Royal College of Paediatrics and Child Health
British Paediatric Surveillance Unit

14th Annual Report 1999/2000

The British Paediatric Surveillance Unit always welcomes invitations to give talks describing the work of the Unit and makes every effort to respond to these positively.
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British Paediatric Surveillance Unit - 14 Annual Report 1999-2000
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Foreword

Confidence and confidentiality

Since it was founded almost 15 years ago the BPSU has depended completely on the active involvement of paediatricians. The surveillance system is based on the orange card which is posted to over 2000 consultant paediatricians in the UK and the Republic of Ireland. Every month the card arrives in the in-tray and each paediatrician makes a decision – do I bother to complete it or do I throw it in the bin? Fortunately in over 90% of cases the decision is made to complete the card and return it to the BPSU office. It is important for the viability of the system that paediatricians are not overloaded with BPSU requests. For practical reasons the conditions under surveillance have to be relatively rare and only about 25% of paediatricians report cases each year. On most occasions all the paediatrician has to do is tick the "nothing to report" box. This "negative" feed-back is very important because it enables Richard Lynn, the Scientific Co-ordinator, to keep track of response rates and investigate the reasons that cards fail to return. It also helps us to estimate the extent to which there is under-reporting of cases.

The conditions on the surveillance card must be sufficiently important for paediatricians to want to make the effort. When a paediatrician has seen a child with a condition under surveillance, ticking the appropriate box on the orange card results in a request for further information, usually in the form of a questionnaire to complete. In itself this hardly an incentive to report cases! The effort involved in completing the questionnaire is not directly to the advantage of either the doctor or the patient. It must be clear that each surveillance project is likely to yield information that will be beneficial to children in general. Studies should attempt to answer a scientific question and should be important for public or child health. The BPSU Executive Committee tries to ensure that proposals that are accepted for the orange card meet these criteria and that questionnaires are well designed - and as brief as possible! The Executive Committee also has an important role in ensuring that BPSU surveys are efficiently organised and properly monitored.

There has been careful examination of the protocols of many BPSU surveys over the years to ensure that they conform to accepted ethical standards for surveillance studies. Since it was established in 1986, over forty investigations of important paediatric conditions have been completed through the BPSU. The findings have been published in over 100 papers and reports which have protected and promoted the health of children. It has been part of the work of the BPSU to ensure that investigators are aware of the need to maintain the confidentiality of the data that are entrusted to them. Surveillance groups have been required to obtain ethical consent for their studies and this has provided a considerable precedent when considering the ethics of BPSU work in the future.

There is a need to maintain high standards of patient confidentiality in an atmosphere of increasing public and professional concern about the issue. In the light of the Data Protection Act 1998, the Common Law duty of confidence, the new Human Rights Act and some GMC guidance it has been suggested that doctors should always obtain explicit patient or parental consent before sharing with other professionals identifiable data required for public health surveillance. On the same basis it has been suggested that surveillance data should be totally anonymised if it is impractical to obtain explicit consent.

The BPSU Executive Committee is concerned that if some of the guidance on patient confidentiality was interpreted in the strictest sense it would seriously prejudice or completely inhibit surveillance that requires complete ascertainment and relies on data linkage. Key information required to protect the health of children would not be obtained in the future. The implications would be similar for public health activities such as the management of public health emergencies and surveillance for infectious diseases via clinician and laboratory reporting. Bodies such as the Public Health Laboratory Service (PHLS) might be unable to fulfil some of their responsibilities.

It is important to draw attention to the difference between epidemiological surveillance and interventional research. The surveillance groups that work via the BPSU collect data about children which they are required to keep in confidence. They do not become involved in patient management and they do not make contact with the children or their relatives. In this way BPSU surveillance is analogous to the surveillance for infectious diseases carried out by the PHLS and its Communicable Disease Surveillance Centre. Authoritative guidance on this important area of epidemiological surveillance is not yet available, although it is recognised that special considerations apply to public health surveillance. A National Advisory Body for Confidentiality and Security is being set up and it will be important to ensure that the BPSU and the PHLS inform this body about the particular nature of epidemiological surveillance.

The BPSU Executive Committee has recently discussed the issues associated with patient confidentiality and has taken action, indeed it has taken a national lead. A report has been sent by the BPSU Executive Committee to the Executive Committee of our College and to the Deputy Chief Medical Officer at the Department of Health. Meanwhile in line with the Caldicott report[1] the BPSU is ensuring that investigators ask for the minimum amount of data about the children in their surveys. The aim is to maintain the anonymity of the patients without prejudicing the studies. To the

ensure good surveillance there is a need to have sufficient information about individuals to validate results and identify duplicate reports.

The issue of obtaining prior parental consent before sharing information is difficult. The College Research Unit found that when prior parental consent was required for a study the data collection process was considerably delayed. After a year of reminders parental consent had been obtained via paediatricians in only 46% of cases. It therefore seems likely that there would be a significant fall in BPSU response rates if obtaining prior parental consent was a necessary part of each surveillance study. The reasons for this can be seen when the BPSU mechanism is considered. Paediatricians are asked to report cases that are seen in the previous month. The orange card may carry up to a dozen different conditions and these change with time, so it is not likely that paediatricians will remember all these and ask parents for permission at the time children are seen. If paediatricians were required to ask permission before reporting clinical details about a child they would have to contact the parents at home and possibly arrange to see them to discuss the study. Experience suggests that when asked almost all parents give their consent, however the administrative work involved in obtaining the consent is considerable. It would probably be necessary for paediatricians to give parents written information. At present that would involve the surveillance group in obtaining ethical consent from a multicentre research ethics committee (MREC) and then from every local research committee (LREC) in the UK before starting surveillance. A prospective study of the new system of review by MRECs has been published recently in the British Medical Journal.[2] The authors obtained MREC approval for their research proposal and then submitted it to 125 LRECs in six regions of England. After 6 months 9 LRECs had still not approved the study and the process had cost over £6,ooo. In the same journal another group setting up a study of the treatment of infantile spasms reported similar experience.[3]

The BPSU argues that it is justified to continue with paediatric surveillance along the lines that have evolved in the past 10 years on the grounds that it would be detrimental to the health of children to do otherwise. However the BPSU Executive Committee will continue to keep the issue of patient confidentiality under review and will work with other groups in the College and elsewhere to ensure that particular consideration is given to epidemiological surveillance. The excellent response of paediatricians indicates that they strongly support the work of the BPSU and recognise the value of the studies that are carried out via the Unit. The challenge is to ensure that patients and carers also support the work. There is a need to inform the public about the benefits of paediatric surveillance. The BPSU maintains contact with a number of patient and carer organisations and will develop these contacts further in order to publicise the work of the BPSU as widely as possible.

Paediatricians worldwide have shown their confidence in the method of surveillance pioneered by the BPSU. This was evident at the second meeting of the International Network of Paediatric Surveillance Units (INoPSU) in Ottawa this June. Dr Angus Nicoll and I attended on behalf of the BPSU and would like to thank the members of the working group that organised the meeting – Jo-Anne Doherty, Danielle Grenier and Andrea Medaglia of the Canadian Paediatric Surveillance Program and Marie Adele Davis of the Canadian Paediatric Society. As a result of their hard work and that of Angus Nicoll, the INoPSU Convenor, the meeting a great success. It was planned in conjunction with the national conference of the Canadian Paediatric Society entitled:“Beyond 2000: Healthy Tomorrows for Children and Youth”.

There are now 11 paediatric surveillance units worldwide (full details are given later in this Annual Report). Most of them were represented at the Ottawa meeting, thanks to generous funding by the Laboratory Centre for Disease Control, Health Canada. Representatives of national paediatric surveillance units were able to exchange information about their own surveillance projects, discuss differences in methodology and make plans for joint studies. We heard some impressive statistics – the 11 units now cover a population of over 50 million children and between them the units have performed studies of 107 different conditions. We hope that this work will continue to thrive, both nationally and internationally.

INoPSU was formed at a meeting in Amsterdam in 1998. Much of its success results from the time and energy given by the Secretariat and in particular Dr Angus Nicoll, the first INoPSU Convenor, and Richard Lynn who has acted as “server” for the Network. Angus Nicoll has now handed over the role of Convenor to Dr Elizabeth Elliott of the Australian Paediatric Surveillance Unit, who was another key person in the founding of INoPSU. It was really exciting to be at the Ottawa meeting and hear the enthusiasm for developing international paediatric surveillance even further. The plan is to have another meeting in the UK in 2002, meanwhile there continues to be active communication between the units via the internet. It seems likely that more countries will be involved quite soon. Richard Lynn was in Lisbon this June giving a lecture to Portuguese paediatricians about the methodology of paediatric surveillance. Apparently there is strong support for a Portuguese unit.

One of the most positive aspects of paediatric surveillance work is that it brings together many different disciplines. This was seen

at the Ottawa meeting and it is also an important feature of the work of the BPSU. Indeed without the support of many different groups the BPSU would not thrive. At present the Department of Health makes a significant and much appreciated contribution to funding of the BPSU. The two Medical Advisors are supported financially by their institutions – Dr Angus Nicoll by the Public Health Laboratory Service and Dr Jugnoo Rahi by the Institute of Child Health. The BPSU Executive Committee consists of representatives from our College, the Institute of Child Health (London), the Public Health Laboratory Service, the Scottish Centre for Infection and Environmental Health and the Faculty of Paediatrics of the Royal College of Physicians of Ireland.

I would like to mention some people who are particularly involved in the running of the BPSU. The Executive Committee meets monthly and the members are warmly thanked for their contributions. Many thanks go to Richard Lynn, the Scientific Co-ordinator, and his assistant Myra Schetman for their hard work and enthusiasm which provides the foundation for all the activities of the BPSU. They are supported by others within the Research Unit of the College, in particular Linda Haines the Principal Research Officer and Professor Richard Cooke, the College Vice-President.

All those who are associated with child surveillance both here and abroad are confident that the work is invaluable in promoting and maintaining child health. Hopefully this Annual Report will clearly demonstrate that the BPSU is doing a worthwhile job. Last November the work of the BPSU was the theme of a successful joint meeting of the RCPCH and the Royal College of Physicians of Edinburgh. We are very grateful to Dr Chris Kelnar and the staff in Edinburgh for co-organising the day and to Professor James Petrie, the President of the Edinburgh College, for his hospitality and support. The meeting was entitled "Key Issues in Child Surveillance" and it aimed to emphasise the importance of paediatric surveillance to the community. The challenge is to influence those who are responsible for shaping policy, particularly in the area of patient confidentiality. However it is perhaps more important that patients and carers are made aware of the great contribution that surveillance studies can make to the health of children in general. That is a task for the BPSU in the coming year.

Finally all of us who are directly concerned with running the BPSU are conscious of the tremendous efforts of the paediatricians who complete the orange cards and the questionnaires. Paediatricians are the key to the success of the Surveillance Unit and they clearly have confidence in it. The excellent response to surveillance studies in the last year indicates that they value the BPSU and their support is appreciated.

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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 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 1999. Reference is also made to studies and activities which have commenced in 2000.

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 1996-2000

The BPSU's key challenges for 1996-2000 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.

February 1996 - BPSU Five year plan

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 offer guidance on the application before it is submitted to the BPSU Executive Committee (BEC). The BEC, which meets every 4-6 weeks, is comprised of consultant paediatricians (general and specialist), epidemiologists and specialists in public health.

If the BEC agrees that the protocol is suited to the BPSU methodology, 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 surveillance objectives of certain conditions. 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 ethical approval. Although 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.

Factors that favour acceptance by the British Paediatric Surveillance Unit

- Scientific importance.
- Rarity of the condition, though short-term or geographically limited studies of commoner disorders are considered.
- Proposals with outcomes of clear importance to public health.
- 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.
- Ethical 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 use laboratory reports to microbiologists. Current studies that are benefiting from such multiple ascertainment include HIV/AIDS, congenital rubella, Reye's syndrome, *Haemophilus influenzae* infection, subdural haematoma and most recently congenital brachial palsy which has benefited from the support of orthopaedic surgeons.

