hospital, PHLS, BPSU, SCIEH
	HIV/AIDS infection in childhood*	P Tookey, A Nicoll, D Goldberg	ICH (London), PHLS, SCIEH
	Invasive *Haemophilus influenzae* infection	P Heath, M Slack, R Moxon	PHLS, Nat Haemophilus Ref. Lab., Oxford
	Progressive intellectual and neurological deterioration*	C Verity, G Devereux, A Nicoll, R Will	Addenbrookes, PHLS, CJDSU
	Reye's syndrome	S Hall, R Lynn	Sheffield Children's Hospital, BPSU
	Severe visual impairment/blindness	J Rahi, I Russell Eggitt, D Taylor, C Gilbert	ICH (London), GOS
	Subacute sclerosing panencephalitis	E Miller, M Bush	PHLS

***** Studies still in progress to July 2001.

Congenital rubella

Key Points

- **There is still a risk of congenital rubella in the UK, though cases are rare.**
- **Five of the seven recently reported cases were imported.**
- **Most recently reported cases are infants with severe rubella damage obvious at birth; it is therefore likely that there are less severely affected infants with congenital rubella who are not being diagnosed.**
- **The current level of MMR uptake may not be enough to prevent circulation of rubella infection in the long term.**

Background

Surveillance of congenital rubella in Scotland, Wales and England started in 1971 with passive reporting by audiologists, paediatricians and microbiologists. Following the introduction of vaccination for schoolgirls and susceptible women post-partum the number of cases of congenital infection and rubella associated terminations declined dramatically, from an average of about 50 births and 740 terminations a year in 1971-75 to an average 23 births and 50 terminations a year in 1986-90. Since there were so few cases, active surveillance was required, and congenital rubella first appeared on the BPSU's orange card in January 1990. BPSU reports from Ireland are also followed up, but not normally included in the published figures.

Since 1988 the combined MMR vaccine has been offered to all children in the second year of life, with a pre-school booster for four year olds introduced in 1996. However, MMR vaccine uptake fell between 1995 and 1998 following adverse publicity about unproven associations between MMR and bowel disease and autism. Although national MMR coverage at 24 months has now stabilised at about 88%, some districts were reporting uptake of only 70% at the end of 2000.[1] Uptake of the pre-school booster has always been at lower levels, and only 75% of 5 year olds had received both MMR1 and MMR2 at the end of 2000. This level is probably not sufficient for the long-term maintenance of a herd immunity level of 85-88% which is required to prevent transmission of wild rubella infection, particularly since very few children now acquire natural infection. Continued surveillance of congenital rubella is vital.

Objectives

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

Case definition

Any child up to 16 years of age who, in the opinion of the notifying paediatrician, has suspected or confirmed congenital rubella with or without defects, based on history, clinical, and/or laboratory findings. Reports of stillbirths associated with congenital rubella infection are also requested.

Analysis

BPSU notifications

Since the beginning of active surveillance in 1990, 120 reports have been made through the BPSU (Table 5). Of the 105 reports from England, Scotland and Wales, 43 are confirmed or compatible, previously unreported cases of congenital rubella, four are possible cases, and twelve had already been reported from another source. The remaining reports were duplicates (19), reporting errors (23) and four where further information could not be obtained. Fifteen reports were from the Republic of Ireland or Northern Ireland, and included three children with confirmed congenital rubella (one born in 1989 and two in 1996), and a fourth possible case (born in 1983). One recent report from Northern Ireland is still outstanding.

Table 5 *Congenital rubella reports to BPSU 1990-2001*

	England, Scotland and Wales	Ireland
Registered Cases	47	4
Already reported	12	2
Outstanding	0	1
Duplicate, error or lost	46	8
Total	**105**	**15**

Among the children born since the beginning of active surveillance in 1990, 36 (69%) of the 52 confirmed or compatible cases (Table 6) were first reported through the BPSU.

Table 6 *Confirmed and compatible congenital rubella births reported to the NCRSP 1971-2001* (England, Scotland & Wales only)*

	Primary source of notification		
Year of birth	**BPSU**	**Other**	**Total**
1964-69	0	39	39
1970-79	1	453	454
1980-89	13	320	333
1990-2001~	36	16	52*
Total	**50**	**828**	**878**
1990	*8*	*4*	*12*
1991	*2*	*1*	*3*
*1992***	*5*	*2*	*7*
1993	*2*	*1*	*3*
1994	*5*	*2*	*7*
1995	*1*	*0*	*1*
1996	*9*	*3*	*12*
1997	*0*	*0*	*0*
1998	*0*	*0*	*0*
1999	*0*	*1*	*1*
2000	*3*	*1*	*4*
2001	*1*	*1*	*2*

* The data for recent years are provisional
~ The data for 1990-2001 include 2 reported stillbirths
** Includes a set of triplets

Recent reports

Six infants have already been reported for 2000/2001. Five of these six cases were imported, with women acquiring infection early in pregnancy in their countries of origin (Africa and the Indian sub-continent). In 1999 a major rubella epidemic in Greece led to isolated outbreaks of infection in the UK, and the only reported case that year, an infant born in December 1999 in Scotland, appeared to be connected to one of these outbreaks.[2,3] There were no congenital rubella births reported in 1997 and 1998. The 12 infants reported in 1996 included eight whose mothers were born and brought up in the UK, all of whom had been eligible for schoolgirl vaccination. These births followed a resurgence of rubella infection in the UK, mainly affecting young men.[4]

The BPSU's orange card has proved to be a rapid and effective reporting system for congenital rubella and was particularly quick to identify the increase in cases in 1996 when all but two of the BPSU reports were made within two months of the infant's birth. In recent years most reported cases of congenital rubella were identified close to the time of birth because of abnormal signs in the infant. Hardly any children with isolated hearing loss due to congenital infection are now reported; any such children would probably remain undiagnosed as they have vaccine induced antibodies following MMR in early childhood. The diagnosed reported cases therefore probably represent only a proportion of the true cases.

About a quarter of the infants reported in the last decade were born to women whose infection was acquired abroad, while about half were born to women who, although they acquired infection in the UK, had only arrived in the country relatively recently. While rubella infection is currently rare in the UK, women who travel abroad during early pregnancy may come into contact with infection. Women who have recently come from countries with less successful, or disrupted vaccination programmes are likely to be at higher risk if there is renewed circulation of rubella.

It is essential that case ascertainment is as rapid and complete as possible, both for imported cases and those where infection was acquired in the UK. Please notify to the BPSU all suspected congenital rubella cases, whether or not they have the associated typical defects. We are grateful to all notifying paediatricians for their co-operation.

Funding

The surveillance of congenital rubella is funded by the PHLS.

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2 Molyneaux P. Congenital rubella infection following documented maternal reinfection. SCIEH Weekly Report 2000; **34**: 85

3 Tookey P, Molyneaux P, Helms P. UK case of congenital rubella can be linked to Greek cases. BMJ 2000; **321**: 766-67

4 Tookey PA, Peckham CS. Surveillance of congenital rubella in Great Britain, 1971-96. BMJ 1999; **318**:769-70

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Encephalitis in children aged two months to three years

Key points

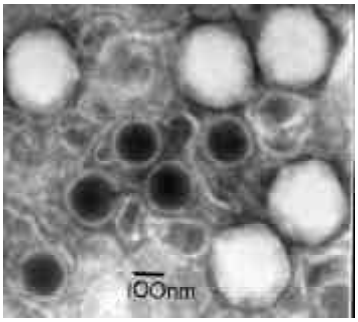
- **Between October 1998 and April 2001 244 children meeting the case definition were reported to the BPSU.**
- **Most confirmed cases presented between 10 and 18 months which is the most frequent age at which primary Human Herpes Virus-6 and -7 (HHV-6 & 7) infections occur.**
- **HHV-6 and HHV-7 infections were identified as commonly as herpes simplex and varicella zoster virus infections.**

Background

Encephalopathy in early childhood makes a substantial contribution to chronic neurological disability and the impact on individual families, frequently exacerbated by diagnostic uncertainty, may be devastating. The causes, however, are largely unknown. The National Childhood Encephalopathy Study (NCES), 1976-1979, suggested an unidentified viral illnesses as a likely cause (i.e. an encephalitis). Identification of the causative agent(s) would help to curtail unnecessary investigation, rationalise treatment and improve reliability of prognosis. Fortunately, more accurate diagnosis of possible agents causing encephalitis has recently become available in the form of new, highly sensitive laboratory methods for detection of nucleic acid (PCR), antibody and antigen. Two newly discovered viruses, human herpesviruses-6 (Figure 6) and -7 (HHV-6 and HHV-7), are obvious candidates for investigation since primary infection normally occurs within the first three years of life, may be associated with febrile convulsions, and there have been isolated case reports of encephalitis.

Figure 6

Electron micrograph of a group of virus particles in a negative contrast preparation showing mature intact virions and naked nucleocapsids.



Objective

To determine the aetiology of encephalitis in children from 2 months old to third birthday and in particular the role of infection with HHV-6 and HHV-7.

Survaillance Case definition

- **Report** any child aged **2 months to third birthday** with acute or subacute encephalitis.

Include encephalitis of **known** infectious or post-infectious aetiology (**unless** due to pyogenic infection)

- **also include** convulsions in a *febrile* child:
  (i) with a total duration of more than half an hour;
  or (ii) followed by coma lasting 2 hours or more;
  or (iii) followed by paralysis or other neurological signs not previously present and lasting 24 hours or more.

Exclude

(i) viral (aseptic) meningitis without encephalopathy;
(ii) the following confirmed causes: pyogenic infections, hypoxic/ischaemic, vascular, toxic, metabolic, neoplastic;
(iii) uncomplicated fits/convulsions or a series of fits convulsions lasting less than half an hour.

If in doubt please discuss with the investigators.

Duration

October 1998 to September 2001.

Methods

Paediatricians are asked to report all cases promptly by telephone to Dr Kate Ward (020 7679 9134 - there is 24 hour cover). Brief initial details of the case are taken, and further investigations are discussed including the collection of relevant samples. Upon notification, filter paper and sponges are sent to the reporting paediatrician for the collection of blood and saliva samples for HHV-6 and HHV-7 testing. Where cerebrospinal fluid (CSF) has been taken for diagnostic purposes, it is sought from the local microbiology laboratory. Dr Ward provides a free diagnostic service for HHV-6 and -7 infection based on acute and convalescent blood, saliva and cerebrospinal fluid. Further diagnostic tests for other virus infections may be undertaken free of charge as required after liaison with the local microbiology laboratory. All results are sent both to paediatricians and microbiologists.

A questionnaire is sent to the reporting paediatrician after about 3 months to allow sufficient time for follow-up. Due to the difficulties of diagnosing encephalitis, which is often a diagnosis of exclusion, a final decision as to whether the case is included

in the survey is based on a detailed analytical case definition. A Working Party judges difficult cases and comprises Professor Euan Ross, Dr Chris Verity and Dr Kate Ward.

Table 7 *Regional distribution of reports.*

Region	Total	Region	Total
East Anglia	10	NE Thames	31
Mersey	10	NW Thames	19
North Ern	8	SE Thames	25
Oxford	15		
South West	14	Wales	17
Trent	38	North Scotland	2
Wessex	14	South Scotland	7
West Midlands	33	West Scotland	6
Yorkshire	20	Northern Ireland	4
		Republic of Ireland	22
Total			**343**

Analysis

At the end of April 2001, 343 children had been reported to the BPSU (140/annum); sixteen from the Republic of Ireland and the remainder from the UK (Table 7). Reports were received from all regions but tended to come from the hospital where the child first presented rather than the Paediatric Intensive Care Unit (PICU) to which they were transferred. Therefore a flier together with filter paper and sponges for collection of saliva and blood is currently being sent as a reminder to all PICUs in the British Isles, those regions that appear to be under ascertaining, i.e. Scotland, Mersey and Northern are being especially targeted.

As regards collection of specimens for HHV-6 and HHV-7 testing, about 55% of cases were reported first by telephone but the rest were only reported retrospectively on the orange card. The investigators received at least some specimens (serum and/or saliva and/or cerebrospinal fluid (CSF)) from approximately nine out of ten cases. CSF has been the most difficult specimen to obtain. Support from local microbiology laboratories has been excellent and we have obtained CSF from seven out of 10 cases where it was taken. CSF is of course the key specimen as testing of other samples can only provide coincidental evidence of possible central nervous system infection. The success rate with retrieval of CSF was highest when cases were reported by telephone rather than retrospectively. The longer the time that elapses after initial presentation of the case, the more likely is the laboratory to have discarded the CSF. Early telephone reporting and immediate despatch of specimens, especially CSF, therefore remain the most important ways in which paediatricians and microbiologists can contribute to the success of the survey and the full virological diagnosis of their patients.

Of the 343 cases reported so far:

- 99 were invalid because of duplication or reporting error (including misdiagnosis and children who were either too old or too young). In 13 cases we did not receive a reply to our request for further information despite reminders.

Of the remaining 244 cases that met the reporting case definition:

- 128 cases fulfilled the analytical case definition
- 53 cases did not fulfil the analytical case definition
- Follow-up has not yet been completed for 63 cases most of whom were reported recently. As explained previously, questionnaires are not sent immediately so as to allow the paediatrician time to confirm the initial diagnosis. Some difficult cases await a decision from the Working Party.

From the above analysis, it can be estimated that the final number of cases per annum will be about 68. This is less than the original estimate of 200 cases per annum which was based on the number of reports received by the NCES. The current much reduced low levels of measles and mumps encephalitis resulting from measles mumps rubella (MMR) vaccination may partly explain the lower number of reports in the BPSU survey. Moreover, although the BPSU reporting case definition is very similar to that of the NCES, there are important differences. The BPSU definition omits infantile spasms and states convulsions in a *febrile* child, i.e. severe febrile convulsions, whereas the NCES definition includes both severe febrile convulsions and 'other' severe convulsions. In addition under reporting may have occurred because of the difficulty of diagnosing encephalitis. This difficulty also explains the observation that only 70% of cases meeting the reporting case definition are confirmed cases when the analytical case definition is used.

Figure 7 overleaf compares the age distribution of the 128 cases that met the analytical case definition with that of the 53 cases that did not fulfil the definition. The most frequent age of presentation of the confirmed cases is between 10 and 18 months old. This is also the most frequent l age for primary HHV-6 and -7 infections in children. In this context the survey has so far identified 8 children with primary HHV-6 infection and 21 children with primary HHV-7 infection. Of the children for whom CSF was available, HHV-6 DNA has been found in 7 and HHV-7 DNA in 8. Notably no similar evidence for HHV-6 or -7 infection has been found so far in the cases that did not meet the definition.

Comment

The study is going very well; both HHV-6 and -7 infections have been found. These results are very encouraging and the investigators are now in a position to begin looking at the clinical picture and outcome of these infections.

As regards other infectious agents, the most commonly suspected cause of encephalitis was herpes simplex and almost all children received a course of acyclovir. However, herpes simplex infection was only confirmed in a few cases; other infections reported in the questionnaires included varicella zoster virus, enteroviruses and adenovirus. Interestingly, HHV-6 and HHV-7 infections were as common as herpes simplex and varicella zoster virus infections.

In summary, from the good progress so far it looks probable that this collaborative work between paediatricians and microbiologists will establish HHV-6 and HHV-7 as significant causes of neurological disease in early childhood. Regardless of the final outcome, it will certainly lead to a firmer scientific

basis for the accurate diagnosis and perhaps prevention of childhood encephalitis.

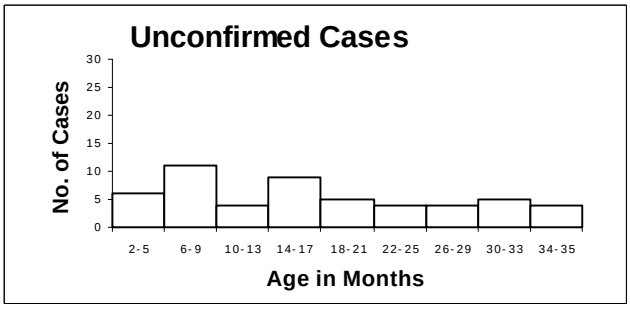
The investigators are very grateful to paediatricians, microbiologists and virologists for taking the time and trouble to support this surveillance project.

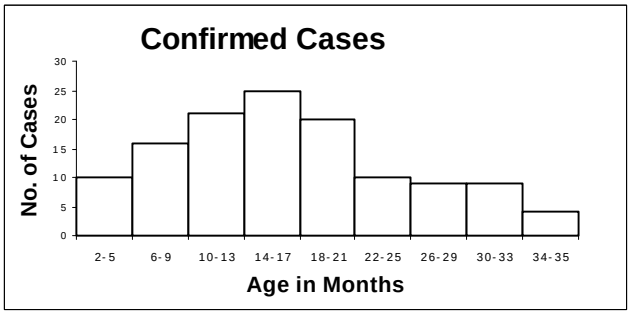
Funding

Wellcome Trust.