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 the surveillance scheme as it allows non-responders 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 at no time does the BPSU office receive patient details. The full process is summarised in Figure 3 opposite.

Figure 1 *BPSU orange card*

British Paediatric Surveillance Unit Report Card

June 2000 [2006]

NOTHING TO REPORT **CODE No [ ]**

If case(s) seen, identify how many

1. HIV & AIDS l
2. *Haemophilus Influenzae* infections 01865 221068/01865 220859 l
3. Haemolytic uraemic syndrome 020 8200 6868 ext 4551(E/W, Eire) 0141 300 1180 ext 1227 (Scotland) l
4. Progressive intellectual & neurological deterioration l
5. Encephalitis in children 2 mths-3 years 020 7679 9134 l
6. Severe visual impairment/ blindness in children l
7. Grp B Streptococcal disease in children less than 90 days old l

8. Congenital Rubella l 9. Reye's Syndrome l 10. SSPE l

Figure 2 *Clinicians section - BPSU orange card*

Clinicians Section **- Please keep if necessary**

British Paediatric Surveillance Unit Report Card
for cases seen in June 2000

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

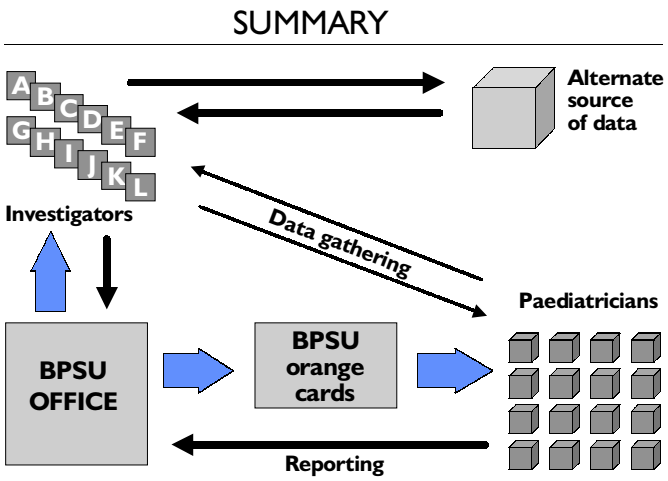
CONDITION	PATIENT	HOSPITAL NO

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 of patient identifiable data collected is strictly limited, though not to an extent that would compromise study aims. The BEC in 2000 is undertaking 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, allowing for the identification of incorrect reports and duplicates, and the speed in which this is achieved 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 1999 for all the conditions under surveillance during 1999. 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 1999, 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 between 85-98%. In the past, studies requesting pathological specimens have had a lower completion rate, though this has not been seen in the current encephalitis and *Haemophilus influenzae* surveys.

Table 3 (page 11) summarises the outcome of the follow-up of all cases reported to the BPSU by the end of 1999 and provides evidence for the high level of accuracy of reporting by participating clinicians. By June 2000, 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 (ie. 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 2000).

Difficulties in case reporting

Though the BPSU has much strength, the BEC 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. 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 reporters 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

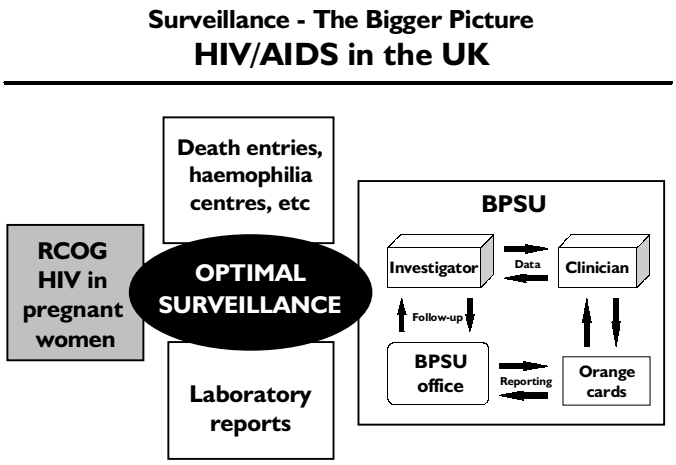
As highlighted, some conditions under study may have necessarily complex case definitions, these can be off putting to reporters and lead to under-ascertainment. Some investigators are coming up with a solution to this problem by devising two kinds of case definition. Firstly, a surveillance definition, 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 influenzae*, 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).

Figure 4



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 by the inflammatory bowel disease (IBD) study which identified cases through the BPSU, adult gastroenterologists and 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.

Using these alternate sources of ascertainment and capture-recapture techniques indicates that on average the BPSU ascertains 80-90% of expected cases.

Funding

For a three-year period until September 2001 the BPSU will be in receipt of a grant from the Department of Health, which 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 1999 the minimum sum was £210 per month.

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

The Unit received a donation from Serono Laboratories towards the costs 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 1999

Several projects were approved in 1999, however only one, on severe visual impairment and blindness, commenced. This was due to delays in receiving ethical approval and funding problems. The severe visual impairment and blindness study (described on page 34) is the first such study to be undertaken in the British Isles. Its main aims are to determine incidence, mode of detection and causes. This study will provide information that has previously not been available about the burden and impact of severe visual impairment and blindness in childhood, which is of relevance to clinical practice and future research. This study is being undertaken with the involvement of the British Ophthalmology Surveillance Unit of the Royal College of Ophthalmologists. The first such project to utlilise ascertainment through two Royal College surveillance units.

February 2000 saw the commencement of the Group B streptococcal disease survey and this winter will see the commencement of the cerebrovascular disease/stroke and stroke-like illness survey. Three further studies have been provisionally approved; vitamin K deficiency bleeding, venous/arterial thrombosis excluding cerebrovascular disease and severe abdominal injuries. Commencement dates have yet to be determined.

Several studies ended in 1999; hepatitis C infection (March), congenital brachial palsy (March), subdural haematoma (April) and inflammatory bowel disease (June). The two-year study on fatal/severe allergic reactions to food ingestion was completed in March 2000. Forty-two studies have now been completed since the BPSU began in June 1986 - those completed prior to 1999 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 1999/2000 relating to these studies and the unit's work totalled 42 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 involved in the RCPCH research division session at the RCPCH scientific meeting. Also the BPSU was the theme for the joint paediatric symposium of the Royal College of Paediatrics and Child Health and the Royal College of Physicians, Edinburgh (see page 41).

Other activities within the Unit include strengthening links with surveillance units from other medical societies. This has led to the initiation of a forum for discussion, it is hoped that this will be come a regular event. The Unit continues to receive requests for information from parents with children with rare diseases and we are in discussions with parent organisations such as Contact a Family on how best to deal with such enquiries. The increase in enquiries to the Unit is due in part to the interest in the BPSU web-site <http://bpsu.rcpch.ac.uk> . Developed in consultation with Radcliffe-online 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. This has led to the establishment of the International Network of Paediatric Surveillance Units (INoPSU). The organisation's first official meeting was held in Ottawa this June, attended by representatives of all the existing units. Plans have been put in placed to increase the flow of information between units. The international scene is described more fully in Chapter 8.

Participation in the scheme during 1999

The BPSU ascertains the names of new consultants primarily through the RCPCH advisory appointment committees, membership office, BMJ adverts or through personal communication. During the year there were 172 new consultants placed on the mailing list whilst 91 were removed, ostensibly following retirement or emigration. The number of consultant paediatricians participating in the scheme during 1999 therefore rose to 1940, an increase of 5.5% on the 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 of subdural haematoma forensic pathologists were included for the first time, and our thanks are extended to the Royal College of Pathologists for supporting this initiative.

Reporting rates for returning the orange cards remains high - the overall response rate for 1999, calculated as a proportion of orange cards returned, was 93.4% (21,643/23,159), slightly down on 1998 (93.6%). Monthly response rates ranged from 90.8 % in August to 96.9% in March, with a median of 93.8%. 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 1% are persistent.

As in previous years, reporting rates varied considerably across the country, as is shown in Figure 5 overleaf. Paediatric reporting in Wales rose from 8th in 1998 to achieve the highest average yearly response rate – 97.3%. Once again the Thames area showed the lowest response rates, North Thames (89.8%) and South East Thames (91.4%) being the lowest. With regard to rank order North and South Scotland rose by 14 and 11 places respectively, while East Anglia and Wessex fell by 15 and 13 places respectively. Noticeable falls were also seen in the South West, 13 and the Republic of Ireland 9 (Table 1). As yet it is not possible to assess the full impact on the BPSU response rate of the newly formed paediatric surveillance units in Wales and Ireland.

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-seven percent (1152) of participants reported no cases in 1999, up on 1998 (52%). Thirty-nine percent (792) reported between one and four cases and only 3% (60) reported five or more cases. The greatest number of cases reported by a single paediatrician was 26. Specialties that had a particularly high level of reporting were the paediatric nephrologists (HUS), paediatric neurologists (PIND, encephalitis, SSPE, Reye's syndrome) and gastroenterologists (IBD). As in previous years community paediatricians report fewer cases, though their continued involvement in the system is important, particularly so with the recent commencement of surveillance into visual impairment and the forthcoming survey on abdominal injury.

Table 1
Regional ranking 1998 and 1999

Region	Rank 1999	Rank 1998
Northern	11	7
Yorkshire	8	4
Trent	7	6
E Anglia	17	2
NWT	15	10
NET	20	19
SET	19	18
SWT	13	8
Wessex	18	5
Oxford	5	14
SWest	4	16
WMids	12	11
Mersey	10	17
NWest	9	12
Wales	1	8
NScot	6	20
SScot	2	13
WScot	16	15
NIre	3	1
RIre	14	3

Figure 5 *Average orange card return rate (%) by area 1999*

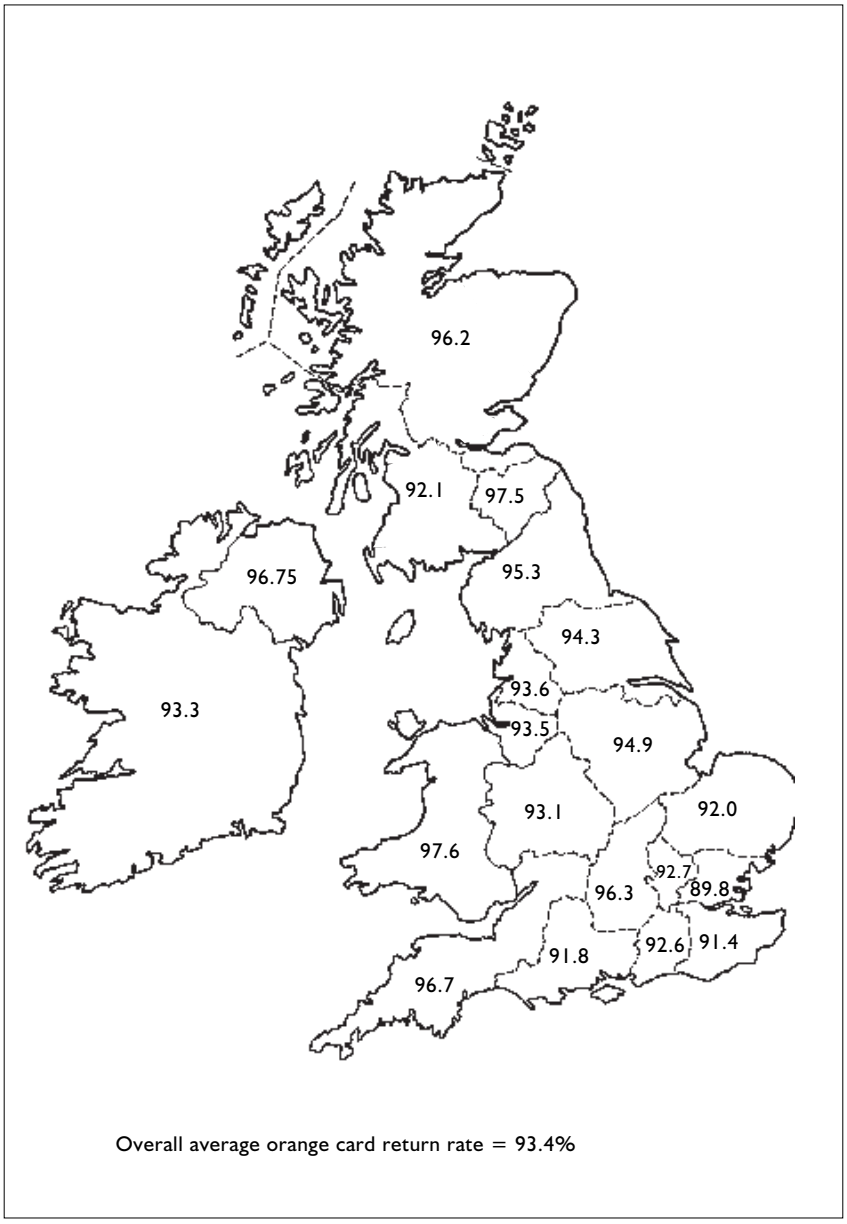


Table 2 *Cases reported from June 1986 - December 1999 for conditions under surveillance during 1999 (cases confirmed by July 2000 shown in brackets)*

Condition under surveillance	Date when reporting began	Reports (confirmed cases)							
		June 1986 to Dec 1989		Jan 1990 to Dec 1992		Jan 1993 to Dec 1995		Jan 1996 to Dec 1998		1999	
HIV/AIDS	1986	137	(90)	495	(386)	359	(215)	488	(326)	202	(119)
Reye's syndrome	1986	149	(76)	71	(31)	57	(21)	31	(21)	12	(5)
SSPE	1986	84	(50)	55	(29)	28	(14)	27	(10)	9	(1)
Congenital rubella	1991	–	–	43	(27)	29	(12)	40	(17)	2	(2)
Hi infection	1992	_	_	25	(20)	146	(105)	200	(126)	69	(45)
HUS	1997	_	_	_	_	_	_	335	(211)	166	(115)
PIND	1997	_	_	_	_	_	_	617	(408)	214	(139)
Congenital brachial palsy	1998	_	_	_	_	_	_	367	(271)	99	(73)
Fatal/severe allergic reactions	1998	_	_	_	_	_	_	124	(96)	129	(90)
Subdural haematoma/effusion	1998	_	_	_	_	_	_	268	(144)	108	(50)
Inflammatory bowel disease	1998	_	_	_	_	_	_	454	(296)	347	(209)
Encephalitis (2-36 months)	1998	_	_	_	_	_	_	55	(31)	138	(57)
SV/Blind	1999	_	_	_	_	_	_	_	_	207	(72)
Total		**370**	**(216)**	**689**	**(493)**	**619**	**(367)**	**3006**	**(1957)**	**1702**	**(977)**

HIV/AIDS Acquired immune deficiency syndrome/human immunodeficiency virus: reports of AIDS in June 1986 included all 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 England 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.

PIND Progressive intellectual and neurological deterioration

SV/Blind Severe visual impairment and blindness

Table 3 *Outcome of follow-up of the cases reported to 1999 for conditions under surveillance during 1999.*

Condition under surveillance	Valid reports (%)		Invalid reports			Not yet known (%)		Total reports
			Duplicates	Errors	(Total %)			
HIV /AIDS	1136	(68)	234	278	(30)	33	(2)	1681
Reye's syndrome	154	(48)	49	112	(50)	5	(2)	320
SSPE	104	(51)	41	34	(37)	24	(12)	203
Congenital rubella	58	(51)	23	29	(46)	4	(4)	114
Hi infection*	297	(68)	25	112	(31)	6	(1)	440
HUS*	326	(65)	137	27	(33)	11	(2)	501
PIND	547	(66)	78	191	(32)	15	(2)	831
Congenital brachial palsy	344	(74)	27	78	(23)	17	(4)	466
Fatal/severe allergic reactions	186	(74)	5	47	(21)	15	(6)	253
Subdural haematoma/effusion	194	(52)	74	52	(34)	56	(15)	376
Inflammatory bowel disease	505	(63)	101	164	(33)	31	(4)	801
Encephalitis (2-36 months)	88	(46)	16	57	(38)	32	(17)	193
SV/Blind	72	(35)	5	60	(31)	70	(37)	207
All	**4011**	**(63)**	**815**	**1241**	**(32)**	**319**	**(5)**	**6386**

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

4 Main findings of studies undertaken in 1999

The study on **congenital brachial palsy** (page 13) has only just been completed but it found that the birth prevalence of this condition was significant at approximately 0.5-1.0 per 1000 live births and that cases were seemingly commoner in large babies. There was an association with assisted deliveries.

Surveillance for **congenital rubella (CRS)** (page 16) in the UK has been underway continuously since 1971. In previous years many cases of CRS have been in babies born to unimmunised women recently arrived in the UK. However this year such cases are exceeded by cases in UK born women including cases born to women who are re-infected with rubella.

A new survey of **encephalitis in young children (2 months to three years)** (page 17) is now identifying cases attributable to Human Herpes Virus 6 and 7 including dual cases.

Severe allergic reaction to food (page 19) sufficiently severe to result in children being hospitalised has been found to be rarer than expected from media reports and allergic reactions with a fatal outcome are proving to be uncommon and deaths very uncommon.

The second survey of **haemolytic uraemic syndrome (HUS)** and *E.coli* O157 (page 21) 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 3 but rare beyond age 11. Most cases are sporadic but cases are reported associated with contaminated food and water and person to person transmissions. The survey reports five deaths and significant long-term morbidity in some children.

The BPSU survey of **HIV and AIDS** (page 23) is the prime source of paediatric data on this condition in the UK. It finds that almost all new infections are now acquired through mother to child transmission and that the greatest number of infections are in London but cases are occurring in all parts of the country. As a result of previous findings it is now professional and Department of Health policy to routinely offer and recommend HIV testing to all pregnant women. Many of the children's infections could have been prevented as mothers were not aware of their infection and so could not take advantage of the many ways that now exist of minimising the risk of mother to child transmission. This is to take place in London but not as yet elsewhere.

The survey of **inflammatory bowel disease (IBD)** in under 20-year-olds (page 25) has found an annual incidence of IBD amongst children < 16 years of 5.3 cases/100,000 with Crohn's disease being twice as common as ulcerative colitis. Children seem to be being diagnosed promptly with a mean time from the onset of symptoms to diagnosis of 0.5 years for children with both Crohn's and ulcerative colitis however management was found to vary considerably between centres.

Surveillance of invasive ***Haemophilus influenzae b* infection (Hib)** (page 27) confirms that Hib vaccination has dramatically reduced invasive disease in the UK and Eire. 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 worldwide 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.

A difficult survey of **progressive intellectual and neurological deterioration in children (PIND)** (page 29) being undertaken to establish whether there is any variant Creutzfeldt-Jakob disease in UK children has proved successful though a few centres are not reporting fully. This has found over 450 cases of PIND due to over 60 different conditions but to date (April 1999) only three cases of variant CJD.

Results from long-term surveillance of **Reye's syndrome** (page 31) 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.

A new survey of **severe visual impairment and blindness** (page 34) commenced in 1999 to determine incidence, mode of detection and causes.

An important enhancement of the long-term survey of **sub-acute sclerosing panencephalitis (SSPE)** (a condition which is a late complication of measles) (page 35) is that it is proving possible to distinguish between 'wild' measles virus and the measles virus used in vaccines. This has found in the cases so far investigated that SSPE is not due to vaccine despite the large amounts of MMR and MR vaccine used in the last five years.

Another difficult but important survey of **subdural haematoma or effusion (SDHE)** (page 36) has found over 150 confirmed cases including 28 deaths. So far there is a male preponderance (a gender ratio of 2 boys to 1 girl) and a mean age is four months. The cases were predominantly but not exclusively due to trauma, which may be abusive, birth trauma or occasionally accidental. Fifty per cent of cases were attributed to child abuse.

5 Surveillance studies undertaken in 1999

Conditions included in the scheme

During 1999, 13 conditions were the subject of surveillance. Five studies were completed: cerebral oedema following DKA, congenital brachial palsy, fatal/severe allergic reactions in childhood, inflammatory bowel disease and subdural haematoma/effusion and one study commenced on severe visual impairment/blindness.

The studies are listed in Table 4 below. Four projects have been given approval but have yet to commence. These include vitamin K deficiency bleeding, cerebral vascular disease/stroke in childhood, severe abdominal injuries and venous/arterial thrombosis.

Table 4 *Studies underway in 1999*

Page	Study	Principal investigators	Research institutions
13	Congenital brachial palsy	G Evans-Jones, S P J Kay, A Weindling	Chester, Leeds, Liverpool Hospitals
16	Congenital rubella*	P Tookey, C Peckham	ICH (London)
17	Encephalitis (2 months - 3 years)*	K Ward, E Ross	King's College Hospital, London
19	Fatal/severe allergic reactions*	A Colver, A Cant, C Macdougall	RVI, Newcastle
21	Haemolytic uraemic syndrome*	M Taylor, B Adak, S Locking, R Lynn	B'ham Children's Hospital, PHLS, SCIEH, BPSU
23	HIV/AIDS infection in childhood*	P Tookey, A Nicoll, D Goldberg	ICH (London), PHLS, SCIEH
25	Inflammatory bowel disease	B Sandhu, A Sawczenko, R Logan	RHSC Bristol, BSG Research Unit
27	Invasive *Haemophilus influenzae* infection*	P Heath, M Slack, R Moxon, N Begg	PHLS, National Haemophilus Ref. Lab., Oxford
29	Progressive intellectual and neurological deterioration*	C Verity, G Devereux, A Nicoll, R Will	Addenbrookes, PHLS, National CJDSU
31	Reye's syndrome*	S Hall, R Lynn	Sheffield Children's Hospital/BPSU
34	Severe visual impairment/blindness*	J Rahi, I Russell Eggitt, D Taylor, C Gilbert	ICH (London), GOS
35	Subacute sclerosing panencephalitis*	E Miller, N Begg	PHLS
36	Subdural haematoma/effusion	C Hobbs, J Wynne, A Childs, A Seal	St James' University Hospital, Leeds

** Studies still in progress to July 2000.*

Congenital brachial palsy (CBP)

Key points

- The birth prevelance of CBP was 0.43/1,000 live births or 1 in 2,300.
- Cases were commoner in larger babies and there was an association with assisted delivery.
- For about 8% of cases no cause could be found.

Background

Congenital brachial palsy (CBP) is generally thought to be due to an injury at birth to part or all of the brachial plexus, although clear evidence of injury is not present in all cases. The commonest type is Erb's palsy (see case definition). The incidence is thought to have declined in the 1950s and 1960s with, for example, a reported annual incidence in 1962 of 0.39 per 1000 live births.[1] There has however been a suggestion that the incidence may have increased in recent years, possibly as babies average birth weight has increased.[2] However, the true incidence in the UK and Republic of Ireland is currently unknown.

The cause is commonly thought to be due to an injury to part, or all of, the brachial plexus at birth due to either local pressure (instruments, fingers, local soft tissue swelling or haematoma) or lateral traction on the fetal head or upper limb causing stretching, rupture or avulsion of the nerve roots of the plexus. This results in weakness or paralysis of the arm. Associated lesions include fractures of the clavicle and proximal humerus, shoulder dislocation, phrenic nerve palsy and Horner's sydnrome. Between 8% to 20% of cases of Erb's palsy have been reported to be bilateral, almost exclusively associated with breech extraction. As well as breech delivery, shoulder dystocia and large fetal weight are common associations, but some cases are unexplained occurring without such factors. Full muscle

recovery is reported to vary widely from as little as 13% to 80% of cases. Similarly the onset of recovery is variable, ranging from two to fourteen weeks and improvements may continue for up to 18 months. Severe cases with little recovery result in serious handicap – the function of the shoulder, elbow, forearm and wrist may be significantly impaired affecting social, physical and educational development. Even in less severe cases, with only residual impairment of shoulder movement, for example, significant disability can result.