Figure 7

Comparison of the age distribution of confirmed and unconfirmed cases.





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Group B streptococcal disease (GBS)

Key Points

- **Group B streptococcal disease (GBS) is an important cause of serious bacterial infection in UK infants (minimum incidence 0.6/1000 live births, mortality 11%). The majority of cases (66%) are early in onset (< 7 days of age, especially days 1-2); 34% are late in onset (7-90 days).**
- **The major mode of clinical presentation is sepsis (50%) followed by meningitis (25%) and pneumonia (20%). Meningitis and focal infections are more common when disease is late in onset and pneumonia and sepsis more common in early onset disease.**
- **A number of demographic, pregnancy and birth factors are associated with GBS disease. These include prematurity and prolonged rupture of membranes. A case control study is underway to define these risk factors more precisely.**

Background

Group B streptococcal disease (GBS) is the most common cause of severe early onset neonatal infection in developed countries. However, in the UK and Republic of Ireland (ROI) the incidence and risk factors for group B streptococcal disease, whether early onset (< 7 days) (EOGBSD) or late onset (7–90 days) (LOGBSD) are not well studied. A passive surveillance study of 25 British centres in the late 1970s estimated a low incidence of 0.3/1000 live births (< 2 months of age). Several studies from the 1980s and 1990s have estimated higher incidence rates (average 0.7/1000). A major weakness of these studies is that they have rarely included major urban and deprived areas. By comparison, the incidence rate of EOGBSD in the USA (prior to widespread antibiotic prophylaxis) was around 1.4/1000.

EOGBSD can be prevented through intra-partum or post-partum antibiotic prophylaxis and various prevention strategies have been proposed; these generally rely on mass screening of pregnant women for carriage of GBS and/or identifying women with specific risk factors for disease. Which strategy should be applied to the UK/ ROI very much depends on the incidence of EOGBSD and on its risk factors. Currently there are a number of ad hoc prevention policies applied in UK settings, some based on local and generally small surveillance studies, others working on the basis of experience elsewhere, especially the USA. In most places policies have yet to be devised, though increasingly centres are feeling the need to do so. There is therefore an increasing need for national guidelines and the gathering of national data. This is a priority of the multiagency-working group convened by the Public Health Laboratory Service. Only with a national study will sufficient data pool be generated to make robust recommendations about policies and practices.

Objectives

1 To determine the incidence of invasive GBS disease in British and Irish infants aged < 90 days.

2 To describe the clinical presentation of cases of invasive GBS disease.

3 To determine the mortality and short-term complication rate of GBS disease.

Methods

Paediatricians were asked to report all cases meeting the case definition. A two page questionnaire was then sent to the paediatrician seeking brief clinical and outcome details. To ensure as complete ascertainment as possible Microbiologists and Consultants in Communicable Disease Control were encouraged to independently report cases to the PHLS Communicable Disease Surveillance Centre, and also to send isolates of GBS to the Streptococcus and Diphtheria Reference

Unit of the PHLS Respiratory and Systemic Infection Laboratory. Characterisation of the serotypes of GBS causing disease in infants is valuable for designing future serotype based conjugate vaccines. Additionally, through the GBS Support Charity, parents of cases were invited to notify cases to the study.

In the Republic of Ireland, microbiology laboratories were contacted by telephone every two weeks.

Case definition

Infants < 90 days of age in whom Group B Streptococcus (GBS) (also called *Streptococcus agalactiae*) was isolated from a normally sterile site eg. blood/CSF/joint aspirate/pleural fluid. Cases diagnosed by surface swabs or antigen testing were not included.

Study duration

February 2000-February 2001.

Results

These are preliminary data as reconciliation of reports from paediatricians, microbiologists and parents is still in progress and data from Republic of Ireland are awaited. Data on short term complications are also not yet complete.

To the 25th April 2001, 416 cases occurring in the surveillance period (to 28/2/01) have been confirmed. The source of confirmed cases was: paediatricians 299 (72%), microbiologists 107 (26%) and parents 10 (2%). The country of origin and the corresponding incidence of GBS disease is shown in Table 8. .

Table 8 *Incidence (95% confidence intervals) GBS disease in infants < 90 days of age.*

Country	Incidence (95% CI)
England	0.62 (0.55-0.68)
Scotland	0.33 (0.19-0.52)
Wales	0.31 (0.15-0.57)
Northern Ireland	0.60 (0.33-1.01)
United Kingdom	**0.58 (0.53-0.64)**

The majority of cases were early in onset i.e. less than 7 days (66%) with the median age of early onset disease was day one and of late onset disease day 29 (figure). Fifty-five percent of cases were male.

The median gestational age of all cases was 38 weeks (range 23-42 weeks) with 40% < 37 and 29% < 35 weeks gestation. Late onset (LO) cases were more likely to be of lower birth weight than early onset (EO) cases: mean weight 2417g versus 2936g ($p<0.001$) with 54% of LO cases < 2500g versus 30% of EO cases ($p<0.001$). Conversely, the mothers of EO cases had longer rupture of membranes than those of LO cases: median 12 hours versus 2 hours ($p<0.001$); 39% versus 14%[3] 18 hours ($p<0.001$).

The clinical presentation is detailed in Table 9.

Table 9 *Clinical presentation of GBS cases*

Clinical presentation	% of all cases	% of EO cases	% of LO cases
Meningitis	24	13	44
Sepsis	54	60	41
Pneumonia	20	26	8
Other	3	0.8	8

The overall mortality of GBS disease was 10.6%. The mortality for EO cases was higher than that for LO cases (11.8% versus 8.5%) and the mortality was higher in those born prematurely than in those born at full term: 16.6% versus 6.1%.

Approximately 56% of EO cases had one or more of the following clinical risk factors: prematurity < 37 weeks, prolonged rupture of membranes[3] 18 hours, or known maternal vaginal GBS carriage during pregnancy. Ten per cent of this group of mothers had received antibiotics in labour.

Of eight possible serotypes of GBS, three serotypes (III, Ia/c,V) caused the majority of cases (> 90%).

Comment

This is the first UK national surveillance study of culture-proven GBS in infants. As indicated, these data are preliminary as a significant number of reports await verification. The final numbers of cases and the corresponding incidence will therefore be higher.

It is apparent that GBS disease occurring during the first three months of life falls into two distinct groups according to the time of onset of disease: early, with the majority of infants developing disease on day one of life; and late, with age of disease spread evenly over the period from 7-90 days of age. These two entities differ in clinical presentation, EO disease presenting predominantly with sepsis and pneumonia and LO disease more likely to present with meningitis and focal infections. EO disease is known to be due to vertical transmission of GBS and consistent with this, prolonged rupture of membranes is a significant risk factor. LO disease is more likely to be due to horizontal acquisition of GBS. Infants of lower birth weight are over-represented in the LO group and it may be postulated that such babies will spend longer in a neonatal unit and be more likely to come in contact with GBS.

The mortality for all UK cases of GBS is notably higher than that quoted from US studies. The reasons for this are not clear.

Prevention of EO GBS disease can be achieved through intrapartum antibiotic prophylaxis (IAP). It is shown in this study that if IAP were administered to women who were identified using the risk factors of prematurity, prolonged rupture of membranes or known GBS genital carriage then, at best, just over 50% of cases may be prevented. It is noteworthy that at least 10% of such women did in fact receive antibiotics in labour

yet their infants developed GBS disease.

Finally, the importance of using multiple sources of reports for a national surveillance study is emphasised by these data as no one reporting system has shown complete ascertainment.

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Haemolytic uraemic syndrome (HUS)

Key points

- **Most cases of HUS in the UK are due to E. *coli* O157.**
- **Most cases are sporadic, outbreaks are uncommon.**
- **There are peaks of HUS incidence in the autumn.**
- **Cases in children have been associated with farm visits, person to person spread, contaminated foods and environmental exposure.**
- **HUS is commoner in children under age 3 and rare beyond age 10 years.**
- **Initial outcome is usually good however long term sequlae is yet to be determined.**

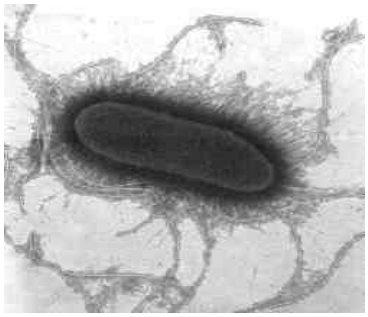
Background

Haemolytic uraemic syndrome (HUS) is the commonest cause of acute renal failure in children in the United Kingdom. In 1995 the Advisory Committee on the Microbiological Safety of Food (ACMSF) produced a report on Verocytotoxin-producing *Escherichia coli* (VTEC). One of the committee's principal recommendations was that a national prospective surveillance study of HUS should be set up.

HUS is a heterogeneous condition characterised by micro-angiopathic haemolytic anaemia (fragmented red blood cells), thrombocytopaenia and acute renal impairment.[4,5] HUS has a number of aetiologies, the most important in the UK has been considered to be verocytotoxin-producing *E. coli* O157 (O157 VTEC).[1,7,8,9,10] O157 VTEC is an emerging infection (Figure 8), it was first identified in the late 1970's and its link with HUS was established early in the 1980's. VTEC of several other serogroups have also been associated with cases of HUS.[1,7] O157 VTEC does not necessarily cause HUS and infections may be asymptomatic. Two HUS sub-types have been defined; diarrhoea-associated (D+) HUS and a group which lacks a diarrhoeal prodrome, (D-) HUS or 'atypical HUS.[4,5] Cases of (D-) HUS have a poorer prognosis and may be familial. VTEC are associated with (D+) HUS.

Figure 8

Verocytotoxin-producing E.coli O157



The fatality rate in cases of HUS may be up to 10% or even higher in institutional settings.[1] Chronic renal failure with consequent human and financial costs is the outcome in another 10% of cases and a further 40% of survivors suffer some renal sequelae. The main reservoir for O157 VTEC is healthy cattle though other animals can carry infection. Humans become infected through the consumption of contaminated foods, particularly minced beef and milk.[1,2,3,11] However outbreaks of VTEC infection including cases of HUS have been associated with a range of vehicles other than beefburgers and milk, such as yoghurt, cheese, salami, raw vegetables, unpasteurised apple juice and water.[1,6] Other important transmission routes of VTEC infection are direct contact with animals and person to person spread in families, schools and institutional settings and elsewhere.[1]

The previous BPSU survey of 1986-1989 found an incidence approaching two per 100,000 child population per annum. Reports of VTEC O157 infections have risen since then; only eight cases were confirmed by laboratories in the UK in 1988; 1156 were reported in 1996. The new study explores the effect of this increase in the VTEC O157 on the epidemiology of HUS.

Objectives

1 To describe the current epidemiology of HUS in children and to include a measure of severe morbidity and mortality.

2 To estimate the proportion of HUS caused by VTEC of all serogroups.

Case definition

A child under 16 years, resident in the UK at time of onset, with all the following:

1 Acute renal impairment, including oliguria and elevated plasma creatinine for age (plasma urea>8mmol/l);

2 Microangiopathic haemolytic anaemia (Hb <10g/l with fragmented red cells);

3 Thrombocytopaenia (platelets < 130,000 x 10^9/l).

in the absence of

Septicaemia, malignant hypertension, chronic uraemia, collagen or vascular disorders.

The above criteria may not all be present simultaneously.

Study duration

February 1997-January 2001.

Methodology

1 **Local hospital:** Paediatricians should report to the BPSU suspect and definite cases of HUS. When required, guidance on diagnosis can be provided by regional specialists in paediatric nephrology. Faecal specimens and serum samples should be submitted to the local microbiology laboratory. These laboratories will carry out culture tests for *E. coli* O157. The recommended method is to plate specimens on sorbitol MacConkey agar containing cefixime and tellurite and test sorbitol non-fermenting colonies for agglutination with an O157 antiserum. Isolates of *E. coli* O157 should be sent to the Laboratory of Enteric Pathogens, Colindale, together with faecal specimens and sera. In Scotland, all samples are now sent to *E. coli* O157 Reference Laboratory in Edinburgh.

2 **Laboratory of Enteric Pathogens (Colindale), *E. coli* O157 Reference Laboratory, Edinburgh:** These laboratories will provide confirmation and typing for all VTEC. For *E. coli* O157 subtyping includes phage typing and DNA-based methods where appropriate. Where *E. coli* O157 is not isolated faecal specimens will be examined for the presence of all VTEC. Serodiagnostic tests for antibodies to *E. coli* O157 lipopolysaccharide will also be performed.

3 **Communicable Disease Surveillance Centre (CDSC) and Scottish Centre for Infection and Environmental Health (SCIEH):** Paediatricians are asked to report promptly by telephone, all cases of suspected HUS to the CDSC project coordinator (tel: 020 820 6868 ext 4551) and in Scotland to SCIEH (tel: 0141 300 1100 ext 1118). Initial summary details will then be taken and recorded. A structured questionnaire designed to collect specific epidemiological and clinical data will then be sent to the reporting paediatricians. The paediatricians will be asked to complete the questionnaires and return them to the BPSU scientific coordinator (Mr R Lynn) or SCIEH (Ms M Locking) at the earliest date possible. Data from the questionnaires will be matched with microbiological data from Colindale and Edinburgh and the information entered onto a database.

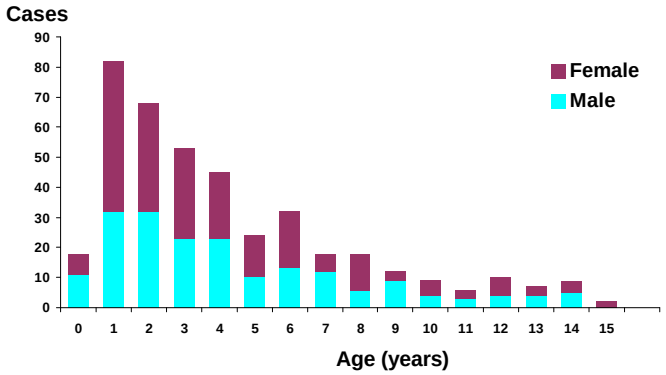
4 **Birmingham Children's Hospital NHS Trust:** Drs C M Taylor and D V Milford advise on clinical aspects of the study on behalf of the British Association for Paediatric Nephrology.

Results and discussion

In the period February 1997 to January 2001 the BPSU, PHLS and SCIEH received 765 reports of suspected HUS cases from paediatricians in the United Kingdom and Republic of Ireland. After de-duplication and verification it was established that 413 of the reports were patients who conformed to the case definition for childhood HUS. A further 29 cases had 2 of the three required criteria for HUS, for the purpose of this report their details have been excluded. The high level of duplicate reporting (252) is a reflection of the substantial proportion of patients referred to specialist paediatric nephrology units by local hospitals. It has been found that reports are often received from both the paediatricians in the hospitals in which the cases were initially seen and also from those in the specialist units to which they were eventually referred. During the year 2000 the BPSU once again undertook with the support of the main referral centres a validation process whereby cases reported were crosschecked with the referral hospitals. Whilst over 80% of cases were seen in the tertiary centres, in order to maintain high levels of case ascertainment it is essential that reporting from both local hospitals and specialist centres is encouraged.

Figure 9

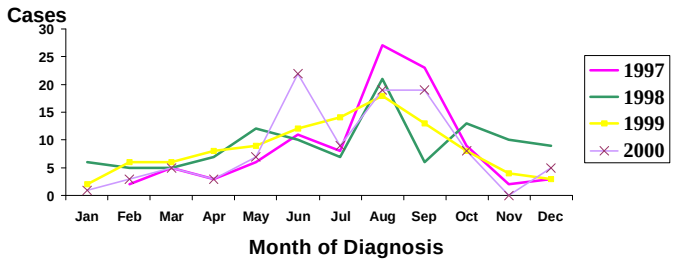
Age and sex distribution of confirmed causes of HUS



The age and sex distribution of clinically confirmed cases of HUS is shown in Figure 9. It can be seen that most reported cases are children of three years of age and below and cases became rare after age 10. The high number of female cases in the age group one to two years is also striking. In total 217 cases were girls and 195 boys.

Figure 10

Seasonal distribution of confirmed cases of HUS



A distinct seasonal pattern has been observed in the reporting of childhood HUS (Figure 10). An early and late summer peak was seen, summer peaks reflecting similar summer peaks in 1997-1998.

Though *E.coli* O157 was the predominate causative agent (288 cases), one case of *E.coli* O26 was reported, other organisms isolated included campylobactor (4), shigella (1), pneumococus (8), salmenella (1), rotavirus (3) in 112 cases no organism was identified or known.