The present therapeutic approach is to use physiotherapy to prevent joint contracture. Although there are reports of encouraging results using microsurgical nerve grafting techniques, the indications for surgery are unclear and controversial, and the effectiveness of the techniques remains unproven.[3] It has been suggested that some infants who could benefit from surgery are not given the opportunity for early expert assessment, being referred too late for surgery to be effective.

Many reported studies are of selected cases; this study provided an opportunity to gather population based data about this important condition.

Case definition

Surveillance – A newborn presenting with a flaccid paresis of the arm (in addition there may or may not be involvement of the hand) with a passive range of motion greater than the active.

An analytic case definition was then applied to all cases reported as fitting the surveillance case definition.

Analytic – CBP occuring in a newborn infant who on clinical examination and observation is found to have a congenital flaccid paresis of the arm (usually one, rarely both) with a passive range of motion greater than the active. In addition, there may or may not be involvement of the hand. Cervical cord injury or cerebral injury e.g. hypoxic ischaemic encephalopathy (HIE) may coexist. X-rays may show fractures of the clavicle or humerus, a dislocated shoulder or paralysis of the hemidiaphragm.

There are three main types of lesion associated with cervical root injury:-

C 5-6 The arm is adducted and internally rotated at the shoulder, the elbow is extended, the forearm pronated, and the wrist (and sometimes the fingers) flexed. This is the classical 'waiter's tip' posture. (Narakas' Group I).[4]

C 5-7 As above, although the elbow may be slightly flexed. (Narakas Group II).

C 5-T1 The arm is totally flail with a claw hand. The arm has a marbled appearance due to vasomotor disturbance. It may (Narakas' Group IV) or may not (Narakas' Group III) be accompanied by a Horner's syndrome.

Objectives

To determine:

1 The incidence of CBP
2 To study its aetiology
3 The natural history of CBP in the first year of life.

Study duration

March 1998 – March 1999

Results

430 cases of suspected CBP were reported. Table 5 summarises the results of the response to the first questionnaire and the calculated incidences of CBP. Of 58 ineligible cases the majority were because of infants being born outside the study period. There were two cases of revised diagnosis.

Table 5 *Breakdown of reported cases*

	UK	Eire	Total
Cases reported	390	40	430
Completed questionnaires	358	33	391
Response rate (%)	92	83	91
Ineligible cases	51	7	58
Confirmed cases	307	26	333
Number of live births	723084*	53524#	776618
Incidence (per 1000 live births per year)	0.42	0.49	0.43

* *Figure for 1998*
\# *April 1998 to March 1999*

Aetiology: There was a striking association with shoulder dystocia (defined as difficulty in delivering the anterior shoulder after delivery of the head) of 212 out of 333 cases (64%) as compared to the estimated rate in the normal population of 0.2 – 1%.

Table 6 summarises the mode of delivery of the study group highlighting the high rate of assisted delivery of 42% and in contrast to the low rate of Caesarian section (2%). The differences are significantly different from what is normally observed.

Table 6 *Mode of delivery (333 cases)*

Mode of delivery	Study Group		England 1994-95
	No:	%	%
Vertex	186	56	73
Assisted delivery	140	42*	10.6
Ventouse	91	27	5
Forceps	49	15	7
Breech	10	3	1
Caesarean section	6	2#	15.5

* $p < 0.0001$ # $p < 0.002$

Note: *The total number of deliveries in the study group slightly exceeds 333 in view of a small number of infants who have a failure of Ventouse delivery who are delivered by forceps.*

Again in comparison to what is normally seen there was an over representation of high birthweight infants in the study group with 54% of affected infants weighing more than the 90th centile for the whole population, (>4065gms), i.e. over half were "large for gestational age" or "macrosomic".

There was a slight preponderance (53%) of male gender mirroring that of the normal population. Fifty percent of cases affected the right arm, 43% the left, 4.5% not known, with five (1.5%) bilateral cases of which only one was delivered by breech extraction. Ninety-four per cent fell into Narakas' Groups I and II with the remainder with more extensive involvement in Groups III and IV.

Associated Injuries: Table 7 summarises the incidence of associated injuries with 26 infants (8%) suffering bony injury of, or adjacent to, the affected arm. Only one case of phrenic nerve injury was reported, although it is possible that a small number of cases were missed if a child x-ray was not performed (phrenic nerve palsy has been reported as a poor prognostic sign[2]). The presence of other nerve lesions and associated soft tissue injury (8 %) is a reflection of trauma.

Table 7 *Associated injuries*

Injuries	No.	%
Bony injuries	26	(8%)
Fracture of clavicle	11	
Fracture of humerus	8	
Shoulder dislocation	7	
Other nerve injuries		
Horner's syndrome	3	
Facial palsy	5	
Phrenic nerve palsy	1*	
Soft tissue injuries		
Facial and other bruising	8	
Cephalhaematoma	4	
Torticollis	4	
Sternomastoid tumour	1	

* *Information unavailable in one third of questionnaires.*

Unexplained cases: In 25 (7.5%) cases there was no reported shoulder dystocia, large birth weight, assisted delivery or associated injury. These cases are the subject of further careful scrutiny and will be reported separately.

Natural history: Second questionnaires requesting information of functional status of the affected arm at six months of age are currently being analysed. Of 333 confirmed cases, completed questionnaires were received on 324 (97%), at a mean age of 23.7 weeks. This information will provide useful information about the likely long-term outcome in the study group and an indication of the proportion of cases in which surgical intervention may be appropriate.

Conclusion

The birth prevalence of CBP in the U.K. and Republic of Ireland in the study period was 0.43 per 1000 live births or 1 in 2300, - a figure remarkably similar to that reported in New York in 1962. Thus the incidence has not fallen in recent years despite improved obstetric practice, during a period in which average birthweight has increased.

The most important associated factors are shoulder dystocia, high birth weight and assisted delivery. The majority of infants, however, do not have extensive lesions. In a small number of cases there is no clear explanation. It is suggested that to reduce the incidence of CBP improvement in methods of the diagnosis of high fetal weight and cephalopelvic disproportion are required.

Funding

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Congenital rubella

Key points

- The risk of congenital rubella continues in the UK, though cases are rare.
- To date only one case has been reported for 1999, following a case of maternal reinfection in pregnancy.
- The risk may be rising again because of a fall off in uptake of MMR in recent birth cohorts.

Background

National surveillance of congenital rubella (CR) started in 1971 with passive reporting by audiologists, paediatricians and microbiologists of cases in Scotland, Wales and England. With the success of the rubella vaccination programme the number of reported cases 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. With so few cases occurring, active surveillance was required, and CR first appeared on the orange card in January 1990. BPSU reports from Ireland are followed up, but not normally included in the published figures.

All children are now offered the combined measles/mumps/rubella (MMR) vaccine in the second year of life, with a pre-school booster for four year olds. However, MMR vaccine uptake in the UK declined from about 93% in 1995 to just under 88% by the end of 1999, following adverse publicity about alleged associations between MMR and bowel disease and autism (later data has found no such association). This level of coverage, combined with a lower uptake of the pre-school booster (only 76% of 5 year olds had received both MMR1 and MMR2 at the end of 1999) may not be sufficient to prevent transmission of wild rubella infection in the long-term.

Objective

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, 112 reports have been made through the BPSU (Table 8). Of the 98 reports from England, Scotland and Wales, 39 are confirmed or compatible, previously unreported cases of congenital rubella, four are possible cases, and ten had already been reported from another source. The remaining reports were duplicates (19), reporting errors (22) and in four further information could not be obtained. Fourteen 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).

Table 8 *Congenital rubella reports to BPSU 1990-2000*

	England, Scotland and Wales	Ireland
Registered Cases	43	4
Already reported	10	2
Outstanding	0	0
Duplicate, error or lost	45	8
Total	**98**	**14**

Among the children born since the beginning of active surveillance in 1990, 32 (70%) of the 46 confirmed or compatible cases (Table 9) were first reported through the BPSU.

Table 9 *Confirmed and compatible congenital rubella births reported to the NCRSP 1971-1999* (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
1990-99**	32	14	46*
Total	**46**	**826**	**872**
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*

* *The data for recent years are provisional*
** *The data for 1990-1999 Include 2 reported stillbirths*
*** *Includes a set of triplets*

Recent reports

Since 1990, 44 liveborn and two stillborn infants with congenital rubella have been reported in the UK. Between 1991 and 1995 most of the 19 mothers of infected infants had either come to Britain as susceptible adults (9), or had acquired infection abroad in early pregnancy (6) (imported cases). In 1996 12 births occurred, following a resurgence of rubella infection, mainly affecting young men[1]. The mothers of these 12 babies included eight women who

were born and brought up in the UK, all of whom had been eligible for schoolgirl vaccination. Two cases were also reported from the Republic of Ireland in 1996. There were no reported congenital rubella cases in 1997 or 1998, but one has recently been reported for 1999, an infant born in December in Grampian, Scotland, to a woman with a retrospectively confirmed reinfection in pregnancy.[2] There was a documented outbreak of rubella in Grampian in the earlier part of 1999, mainly affecting university students, which was epidemiologically linked to an outbreak in Greece.[3]

The estimated risk of fetal infection following first trimester maternal reinfection is 8%[4], considerably lower than that following primary maternal infection. 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 have been reported in recent years with sensorineural hearing loss as an isolated defect, and it is likely that there is underdiagnosis of such cases. Few 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.

It is essential that case ascertainment is as complete as possible. Please report to the BPSU all suspected congenital rubella cases, whether or not they have the associated typical defects. The investigators are grateful to the notifying paediatricians for their co-operation.

Funding

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Encephalitis in children two months to three years

Key points

- Between October 1998 and April 2000 178 children have been reported to the BPSU meeting the case definition.
- Most of the confirmed cases presented between 10 and 18 months old.
- HHV-6 and HHV-7 infections were commonly identified as causes of encephalitis Other causes were 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 because of new, highly sensitive laboratory methods for detection of nucleic acid (PCR), antibody and antigen. Two newly discovered viruses, (Figure 6 overleaf) human herpes viruses-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 due to these viruses.

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.

Surveillance 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.

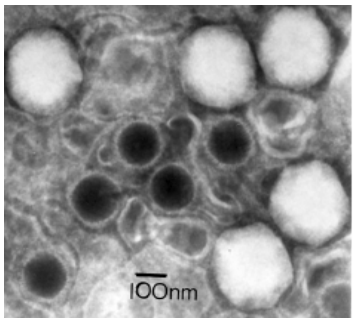
Exclude
(i) viral (aseptic) meningitis without encephalopathy;
(ii) the following confirmed causes: pyogenic infections, hypoxic/ischaemic, vascular, toxic, metabolic, neoplastic;
(iii) uncomplicated fits/convulsions or a series of fits convulsions lasting less than half an hour.

If in doubt please discuss with the investigators.

Duration

October 1998 to April 2001

Figure 6 *Electron micrograph of a group of virus particles in a negative contrast preparation showing mature intact virions and naked nucleocapsids.*



Coverage

UK and Republic of Ireland.

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. Pre-paid packages are supplied for return of specimens to Dr Ward who provides a free diagnostic service for HHV-6 and -7 infection based on acute and convalescent blood, saliva and cerebrospinal fluid (CSF), if available. CSF should be sent to the local microbiology laboratory for routine testing together with a request to forward an aliquot to Dr Ward for free HHV-6 and -7 testing; 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.

Analysis

At the end of April 2000 a total of 250 children had been reported to the BPSU; 15 from the Republic of Ireland and the remainder from the UK. About 55% of cases were reported first by telephone but the rest were only reported retrospectively on the orange card.