Table 10 *Comparison of National Surveillance Unit HUS data*

Unit	Study Duration	Cases	Incidence		Mortality	Predominant Organism
			< 15 yrs	< 5 years	(%)	
Australia	6.5	137	0.6	1.3	6.6	O111:H-
UK/Ireland	4	413	0.8	1.5	2.6	O157:H7
New Zealand	3	28	1.03	2.13	7.4	O157:H7
Switzerland	4	70	1.4	3.5	4.3	non-O157:H7
Canada	0.7	76	1.2	2.08	2.6	O157:H7

Minimum annual estimate per 100,000 children

Where outcome was known (97.5%) 86.0% of children have appeared to recover normally, 11.6% have had an abnormal/ unclear outcome. Long term sequelea of children contracting *E.coli* O157 induced HUS is unknown, continuous follow-up would be useful. Unfortunately 11 children (2.6%) died of these 8 were under the age of 4.

This is the last year of surveillance through the BPSU however SCIEH will continue to monitor the situation in Scotland and with the help of the British Paediatric Nephrology Association the PHLS also hope to continue to monitor trends in incidence.

HUS surveillance is also currently being undertaken in several other national surveillance units allowing useful data comparison. As you will see from Table 10 the incidence rate in under fives in Switzerland and New Zealand is twice that of Australian, the British Isles and Canada. The death rate in the last two being half of the other countries. It is interesting to note that Australia has few *E.coli* O157:H7 reports, *E.coli* O111:H- being the predominant organism, this is also the case for Switzerland. In contrast in New Zealand O157:H7 predominates. The collection of data by other national surveillance units will, through INoPSU, allow for future international comparisons.

** References (1-10) available from principal researcher (in bold) on request.*

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HIV/AIDS infection in childhood

Key points

- **Almost all new infections are acquired through mother to child transmission.**
- **Interventions can reduce vertical transmission of infection from mother to child to less than 2%. HIV testing should be offered and recommended to all pregnant women as an integral part of antenatal care.**
- **Annual follow up of infected and indeterminate children through contact with the appropriate paediatrician continues. Follow up of uninfected children to explore any adverse effects of exposure to prophylactic antiretroviral therapy is currently being established.**

Background

National surveillance of paediatric HIV infection and AIDS began in 1986 and is based on a combination of paediatric, obstetric and laboratory reporting schemes.

Almost all children now living with HIV in the UK and the Republic of Ireland acquired their infection through mother to child transmission. All the children known to have acquired infection during the course of treatment for haemophilia were born before 1984. There are a small number of children who probably acquired infection as a result of nosocomial transmission outside the UK, and a very few for whom sexual transmission or injecting drug use is the likely source.

Antiretroviral treatment for the pregnant woman and her newborn infant, delivery by elective caesarean section and the avoidance of breastfeeding have dramatically reduced vertical transmission rates, and it is now rare for a woman whose infection is diagnosed prior to delivery to have an infected infant. All pregnant women should now be offered and recommended an HIV test as a routine part of antenatal care. National targets have been set for the uptake of antenatal testing (90% by end 2002), and detection of infection in pregnancy (80% by the end of year 2002) in order to reduce the proportion of infected infants.[1] In the first half of the year 2000 at least 73% of infected women in inner London,

65% in outer London and 78% in Scotland were diagnosed and reported to the surveillance programme, a considerable improvement on previous years (comparable rates for 1997 were 43%, 21% and 27% respectively). Although improvements were slower to appear elsewhere, they are now starting to be apparent.[2]

Objective

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

Case definition

Any child less than 16 years of age who has AIDS, or is HIV antibody positive, or with positive virus culture, polymerase chain reaction (PCR) or antigen detection, or any other laboratory marker of HIV infection. Also any child born to a woman known to be HIV infected at the time of that child's birth regardless of the child's infection status.

Study duration

The survey began in June 1986 and is reviewed annually.

Analysis

By the end of January 2001 there had been 1976 reports through the BPSU. One thousand one hundred and sixty-seven children born to HIV infected women, and therefore at risk of vertical transmission, were reported (Table 11), together with 48 children who were infected in the course of treatment for haemophilia, 25 infected through blood or tissue transfer and six for whom the transmission route cannot be established. Three hundred and twenty-five of the remaining reports were duplicates, and there were also 317 reporting errors. Eighty-eight reports were still under investigation.

Table 11 *Infants born to HIV infected women, and confirmed cases of paediatric HIV infection (notified by 31 January 2001)*

Transmission route (actual or potential)	BPSU Reports	Reports from other sources	Total
risk of vertical transmission	1167	1148	2315
haemophilia treatment	48	219	267
blood transfusion/products	25	17	42
other/not yet established	6	27	33

* NB For infection status of children at risk of vertical transmission see table 12

A further 1411 reported cases have been identified from other sources (see Endnote) including 1148 children born to HIV infected women, 219 children with haemophilia, 17 infected through blood transfusion and 27 where the route of transmission is at present unclear. Data from all sources are combined each quarter and form the basis of the national surveillance of HIV infection and AIDS in children, with UK summary tables appearing on a quarterly basis in the Communicable Disease Report (England, Wales and Northern Ireland) (available at www.phls.co.uk) and the SCIEH Weekly Report (Scotland).

All reporting is voluntary and confidential. Follow up of the surviving young people infected during the course of treatment for haemophilia is undertaken by the UK Haemophilia Centre and the PHLS AIDS and STD Centre. All other children are followed-up yearly to monitor their clinical and immunological status and for those at risk of vertical transmission, to determine their infection status.

By the end of January 2001, 2315 children born to HIV infected mothers had been reported (Table 12); about 12% of these children were born abroad. Transmission rates cannot be estimated from these data as there is a bias towards the reporting of symptomatic children, but 792 had confirmed infection, 534 were of indeterminate status and 989 were known to be uninfected. Two hundred and eleven (9%) children were reported from the Republic of Ireland, 223 (10%) from Scotland, 1557 (67%) from the Thames regions and 324 (14%) from the rest of England, Wales and Northern Ireland, about 15% of indeterminate and infected children were known to have died.

Growing numbers of mainly uninfected children have had perinatal exposure to antiretroviral therapy and mechanisms are being established for on-going follow up of these children, in order that any unexpected or unusual sequelae of treatment can be recognised as early as possible.

Thanks go to all members of the RCPCH, particularly those paediatricians who have reported cases and completed questionnaires, for their continued support and diligence.

Funding

This study is funded by the Department of Health, and additional support is received from the collaborating institutions and the Medical Research Council.

Table 12 *Infection status of children born to HIV infected women (notified by 31 January 2001)*

Region of first report	Infected	Indeterminate	Not Infected	Total
Thames regions	576	385	596	**1557**
Rest of England, Wales & Northern Ireland	135	72	117	**324**
Scotland	39	35	149	**223**
Republic of Ireland	42	42	127	**211**
TOTAL	**792**	**534**	**989**	**2315**

Endnote

Additional sources include: an obstetric reporting scheme run under the auspices of the Royal College of Obstetricians and Gynaecologists; reports to the UK Haemophilia Centre; laboratory reports to the Public Health Laboratory Service AIDS Centre at the Communicable Disease Surveillance Centre, and the Scottish Centre for Infection and Environmental Health; reports made directly to the coordinating centre at the Institute of Child Health in London.

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Invasive Haemophilus influenzae infection

Key points

- **Hib vaccination continues to ensure a low incidence of invasive Hib disease throughout the UK and Republic of Ireland in comparison with the pre vaccine era.**
- **A substantial number of Hib cases could still be avoided by timely vaccination.**
- **The majority of Hib cases in vaccinated children occur in the absence of any obvious predisposing clinical risk factors.**
- **The incidence of Hib disease in the population has shown a progressive increase over the past two years, the significance and causes of which are unclear.**
- **While Hib has now been removed from the orange card reporting scheme, ongoing notification of cases is encouraged in order to continue to monitor the effectiveness of this vaccination programme.**

Background

Haemophilus influenzae type b conjugate vaccines were introduced into the national immunisation schedules of the United Kingdom (UK) and Republic of Ireland (ROI) in October 1992. Infants are given a three dose primary course without boosting, in line with the routine accelerated schedule for other infant immunisations at 2, 3 and 4 months of age. The first year of the programme was supplemented by a catch up campaign, in which a single dose of conjugate vaccine was administered to children aged 1 to 4 years.

In September 1992 the BPSU included invasive *H influenzae* infection occurring after Hib immunisation in its reporting scheme. In 1995, the case definition was broadened to further include cases occurring in unvaccinated children. Data collected has allowed the estimation of vaccine effectiveness, in relation to both the pre vaccine era and the ongoing incidence of cases in the unvaccinated population. In the later years of the study, we can be more confident that estimates of efficacy truly represent the effect of the primary infant series, as those children who took part in the initial catch up campaign have grown older. This information also allows us to make some assessment of the duration of protection offered by a primary conjugate vaccination series without booster. Ongoing post licensure surveillance plays an important further role in monitoring the longer term effects of an immunisation programme on the population, in particular, ensuring that no new populations of 'susceptibles' are generated.

Study duration

The study began in September 1992. Surveillance of invasive *Haemophilus influenzae* infection through the BPSU ceased in October 2000. Ongoing notifications to the PHLS Haemophilus Reference Unit (HRU), the Communicable Disease Surveillance Centre, Colindale (CDSC), the Scottish Centre for Infection and Environmental Health (SCIEH) and the Oxford Vaccine Group (OVG) have been used to generate figures to March 2001 for comparison with previous years' reports.

Objectives

To identify cases of invasive *H influenzae* disease occurring in children regardless of their vaccination status enabling:

1 Estimation of the effectiveness of Hib conjugate vaccines in British and Irish children.

2 Determination of the importance of disease due to non type b *H influenzae*.

3 Documentation of host factors and the clinical presentation of the disease, and in cases of vaccine failure, the collection of acute and convalescent concentrations of Hib antibody.

Case definition

Definite: A child between 0-16 years of age in whom *H influenzae* is cultured from a normally sterile site eg CSF/blood/joint aspirate. The child should be notified regardless of vaccination status.

Examples of invasive diseases include meningitis, pneumonia, bacteraemia, epiglottitis, septic arthritis and osteomyelitis.

Probable: Where antibiotics are administered prior to cultures being taken, the clinical disease is compatible with invasive Hib disease (as listed above) and either:

Hib antigen is detected in fluid from a normally sterile site.

Or

A four-fold rise in Hib antibody between acute and convalescent serum specimens is recorded.

True vaccine failure: the occurrence of invasive Hib disease after three doses of vaccine, or more than one week after two doses given in the first year of life, or more than two weeks after a single dose given to a child over twelve months of age.

Apparent vaccine failure: Hib disease that occurs after vaccination has been given but before protection could be reasonably expected to develop, for example, disease occurring after one dose in the first year of life.

Paediatricians are asked to report cases as soon as possible, preferably by telephone, if *H influenzae* is isolated from a normally sterile site in a child under 16 years of age irrespective of his/her vaccination status. Telephone reporting is needed because a sample should be sent promptly to the PHLS Haemophilus Reference Laboratory at the John Radcliffe Hospital, Oxford, where the serotype of the organism is determined by standard microbiological techniques and capsular genotyping using a polymerase chain reaction (PCR) technique. In cases of vaccine failure, attempts are made to collect acute and convalescent specimens of serum.

Results

By the study's completion date at the end of October 2000, 719 reports meeting the case criteria had been made including 517 in vaccinated and 202 in unvaccinated children. Ongoing surveillance through the HRU, CDSC, SCIEH and OVG to the end of March 2001 identified 67 additional cases (52 vaccinated, 15 unvaccinated). Of this total, 225 cases represented true vaccine failures (TVFs) and 81 were apparent vaccine failures (AVF). There were 19 possible vaccine failures where a course of vaccination was received and an isolate of *H influenzae* obtained but not typed. Amongst vaccinated children there were 198 with invasive disease due to non capsulate strains of *H influenzae* and 46 with non b capsulate strains (type f 35, type e 9, type c 1, type a 1).

Two hundred and sixteen of the 225 TVF were vaccinated in the first year of life: 202 received three doses and 14 received two doses. Nine were vaccinated when older than 12 months of age. Of those UK born and vaccinated in the first year of life (199), 35 developed disease between 5 and 11 months of age, 52 between 12 and 23 months of age, 52 between 24 and 35 months of age, 34 between 36 and 47 months of age, 17 between 48 and 59 months of age, 5 between 60 and 71 months of age and 4 older than 71 months of age. Surveillance has therefore allowed the following point estimates of the effectiveness of three doses in infancy to be made: 99.4% (95% Confidence Interval 99.0, 99.6) for children aged 5-11 months, 97.9% (97.2, 98.4) for those aged 12-23 months, 95.5% (93.9, 96.7) between 24-35 months of age, 95.1% (93.0, 96.8) between 36-47 months of age, 89.9% (82.9, 94.5) for those aged 48-59 months of age and 97.1% (91.2, 99.4) for those 60-71 months of age. For the whole period from 5 to 71 months of age, the estimate is 97.4% (96.9, 97.8).

The modes of presentation and associated medical and immunological conditions amongst the cases of TVF are detailed in Table 13. Data relating to clinical risk factors and immunophenotype was not available for all cases, and the relevant denominators of children for whom this information was know are given. Among all TVFs there have been 7 deaths (3%). Among AVF there have been 4 deaths (5%).

Convalescent sera were available in 163 cases of TVF. Forty-three (26%) demonstrated a convalescent antibody response less than 1.0 µg/ml, the level of antibody thought to correlate with long term clinical protection. Of these, we have information on responses to a booster dose of vaccine in 24 cases, of whom all but one achieved a protective level of antibody.

The majority of *H influenzae* isolated from unvaccinated children have been non capsulate strains (136/217). Ninety one reports have been made in children in the first month of life (six of these were type b). Hib has been isolated from 71 children, of whom 24 were aged less than six months. There have been five deaths attributable to type b infection.

Table 13
Presenting illness and associated conditions of TVF Sept 1992 – March 2001

Presenting illness (n=225)	Number	Associated condition	Number of cases where risk factor data known	Number with risk factor
Meningitis	117	Prematurity	206	22
Epiglottitis	44	Immunoglobulin deficiency	137	36
Bacteraemia	33	Clinical risk factor	203	24
Pneumonia	11	Malignancy		8
Cellulitis	11	Dysmorphic syndrome		5
Septic arthritis	5	Downs syndrome		3
Other	4	Chromosomal anomaly		2
		Neutropaenia		1
		Other		5

From November 1995 all cases of Hib, regardless of vaccination status, have been surveyed enabling the incidence of Hib disease to be calculated. The incidence in children <5 years of age for the years 1996-2000 is shown in Table 14. A significantly increased incidence is observed in the year 2000 in comparison with all previous years.

Table 14
Incidence of Hib disease in UK children < 5 years of age
Jan 1996 – Dec 2000

Year	Cases	Incidence rate per 10^5	(95% CI)
1996	30	0.83	(0.53, 1.1)
1997	29	0.84	(0.54, 1.1)
1998	23	0.63	(0.37, 0.89)
1999	39	1.1	(0.7, 1.4)
2000	66	1.8	(1.4, 2.3)

Conclusions

Estimates of efficacy for three doses of Hib conjugate vaccine in infancy continue to show high levels of protection against invasive type b disease. As previously observed, this is greatest in the first year of life and wanes slightly thereafter. In the year 2000, there was an overall reduction of 94% in the incidence of Hib disease in children under five years in comparison with the pre vaccine era. Of the unvaccinated children in whom invasive Hib disease occurred, 47/71 (66%) were 6 months of age or older at the time of presentation. Timely vaccination may have prevented these cases. Vaccination coverage remains at 92-93% by the age of one year, leaving room for improvement. Overall, when the incidence rate of disease in vaccinated children was compared with those not vaccinated, immunisation was accountable for an 80% reduction in risk of disease.

The increase in the incidence of Hib cases noted last year has been repeated again in the year 2000. This has occurred in children of all age groups, and has not been associated with an increase in clinical factors which may contribute to disease risk. Further evaluation of trends in carriage and population immunity contributing to this increase is required. Of particular note is the more widespread use since January 2000 of combination vaccines incorporating acellular Pertussis, which have been shown to reduce primary antibody responses to Hib conjugates. Information obtained from such analyses is important to the continuing assessment of the adequacy of the current immunisation schedule.

The investigators are very grateful for the ongoing willingness of paediatricians, microbiologists and public health physicians to contribute details regarding cases of invasive *Haemophilus* disease. While reporting by clinicians will no longer continue through the orange card scheme, surveillance will still continue with case ascertainment by microbiologists and CCDCs. Clinicians looking after children with suspected invasive *Haemophilus influenzae* disease are invited to contact the authors listed below.

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Progressive intellectual and neurological deterioration in children (PIND)

Key Points

- **Four cases of vCJD (three definite and one probable) were reported to the study in 1999 and 2000. There is concern that more cases may appear.**
- **We want to hear about all children with progressive intellectual and neurological deterioration even if a diagnosis has already been made! This is important to ensure that ascertainment is as complete as possible.**

Background

Active prospective surveillance of UK children with progressive intellectual and neurological deterioration (PIND) commenced in May 1997 and will continue until April 2002 with a possible extension thereafter. Funded by the Department of Health, it is being carried out via the BPSU in coordination with the National Creutzfeldt-Jakob Disease Surveillance Unit in Edinburgh (NCJDSU) and the Public Health Laboratory Service (PHLS).

Paediatric PIND includes an important group of conditions which have not previously been investigated epidemiologically in the UK. The main aim of the survey is to determine whether or not any children in this group have developed variant Creutzfeldt-Jakob disease. The appearance of variant CJD (vCJD) in patients as young as 16 years of age[1] raised the possibility vCJD could occur in younger children. The detection of vCJD in UK children has important implications for both paediatrics and child health and there was a call for further epidemiological surveillance to investigate this issue.[2] The presentation of vCJD is not typical of classical CJD, and therefore the clinical

presentation of any cases in children is difficult to predict. The strategy is to detect suspected vCJD cases by looking at a broader group of conditions causing progressive intellectual and neurological deterioration in children (PIND). In this way, not only are vCJD cases detected, but also unique epidemiological data on a variety of conditions causing PIND are obtained.[3]

The researchers use a detailed questionnaire to gather information via a telephone interview or site visit to review the case notes. An Expert Neurological Advisory Group consisting of seven paediatric neurologists supports the research team by meeting quarterly, discussing all newly notified anonymised cases, and classifying them according to study categories. There is further follow up of undiagnosed cases via the local paediatricians.

Objectives

- 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) - in order to determine the incidence and distribution of PIND.
- To evaluate cases presenting with PIND in order to classify them and investigate the possibility that v CJD is occurring in children.

Study Duration

May 1997 to April 2002 (5 years) - extended in 2000 from three years to five years.

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.

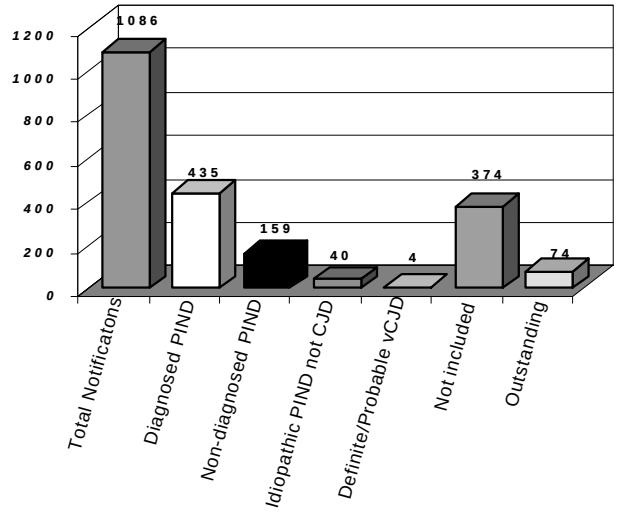
Reports restricted to: Cases seen in the last month but including those whose conditions began earlier (i.e. including "old cases" of children in follow-up (if seen in that month).

Current Status

By the middle of March 2001 a total of **1086** children had been reported via the BPSU. Of these the Expert Group has discussed **785** cases. **Four** children are placed in the Definite or Probable vCJD category (3 Definite, 1 Probable); **435** have been classified as having a recognised cause of PIND; **159** have been classified as meeting the surveillance case definition and are still under investigation; **40** have been classified as Idiopathic PIND - not vCJD; **147** have been classified as "Not PIND"

Of the remaining **301** notifications: **227** are "No Cases" i.e. reported in error, duplicate report, no traceable clinical information and **58** are in the process of being followed-up with 16 of those (so far) due for discussion at the May 2001 Expert Group meeting.

Figure 11
PIND Surveillance – Current Status



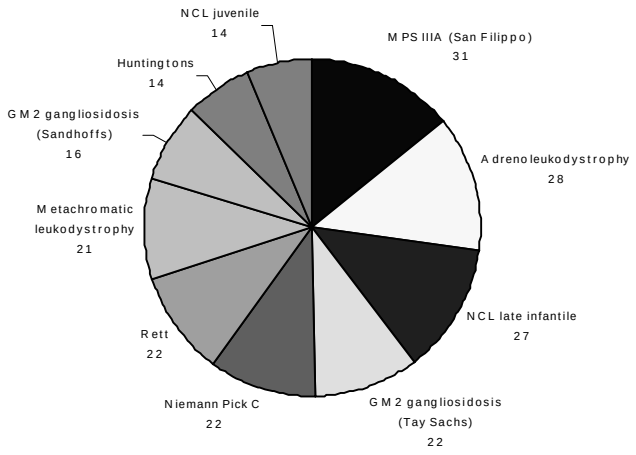
Definite/Probable cases of vCJD

Four cases of vCJD (three definite and one probable) have been notified – the youngest was a girl aged 12 years at onset. The other three were a girl aged 14 years and two boys aged 15 years at onset. Three have died and neuropathology has confirmed vCJD.

Children with PIND who have definite diagnoses other than vCJD

The study is producing unique population-based data on the causes of PIND. The majority of children with PIND have a confirmed diagnosis or likely underlying diagnosis which is not vCJD. In the 435 children with a confirmed diagnosis there were 89 different neurodegenerative conditions. The ten most commonly occurring diagnoses are shown in Figure 12.

Figure 12
The ten most commonly occurring confirmed PIND diagnoses



Variation In Reporting By District

Geographical analysis by hospital of report and by residence reveals significant variations. A few hospitals have not reported any cases. There are some areas with considerably higher rates of incidence of PIND, particularly areas where there is known parental consanguinity. Yorkshire remains the region with the highest number of reports - 139; with North East Thames second at 117 and West Midlands third at 116 reports.

Interim Conclusions

PIND surveillance has been running for almost four years now (in September 2000 the Department of Health approved a two-year extension). Three cases of vCJD in children under 16 years of age at first presentation were notified to the study in 1999 and one in 2000. There were three cases of definite vCJD and one case of probable vCJD. One girl was age 12 years at onset, the youngest ever case of vCJD. There have been no other children with the clinical features of vCJD, however there is concern that more childhood cases may appear. Three years is a short time to perform surveillance for a disease about which there are still many unanswered questions - for example, the number of children who may be incubating vCJD, the length of the incubation period, and the exact nature of transmission.

PIND surveillance is working very well and is yielding valuable information about the conditions that lead to PIND in children. Paediatricians are still responding enthusiastically with a median number of 24 notifications per month. The PIND surveillance team is very grateful to the members of the Expert Neurological Advisory Group (Prof J. Aicardi, Dr P. Baxter, Dr S. Green, Prof. B. Neville, Prof. R. Robinson, Dr R. Surtees and Dr J. Wilson) for all their work in classifying cases and for the cooperation of UK paediatricians in support of this surveillance project.

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Reye's syndrome

Key Points

- **Surveillance of Reye's syndrome via the BPSU ceased in Mayl 2001.**
- **The incidence of "classic" Reye's syndrome has dropped dramatically since June 1986.**
- **Diagnostic vigilance, however, needs to be maintained, especially in the setting of an influenza epidemic.**
- **Continued monitoring of classic, aspirin-associated Reye's syndrome is essential. Such cases should be treated as an adverse drug reaction and reported on a "yellow card" to the Committee on Safety of Medicines.**
- **Most cases reported in recent years, although satisfying the diagnostic criteria, have been atypical.**
- **It is essential to investigate fully, patients presenting with a Reye-like illness *or* with sudden death associated with cerebral oedema and fatty liver, for the relevant inherited metabolic disorders.**

Background

Surveillance of Reye's syndrome began in August 1981 as a venture shared between the (then) British Paediatric Association and the Public Health Laboratory Service Communicable Disease Surveillance Centre (CDSC). Responsibility for case ascertainment was transferred to the BPSU in June 1986. The administration of the scheme was transferred from CDSC to the Department of Paediatrics at Sheffield in 1995.

In the early years, the surveillance data demonstrated that the incidence of Reye's syndrome in the British Isles was similar to that in the United States, where national surveillance of this condition has been in place since the mid-seventies. However, British and Irish cases occurred at a younger mean age, there was no clear seasonal (winter) peak, no striking association with influenza and chickenpox (although such cases did occur), and a higher case fatality rate.

In 1984/85 a risk factor study, mounted on to the surveillance database, showed an association between Reye's syndrome and consumption of aspirin. In response both to this and to similar findings in the United States, the Committee on Safety of Medicines issued public and professional warnings in 1986 about the use of aspirin in children. Since then, products that contain aspirin have been required to carry warning labels which state " Do not give to children under 12 except on the advice of a doctor". From April 1998, aspirin-containing medications are additionally required to state on patient information leaflets : "There is a possible association between aspirin and Reye's syndrome when given to children with a fever."

There is increasing recognition that a number of inherited metabolic disorders - most notably those affecting fat oxidation, amino acid metabolism and ureagenesis, may present as a 'Reye-like' illness, which is *clinically and pathologically indistinguishable from Reye's syndrome*. The surveillance questionnaire, although currently in its simplest and shortest format since 1981, therefore seeks information on whether patients have been investigated for these disorders.

In addition to BPSU reporting, cases are also ascertained via death entries provided by the Office for National Statistics, the General Register Office for Scotland, the Northern Ireland Statistics and Research Agency, and via laboratory reports to CDSC.

Objectives

To describe the epidemiological and clinical features of Reye's syndrome in the British Isles, to monitor long term trends, and to provide a database for detailed clinical, laboratory, and aetiological studies.

Study duration

June 1986-April 2001.

Case definition

A child under 16 years old with:

unexplained non-inflammatory encephalopathy, and *one or more of*:

- serum hepatic transaminases elevated to at least three times the upper limit of normal;
- blood ammonia elevated to at least three times the upper limit of normal;
- characteristic fatty infiltration of liver (biopsy or autopsy).

Since this definition is relatively non-specific, cases reported from surveillance year 1994/5 onwards, whose diagnosis has not been revised, have been allocated a "Reye-score".[1] Because of the non-specificity of the case definition and because there may still be "Reye-like" inherited metabolic disorders as yet undiscovered, **a case of Reye's syndrome can rarely, if ever, be described as confirmed;** it is better designated as "compatible with" the diagnosis.

Study duration

Ascertainment of cases via the BPSU began in June 1986 and ended in April 2001.

Analysis

Between August 1981 and April 2001 a total of 632 suspected cases of Reye's syndrome were reported (Table15 overleaf), but the diagnosis was subsequently revised in 164 (26%). Eighty one (49%) of the revisions were to one of the 'Reye-like' inherited metabolic disorders. Two hundred and thirty nine (53%) of the total 450 cases compatible with a diagnosis of Reye's syndrome died.

In the year to July 31st, 2000, four reports of new cases were received and further information was provided on all of them. One of the four diagnoses was later revised, leaving three patients whose clinical and pathological features were compatible with the case definition of Reye's syndrome. Three of the cases were first reported via the BPSU, one was ascertained only via a death entry. ***In the period August 1st 2000 to April 30th 2001***, three reports were received, further information was provided on two. One of the diagnoses was later revised; in the other case a specific alternative diagnosis was not reached, but an inherited metabolic disorder was so strongly suspected that Reye's syndrome was not recorded as a cause of death.

Cases compatible with a diagnosis of Reye's syndrome (surveillance year 99/00, N=3):

There was one male and two females; the ages were 2 months, 14 months and 23 months. Their illnesses were in November, January and April. All lived in England - there were no reports this year from Northern Ireland, Republic of Ireland, Wales or Scotland.

One child, whose investigations for an inherited metabolic disorder were negative, recovered completely. Of the two who succumbed, both died suddenly and unexpectedly during relatively mild viral-type upper respiratory and gastroenteritic illnesses respectively. The diagnosis of Reye's syndrome was made at autopsy on the basis of cerebral oedema and a characteristic histological appearance of the liver. Investigations on both for inherited metabolic disorders were negative. Virological investigations on all three cases were also negative. Only one patient had received preadmission medications: paracetamol and ibuprofen.

The 'Reye Scores' (possible range 1-25) were 9,12 and 15. The median scores in the previous five years were 12, 12, 13, 13 and 16 respectively.

Revised diagnosis cases

The one case in 99/00 was a nine month old boy who died suddenly during an episode of gastroenteritis. Although the autopsy findings led to a preliminary diagnosis of Reye's syndrome, subsequent investigations revealed medium chain acyl coA dehydrogenase deficiency. Of the two cases in 00/01, one was a two month old boy who died suddenly during an upper respiratory illness. An inherited metabolic disorder was suspected on grounds of extensive fatty change in liver, kidneys, heart and muscle, but investigations were negative. The other patient was a four year old girl presenting with encephalopathy and abnormal liver function tests after a gastroenteritic illness in whom the subsequent diagnosis was pneumococcal meningitis and cerebrovascular accident complicating sickle cell anaemia.

Comment

This Annual Report will be the last in the series which started in 1981/82, when surveillance of Reye's syndrome began. As the first clinical reporting scheme involving paediatricians in the UK and Ireland in the epidemiological surveillance of rare disorders of public health importance, the Reye's syndrome surveillance scheme was a forerunner of the BPSU. It is fitting that the total cases in the last complete surveillance year, three (none of whom had classic, aspirin associated Reye's syndrome), equals the lowest total recorded in 19 years and that, so far up to the end of surveillance in April 2001, there have been no cases

at all. It is fitting because the trends vindicate the public health action taken on the use of aspirin in children in 1986 which, as also reported in the United States, represents a triumph for primary prevention of a devastating childhood illness.[2]

National surveillance of Reye's syndrome through paediatrician reporting has now ceased, but two important issues remain:

First - *classic, aspirin-associated Reye's syndrome* has now become so rare that some clinicians have dismissed it as being no longer of any clinical importance. However, this is a dangerously complacent view of a disease capable of re-emergence during a major influenza epidemic or pandemic (it is now 10 years since the annual influenza incidence rose to epidemic levels and even these were not as high as in the last major epidemic in the 1970s) if aspirin warnings are disregarded or ignored because the child is over 12. The decline of Reye's syndrome means that a new generation of paediatricians in training and young consultants will certainly never have seen or heard about a case and are unlikely to have read about it or had it included in educational materials. Furthermore, it is likely to be under-recognised by physicians caring for teenagers and older adults with acute encephalopathy. Thus if there is a resurgence, the "old days" of late diagnosis, late or inappropriate treatment and poor outcome in terms of mortality and brain damaged survivors may be seen again.

It is, therefore, most important that Reye's syndrome is not forgotten or removed from the differential diagnosis of a child presenting with encephalopathy following a viral prodrome. The incidence should continue to be monitored, if less intensively than via the BPSU. Methods of achieving this are currently under consideration, but in the meantime it is *essential* that such cases are considered as an adverse drug reaction to aspirin and reported to the Committee on Safety of Medicines via the "yellow card". This will reveal any upsurge in the event of an influenza epidemic which might require action in the form of public education, and will inform any re-evaluation by the regulatory authorities of the upper age limit on the warning.[3]

Second - because the classic form of the illness has become so rare, it is now more likely that a patient presenting with a Reye's syndrome-like illness has an inherited metabolic disorder especially if the child is aged under three years (although these disorders can present in later childhood or even in adult life).[4] All of the six cases reported in 99/00 and 00/01 for whom further

Table 15
Reye's Syndrome Surveillance 1981/82 - 2000/01†

Reporting period (August-July)	Total reports from the British Isles	Revised diagnosis (inherited metabolic disorder in brackets)		Cases of Reye syndrome*	Number of deaths (of cases)
1981/82	47	7	(3)	40	26
1982/83	69	10	(6)	59	34
1983/84	93	12	(3)	81	36
1984/85	64	8	(2)	56	32
1985/86	53[1]	13	(4)	39	22
1986/87	47	21	(11)	26	13
1987/88	44	12	(3)	32	19
1988/89	31	13	(6)	18	9
1989/90	24[1]	8	(5)	15	7
1990/91	25	13	(8)	12	5
1991/92	23[2]	6	(5)	15	6
1992/93	21[3]	10	(6)	5	4
1993/94	20[4]	13	(7)	3	3
1994/95	17[2]	3	(2)	12	3
1995/96	18[1]	2	(1)	15	7
1996/97	7	2	(2)	5	4
1997/98	11	4	(2)	7	5
1998/99	11	4	(3)	7	2
1999/00	4	1	(1)	3	2
2000/01	3†	2	(1)	0	0
TOTAL	632	164	(81)	450	239

* *Compatible with the diagnosis (see text)*

† *to April 01*

1 *Follow-up not received for one case*

2 *Follow-up not received for two cases*

3 *Follow-up not received for five cases and one case did not meet the case definition*

4 *Follow-up not received for five cases*

Note: numbers may differ from previous versions of this table because of late ascertainment of cases and revised diagnosis

information was provided were atypical for classic Reye's syndrome and five were under two years of age. Three of them subsequently did have a revised diagnosis -to an inherited metabolic disorder in two. The observation that all reported cases in these last one and a half surveillance years had at least some investigations for inherited metabolic disorders and that numbers of reports of atypical cases have also declined in recent years, suggests that diagnostic awareness of these conditions has increased.