As regards collection of specimens for HHV-6 and HHV-7 testing, the investigators have received some specimens (serum and/or saliva and/or CSF) from about nine out of ten cases. CSF has been the most difficult specimen to obtain. Support from local microbiology laboratories has been excellent and the investigators have obtained CSF from seven out of 10 cases where it was taken. CSF is the key specimen as testing of other samples can only provide circumstantial evidence of possible CNS infection. The success rate with retrieval of CSF was highest when cases were reported early rather than retrospectively. The longer the time that elapses after initial presentation of the case, the more likely the laboratory is to have discarded the CSF. Early telephone reporting and immediate dispatch of specimens, especially CSF, therefore remain the most important ways in which paediatricians and microbiologists can contribute to the success of the survey. This can also contribute to making virological diagnosis of their patients.

Of the 250 cases reported so far:

- 72 were invalid because of duplication or another error (including 21 children who were either too old or too young).

Of the remaining 178 cases that met the reporting case definition:

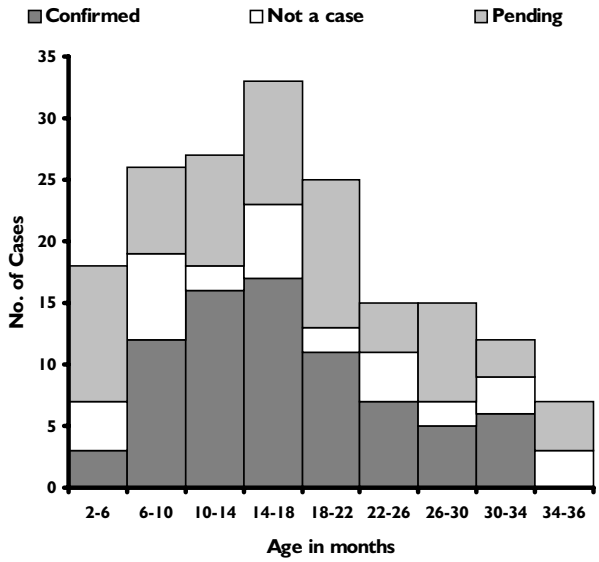
- 77 cases fulfilled the analytical case definition
- 33 cases did not fulfil the analytical case definition

Follow-up has not yet been completed for 68 cases of which questionnaires have not yet been received for 44 children most of whom were reported recently.

These numbers are less than the number of reports received in the NCES and it is likely that there is some under reporting. This may reflect difficulties of diagnosing encephalitis, which is often a diagnosis of exclusion. This difficulty also explains the observation that only two thirds of cases meeting the reporting case definition are confirmed after final analysis.

The age distribution of the 178 cases that met the reporting case definition is shown in Figure 7. The modal age of presentation of the 77 confirmed cases is between 10 and 18 months old. This is at variance with the NCES findings where the peak presentation was in the first year of life. The explanation for this difference is unclear and will only be resolved at the end of the survey when a detailed comparison with the results of the NCES will be undertaken.

Figure 7 *Age distribution of the 178 cases that met the reporting case definition*



Comment

The study is going well; a number of primary HHV-6 and HHV-7 infections and even two dual infections have been found. To date HHV-6 has been identified in the CSF of 5 children and HHV-7 in the CSF of 7 children. The investigators are now looking at the clinical picture and sequelae accompanying these infections.

As regards other infectious agents, the most commonly suspected cause of encephalitis was herpes simplex and almost all these children received a course of acyclovir. However, herpes simplex infection was only confirmed in 9 cases; other infections reported in the questionnaires included varicella zoster virus (7 cases), enteroviruses (4 cases) and adenovirus (1 case). Thus, 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.

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Fatal/severe allergic reaction to food ingestion

Key points

- Severe allergic reactions to food in childhood are rare.
- Severe allergic reactions to food leading to childhood deaths are very rare.
- The ethics of contacting bereaved families are challenging and mechanisms to do so involving professionals not involved in our study have not been effective so far.

Background

A number of recent studies have suggested that allergic reactions to foodstuffs in children may be becoming commoner.[1] However, these studies either used proxy measures, such as skin prick tests and radio allergo sorbent test (RAST) levels[2], or weak methods in which case definition was imprecise, case ascertainment restricted to those referred to a clinic, or comparisons made with unreliable historical data.[3,4]

Some reactions to food may be very severe or even fatal[5], but there is even less evidence about the incidence of such severe reactions. Where case series are reported[6-8] fatal allergic reactions in children under eight are extremely rare. Seemingly no population-based studies have been undertaken in the United Kingdom or North America. A preliminary search by the Office of National Statistics (ONS) revealed only one death of a child from an allergic reaction in England and Wales in 1993 and 1994. Most paediatricians have never been involved with a case of very severe reaction and there may be a gross miss-match between the perceived risks and actual incidence of severe allergic reactions.

In spite of the absence of reliable data, prescriptions of adrenaline in the form of inhalers or auto injection devices have become more common, the assumption being that it may save lives and/or prevent severe symptoms. There is still uncertainty as to whether adrenaline is life saving[9] but even if it is assumed that it may sometimes help, there are disadvantages with using adrenaline including:

- Potentially dangerous side effects if administered on a 'if in doubt, give it' basis, such side effects may be more dangerous than possible allergic reaction.[10-12]
- Teachers are anxious about having to decide when to administer adrenaline – these may need special training, reinforced each year.
- The prescription will potentially be required for life.
- Although relieving parental anxiety in situations where there is considerable risk, prescribing adrenaline may create unnecessary anxiety if the risk has been exaggerated.

Objectives

1 To estimate the incidence of fatal and very severe allergic reactions to food in children.
2 To describe the circumstances in which these reactions occurred.
3 To describe the clinical course and management of these cases.
4 To determine whether such children have had previous reactions and whether the severity of previous reactions predicts later severe reactions.

Case definition

A child under 16 who has died from allergic reaction to food ingestion or an unknown allergen in the last month.
Or
A child under 16 who has been admitted to a hospital ward because of an allergic reaction to food ingestion or an unknown allergen within the last month.

Excluded

1 Children spending a few hours under observation without treatment in an accident and emergency department or day unit.
2 Children whose only symptoms of a possible allergic reaction are asthmatic and the allergen is unknown.

Study duration

March 1998 - February 2000.

Method

It was assumed that all children admitted to hospital for severe allergic reactions would have come under the care of a paediatrician and that these cases would therefore probably be identified through the BPSU.

It cannot be assumed that paediatricians will have become aware of all deaths due to severe allergic reaction; particularly if the child died at home or in an A&E department. These cases will also be identified through the ONS in England and Wales and their counterparts in Scotland and Ireland. For the very small number of children who die (one or two per year are expected), a member of the investigating team may need to visit the parents for more details (see notes below) This would only be undertaken if the parents have given written consent following a discussion with the reporting clinician or, if the case has been accessed via the ONS, their family doctor.

Results

Prospective reporting appeared for the final time on the February 2000 'orange card'. The last few reports are still being received.

As of late April 2000, 265 reports have been received over the two year study period of which 242 remain on the database, 21 cases have not met the reporting criteria and in two the respondents cannot trace or recall the case. The 242 remaining cases includes 25 where full data are still awaited. The investigators expect to be able to gain full information on most of these on the basis of their previous experience. There are, however, three cases in this group where the relevant respondent has still been unable to confirm details of the case despite significant effort on their behalf. The follow-up rate on reported cases is therefore currently 90% of reported cases but should rise to 98%.

During the first year (BPSU annual report 1999), 26% of reported cases met the criteria for a severe case. Second year reporting appears broadly similar. The two year data are, however, still incomplete. The number of deaths still remains very small, although confirmation from searches by the ONS is still awaited. The investigators expect to have completed this shortly and to submit the incidence data for publication by the end of 2000.

Given the potential significance of these results, there is a clear wish to ensure the data are clearly understood and appropriately presented. This can only be undertaken in full publication form thus the limited incidence data presented at this time.

Retrospective and prospective deaths search - The ONS have run preliminary searches for deaths for the United Kingdom and the Republic of Ireland. The ONS (England and Wales) has performed their main search for 1993 to 1998. This has used all relevant codes, text searches of all reasonable text strings (e.g. any mention of food or of a list of potential specific food allergens) in all recorded fields. Code searches were subsequently reviewed in the light of the result of text searches and after noting the coding of cases identified prospectively. Three probable deaths have been identified in the 1993-98 period. Preliminary searches in Scotland, Northern Ireland and the Republic of Ireland (where searches are limited to code searches) have revealed no further cases despite use of the adjusted codes as mentioned above.

The final searches by the ONS will be undertaken after a short time lag to ensure data up to the end of our reporting period has been fully entered on their databases. Death numbers for our study period cannot be confirmed until this has been done.

In setting up this study, considerable effort was made to put in place mechanisms for gaining further information about deaths identified in this way in an ethically acceptable manner. Ethics approval was gained for initial contact being with the family's GP who could make a judgment about the best way to approach the family and could gain informed consent on our behalf and with our support. Unfortunately this process has resulted either in the response from the GP that it would be inappropriate to contact the families or in no response at all. This limits the ability to gain information on cases identified by ONS prior to the reporting period.

Interim conclusions

The overall reporting rate has been encouraging and all involved in this project are grateful for the interest shown.

Incidence - Although unable to release our full two year data until publication, the second year reporting has broadly followed the pattern of the first. This was of 26 severe cases from 105 documented cases at the time of report reporting

Circumstance and clinical management - The descriptive part of our work (on circumstances, clinical course and associations such as asthma) will be undertaken after full case ascertainment.

Previous reactions - Again this work will be undertaken shortly. For the future, however, the possibility has arisen of tagging cases identified as having suffered severe reactions on the basis of their NHS number. Subsequent deaths could therefore be logged. This would be subject to further funding and ethics approval but could add an exciting long term prospective element to our study.

General - The final conclusions are likely to be very controversial, therefore have to be very confident about case ascertainment. Other channels for further cases ascertainment have been explored (including the Anaphylaxis Association) which have so far yielded no additional cases. The integrity of the study still rests primarily with the vigilance of BPSU respondents. If BPSU respondents

become aware of a case that occurred during our reporting period (March 1998 until February 2000) we would still like to know about it and contact can be made directly (details below) or via the BPSU.

Funding

Research & Development Northern and Yorkshire Small Grant Fund.

References

(1-12) available from principal investigators on request.

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Haemolytic uraemic syndrome (HUS)

Key points

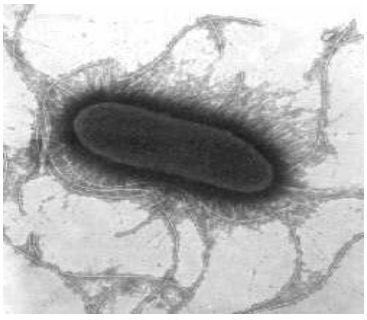
- Most cases of HUS in the UK are due to *E.coli* O157.
- Most cases are sporadic, outbreaks are uncommon.
- There are peaks of HUS incidence in the autumn.
- Cases in children have been associated with farm visits, person to person spread, contaminated foods and environmental exposure.
- HUS is commoner in children under age 3 and rare beyond age 11 years.
- Initial outcome is usually good however long term sequlae is yet to be determined.
- The incidence and death rates in under fives is similar to Australia but half that seen in Switzerland and New Zealand.

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 *Verocytoxin-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

The survey started in 1997 and is reviewed annually.

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 should be sent to the *E.coli* O157 reference laboratory in Edinburgh. As part of the follow-up after one year a urine sample should be submitted.

2 Laboratory of Enteric Pathogens (Colindale), Department of Medical Microbiology (Aberdeen): 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 (Dr M Locking) at the earliest date possible. Data from the questionnaires will be matched with microbiological data from Colindale and Aberdeen and the information entered onto a database.

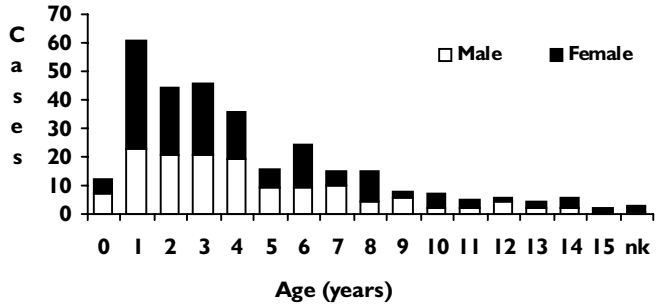
4 Birmingham Children's Hospital NHS Trust: Drs C M Taylor and D V Milford advise on clinical aspects of the study on behalf of the British Association for Paediatric Nephrology.