We are most grateful to all the paediatricians who, over the past 20 years, have reported cases and provided further information.

Funding

The Reye's syndrome surveillance scheme is funded by the National Reye's Syndrome Foundation of the UK, to whom the investigators are most grateful.

References

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3 Hall SM and Lynn R. Reye's syndrome. New Engl J Med 1999; 341: 845-846

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Severe visual impairment and blindness

Key Points

- **Surveillance of severe visual impairments ended in December 2000 but 1 year follow- up data an all notified cases are being collected.**
- **A larger than anticipated number of eligible children have been identified.**
- **Interesting findings are emerging which it is hoped will be helpful to clinical practice and service provision.**

Background

Information on the incidence and causes of severe visual impairment and blindness in childhood is important for the development and evaluation of preventive strategies, for aetiological research and for provision of services for affected children and their families. Currently, this information is not readily available from routine sources at a national level.

Objectives

1 To determine the incidence of severe visual impairment and blindness in childhood in the UK and Republic of Ireland, for children with isolated visual loss and those with other impairments.

2 To describe the causes of severe visual impairment and blindness in children, using a standardised classification based on anatomical site(s) affected and underlying or associated cause(s).

3 To determine the mode of detection and timing of ophthalmic assessment of affected children, including the proportion detected through routine screening or surveillance examinations.

4 To ascertain current national practice regarding partial sight or blindness certification of eligible children.

Case definition

Any child under 16 years *newly diagnosed (suspected or confirmed)* as severely visually impaired or blind *due to any disorder*, to include:

- a child whose visual acuity cannot be measured formally but who has clinical features consistent with severe visual impairment or blindness (e.g. is unable to follow a light)
- a child who is eligible for certification as blind or partially sighted
- a child whose corrected distance visual acuity is less than 6/60 (or equivalent) in the better eye

Children with unilateral visual loss or born outside the UK or Ireland are ineligible.

Study duration

September 1999 - December 2000.

Methodology

Surveillance for the study was undertaken, simultaneously but independently, through the British Paediatric Surveillance Unit and the British Ophthalmological Surveillance Unit (BOSU), from 1st September 1999 until 31st December 2000. Eligible children were identified using both sources in order to ensure high ascertainment, particularly of children with multiple impairments, and to allow as complete data as possible to be obtained about each child.

Results

To date, more than 350 confirmed cases have been identified, 46% through the BPSU alone. Other notifications are awaiting confirmation. **At present, follow up information is being sought one year after notification on all cases**. This will allow final confirmation of their eligibility and updating of previously reported data, as necessary. So far, follow up data have been collected on children notified during the first six months of the surveillance study.

Interim analysis of findings at notification shows:

- children of low birth weight are over-represented, compared with the national picture
- about half of the children have additional *non-ophthalmic* impairment(s)
- in about half of the children, visual loss was *suspected* by parents before contact with a health professional, about half presented symptomatically
- in almost two thirds of all children, visual impairment was first *detected* by a non-ophthalmic health professional, most commonly by hospital based paediatricians
- disorders of the cortex / visual pathways, retina, and optic nerve are the most common causes of visual impairment
- the anatomical pattern differs between those with visual impairment alone and those with other impairment(s).

The study continues to progress well, with interesting findings starting to emerge which we hope will be relevant to clinical practice and service provision. Final analysis of the data will be undertaken once the process of collecting and validating follow up data has been completed, towards the beginning of 2002.

We are very grateful to all paediatricians for notifying their patients for inclusion in the study and providing initial and follow up information about them. Should any paediatrician have any patients eligible for inclusion in the study, but as yet unreported, we would be very grateful to know about them.

Funding

National Eye Research Centre, Children Nationwide Medical Research Trust and British Council for Prevention of Blindess.

Selected references

(Further references available from investigators or BPSU office).

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2 Rahi JS, Dezateux C. Epidemiology of visual impairment in Britain. Arch Dis Child 1998; **78**: 381-386

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Subacute sclerosing panencephalitis (SSPE)

Key Points

- **SSPE continues to occur in the UK though it is extremely rare.**
- **Detailed virological analyses of samples from the reported cases indicate that all these were due to so-called 'wild' virus and none were due to immunisation.**

Background

A register of cases of subacute sclerosing panencephalitis (SSPE) was set up by Professor George Dick in 1970 at the request of the Joint Committee on Vaccination and Immunisation. The object was to establish the incidence of SSPE in the UK so that any change following the introduction of measles vaccination in 1968 would be recognised. In 1980 the Register was transferred to Dr Christine Miller, formerly of the Epidemiology Research Laboratory, now the PHLS Communicable Diseases Surveillance Centre (CDSC), in 1989 to Dr Norman Begg and in 1993 to Dr Elizabeth Miller.

Initially paediatricians and neurologists were asked through the medical press to notify cases to the Register; clinical and laboratory details were then requested from the clinician. From 1980 an annual letter was sent to every paediatrician and neurologist listed in the Medical Directory, asking for a slip to be returned to state whether or not a case had been seen.

SSPE was included in the BPSU reporting system from its inception in 1986 until July 1994, when it was removed from the card. In the following year, with only a passive surveillance system, no cases were brought directly to the attention of CDSC.

However, two cases came to the attention of the investigators later and one case through a media report, and one through a "Yellow Card" adverse event notification to the Committee on Safety of Medicines. SSPE was returned to the BPSU card in September 1995 in order to assess whether or not the apparent decline in incidence was a true reflection of the burden of disease.

The number of cases arising since 1982 has fallen. This follows about ten years after the decline in measles, which resulted from the introduction of vaccine (PHLS CDSC, unpublished data). However, under-reporting may also be responsible and as the incidence appears to fall the importance of complete notification increases.

Objective

To monitor the incidence of SSPE.

Study duration

June 1986-June 2001.

Methods

When a case is reported, the paediatrician is asked to provide brief clinical details on a one-page proforma. Analysis is initially made only on England and Wales data. If available, diagnostic specimens (CSF, fresh biopsy material, fresh frozen brain tissue or fixed brain tissue) are analysed using the polymerase chain reaction and direct sequencing to detect and classify viral genome. Serum and CSF samples are also examined for evidence of intrathecal measles antibody production.

Case definition

A typical history: usually insidious onset of mental deterioration followed (usually within a few months) by motor dysfunction, finally a progressive decerebration and ultimately death and one of the following:

1 raised measles antibody titres in the serum and CSF indicative of intrathecal antibody production and a higher level in the CSF compared to serum,

2 typical EEG changes,

3 typical brain histology or other evidence of measles virus in brain tissue.

A definitive case requires the presence of 1 and 2.

Cases identified as SSPE should also be reported to the PIND surveillance project see page 25.

Recent results and progress

Two new cases were reported through the BPSU with onset in 2000. The diagnosis was confirmed in each case at the Enteric, Respiratory and Neurological Virus Laboratory (ERNVL), Colindale, (a WHO Global Measles Reference Laboratory) using paired serum and CSF samples. Age at onset was four years (immigrant who had had measles before coming to the United Kingdom two years previously) and fifteen years respectively. A further case was confirmed at ERNVL through molecular investigation, the strain identified from brain biopsy was an historic wild type strain belonging to genotype D1. Genotype D1 is currently inactive in the United Kingdom but was one of the predominant wild type strains of measles virus circulating in the UK in the 1970s. Age at onset was 21 years.

The referencing of strains used is in accordance with the WHO classification of reference strains to be used for genetic analysis of wild-type measles viruses.

Funding

Public Health Laboratory Services

References

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2 Jin L, Richards A, Brown DWG. Development of a dual target PCR for detection and characterization of measles virus in clinical specimens. Molec and Cell Probes 1996;**10**:191-200

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6 New studies for 2001

Cerebrovascular disease, stroke & like illness

Background

Cerebrovascular disorders in childhood are associated with significant mortality and considerable residual handicap, both physical and cognitive. For the United Kingdom, however, the actual numbers of children affected annually by stroke remains unknown. This study, run through the British Paediatric Surveillance Unit, is a prospective observational study of one year's cases with independent surveying of British neurosurgeons, cardiac surgeons, cardiologists, paediatric radiologists and haematologists/oncologists.

The aetiology of stroke and cerebrovascular disease in childhood remains a puzzle in a significant proportion of cases and even where there appears to be an association, causation may remain unproven. Management strategies have been developed for certain conditions, but there is no overall policy yet. The most important questions that doctors face is how far to investigate children with cerebrovascular disease or stroke, whether to refer and whether to treat. The initial surveillance study will look at current practice.

Objectives

1 To estimate the incidence of stroke, stroke-like illness and cerebrovascular disease in all children between birth (at >37 weeks gestation) and 16 years.
2 To determine the national and regional patterns of presentation and of neurological referral.
3 To assess aetiology considered at the time of diagnosis in incident cases, and to describe current practices, management and prevention.

Study duration

January 2001- January 2002.

Case definition

Any child from birth (at >37 weeks gestation) and the 16th birthday with cerebrovascular disease and/or stroke or stroke-like illness. The W.H.O. definition of stroke is: "A clinical syndrome of rapidly developed clinical signs of focal or global disturbance of cerebral function lasting greater than 24 hours or leading to death with no obvious cause other than that of vascular origin".

To Include children with cerebrovascular disease presenting in other ways e.g.

- haemorrhage or infarct in a vascular territory with disturbance of cerebral function for less than 2 hours
- moyamoya
- venous sinus thrombosis
- Sturge-Weber syndrome presenting as (e.g.) epilepsy
- Vein of Galen malformation presenting as or e.g. cardiac failure
- 'stroke-like episodes' lasting more than 24 hours without an obvious vascular cause e.g. in migraine or metabolic disease
- focal intracerebral haemorrhage or ischaemic infarct related to severe head injury

This does not automatically exclude prior illness e.g. infection or events e.g. head trauma, provided that this is linked to the clinical presentation via a vascular mechanism

Exclude

- non-cerebral venous and arterial thrombosis
- subdural/extradural haematoma
- neonatal intraventricular haemorrhage and periventricular leukomalacia
- hemiparesis after seizures (Todd's paresis) unless cerebrovascular disease

Funding

Stroke Association

Reference

Stroke in Childhood. Kirkham F.J. Arch Dis. Child. 1999; **8**1:5-89

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Vitamin K deficiency bleeding

Background

The BPSU survey of Haemorrhagic Disease of the Newborn 1988-90 clearly demonstrated that the condition remains a cause of death and handicap which is preventable by vitamin K prophylaxis.[1] Intramuscular prophylaxis gave more reliable protection than oral in the doses then used. In 1992 wide publicity in the popular press has been given to studies suggesting a link between vitamin K prophylaxis administered to neonates and subsequent development of childhood cancer.[2] Subsequent studies have given some reassurance but it may never be possible to exclude a 10% increase in risk. As a result, paediatricians have repeatedly reviewed their prophylaxis recommendations and many parents are anxious about the use of vitamin K in any form. More In 1996 Konakion MM Paediatric became licensed for oral prophylaxis and is increasingly used. There is no uniformity of practice and so continued surveillance for VKDB remains essential.

The first and second BPSU surveys of Vitamin K Deficiency Bleeding (VKDB) were carried out between 1989-90[1] and in 1993-4[3] and demonstrated that:

- VKDB was still occurring in the British Isles despite widespread use of vitamin K prophylaxis
- VKDB is a significant cause of preventable mortality and morbidity.

Vitamin K is now given in four common but very different regimens. In 1993 one or two units gave no routine prophylaxis, some gave a single oral dose, some gave multiple oral doses and some gave intramuscular vitamin K to all infants.[4] The relative risk of bleeding in infancy is maximum in the first and minimum in the last of these groups with dramatic differences across the groups; babies given no prophylaxis (including those whose parents have refused it) are eighty times more likely to bleed than those given intramuscular prophylaxis.[5] Errors in administration of the planned regimen or parental refusals would tend to mask these differences.[5]

Surveys of vitamin K prophylaxis in the United Kingdom in 1988 and 1993[4] showed an increase in the number of infants receiving prophylaxis orally and since that then there has been an increase in the number of infants receiving multiple oral prophylaxis regimens with Konakion K MM (Roche) or other preparation.

Unsuspected liver disease continues to be a high risk factor for VKDB.[1,6]

Study duration

January 2001-January 2003.

Research Questions

1 Have the recent changes in vitamin K prophylaxis regimens, with the introduction of vitamin K MM in various dosages, altered the prevalence of VKDB?
2 Do failures to achieve the planned prophylaxis regimen remain a major cause of morbidity?
3 Do the newer regimens and preparations reduce the risk of VKDB when there is co-existing liver disease?
4 When vitamin K is **NOT** given, is this because
   a) policy of the maternity unit?
   or b) parents chose not to follow recommended policy?
   or c) policy inadvertently not followed?
5 Was there delay in presentation when the significance of apparently trivial warning was not appreciated?

Case definition

Any infant under 6 months of age with spontaneous bruising/ bleeding or intracranial haemorrhage associated with prolonged clotting times, not due to an inherited coagulopathy or disseminated intravascular coagulation.

NOTE: The same definition was used for "Haemorrhagic disease of the newborn" in the previous BPSU survey.[1] An Expert Committee convened at the request of the Department of Health and chaired by Professor David Hull agreed that the term "Haemorrhagic disease of the newborn" was potentially misleading - it did not mention vitamin K or exclude other causes of bleeding and it erroneously implied a condition confined to the newborn period and was sometimes confused with "Haemolytic Disease of the Newborn". The new term, Vitamin K Deficiency Bleeding, was agreed to be more informative and correct[7] and so has been adopted internationally and so will be used in this survey.

Please note that measurement of clotting parameters before the administration of blood products or vitamin K remains very important. This is particularly so in relation to agreed international criteria for diagnosis, which are essential in comparing data with other countries who have different regimens of prophylaxis.

Funding

Department of Health.

References

Available from investigators or BPSU office.

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Congenital Cytomegalovirus (cCMV)

Background

Primary or recurrent maternal CMV infection in pregnancy can result in fetal infection. Although most infants have no associated problems, cCMV can cause neonatal death or severe disease, and long-term disability in 10-20% of infected children. The incidence of cCMV ranges from 0.3% to 2% of all live births worldwide; earlier British studies suggest an incidence of 3-4/1000 live births, but this varies in different population groups, and may have changed over time. Congenital infection can only be confirmed on the basis of samples collected in the first three weeks of life. Detection of CMV in later samples is likely to reflect infection acquired at delivery or postnatally, which is common, but rarely associated with adverse outcome. In Britain about 20% of children probably become infected by 12 months of age.[1] About 10% of congenitally infected infants are symptomatic at birth, and most of these have long-term complications, for example cerebral palsy, mental retardation and sensorineural hearing loss (SNHL).[2-4] In contrast, most asymptomatic infants develop normally, although a minority have neurological sequelae, usually SNHL.[5-9] Infants with cCMV who are asymptomatic at birth or have non-specific symptoms are unlikely to be identified. This surveillance study is part of a planned programme of work, and a parallel research project to investigate the contribution of cCMV to serious congenital hearing loss is being developed.

Study duration

February 2001-February 2002.

Case definition

Any infant with confirmed or suspected cCMV infection born in the UK or Republic of Ireland since 1 January 2001.

Confirmed cases: any infant with cCMV infection, confirmed by PCR or virus isolation from urine, blood, saliva or tissue taken at biopsy within 3 weeks of birth.

Suspected cases*:* any infant with symptoms compatible with cCMV infection aged under 12 months with CMV isolated from urine, blood, saliva or tissue taken at biopsy after 3 weeks of age, and/or with CMV specific IgM after 3 weeks of age.

Methods

Reporting paediatricians will be sent a brief questionnaire seeking demographic and clinical information on receipt of their notification, and a second brief questionnaire to establish the child's clinical status at one year of age.

Laboratory techniques have recently been developed to detect CMV DNA in dried blood spots by PCR, and it may be possible to make a retrospective diagnosis for infants with suspected cCMV identified after three weeks of age, if the Guthrie card can be retrieved and a sample is available. We will attempt to do this.

As part of this study we will also offer testing of viral load in urine and blood for children with confirmed cCMV infection. Samples will be processed at the Royal Free Hospital as part of on-going research into CMV disease and outcome carried out there. Paediatricians wishing to take advantage of this offer should store at least two blood samples on occasions when blood is being taken for clinical purposes during the 12 months after diagnosis. Blood can be stored whole, in citrate anti-coagulant, at -20°C; one or two urine samples could also be stored, also at -20°C. Viral load will be assessed in these samples at a clinically appropriate time, or at a later date to explore the relationship with neonatal symptoms, severity of neonatal disease, and sequelae of congenital infection. Further details will be supplied to reporting paediatricians.