Results and discussion

In the period February 1997 to February 2000 the BPSU, PHLS and SCIEH received 465 reports of suspected HUS cases from paediatricians in the United Kingdom and Republic of Ireland. After de-duplication and verification it was established that 310 of the reports were for patients who conformed to the case definition for childhood HUS. The high level of duplicate reporting 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 1999 the BPSU undertook with the support of the main referral centres a validation process whereby cases reported were cross-checked with the referral hospitals, this process identified several previously un-reported cases, especially in London and Scotland.

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 with cases over the age of 11 rare. The high number of female cases in the age group one to two years is also striking. In total 169 cases were girls and 141 boys.

Figure 9 *Age and sex distribution of confirmed cases of HUS*



A distinct seasonal pattern has been observed in the reporting of childhood HUS (Figure 10). A late summer peak was seen once again in 1999 reflecting similar peaks in 1997-1998.

Though *E.coli* O157 was the predominate causative agent (205 cases), other organisms isolated included campylobactor (4), shigella (1), pneumococus (2), in 92 cases no organism was identified or known.

Where outcome was known 88.5% children have appeared to recover normally, 9% have had an abnormal/unclear outcome. Long term sequelea of children contracting *E.coli* O157 induced

Figure 10 *Seasonal distribution of confirmed cases of HUS*

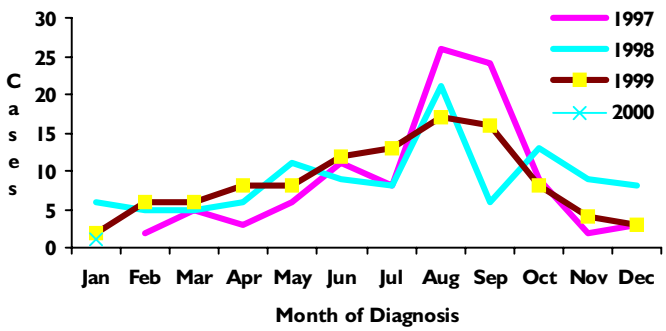


Table 10 *Comparison of National Surveillance Unit HUS data*

Unit	Study Duration	Cases	Incidence		Mortality	Predominant Organism
			<15 yrs	<5 years	(%)	
Australia	5	108	0.7	1.5	2.8	0111/013/0157
Britain	2	193	0.8	1.5	2.6	0157
New Zealand	1	14	1.6	3.9	7.0	0113
Switzerland	2	41	1.5	4.0	5.0	non-0157

Minimum annual estimate per 100,000 children

* data as of 1.10.99

HUS is unknown, continuous follow-up would be useful. Unfortunately 5 children (2.5%) died.

Data from reports of *E.coli* O157 indicates that most cases of VTEC are sporadic but that transmission occurs through farm visits, contaminated food and water and person to person contact.

HUS surveillance is currently being undertaken in several other national surveillance units allowing useful data comparison. As you will see from Table 10 the incidence rate in Switzerland and New Zealand is twice that of Australian and the British Isles as is the death rate. It is interesting to note that Australia has few *E.coli* O157 reports, *E.coli* O111 being the predominant organism. This is also the case for New Zealand and Switzerland. In contrast in nearby New Zealand O157 predominates. With Germany and Canada now collecting data it is hoped an international comparison will now be undertaken through INoPSU.

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

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HIV/AIDS infection in childhood

Key points

- Reports of HIV infected children are increasing.
- Almost all new reports of infections represent mother to child transmission.
- Cases continue to be reported where the child's diagnosis with AIDS preceded diagnosis of infection in the mother.
- The greatest number of infections are in London, but cases occur in all parts of the country.
- Interventions can reduce vertical transmission of infection from mother to child to less than 5%. It is therefore now national policy to offer and recommend HIV testing to all pregnant women in all parts of England as an integral part of antenatal care. This should be in place by December 2000.
- The proportion of maternal infections diagnosed antenatally has improved considerably in London but this is not yet the case elsewhere in the UK (data up to mid 1999).

Background

National surveillance of HIV infection and AIDS began in 1986 in order to monitor the incidence and prevalence of paediatric infection. It is based on a combination of paediatric, obstetric and laboratory reporting schemes.

Most cases of paediatric HIV infection and AIDS are children born to women infected with HIV; it is now possible to establish the infection status of these children by three to four months of age. Interventions such as antiretroviral treatment for the pregnant woman and her newborn infant, delivery by caesarean section and the avoidance of breastfeeding have dramatically reduced transmission rates. Furthermore, prophylaxis for infected infants can reduce the incidence of pneumocystis carinii pneumonia (PCP), a major cause of HIV-related morbidity and mortality in the first year of life.

These options can only be considered by women if they are aware of their HIV infection. National guidelines are now in place which state that HIV testing should be offered and recommended to all women as a routine part of antenatal care.[1] In the first half of 1999,

71% of HIV infected pregnant women in Inner London had their infection diagnosed by the time their baby was born, and the antenatal detection rate (the proportion of previously undiagnosed women diagnosed antenatally) exceeded 50% for the first time.[2] Diagnosis rates also improved in Scotland, and although similar improvements have not yet been confirmed elsewhere, there are anecdotal reports of improvements in some units which have started to implement the policy. It is vital that this process continues so that HIV-infected women can be offered treatment and advice, vertical transmission rates can be minimised and infected infants receive optimum care.

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 2000 there had been 1600 reports through the BPSU. Nine hundred and seventy-five 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 four for whom the transmission route cannot be established. Two hundred and seventy-four of the remaining reports were duplicates, and there were also 274 reporting errors. Sixty-seven reports are still being investigated.

A further 1150 reported cases have been identified from other sources (see Endnote) including 894 children born to HIV infected women, 219 children with haemophilia, 17 infected through blood transfusion and 20 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) and the SCIEH Weekly Report (Scotland).

All reporting is voluntary and confidential. Virtually all of the surviving young people infected during the course of treatment for haemophilia are now over 16 years old, and their follow-up 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 2000, among the 1869 children born to HIV infected mothers (Table 12), 664 had confirmed infection, 416 were then of indeterminate status and 789 were known to be uninfected. Transmission rates cannot be estimated from these data as there is a bias towards the reporting of symptomatic children. One hundred and sixty-eight (9%) of these children had been reported from the Republic of Ireland, 208 (11%) from Scotland, 1248 (67%) from the Thames regions and 245 (13%) from the rest of England, Wales and Northern Ireland.

Growing numbers of mainly uninfected children have had perinatal exposure to antiretroviral therapy and mechanisms are being established for monitoring both short and long-term outcomes in such 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, which funds the routine collation of data each quarter and the transfer to national surveillance centres.

Table 11 *Infants born to HIV infected women, and confirmed cases of paediatric HIV infection (notified by 31 January 2000)*

Transmission route ***(actual or potential)***	**BPSU Reports**	**Reports from other sources**	**Total**
risk of vertical transmission	975	894	1869
haemophilia treatment	48	219	267
blood transfusion/products	25	17	42
other/not yet established	4	20	24

Table 12 *Infection status of children born to HIV infected women (notified by 31 January 2000)*

Region of first report	**Infected**	**Indeterminate**	**Not Infected**	**Total**
Thames regions	486	300	462	**1248**
Rest of England, Wales & Northern Ireland	105	55	85	**245**
Scotland	35	29	144	**208**
Republic of Ireland	38	32	98	**168**
TOTAL	**664**	**416**	**789**	**1869**

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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Inflammatory bowel disease (IBD) in under 20-year-olds

Key points

Based on preliminary data

- A preliminary estimate incidence of 5.3/100,000/year was observed in the UK/ROI population.
- The incidence of Crohn's disease was twice that of ulcerative colitis.
- IBD was seemingly over represented among Asian children.
- 10% of cases were in children under 10 and 3% in under fives.
- The period from first symptoms to diagnosis varied between regions.

Background

Whilst the incidence of ulcerative colitis (UC) appears static or falling, some recent reports suggest there has been an increase in the incidence of Crohn's disease (CD) in industrialised countries. If confirmed these findings may be consistent with an environmental trigger. However, epidemiological studies to assess environmental factors that may affect susceptible individuals are difficult to undertake because of the small numbers of affected children attending single centres. Equally, conflicting reports on aetiology have highlighted the need for current data on disease incidence and clinical cause.

Paediatric inflammatory bowel disease (IBD) is considered to present a number of additional clinical problems to those seen in adult disease. These include delay in diagnosis, growth failure in more aggressive disease and a higher potential for malignant change. The delay in diagnosis in part probably reflects the lack of specificity in presenting symptomatology and may prevent the initiation of effective therapy. However, many of these impressions are based on occasional reports from specialist centres. Some retrospective data related to this are available from Scotland and Wales but none from England. There have been no previous prospective studies to document clinical patterns and disease prevalence in the UK so the incidence of inflammatory bowel disease in childhood in the UK remains unknown[1].

The incidence of inflammatory bowel disease is thought to rise rapidly in the teenage years. Since an apparent increase in incidence could simply be the result of earlier diagnosis (shortening of time between symptom onset and diagnosis), it is important to have reliable data throughout the 16-19 year age group, some of whom may present to a paediatrician and others to an adult gastroenterologist.[1] This study is therefore being carried out in collaboration with the newly formed British Society of Gastroenterology Research Unit. This collaboration, including raising the reporting age to 20 years, should ensure optimal reporting of adolescent cases.

A prospective UK study on IBD is also needed in order to plan appropriate care facilities, devise effective treatment strategy and direct research into this chronic disease. Furthermore in order to properly undertake future epidemiological studies on IBD, particularly to investigate environmental factors incidence data are required.

Study duration

June 1998-June 1999.

Case definition

Reporting case definition: Any individual under 20 years of age at diagnosis, and resident in the United Kingdom or Republic of Ireland who in the opinion of the notifying doctor has newly diagnosed inflammatory bowel disease (Crohn's disease, ulcerative colitis or indeterminate colitis), based on history, clinical, laboratory, radiological and/or endoscopy findings. Cases to include children with isolated oral granulomatous disease and isolated peri-anal disease.

Objectives

To identify:

1 The annual incidence of inflammatory bowel disease (including Crohn's disease, ulcerative colitis or intermediate colitis) presenting in childhood/adolescence (under 20 years of age).

2 The average period between onset of first symptoms to presentation to a GP, or other doctor to diagnosis.

3 The site and extent of the disease process at diagnosis.

4 The basis for the diagnosis and the treatment given to the child.

Method

Reporting paediatricians are sent a questionnaire to gather information on symptomatology, time between onset of symptoms, diagnosis, the method by which the diagnosis was made and the mode of management. Histology slides are requested for one in ten reported cases and returned to the reporting physician after having been reviewed by two independent paediatric pathologists.

All members of the British Society of Gastroenterology (BSG) are also asked to report cases through their Research Unit (the majority of adult gastroenterologists and gastrointestinal surgeons belong to the BSG). Data are then combined to produce an optimal data set.

Analysis – interim data

These interim findings are based mainly on the BPSU data with additional data from the National Register (NR), co-ordinated by the Inflammatory Bowel Disease Working Committee of the British Society of Paediatric Gastroenterology and Nutrition and the BSG surveys. At the time of writing a complete data set is still awaited from these organizations. Once available final analyses will be undertaken.

BPSU data (under age 16)

This is the first national prospective study of paediatric IBD reported in the world.

During the 13 month study period 966 IBD reports were received through the surveillance mechanism:

- 339 clinicians made reports from 204 institutions
- 70% of clinicians returned their questionnaires within 9 weeks of the report being received by the BPSU

65% (623) of reports were confirmed as cases of IBD under age 16 years, 35% were not valid and 15 late reports are unconfirmed but probable cases. The not valid include 163 duplicates and the remainder includes mistaken diagnoses, older children etc.