Funding

Institute of Child Health (London).

References

Available from the investigators or BPSU office

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Thrombosis in childhood

Background

Symptomatic thrombotic events, venous and arterial, are rare in childhood, particularly after the neonatal period, and the incidence in the UK is unknown. A Canadian Registry of DVT/PE in children (age 1 month to 18 years) prospectively identified 137 patients, giving an incidence of DVT/PE of 5.3/10,000 hospital admissions, or 0.07/10,000 children in Canada. Infants under one year of age and teenagers predominated (18% and 50% respectively) with an equal sex distribution. Two retrospective reviews report an incidence of clinically symptomatic DVT in children and PE in adolescents/young adults of 1.2 and 7.8 cases per 10,000 hospital admissions. Advances in tertiary care paediatrics with its accompanying increase in invasive procedures, and a growth in organ transplantation, may be contributing to an increase in incidence.

Current management decisions for children with thrombosis are directly extrapolated from treatment recommendations for adults with no further validation. To accept recommendations for adult patients as optimal management for paediatric patients, these two patient populations and their thrombotic problems have to have basic features in common. These parameters include the primary underlying disorder, the distribution of vessels involved, the interaction of anticoagulant and thrombolytic drugs with the haemostatic system, the pharmacokinetics of these drugs and the risk of serious complications of the disease and treatment. Available data suggests there are important differences.

DVT involves the upper system in between 26-36% of children

(due to the use of central venous catheters) compared to 1-2% of DVT in adults. Idiopathic DVT is rare (4% in the Canadian Registry and 2% in the literature) in contrast to approximately 30% of adult DVT, and more than 95% of children with DVT/PE have one or more predisposing factors. The role of acquired and inherited thrombophilia in children remain unclear.

There have been no comparative studies evaluating the sensitivity and specificity of diagnostic procedures in children, and given the differences in the size and location of vessels involved, it is unlikely that the results from comparative studies in adults can be extrapolated to children.

There is a profound effect of age on plasma concentration of coagulation proteins, with secondary effects on the regulation of thrombin and plasmin. This subsequently influences the pharmacokinetics of anticoagulants which strongly suggest that optimal therapy for children with thrombo-embolic disease and its complications may differ significantly from adults.

Objectives

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

Study duration

February 2001- February 2002.

Case definition

Any child aged between one month (or 44 weeks post-conceptional age) and 16 years newly diagnosed with an objectively documented venous or arterial thrombosis.

Exclude: children with stroke whether this is arterial or due to sino-venous thrombosis.

Funding

Local hospital research funds.

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Internal abdominal injuries due to child abuse in children under 14 years

Background

In the course of a two-year study of severe child abuse in Wales using the Welsh Paediatric Surveillance Unit, four cases of abdominal injury due to child abuse were ascertained two of which were fatal (WPSU). The WPSU uses similar methodology to the BPSU. If figures from Wales are representative of the United Kingdom as a whole than abdominal injury is the second most common cause of death in childhood from abuse after sub-dural haematoma. Although abdominal injury is a well-recognised form of child abuse there is only a small literature on the subject. The paediatrician may therefore be in difficulties in analysing these cases for the child protection process. We understand that there are undoubtedly some cases of abuse where there is evidence of abdominal injury such as bruises but no evidence of internal injury. There are major difficulties of attempting a BPSU study on this. Although clearly important, they do not form part of this study.

We would use as controls for this study cases of unintentional internal abdominal injury from the Trauma Audit and Research Network (Professor David Yates), this covers 60% of the Accident Departments in the UK.

Objectives

To identify:

1 what is the incidence of abdominal injury due to abuse?
2 what organs are involved?
3 what are the diagnostic features both in the differential diagnosis of abuse versus accident and the diagnosis of injury?
4 were there factors prior to diagnosis that could have prevented the abuse?
5 what was the Child Protection outcome?

Study duration

March 2001-March 2002.

Case definition

Children 0-14 years diagnosed as having an internal injury of the abdomen due to child abuse. For inclusion cases would be referred for at Case Conference or other Multidisciplinary child protection meeting.

Include - traumatic damage or rupture of any abdominal viscera including deaths.

Exclude - abdominal bruising alone.

Funding

Local sources in Wales.

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7 The International Perspective

Background

Following the success of the BPSU, the same methodology was adopted and adapted in the 1990's to other countries whose paediatric services are amenable to an active surveillance approach. Within Europe this led in 1992 to units in the Netherlands and Germany and in 1994 Switzerland. The European paediatric surveillance units then met and communicated regularly in order to discuss surveillance protocols.

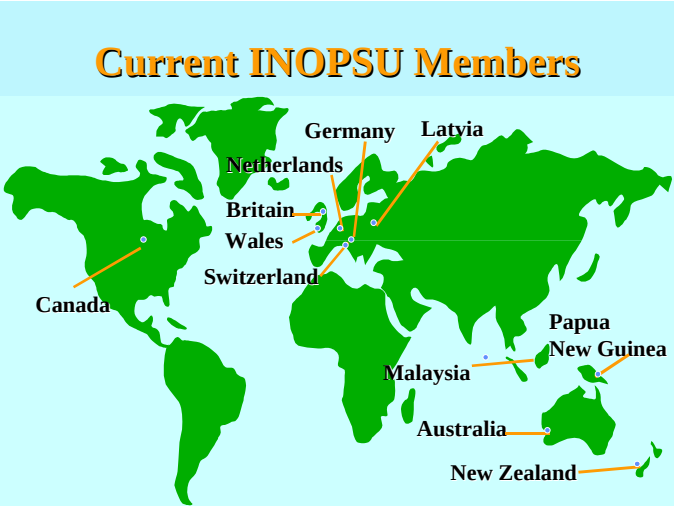
The European initiative was also the stimulus for the development in 1992 of an Australian unit and later the Malaysia unit (1994) to be followed more recently by units in Canada (1996), Papua New Guinea (1996), New Zealand and Latvia (1997). Portugal has recently set up a unit, and commenced surveillance in 2001. Interest has also been shown in Belgium, Greece /Cyprus and the Czech Republic. Wales (1995) and Republic of Ireland (1997) developed surveillance units using a similar methodology to the BPSU, though they are concentrating on less rare disorders.

Through the use of active ascertainment the ten units provide an efficient, effective framework for case-finding for investigators who wish to study rare conditions in children. These include infections, infection-related conditions, vaccine-preventable diseases, congenital and inherited (genetic) diseases, unusual injuries or therapies and rare complications of common diseases. The units frequently encourage, facilitate or elicit studies but only occasionally undertake research themselves.

The director of the Australian unit keeps in contact with those of units in Papua New Guinea, New Zealand and Malaysia. Given the existence of at least ten national paediatric surveillance units undertaking similar work and this level of informal contact it was accepted byall that the time had come to formalise these links into a network.

In 1996 the proposal to form an International Network of Paediatric Surveillance Units (INoPSU) was accepted in principle by all units existing at that time. Now all the units contact each other for results, sharing of protocols, putting researchers in touch with each other and a common international report is shared as part of national reports.

International Network of Paediatric Surveillance Units (INoPSU)



The network was formed in August 1998 at a meeting of the 10 units expressing a desire to link with each other. This took place at the 22nd International Congress of Paediatrics in Amsterdam, The Netherlands. The first INoPSU conference was held in June 2000 in Ottawa, Canada sponsored by Health Canada and was attended by representatives of most of the existing units.

A document known as the Amsterdam-Ottawa Note detailing the functions and structure of the network has been agreed and will posted on the INoPSU website (www.inopsu.com).

The mission of INoPSU is *the advancement of knowledge of 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*. These include the following agreed in Amsterdam:

- facilitate communication and cooperation between existing national paediatric surveillance units;
- to assist in the development of new units;
- to facilitate sharing information and collaboration between researchers from different nations and scientific disciplines;
- to share information on current, past and anticipated studies and their protocols, and on conditions that have been nominated for surveillance but are not selected;
- to encourage the use of identical protocols to potentially enable simultaneous or sequential collection of data on rare paediatric disorders in two or more countries;
- to share and distribute information of educational benefit to constituent units, notably on study and surveillance methodologies;

- to share school techniques and models of evaluation for units;
- to peer review and evaluate existing and proposed units;
- to identify rare disorders of mutual interest and public health importance for cooperative surveys through each national unit;
- to collaborate with and provide information to other groups interested in rare childhood diseases such as parent support groups;
- to respond promptly to international emergencies relating to rare childhood conditions where national and international studies can make a contribution to science or public health;
- To vigorously encourage the promulgation of the benefits of surveillance to the whole community including the general public, patient groups, health care staff and decision makers;
- To promote guidance to national units and others as to how surveillance can be carried out without prejudicing data protection, patient confidentiality and ethical standards.

The founding units are: Australian Paediatric Surveillance Unit (APSU); British Paediatric Surveillance Unit (BPSU); Canadian Paediatric Surveillance Programme (CPSP); German Paediatric Surveillance Unit (ESPED); Latvian Paediatric Surveillance Unit (LPSU); Malaysian Paediatric Surveillance Unit (MPSU); Netherlands Paediatric Surveillance Unit (NSCK); New Zealand Paediatric Surveillance Unit (NZPSU); Papua-New Guinea Paediatric Surveillance Unit (PNGSU); Swiss Paediatric Surveillance Unit (SPSU).

The Welsh Paediatric Surveillance Unit has now joined this group and the British Ophthalmological Surveillance Unit has joined as an associate member. Both the Irish and Portuguese units intend to submit applications to join.

In order to carry out the aims and direct the activities of INoPSU a secretariat has been set up. From 2000 Professor Elizabeth Elliott (APSU) will act as convenor, taking over from Dr Angus Nicoll (BPSU). Also on the secretariat are Dr Rudi von Kries (Germany), Professor Victor Marssault (Canada), Dr Chris Verity and Richard Lynn (BPSU). The British Paediatric Surveillance Unit will continue to act as server. INoPSU has recently published its first collaborative paper (Elliott EJ, Nicoll A, Lynn R, Marchessault V, Hirasing R, Ridley G, on behalf of the secretariat and members of the international network of paediatric surveillance units. Rare disease surveillance: An international perspective. Paediatr Child Health. 2001; 6(5):251-59).

Current work being undertaken in individual units is highlighted as follows:

Australian Paediatric Surveillance Unit (APSU)

The APSU commenced surveillance in May 1993 and currently surveys approximately 944 clinicians in child health on a monthly basis, covering a child population of 3.9 million. The overall response rate was 96% in 2000. APSU introduced email reporting in 1997 and currently 50% (472) of clinicians have elected to use this service. Workload for the individual clinician was generally low for 2000 with 16% of clinicians reporting one case, 8% reporting between two and three cases and less than 2% reporting four or more cases. Seventy-six percent clinicians did not report a case of any condition under surveillance and hence were not required to complete a questionnaire.

Conditions surveyed in 2000 include acute flaccid paralysis, CHARGE association, congenital cytomegalovirus infection, congenital and idiopathic nephrotic syndrome, congenital rubella, haemolytic uraemic syndrome, Hirschsprung disease, HIV/AIDS, invasive haemophilus influenzae infection, Munchausen by Proxy Syndrome, neonatal herpes simplex virus infection, Prader-Willi syndrome, Rett syndrome and vitamin K deficiency bleeding. The year 2001 has seen the commencement of three new studies, adverse effects from complimentary or alternative medicine, fetal alcohol syndrome and hospitalised pertussis in infancy.

A key highlight of the year 2000 was the World Health Organisation certification of the Western Pacific region as polio-free. Surveillance of acute flaccid paralysis (AFP) by the APSU has been a crucial part of the accreditation process. While the area was declared polio-free in October 2000, surveillance, including by the APSU, must continue to detect imported cases.

Studies through the APSU have given rise to more than 70 publications and a wide range of presentations (151) that have informed the general public and the wider medical community.

APSU has maintained close links with INoPSU members with the recent appointment of APSU's Director, Assoc Prof Elizabeth Elliott, as the convenor of INoPSU. The first INoPSU newsletter has been published and web-sites for INoPSU (http://www.inopsu.com) and the APSU (http://apsu.inopsu.com) have been developed. The web-sites were developed 'in-house' by APSU staff. News and contact details of individual paediatric surveillance units worldwide may be accessed through the INoPSU web-site.

1 Morris A, Ridley G, Elliott E. The Australian Paediatric Surveillance Unit- A progress report. J Paediatr Child Health. In press.

Contacts

Professor Elizabeth Elliott (Director), Dr Greta Ridley (Assistant Director), Dr Anne Morris (Assistant. Director), Ms Diana Redmond (Scientific Officer), Ms Gabrielle Williams (Senior Administrator), and Ms Jennifer Fowler (Secretary) APSU, The Children's Hospital at Westmead, Locked Bag 4001, Westmead, NSW 2145 Australia. Tel: ++61 2 9845 3005/2200, Fax: ++61 2 9845 3082, E-mail: apsu@chw.edu.au

Canadian Paediatric Surveillance Program (CPSP)

The Canadian Paediatric Surveillance Program (CPSP) was established in January 1996 as a joint pilot project under the auspices of the Canadian Paediatric Society and the Laboratory Centre for Disease Control. As a result of a successful call for studies in the fall of 1998, the CPSP has grown steadily over the years from three initial studies in 1996, to six in 1999 and ten in 2000. The CPSP currently surveys more than 2300 paediatricians and sub-specialist participants, covering a child population of approximately 6.3 million, making the CPSP the largest national paediatric surveillance unit in the world. In 2000, the overall initial response rate to the monthly card was 82%, with an overwhelming 95% voluntary completion rate for follow-up detailed reports.

Conditions surveyed in 2000 include acute flaccid paralysis (AFP), anaphylaxis – severe allergic reaction, cerebral oedema in diabetic ketoacidosis, congenital rubella syndrome, Creutzfeldt-Jakob disease (CJD) /progressive intellectual and neurological deterioration, hemorrhagic disease of the newborn, hemolytic uremic syndrome, neonatal herpes simplex virus, Smith-Lemli-Opitz syndrome and subacute sclerosing panencephalitis. Early in the year 2001, the CPSP commenced surveillance for two new studies on hepatitis C infection and neonatal live faiure/perinatal hemochromatosis. In the fall of 2001, CHARGE association/syndrome and necrotizing fasciitis will be added to the card.

Results from the past year have reaffirmed that the system is working, allowing us to identify and collect information on these rare diseases with public health importance. For example, with only five cases in four years, hemorrhagic disease of the newborn study results have supported the Canadian Paediatric Society's guidelines on the administration of intramuscular vitamin K to new born babies. Increased awareness and earlier diagnosis of the treatable inherited disease Smith-Lemli-Opitz (SLO) syndrome will improve the general health, behaviour and quality of life of affected patients and their families, and if the incidence is found to be sufficiently high, may indicate the need for newborn screening of SLO. The rarity of subacute sclerosing panencephalitis cases (two in four years) is both a tribute to the success of the measles immunisation program, as well as reassurance about the safety of the measles vaccine.

In the coming year, consideration will be given to proposed new studies on rickets, lead toxicity and autism.

The CPSP has also developed its own website sited at http://www.cps.ca/english/proadv/CPSP/CPSP.htm

Contacts

Ms. Jo-Anne Doherty, MSc, Chief, Division of Disease Surveillance, Center for Infectious Disease Prevention and Control, Health Canada, Tunney's Pasture, 0603E1 Ottawa ON K1A 0L2. Tel: 613 946 2328, Fax: 613 946 8808, E-mail: jo-anne_doherty@hc-sc.gc.ca

Andrea Medaglia, CPSP coordinator, 100-2204 Walkley Rd., Ottawa ON K1G 4G8. Tel: 613 526 9397 ext. 239, Fax: 613 526 3332, E-mail: andream@cps.ca

German Paediatric Surveillance Unit (ESPED)

Encouraged by the success of the BPSU, a German adaptation of the surveillance scheme called the ESPED was initiated in July 1992 to cover the country which has the largest child populations of any of the units (around 14 million). The surveillance system differs from the original British methodology in that cards are sent to paediatric department heads to complete. The response rates for the 500 groups of clinicians have risen significantly from 75% in 1992 to 95% in 1999, with the follow-up rate of completion of questionnaires in the range of 60 to 100%.

A number of studies have been completed. These include Reye's syndrome, Ondine's curse (primary failure of respiratory regulation), Kawasaki disease, acute renal failure and acute liver failure, HUS, HSES, fatal/near fatal asthma and neonatal infection due to fungi (candida).