Only 1% of the reports to the BPSU were aged over 16. It is not clear if this reflects paediatric practice, or whether notifying paediatricians were unaware that all cases under 20 were to be included. There were few duplicate reports and an impression was made that smaller centers expected the tertiary referral centers to make the report. Only 6% of reports represented prevalent cases. A few centers seemed to make no valid reports to either the NR or BPSU.

Overall 84% of all IBD cases during the study period were identified by the BPSU. An additional 55 cases were registered with the National Register but not reported to the BPSU (all from larger metropolitan centers) and 65 previously unknown cases under the age of 16 were registered with the BSG.

The minimum number of new cases of IBD in children aged less than 16 years (from 1.6.98 – 30.6.99) in the UK and the Republic of Ireland (ROI) was 743. Using 1997 population estimates the overall incidence of inflammatory bowel disease in children aged less than 16 years was 5.3/100,000 in 1998/9, equivalent to around 685 new cases per annum.

The estimated incidence figure of 5.3 per/100,000/year is the highest figure to date reported for the UK/ROI (a 1993 retrospectively study from South Wales recorded an incidence of 3.8/100,000). The only comparative data is that from Scandinavia. In Sweden the incidence of IBD was found to have increased from 4.2/100,000 in 1984/6 to 7.0/100,000 in 1993/5, in two similarly conducted prospective studies. The apparent increase in the incidence of IBD in the UK and ROI may possibly thus be genuine (rather than due methodological differences), as the rate of increase is very similar to that documented in Sweden. The data appear to support clinician's impressions that the incidence of IBD is truly increasing, but only a repeat prospective study can definitively confirm this impression as this and the South Wales survey are not strictly comparable.

The incidence of Crohn's Disease (CD) was twice that of ulcerative colitis (UC) which is the reverse of what is observed in the adult population.

IBD was over-represented amongst children with an Asian background in the UK. Furthermore colitis was more common than Crohn's Disease in this group (i.e. the reverse to that of the Caucasian and Afro-Carribean groups). It is not clear whether this is due to environmental or genetic factors. However there was a very strong genetic component amongst certain ethnic groups, a positive family history was recorded in 47% of Pakistani children.

The mean age at diagnosis was 11.8 years (median 12.6 years). 13% of cases developed in children aged less than 10. There was a small number of very young children developing the disease - just over 3% of cases are aged under five. Although the median delay period from onset of symptoms to diagnosis was five months, 25% of children seemingly had symptoms for more than one year before diagnosis. The length of delay varied significantly between regions. In some regions a significant factor in the delay appeared to be a prolonged diagnostic process.

Thirty per cent of cases were reported from institutions seeing less than five cases a year. In many smaller institutions there appeared to be no "lead" paediatrician involved in coordinating care, with management seemingly being spread amongst different clinicians. A paediatric gastroenterologist was not involved in the initial management of 35% of cases. Patterns of investigation and treatment varied between institutions and between different types of clinicians.

Comment

This data provides some indication that the incidence of IBD may have increased recently. This survey has highlighted the need for increased awareness of the condition amongst all doctors, the need

for significant improvements in the overall provision for children and their families, and the urgent need for further research both to determine the optimum care pathways and to understand any precipitating environmental triggers.

Interim data have been presented (in poster format) at the 1999 meeting of ESPGHAN (Warsaw) and at a plenary session of the RCPCH (April 2000) and an oral presentation at the First World Congress of Paediatric Gastroenterology, Boston will take place (August 2000).

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In collaboration with Professor R Logan, British Society for Gastroenterology Research Unit and the IBD Working Committee (chair Dr Hugh Jenkins) of the British Society of Paediatric Gastroenterology and Nutrition.

Invasive Haemophilus influenzae infection

Key points

- Hib vaccination has resulted in a dramatic decline in invasive Hib disease in children in the UK and Republic of Ireland.
- True vaccine failures are occurring rarely, a substantial number have an underlying predisposing condition.
- Paediatricians should support higher Hib vaccine coverage in the UK and ROI and encourage timely Hib vaccination because a significant proportion of Hib cases are still avoidable.
- Hib immunity in immunised children declines with age (time since primary immunisation) though the fall is small in real terms.

Background

In October 1992 *Haemophilus influenzae* type b (Hib) conjugate vaccines were introduced for routine immunisation of infants in the United Kingdom (UK) and the Republic of Ireland (ROI). The acceptance and uptake of vaccine has been high and the incidence of Hib disease has fallen dramatically.

In September 1992 the BPSU included invasive *H.influenzae* infection occurring after Hib immunisation in its reporting scheme and in November 1995 widened the case definition to include all children with invasive *H.influenzae*, regardless of vaccination status. Following the dramatic decline in invasive Hib that was seen following the introduction of Hib immunisation in 1992, the surveillance mechanism has identified children in whom vaccination is unsuccessful as worthy of further immunological evaluation and follow-up and allowed preliminary estimates of vaccine effectiveness to be made. The continuation of surveillance is addressing the important issue of the duration of protection provided by primary immunisation. Protection against Hib disease is required until children are at least five years of age by which time natural immunity has usually developed. The absence of a second year Hib booster in the UK and ROI (most other countries include such a booster) therefore necessitates careful monitoring of the programme. The widening of the case definition, in 1995, aims to ensure complete case ascertainment and to identify pockets of continuing transmission. Such information will aid in targeting control measures and deciding future vaccination strategies.

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.

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.

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.

Study duration

The study began in September 1992 and is reviewed annually.

Results

By 1 March 2000, 672 reports that met the case criteria had been made including 434 cases in vaccinated and 172 in unvaccinated children. One hundred and sixty-two cases represented true vaccine failures (TVF), 78 apparent vaccine failures (AVF) and 18 were possible vaccine failures (course of vaccination received, isolate of *H.influenzae* obtained but not typed). Amongst vaccinated children there were 139 with invasive disease due to non capsulate strains of *H.influenzae* and 37 with non b capsulate strains (type f 28, type e 7, types a and c one each).

One hundred and fifty-three of the 162 TVF were vaccinated in the first year of life: 140 received three doses and 13 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 (129), 17 developed disease between five and 11 months of age, 43 between 12 and 23 months of age, 36 between 24 and 35 months of age, twenty between 36 and 47 months of age, ten between 48 and 59 months of age and three between 60 and 71 months of age. Surveillance has therefore allowed the following point estimates of vaccine effectiveness to be made (three doses in infancy): 99% (95%CI 99-100%) for children aged 5-11 months, 98% (97-99%) for those aged 12-23 months, 96% (94-97%) between 24-35 months of age, 96% (94-98%) between 36-47 months of age, 91% (83-96%) for those aged 48-59 months of age and 96% (88-99%) for those 60-71 months of age. For the whole period from five to 71 months of age, the estimate is 98% (98-99%).

The modes of presentation and associated medical and immunological conditions amongst the cases of TVF are detailed in Table 13. Overall 48 of 123 (39%) TVF, for whom all information was available, were shown to have an associated condition. Among all TVF there have been 7 deaths (4%). Among AVF there have been 3 deaths.

Table 13 *Presenting illness and associated conditions of true vaccine failures (TVF) Sept 1992 – March 2000*

Presenting Illness		Associated condition	
Meningitis	93	Prematurity	20
Epiglottitis	28	Chromosomal abnormality	5
Bacteremia	18	(includes 3 Down's syndrome)	
Pneumonia	9	Malignancy	6
Cellulitis	8	Dysmorphic syndrome	5
Septic arthritis	3	Cyclical neutropenia	1
Other	3	Immunosupression	1
		Immunoglobulin deficiency	35

Convalescent sera were available in 122 cases of TVF. Thirty-six (30%) demonstrated a poor antibody response to disease (<1ug/ml), necessitating a booster dose of vaccine.

The majority of *H.influenzae* isolated from unvaccinated children have been non capsulate strains (108/172) with a predominance of neonatal disease, especially in premature infants. Hib has been isolated from 55 children, four of whom died.

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 1996-1999 is shown in Table 14.

Table 14 *Incidence of Hib disease in UK children < 5 years of age*

Year	Cases (incidence, 95% CI)
1996	30 (0.8, 0.5-1.1)
1997	29 (0.8, 0.5-1.1)
1998	23 (0.6, 0.4-0.9)
1999	39 (1.1, 0.7-1.4)

Comment

This surveillance continues to demonstrate high levels of protective efficacy of the Hib conjugate vaccines when given at 2, 3 and 4 months of age in the UK. The overall Hib incidence in children < 5 years of age in 1999 represents a 97% reduction compared with the incidence pre-vaccination. The incidence in 1999 is however, slightly higher than in previous years (Table 14) and emphasises that continued surveillance is vital.

Although the majority of *H.influenzae* isolates in UK children are now non – type b, Hib is still occurring in unvaccinated children. Amongst unvaccinated cases, 32 / 55 (58%) were of an age that timely vaccination may have prevented disease. The risk of Hib disease in an unvaccinated child in 1998 was 23 fold higher relative to a vaccinated child. National Hib vaccine coverage rates of 92-93% for 3 doses by 12 months of age allow room for improvement. Timely vaccination and high vaccine uptake remains vital if this disease is to be eliminated.

For Hib cases occurring in vaccinated children, a significant proportion have underlying conditions which may have predisposed them to vaccine failure. A statistically significant decline in vaccine efficacy as children get older is now apparent, this decline is small in real terms and absolute estimates of vaccine

efficacy remain very high up to and including 6 years of age. Whether a booster dose in the second year of life would have a significant impact on numbers of Hib cases and whether it would be a cost effective strategy requires ongoing evaluation.

The investigators are most grateful for the collaboration of paediatricians, microbiologists and public health physicians in this study.

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Progressive intellectual and neurological deterioration in children (PIND)

Key points

- Surveillance of variant Creutzfeldt-Jakob Disease (vCJD) through PIND is feasible.
- The majority of children notified to the PIND study have some other diagnosis which is not vCJD.
- Three cases of vCJD have been notified in 1999 - two cases of Definite vCJD and one case of Probable vCJD.

Background

Active prospective surveillance of UK children with progressive intellectual and neurological deterioration (PIND) commenced in May 1997 and is expected to continue until April 2002. Funded by the Department of Health, it is being carried out via the British Paediatric Surveillance Unit (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 is to determine whether or not any children in this group have developed vCJD. The appearance of vCJD in patients as young as 16 years of age[1] first suggested the possibility that vCJD is occurring in 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 PIND conditions are obtained.

The investigators 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

1 To carry out active prospective surveillance of UK children with paediatric neurological conditions (including those with specific diagnoses) defined by their common presentation - Progressive Intellectual and Neurological Deterioration (PIND) - to determine the incidence and distribution of PIND.

2 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 - recently extended from three 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:

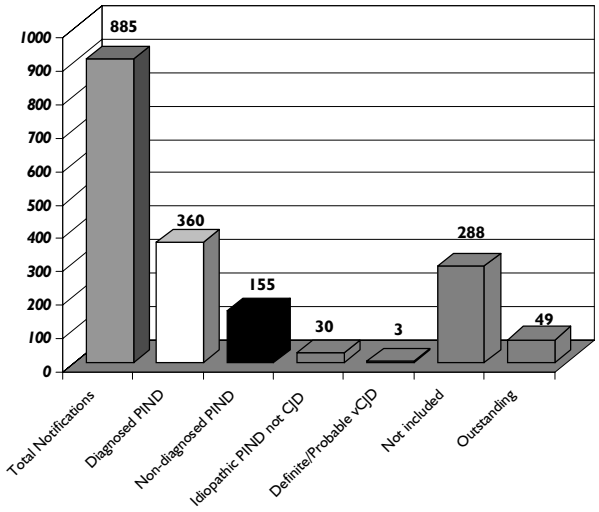
- Children who meet the case definition even if specific neurological diagnoses have been made.
- Metabolic disorders leading to neurological deterioration.
- Seizure disorders if associated with progressive deterioration.
- Children that have been diagnosed as having neurodegenerative conditions but 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 beginning of May 2000 a total of 885 children had been reported via the BPSU. Of these the Expert Neurological Advisory Group has discussed 655 cases. 360 have been classified as having a recognised cause of PIND; 155 have been classified as meeting the surveillance case definition and are still under investigation; 30 have been classified as Idiopathic PIND - not vCJD; three children have been placed in the Definite or Probable vCJD category (2 Definite, 1 Probable); 107 have been classified as "Not PIND" (and therefore not included).