In 1999 the conditions under surveillance were: invasive infection with *Haemophilus influenzae* type b; insulin dependent diabetes mellitus in under fives; neonatal stroke; haemorrhagic shock encephalopathy syndrome; multiple sclerosis; systemic pneumococcal infection; haemorrhagic disease of the newborn; severe pertussis and severe aseptic meningitis following MMR vaccination, transient myeloproliferative syndrome in newborns with Down syndrome; organoacidopathia and fatty acid oxidation defects, glucose transporter defect (GLUT1).

Studies under consideration include imported parasitical diseases (malaria, schistosomiasis and kala azar), and neonatal streptococcus B infections and intersexual genital malformations

Contacts

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Beate Heinrich, ESPED Office, Universitats-Kinderklinik, Moorenstrasse 5, 40225 Duesseldorf, Germany E-mail: heinrich@med.uni-duesseldorf.de

Irish Paediatric Surveillance Unit (IPSU)

Set up in 1996 by the Faculty of Paediatircs of the Royal College of Physicians (Ireland) in cooperation with the Ulster Paediatric Society, the IPSU compliments the work of the British Paediatric Surveillance Unit by surveying for more common disease in the Ireland, North and South. Surveillance is achieved through a monthly prepaid postcard circulated to around 150 members of the Irish Paediatric Society. Studies being undertaken in 2001 include tuberculous meningitis, status epilepticus, coeliac disease, nephrocalcinosis, diaphragmatic hernia and neural tube defects. As yet the IPSU is not a member of INoPSU but are in the process of applying.

Contact

Professor D Gill, Children's Hospital, Temple Street, Dublin 1, Republic of Ireland. Tel: 003531 8741751, Fax: 003531 8748355, E-mail:gilld@iol.ie

Latvian Paediatric Surveillance Unit

The Latvian paediatric surveillance system began in 1997. The active mailing of a surveillance card has recently been adopted. As there are only two major children's hospitals in Latvia cards have been sent to a comparatively few clinicians. Response rates are dipped this past year to 60%, but are again increasing. In 1999 the following were reported stomach atresia (1), oesophageal atresia (1), histiocytosis (1), congenital nephrosis – Finnish type (1), medullary sponge kidney (1), policystic kidney disease (1), HIV/AIDS (3), tuberculosis under 14 (135), cystic fibrosis (3); paediatric pulmonary disease (6), leukemias (23). In 2000 2 cases of haemolytic uraemic syndrome was seen.

Contact

Professor E Bikis, Skolas Street 3-105, Riga, Latvia.
Tel: ++371 760571, Fax:++ 371 7240662,
E-mail: aspedlat@com.latnet.lv

Malaysian Paediatric Surveillance Unit (MPSU)

The MPSU was established in December 1993 and surveillance began in September 1994 under the auspices of the Malaysian Paediatric Association. It covers all of Malaysia with a child population of 7.6 million. The unit has adopted the classical BPSU methodology with cards being circulated to around 400 paediatricians and surgeons. The initial response rate is encouraging at 75%, having risen as the system becomes more familiar to respondents. Only 13% of respondents have never returned a card. Initially four conditions were under surveillance, paediatric HIV and AIDS, neonatal meningitis, acute fulminant liver failure and death from asthma. 1998 saw commencement of surveillance for Duchenne muscular dystrophy and in 1999 for neonatal congenital heart disease.

Contact

Dr Jacqueline Ho, Dr HSS Amar, Department of Paediatrics, Hospital Ipoh, 30990 Ipoh, Malyasia. Tel: ++605 253 333, Fax: ++605 253 1541, E-mail: jho@pc.jaring.my

Netherlands Paediatric Surveillance Unit (NSCK)

The Dutch Paediatric Surveillance Unit started surveillance in October 1992. Around 450 paediatricians in general hospitals receive the monthly card. The child population (0-14 years) is 2.91 million. As in Germany, the reporting methodology has been modified to suit local organisation of care. The eight university hospitals have each nominated specific personnel to respond for separate disorders and to be responsible for reporting all cases in that hospital. The overall response rate for the paediatricians receiving the card has risen from 83% in 1992 to 92% in 2000. The follow-up rate is also high at over 90%. In 1998, 14% of the clinicians reported one case, 9% reported 2 cases, 49% reported 3 or more cases while 29% of clinicians did not encounter a case of the conditions under surveillance. The importance of full case ascertainment has been realised and where possible alternative complementary data sources have been recruited for particular disorders. For example, surveillance of diabetes was strengthened by the inclusion of the Dutch Diabetic Association, while surveillance of invasive *Haemophilus influenzae* infection was improved by using reports from the Netherlands Reference Laboratory for bacterial meningitis.

A number of studies have been completed. These were sickle cell disease and thalassaemia major, postneonatal mortality in premature and dysmature born children, haemolytic disease of the newborn (non ABO non RhD), haemorrhagic disease of the newborn, invasive *Haemophilus influenzae* infection, congenital rubella, venous thromboembolic complications and hospital admissions due to rotavirus infections.

In 2000 the conditions under surveillance were: acute flaccid paralysis (15 reports), coeliac disease (204 reports), insulin dependent diabetes mellitus (443 reports), group B streptococcal infections (295 reports), HIV/AIDS (77 reports), neural tube defects (77 reports), hospital admissions due to pertussis (100 reports), congenital adrenal hyperplasia (25 reports), inflammatory bowel disease (71 reports) and Neonatal allo-immune thrombocytopenia (35 reports)

In 2001 adverse reactions to drugs and atypical mycobacterial infections were added.

Contact

Professor S P Vanloove-Vanhorick, Rob Rodrigues Pereira (paediatrician), TNO Prevention and Health, Postbus 2215, 2301 CE Leiden, Netherlands. Tel: 0031 71 5181838, Fax: 0031 71 5181662, E-mail: r.pereira@pg.tno.nl

New Zealand Paediatric Surveillance Unit (NZPSU)

The NZPSU, established in 1997, is co-directed by Professor BarryTaylor and Dr Nigel Dickson. From the beginning the NZPSU has received financial support from the New Zealand Ministry for Health to provide active surveillance of acute flaccid paralysis as part of WHO's polio eradication initiative. Covering a child population of 0.83 million, each month over 180 paediatricians are circulated with a surveillance card. The response rate has remained high at 94%, while the completion rate has been 100% for most conditions. Nine conditions are currently being surveyed. These are acute flaccid paralysis, congenital rubella, perinatal HIV exposure, haemolytic uraemic syndrome, vitamin K deficiency bleeding, subdural haemorrhage under the age of 2, fetal alcohol syndrome, Kawasaki Disease and Bronchiectasis.

The unit is working closely with the APSU. Protocols and questionnaires developed for some APSU studies are being used for some NZPSU studies. This process will allow identical data to be collected simultaneously in two geographically distinct populations.

Contact

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Papua New Guinea Surveillance Unit (PNGSU)

This unit began in 1996 and is closely associated with the Paediatric Association of Papua New Guinea. Covering a national child population of 1.92 million there are currently 40 respondents, including all paediatricians in the country and some general physicians in the more remote areas. Response rate for the year to June 199 was 78.6%. Since 1996 surveillance has been undertaken for 11 conditions. Current studies are acute flaccid paralysis (57 cases); insulin dependent diabetes mellitus (8 cases); congenital hypothyroidism (41 cases) neurologic endemic cretinism (5 cases), renal tubular acidosis(27 cases); sub-acute sclerosing panencephalitis (112 cases); necrotising enterocolitis and HIV/AIDS (64 cases). It is hoped that this year will see the commencement of nephrotic syndrome.

Contact

Dr Graham Ogle Co-ordinator PNG Paediatric Surveillance Unit. C/o HOPE Worldwide (PNG), POBox 3478, Boroko, NCD, Papua New Guinea. Tel: ++675 325 6901, Fax: ++675 323 0419, E-mail: Graham_Ogle@hopeww.org OR hopepng@datec.com.pg

Portuguese Paediatric Surveillance Unit (PPSU)

This is the newest of the Units established in June 2000. Surveillance commenced in March 2001. Studies to be investigated include Group B streptococcal disease, Kawasaki disease, haemolytic uraemic syndrome and insulin dependent diabetes melitus in under fives. For further information visit their website (http://www.spp.pt) Currently the PPSU is not a member of INoPSU but will be applying at the earliest possible opportunity.

Contact

Dr M Coelho, Co-ordinator, Portuguese Paediatric Society, R. Amílcar Cabral, 15 - r/c I 1750-018 Lisbon, Portugal. Tel: (++351) 21 757 46 80 / 99 90, Fax (++351) 21 757 76 17, E-mail: coelhom@mail.telepac.pt

Swiss Paediatric Surveillance Unit (SPSU)

The SPSU was established in early 1995 under the auspices of the Swiss Paediatric Association and the Federal Office of Public Health. The German unit provided the software to run the system.

Report cards are circulated to a willing paediatrician at each of the 38 paediatric teaching clinics representing about 250 hospital or clinic-based paediatricians (i.e. not to those delivering primary care) and covering a total child population of 1.3 million children. The response rate for the initial cards was 100% in each year, and 96-98% for the complementary questionnaires. The seven conditions under surveillance in 2000 were: acute flaccid paralysis (12 cases), congenital rubella syndrome (0 cases), haemolytic uraemic syndrome (15 cases), vitamin K deficiency bleeding (3 cases), tick-borne encephalitis (5 cases), varicella/zoster (52 cases) and acute rheumatic fever (2 cases). The study on cystic periventricular leukomalacia has been completed in December 1997. The study on congenital toxoplasmosis ended December 1998, with a total of 21 confirmed cases. The study on vitamin K deficiency bleeding ended December 2000, with a total of 19 confirmed late-onset cases. In 2001, neural tube defect was included in the surveillance.

Contact

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Welsh Paediatric Surveillance Unit (WPSU)

The Welsh Paediatric Surveillance Unit (WPSU) was set up in 1994 as a joint venture between the University of Wales Departments of Public Health Medicine (Prof. S. Palmer) and Child Health (Prof. J. Sibert). The management of the system was reorganised in 1996 in conjunction with the Welsh Paediatric Society, which supports the system. Funding has also been obtained from the Welsh Office for Research and Development and latterly the National Assembly for Wales.

The Welsh system looks at conditions considered too common for a UK study or too uncommon for a local hospital to perform. The WPSU uses the same methodology as the BPSU with whom we have a very close relationship. We discuss all our new projects with the BPSU to ensure that there is no overlap and have consequently suspended one study on subdural haemorrhages in the past.

Monthly green cards are distributed to consultant paediatricians and senior doctors of whom there are approximately 119. This covers a child population of 650,000. The overall response rate for 2000 was 100%.

Mailings can be extended to include consultant physicians and surgeons in Wales particularly where it is considered that older children may be affected. This has been very successful in studies involving acute and chronic renal failure and inflammatory bowel disease. Paediatricians along the border of England and Wales have also been very helpful where some Welsh children have been treated outside the confines of Wales.

Doctors in training may initiate studies under supervision and thereby encourage a culture of audit and research. We are not in a position to record responses by email at the moment but there are many Welsh paediatricians who are enthusiastic about such a system and this is currently being considered.

The following studies have been completed successfully: acute and chronic renal failure, severe child abuse, the critically ill child, coeliac disease, inflammatory bowel disease, children in housefires, subdural haemorrhage (1 case), congenital adrenal hyperplasia. Two studies were unsuccessful and were withdrawn:

ingestion of household products and haemoglobinopathy. Current studies include newly diagnosed malignant disease, newly diagnosed diabetes, Marfan syndrome, childhood tuberculosis, subdural haemorrhage (2) and facial palsy.

The unit hopes to provide the Welsh National Assembly with data that can assist in the planning of Health Care for Children in Wales, to act as a resource for the determination of the epidemiology of diseases in childhood and to assist audit and research.

Contacts

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Table 16
National paediatric surveillance units status circa end 2000

Country	Child population (106- aged 0-15 years)	Established	Respondents	Reply paid	Response rate **(E-mail reporting)	Fee for study
Australia	3.9	1992	942	Yes	96%**	Yes
UK/Rep of Ireland	12.8	1986	2005	No	93%	Yes
Canada	6.3	1996	2294	Yes	82%	Yes
Germany	14.0	1992	468*	No	94%	Yes
Latvia	0.7	1996	22	No	60%	No
Malaysia	7.7	1994	395	Yes	75%	No
Netherlands	2.9	1992	445	Yes	92%	Yes
Papua New Guinea	1.9	1996	40	Yes	79%	No
New Zealand	0.8	1997	165	Yes	94%	No
Switzerland	1.3	1995	40*	Yes	99%	No
Wales	0.65	1994	119	No	100%	No
Republic of Ireland	1.1	1996	135	Yes	85%	Yes
Portugal	1.8	2001	1500	Yes	nk	Yes

* Heads of paediatric centres

Appendix A Completed Studies 1986-2000

By mid-2000 the British Paediatric Surveillance Unit had completed forty studies. Information about these studies has been included in previous annual reports of the BPSU, which are available from the BPSU office. The studies, principal investigators and definitive papers are listed below. For addresses see the list at the end of this report.

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

Haemorrhagic shock encephalopathy syndrome
Completed: June 1986 – December 1988
Investigator: Dr S Hall
Published Paper: *Haemorrhagic Shock Encephalopathy Syndrome in the British Isles. Bacon* CJ, Hall SM. Arch Dis Child 1992; **67**: 985-993

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

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

Lowe syndrome
Completed June 1986 – February 1988
Investigator: Dr C McKeown
Published Paper: *Lowe Syndrome*. McKeown C. BPSU 2nd Annual Report. 1987. BPSU London

Neonatal herpes
Completed: June 1986 – Dec 1991
Investigator: Ms PA Tookey, Professor C S Peckham, Dr R Dinwiddie
Published Paper: *Neonatal herpes simplex virus infection in the British Isles*: Tookey P, Peckham CS.
Paediatr Perinat Epidemiol 1997; **10**: 432-442

Insulin dependent diabetes in under fifteens
Completed: January 1988 – December 1988
Investigator: Professor J D Baum
Published paper: *Incidence of Insulin Dependent Diabetes in Children Aged Under 15 Years in the British Isles During 1988*: Metcalfe MA, Baum JD. BM J 1991; **302**: 443-7

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

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

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

Congenital toxoplasmosis
Completed: June 1989 – May 1990
Dr S Hall
Published paper: *Screening for Toxoplasmosis during Pregnancy*: Peckham CS, Logan S. Arch Dis Child 1993; **68**: 3-5

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

Acute rheumatic fever
Completed: January 1990 – December 1990
Investigator: Dr C Boyd-Scobie, Dr S Hall
Acute Rheumatic Fever. Boyd-Scobie, Hall S.
Published paper: BPSU Fifth Annual Report 1990. BPSU London 1990

Rett syndrome
Completed: April 1990 – June 1990
Investigator: Dr A Kerr
Published paper: *Rett Syndrome: British Longitudinal Study (1982-1990) and 1990 Survey*. In Mental Retardation and Medical Care.
Roosendaal JJ (ed.). Uitgeverij Kerckebosch, Zeist 1991

Measles, mumps, rubella-meningococcal meningitis
Completed: Jan 1990 – Dec 1991
Investigator: Dr N Begg
Published paper: *Meningoencephalitis associated with MMR vaccine*: Maguire HC, Begg NT, Handford SC. Communicable Disease Report 1991; **1** (**6**): R57-R59

Chemistry set poisoning
Completed: Jan 1991 – April 1992
Investigator: Dr E Mucklow
Published paper: *Chemistry Set Poisoning*: Mucklow ES. Internat Journ Clin Pract 1997; **51**.5: 321-23

Acute flaccid paralysis
Completed: July 1991– June 1994
Investigator: Dr N Begg
Published paper: *Polio Eradication: Surveillance Implications for the United Kingdom*: Salisbury DM, Ramsay ME, White JM, Brown DW. Infect Dis 1997; **175 (Suppl 1)**: S156-9

Androgen insensitivity syndrome
Completed: Sept 1991 – Aug 1993
Investigator: Professor IA Hughes
Published paper: *Androgen Insensitivity syndrome: a survey of diagnostic procedures and management in the UK*. Viner RM, Teoh Y, Williams DM, Patterson MN, Hughes IA. Arch Dis Child 1997 **77** 305-309

Long term parenteral nutrition
Completed: Feb 1992 – April 1992
Investigator: Professor D Candy, Professor E Ross, Dr S Devane
Published paper: *Survey of children on long term parenteral nutrition, UK and Eire 1992*. Devane S P. Abstract RCPCH Scientific Meeting 1993

Insulin dependent diabetes in under fives
Completed Jan 1992 – Dec 1992
Investigator: Professor JD Baum, Ms E Wadsworth
Published Paper: *Insulin dependent diabetes in children under five: incidence and ascertainment validation for 1992*. BMJ 1995; **67**: 700-703
Dermatoglyphics, fetal growth and insulin dependent diabetes in children under five: Shield JP, Wadsworth EJ, Hobbs K, Baum JD. Arch Dis Child 1995 **72(2)**: 159-60

Juvenile dermatomyositis
Completed: June 1992 – Dec 1993
Dr D Symmons, Dr A Sills*
Published Paper: *The incidence of juvenile dermatomyositis: results from a nationwide study*: Symmons DP, Sills JA, Davis SM. Br J Rheumatol 1995; **34**: 732-736

Congenital dislocation of the hip
Completed April 1993 – July 1993
Investigator: Dr C Dezateux
Published Paper: *A national survey of screening for congenital dislocation of the hip*: Dezateux C, Godward S. Arch. Dis. Child. 1996; **74**: 445-448
Screening for congenital dislocation of the hip in the newborn and young infants. Dezateux C, Godward S. Edinburgh 1997; Churchill Livingstone

Haemophagocytic Lymphohistiocytosis
Completed September 1991 – August 1994
Investigator; Professor S Strobel, Dr M Taylor, Dr J Pritchard
Published Paper: *10th BPSU Annual Report 1995/96*. BPSU London 1995

Non-accidental poisoning/ Munchausen syndrome by proxy
Completed September 1992 – August 1994
Investigator: Dr P Davis, Professor J Sibert, Professor SR Meadow, Dr R McClure
Published paper: *The epidemiology of Munchausen Syndrome by Proxy, Non-accidental poisoning and Non-accidental suffocation*: McClure RJ, Davis PM, Meadow SR, Sibert JR. Arch Dis Child 1996; **75**: 57-61

Neonatal necrotising enterocolitis
Completed October 1993 – October 1994
Investigator: Professor A Lucas, Ms R Abbott
Published Paper: *Neonatal necrotising enterocolitis: 11th BPSU Annual Report 1996/7*. London 1998

Vitamin K deficiency bleeding
Completed January 1993 – December 1994
Investigator: Dr A McNinch, Dr J Tripp
Published paper: 9th BPSU Annual Report 1993/94. BPSU London 1994

Biliary Atresia
Completed March 1993 – February 1995
Investigator: Dr JP McKiernan, Dr D Kelly
Published paper: *The frequency and outcome of biliary atresia in the UK and Ireland*. McKiernan JP, Baker AJ, Kelly D Lancet 2000; **355**: 25 – 29

Transient and permanent neonatal diabetes

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

Adverse neonatal outcomes of delivery or labour in water

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

Congenital syphilis

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

Congenital cataract

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

Medium chain acyl-CoA dehydrogenase

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

Pyroxidine dependent seizures

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

Neonatal Meningitis

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

Cerebral oedema and death following diabetic ketoacidosis

Completed: October 1995 – September 1998
Investigator: Dr J Edge, Dr M Hawkins
Published paper: *The risk and outcome of cerebral oedema developing during diabetic ketoacidosis*. Edge JA, Hawkins MA, Winter DL, Dunger DB, Arch Dis Child 2001; **85** 16-22

Hepatitis C virus (HCV) infection

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

Congenital brachial palsy

Completed: March 1998 – March 1999
Investigator: Dr G Evans-Jones, Mr S P J Kay, Professor M Weindling
Published Paper: 14th BPSU Annual Report 1999/00. London 2000

Subdural haematoma and effusion

Completed: April 1998 – April 1999
Investigator: Dr C H obbs, Dr J Wynne, Dr A M Childs
Published Paper: 14th BPSU Annual Report 1999/00. London 2000

Inflammatory bowel disease in under 20 year olds

Completed: June 1998 – June 1999
Investigator: Professor B Sandhu, Dr A Sawczenko
Published Paper: *Prospective survey of childhood inflammatory bowel disease in the British Isles*. Sawczenko A, Sandhu B K Logan, R F A, Jenkins H, Taylor C J, Mian S, Lynn R. Lancet 2001; **357**, 1095-96

Fatal/Severe allergic reactions to food ingestion

Completed: March 1998 – February 2000
Investigator: Dr A Colver, Dr A Cant, Dr C MacDougal
Published Paper: 14th BPSU Annual Report 1999/00. London 2000

Appendix B Published papers 2000-2001

HUS Surveillance - What Does it Tell Us About VTEC? - Adak GK, Lynn RM & O'Brien SJ
Supplement to SCIEH Weekly Report 8 February 2000

The frequency and outcome of biliary atresia in the UK and Ireland. McKiernan JP, Baker AJ, Kelly D. Lancet 2000; **355**: 25 - 29

Active surveillance of hepatitis C infection in the UK and Ireland. Gibb DM, Neave PE, Tookey PA, Ramsay M, Harris H, Balogun K, Goldberg D, Mieli-Vergani G, Kelly D. *A*rch Dis Child 2000; **82(4)**: 286-91

Achievements of the BPA - the British Paediatric Surveillance Unit: Ross EM, Lynn RM. The RCPCH at the Millennium 2000 pg 63-67 Ed B Valman, MPG Books 2000

Congenital and infantile Cataracts in the United Kingdom: Underlying or Associated Factors: Rahi JS, Dezateux C and the British Congenital Interest Group. IOVS 2000; **41(8)**: 2108-2114.

Clinical Immunological Risk Factors Associated with Hib Conjugate vaccine failure in Childhood. Heath PT, Booy R, Griffiths et al Clinical Infectious Disease 2000; **31**: 973-80

Non Type b Haemophilus influenzae Disease:Clinical and Epidemiological Characteristics in the Hib Vaccine Era. Heath PT, Booy R, Azzopard HJ, Slack MPE, et al. Paediar Infect Dis J 2000; **20**: 300-5.

Antibody Concentration and Clinical Protection after Hib Conjugate Vaccination in the United Kingdom. Heath PT, Booy R, Azzopardi HJ et al. JAMA 2000; **284**: 2334-2340

Public Health Outputs from the British Paediatric Surveillance Unit and similar clinician-based surveillance mechanisms. Nicoll A, Lynn RM, Rahi J, Verity C, Haines L. J R Soc Med 2000; **80**: 580-585

Variant Creutzfeldt disease in UK children: a national surveillance study. Verity CM, Nicoll A, Will R, Devereux G, Stellitano Ll. Lancet 2000; **356**: 1224-7

Decrease in effectiveness of routine surveillance of Haemophilus influenzae disease after introduction of conjugate vaccine: comparison of routine reporting with active surveillance system. Olowokure B, Hawker J et al BMJ 2000; **321**: 731-32

UK case of congenital rubella can be linked to Greek cases. Tookey P, Molyneaux P, Helms P. BMJ 2000; **321**: 766-67

Pregnancy is still a contraindication to rubella vaccination. Tookey P. BMJ 2001; **322**: 1489

Congenital and infantile Cataracts in the United Kingdom: Underlying or Associated Factors: Rahi JS, Dezateux C and the British Congenital Interest Group. *IOVS* 2000; **41(8)**: 2108-2114.

Mother-to-child transmission of hepatitis C virus: evidence for preventable peripartum traansmission. Gibb D, Goodall R et al. Lancet 2000; **356**: 904-07

Pneumocystis carinii pneumonia and cytomegalovirus infection in children with vertically acquired HIV infection. Williams AJ, Duong T, McNally LM, Tookey PA, Masters J, Miller R, Lyall EGH, Gibb DM. AIDS 2001; **15**: 335-39

Key issues in child health surveillance. Lynn RM. Proc R Coll Physicians Edinb 2001; **31**: 39-45.

Neonatal meningitis in England and Wales: 10 years on. Holt DE, Halket S, de Louvois J, Harvey D. Arch Dis Child Fetal Neonatal Period Ed 2001; **84**: F85-F89

Is regional paediatric surveillance useful? Experience in Wales R H J Morgan, O'Connell H, Sibert JR, Lynn RM Z E Guildea, Palmer S. Arch Dis Child 2001; **84**: 486-487

The risk and outcome of cerebral oedema developing during diabetic ketoacidosis Edge J A, Hawkins M M, Winter D L, Dunger D B, Greene S Arch Dis Child 2001; **85**: 16-22

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

An international network of paediatric surveillance units: A new era in monitoring uncommon diseases of childhood. Elliott E, Nicoll A, Lynn RM, Marchessault V, Hirasing R (INoPSU Secretariat), on behalf of INoPSU members. Paediatr Child Health 2001; **6(5)**: 251-252

Appendix C Recent presentations

RCPCH Annual Scientific Meetings 2000 & 2001

Results of the first prospective survey of the incidence, presentation, and management of inflammatory bowel disease in the United Kingdom and the Republic of Ireland. Sawczenko A, Sandhu B (on behalf of the BSPGN IBD group). York 2000

Congenital brachial palsy – incidence and aetiology. Evans-Jones G., Kay SP, Ward A, Weindling AM. York 2000

Subdural haematoma/effusion in infancy – report of a national epidemiological study in conjunction with the BPSU. Hobb C, Wynne J. York 2000

Progressive Intellectual and Neurological Deterioration (PIND) in Children. Verity C, Nicoll A, Will R, Devereux G. York 2000

Are children in the UK developing vCJD? The BPSU study of progressive intellectual and neurological deterioration in children. Verity C, Nicoll A, Will R, Devereux G, Stellitano L. York 2001

Group B streptococcal disease (GBS) in UK infants less than 90 days of age: A national surveillance study. Heath P, Nicoll A. York 2001

Antenatal HIV testing – making a difference. Tookey P A. York 2001

Prospective national data on IBD in children aged less than five. Sawczenko A, Sandhu B. York 2001

Childhood encephalitis and human-herpesviruses-6 and-7 (HHV-6 & -7) infection. Ward K N. Ross E R. York 2001

Surveillance of Haemolytic Uraemic Syndrome in the UK and Ireland (1997-2000). Adak G K, Lynn RM M, O'Brien S, Locking M. York 2001

Other Conferences & Meetings

Hib antibodies and field efficacy of Hib vaccines in the United Kingdom. Food and Drug Administration. Center For Biological Evaluation and Research. Vaccines and Related Biological Products Advisory Committee. Heath P. Maryland, USA. January 2000.

The early years and recent progress. Advances in Paediatrics Public Health/Population. Nicoll A, Lynn RM. RSM London February 2000

Paediatric Surveillance – How to set up an active reporting system. Lynn RM. Lisbon, Portugal June 2000

National antenatal HIV targets – are they achievable? PHLS 25th Annual Scientific Conference, Cliffe S, Nicoll A, Tookey PA. Warwick September 2000

Haemolytic Uraemic Syndrome Surveillance – What does it tell us about VTEC? PHLS 25th Annual Scientific Conference, University of Warwick. O'Brien SJ, Adak GK, Lynn RM, Reilly WJ, Smith HR. Warwick September 2000

Synergy between clinical and laboratory surveillance for describing the epidemiology of VTEC O157. World E.coli o157 conference O'Brien S, Adak GK, Lynn RM, Locking M . Kyoto, Japan. September 2000

Congenital rubella. Royal Society of Medicine, Section of Paediatrics and Child Health. Tookey PA. RSM London, October 2000

Are UK Children developing CJD? Royal Society of Medicine Section of Paediatrics and Child Health, Devereux G. RSM London, October 2000

Encephalitis in children – BPSU Surveillance study. Royal Society of Medicine Section of Paediatrics and Child Health. Ward K. RSM London October 2000

HIV in pregnancy and childhood – the changing picture. World AIDS Day conference 2000. Tookey PA. Worthing NHS Trust, November 2000

Why does paediatric surveillance help children? Rare Disease Alliance Conference, London. Verity C. December 2000

Active surveillance of rare paediatric disease. Birmingham March 2001 Lynn RM

Aspects of Paediatric Surveillance – Royal Hospital for Sick Children, Glasgow. Lynn RM. Scotland June 2001

Appendix D Support groups and contacts

Severe Allergic Reactions
The Anaphylaxis Campaign, The Ridges, 2 Clockhouse Road Farnborough, GU14 7QY

Congenital Rubella
Sense, 11-13 Clifton Terrace, London N4 3SR

Progessive Intellectual Neurological Degeneration
Creutzfeldt-Jakob Disease Support Network, Birchwood, Heath Top, Ashley Heath, Market Drayton, TF9 4QR
Batten Disease Family Association, c/o Heather House, Heather Drive, Tadley, Hampshire, RG26 4QR
The Society for Mucopolysaccharide Diseases, 46 Woodside Road, Amersham, HP6 6AJ
Climb, (formerly the Research Trust for Metabolic Diseases in Children (RTMDC.), The Quadrangle, Crewe Hall , Weston Road, Crewe, CW2 6UR
Adrenalleukodystrophy (ALD), ALD Family Support Trust, 30-32 Morley House, 320 Regent Street, London, W1R 5AB
Niemann Pick Disease Group, Kingslaw House, East Brae, East Wemyss, Fife KY1 4RS, Scotland UK

Encephalitis Effects
Encephalitis Support Group, 44a Market Place, Malton, YO17 7LH

Group B streptococcal disease
Group B Strep Support, PO Box 203, Haywards Heath, and RH16 1GF

Haemolytic Uraemic Syndrome
HUSH, PO Box 159, Hayes, UB4 8XE

HIV/AIDS
Barnardos Positive Options, William Morris Hall, 6 Somers Road Walthamstow, London, E17 6RX
Positively Women, 347-349 City Road, London EC1V 1LR

Meningitis
National Meningitis Trust, Fern House, Bath Road, Stroud, Gloucestershire.

Meningitis Research Foundation, Unit 9 Thornbury Office Park Midland Way, Thornbury, Bristol, BS35 2BS

Reye's Syndrome
Reye's Syndrome Foundation of the UK, 15 Nicholas Gardens, Pyrford, Woking, Surrey GU22 8SD

Stroke/Stroke like illness
The Stroke Association, CHSA House, Whitecross Street London, EC1Y 8JJ
Different Strokes, 162 High Street, Watford WD1 2EG
Sturge-Weber Foundation (UK), Burleigh, 348 Pinhoe Road Exeter EX4 8AF

Visual impairment/blindness
LOOK, Queen Alexandra College, 49 Court Oak Road Birmingham, B17 9TG
Vision Aid, Guy Salmon House 22a Chorley New Road, Bolton BL1 4AP
Henshaw's Society for the Blind, John Derby House, 88-92 Talbot Road, Old Trafford, Manchester, M16 0GS
RNIB 224 Great Portland Street, London W1N 6AA
SENSE – 11-13 Clifton Terrace, London N4 3SR

For information on a variety of rare childhood disorders a directory of support groups and their addresses has been produced by:

'Contact a Family'

209-211 Old Street, London EC1V IJN. Tel: 0207 383 3555. www.cafamily.org.uk

Useful web-site addresses

Communicable Disease Surveillance Centre of the Public Health Laboratory Service
http://www.phls.co.uk/

Contact a Family (CaF)
http://www.cafamily.org.uk

Office of National Statistics
http://www.statistics.gov.uk

Organising Medical Networked Information
http://www.omni.ac.uk/

Royal College of Paediatrics and Child Health
http://www.rcpch.ac.uk

On-Line Mendelian Inheritance in Man (OMIM)
http://www3.ncbi.nlm.nih.gov/Omim/

National Organization for Rare Disorders (NORD)
http://www.rarediseases.org/

Paediatric Aids Resource Centre
http://www.ed.ac.uk/~clah/parc.html

Pedinfo
http://www.pedinfo.org

Further useful web-sites are available from the
Guide to the Internet Sites in the Area of Paediatrics and Child Health
produced by the RCPCH.

Appendix E Contact addresses

Dr G K Adak, Central Public Health Laboratory, 61 Colindale Avenue, London NW9 5HT

Dr P Baxter, Consultant Paediatric Neurologist, Ryegate Children's Centre, Sheffield Children's Hospital, Sheffield S10 2TH

Dr E Bikis, Skolas Street 3-105, Riga, Latvia

British Society of Gastroenterology, 3 St Andrews Place, Regent's Park, London NW1

British Ophthalmological Surveillance Unit, 17, Cornwall Terrace, Regent's Park, London NW1 4QW

Professor D Candy, Department of Child Health and Community Paediatrics, King's College School of Medicine and Dentistry, London SW5

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Dr A Clarke, University of Wales, Heath Park, Cardiff CF4 4XW

Professor R Cooke, Liverpool Women's Hospital, Crown St, Liverpool, Merseyside LB7SJ

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Dr E G Evans-Jones, Countess of Chester Hospital, Liverpool Road, Chester, CH2 1UL

Faculty of Paediatrics of the Royal College of Physicians of Ireland, 6 Kildare Street, Dublin 2, Republic of Ireland

Dr J Fogarty, Department of Public Health Medicine, Merlin Park Hospital, Galway, Republic of Ireland

Dr B Gibson, Dept of Hematology, RHSC Yorkhill, Glasgow, G3

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Dr A Kerr, Quarrier's Homes, Bridge of Weir, Renfrewshire PA1 3SA

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Office of National Statistics, 1 Drummond Gate, London SW1V

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