Figure 11 *PIND Surveillance - Current Status*



Of the remaining 230 notifications 181 were not included (reported in error, duplicate report, no traceable clinical information). Forty-nine reports are in the process of being followed-up.

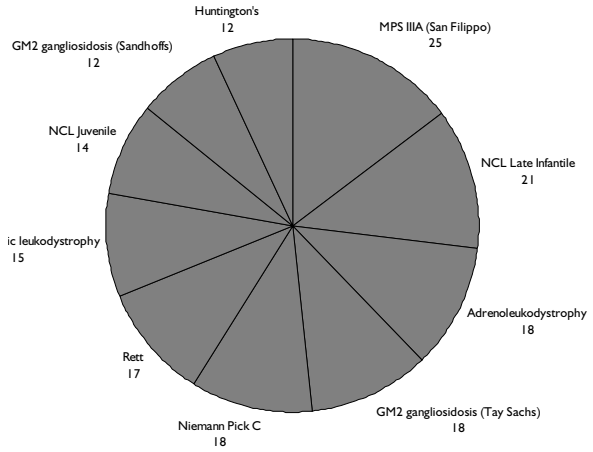
Definite/probable cases of vCJD: Three cases of vCJD (two Definite and one Probable) have been notified - the youngest was aged 12 years at onset. Of the other two, one boy was aged 15 and one girl was aged 14 years at onset. Two of them have died and neuropathology has confirmed vCJD.

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 360 children with a confirmed diagnosis there were 88 different neurodegenerative conditions. The ten most commonly occurring diagnoses are shown in Figure 12.

Variation in reporting by district

Demographic analysis reveals interesting variations in reporting rates between paediatric centres. Yorkshire remains the region with the highest number of notifications - 119.

Figure 12 *The ten most commonly occurring confirmed PIND diagnoses*



Interim conclusions

PIND surveillance has been running for just over three years now and has recently been approved by the Department of Health for 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 - two 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.

PIND surveillance is working very well; paediatricians are still responding enthusiastically with a median number of 25 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.

Funding

Department of Health.

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Reye's syndrome

Key points

- The incidence of "classic" Reye's syndrome has dropped dramatically since June 1986.
- Occasional aspirin associated cases continue to occur, predominantly in children aged 12 years and over.
- Continued monitoring of Reye's syndrome is essential to determine whether current advice on aspirin for children requires modification.
- Most cases now reported, although satisfying the diagnostic criteria, are 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 USA, 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 USA, 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 has been 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.

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

The BPSU involvement with this study began in June 1986 and is reviewed annually.

Analysis

Between August 1981 and July 1999 a total of 625 suspected cases of Reye's syndrome were reported (Table 15), but the diagnosis was subsequently revised in 161 (26%). Seventy nine (49%) of the revisions were to one of the 'Reye-like' inherited metabolic disorders. Two hundred and thirty seven (53%) of the total 447 cases compatible with a diagnosis of Reye's syndrome died. The figures for 1997/98 in the Table differ slightly from those in last year's report because of a late ascertainment of a diagnostic revision - a five year old boy who had anicteric hepatitis A with hyperammonaemia and hypoglycaemia.

In the year to July 1999, 11 reports of new cases were received and further information was provided on all of them. Four of the 11 diagnoses were later revised, leaving seven patients whose clinical and pathological features were compatible with the case definition of Reye's syndrome. Nine of the cases were first reported via the BPSU, two were ascertained only via death entries. In addition to these 11 cases, two further death entries were received: one was for a child first reported to the BPSU in 1993, who died from the neurological sequelae of Reye's syndrome aged six years; the other was a 23 year old woman whose main cause of death was pneumonia, with Reye's syndrome recorded as the underlying cause. This case had not previously been reported and further enquiry revealed that

Reye's syndrome had been diagnosed at the age of 4 months in 1976 before the surveillance scheme began.

Cases compatible with a diagnosis of Reye's syndrome (N=7):

There were six males and one female; the ages ranged between 2 months and 13 years with a median of 2 years 5 months. Five lived in England, and two in Northern Ireland. There were no reports from the Republic of Ireland, Wales or Scotland. One patient was ill in June, the remainder had their onsets between September and March.

Five children recovered completely. Of the two who died, one was a five year old who also had congenital cytomegalovirus infection with spastic quadriplegia and epilepsy. The other was a two year old in whom the diagnosis was made at autopsy on the basis of cerebral oedema and a fatty liver. The child had died suddenly during an episode of gastroenteritis. Investigation of post mortem urine and liver for disorders of fat oxidation and amino acid metabolism did not reveal an inherited metabolic disorder.

Three cases had had no pre-admission medications other than oral electrolyte solutions for gastroenteritis; one, the patient with congenital cytomegalovirus infection, was taking sodium valproate; none had received paracetamol. Three patients had taken aspirin, of whom two were aged over 12 years and one was nine months old.

Six of the seven patients had had a pre-encephalopathic viral-type prodrome - flu-like in three, and gastroenteritis in three. Virological investigation confirmed influenza B infection in one of the older cases who had taken aspirin; in none of the others was there a confirmed microbiological diagnosis.

Five patients were reported to have had a range of investigations for inherited metabolic disorders. In one case this information was unavailable; the other patient, a two-month-old infant, was not investigated.

The 'Reye Score' (possible range 1-25) ranged between 8 and 20 with a mean of 15 and median of 16. The median compares with 12, 12, 13 and 13 in the previous four years respectively.

Revised diagnosis cases (N = 4)

One patient was a 25month old boy, who developed an influenza-like illness and pneumococcal bacteraemia and who died. A fatty acid oxidation defect, probably long chain hydroxyacyl dehydrogenase deficiency, was reported. Another, a 13 month old boy, had an influenza-like illness preceding encephalopathy; he survived and cytochrome oxidase deficiency was the revised diagnosis. The third was a nine month old male with a two day history of gastroenteritis who died suddenly. Reye's syndrome was initially diagnosed on the basis of the autopsy findings, but further investigation revealed medium chain acyl coA

Table 15 *Reye's syndrome surveillance 1981/82 - 1998/99*

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	13	(4)	39	22
1986/87	47	21	(11)	26	13
1987/88	44	12	(3)	32	19
1988/89	31[1]	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[5]	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
TOTAL	625	161	(79)	447	237

* *Compatible with the diagnosis (see text)*

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

dehydrogenase deficiency. Details were unavailable on the final case, but the child survived and the diagnosis was reported as still uncertain.

Comment

The findings for 1998/99 differed little from those in the previous five years: the annual total Reye's syndrome cases remained under 10, compared to a peak of 81 during the years before the 1986 aspirin warning; the number of deaths, two, was the lowest yet recorded; two other deaths were ascertained, but they were both the consequence of serious brain injury from Reye's syndrome acquired some years ago. These trends are continuing in the current surveillance year: by June 2000 only three reports had been received, compared with seven in the same period last year.

Only two of the seven non-revised cases could be described as having "classic" or North American-type Reye's syndrome [1,2], both were over 12 and both had received aspirin. The two who died were both atypical: one child had pre-existing neurological damage and was taking sodium valproate which is, rarely, associated with a Reye-like syndrome; the other died suddenly during an episode of gastroenteritis. These patients illustrate the low specificity of the standard case definition and in fact the former could equally be allocated to the revised diagnosis category, as her encephalopathy might have been "explained" by the valproate. The ages of the other three patients ranged from two to 19 months, again, atypical [2] and it is possible that they had unrecognised inherited metabolic disorders, although none were found in the two who were investigated (one of these latter was the infant who had been given aspirin and it is of concern that the warning label was not heeded in this case).

This year, as in the previous four years, there was a winter predominance in onsets which is an epidemiological feature of "classic" Reye's syndrome; however, it is also compatible with that of the presentation of Reye-like inherited metabolic disorders since encephalopathic episodes in these too, are likely to be precipitated by common childhood viral infections, which are more prevalent in winter.

During 1999 anonymised data from the surveillance scheme were requested by the Medicines Control Agency for a paper to be put before the Committee on Safety of Medicines . This paper reviewed the case for increasing the age limit on the UK aspirin warning to include teenagers (as it does in the USA) and was partly prompted by the observation that, of 17 aspirin-associated cases reported since June 1986, 10 have been aged over 12. [3] The Committee on Safety of Medicines reached its decision last November: it "was of the opinion that there is currently insufficient evidence of a causal association in these children, and therefore advised that extension of the existing advice to include children aged 12 years and above could not presently be justified". This was a disappointing decision, especially in view of the two aspirin associated cases over 12 in the year under review. However, the Committee went on to advise that: "monitoring of the incidence of Reye's syndrome should continue, as clearer trends may emerge in the future". They further noted that " a review of this issue might well be appropriate when additional information is available". As a result of this, the Medicines Control Agency have informed us that it is "essential to continue monitoring the incidence of Reye's syndrome in the UK".

The investigators are most grateful to all the paediatricians who report cases and who provide 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.

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Severe visual impairment and blindness

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. This information has not been previously 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 blind certification of eligible children.

Since September 1999, eligible children (as defined below) have been sought, simultaneously but independently, through the BPSU and the British Ophthalmological Surveillance Unit. Both sources are being used to ensure high ascertainment, particularly of children with multiple impairments, and to enable both paediatric and ophthalmic information to be collected about each child.

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.

Results

There has been a very good response from paediatricians. Over 150 eligible children have been notified in the first six months of the study.

Of these children:

- 50% are boys
- 43% have additional non-ophthalmic impairment(s)
- 16% are South Asian (Indian, Pakistani, Bangladeshi)
- 23% were < 2500 g at birth
- 54% presented symptomatically, whilst in 30% visual impairment was detected during a routine examination

The three most common groups of disorders are those affecting the cortex / visual pathways, the retina, and the optic nerve. However, the anatomical pattern differs between those with visual loss alone and those with other impairments. In 59% of children prenatal aetiological factors were implicated or identified.

The study is progressing well with interesting findings emerging which the investigators believe will be important to clinical practice and service provision. All involved in the study are very grateful to all paediatricians who have notified cases to the BPSU and provided information about them. The investigation team would request all paediatricians to continue to notify *newly diagnosed* severely visually impaired or blind children *whether or not the children have been notified by an ophthalmic colleague*, to enable high ascertainment of all eligible cases, and complete data collection to be achieved.

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Subacute sclerosing panencephalitis

Key points

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

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 (PCR) 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 29.

Study duration

1986-2001 (reviewed annually)

Recent results and progress

There has only been one new case of SSPE in the UK reported with onset in 1999. A brain tissue sample was analysed in the Enteric and Respiratory Virus Laboratory at Colindale for diagnostic purposes: the proposed measles virus genotype was identified as D-5, one of the predominant wild types of measles virus in the UK and throughout Europe. The age at onset was 14yrs.

Ten cases of SSPE have now been investigated at the Enteric and Respiratory Virus Laboratory at Colindale through PCR and genetic sequencing of the causative measles virus, and none has been related to the vaccine-like strain (genotype A). 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.

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Subdural haematoma/effusion (SDH)

Key points

- This study found an incidence around 10.9/100,000/year infants aged 0-1 years and 20.8/100,000/year for 0-2 years.
- About 50% of cases were attributed to child abuse
- At preliminary follow-up around 50% of children were normal neurologically and developmentally.

Background

Subdural haematoma/effusion (SDH) is an important cause of death and neurological disability in childhood. Over half the cases of SDH present without evidence of skull fracture or other sign of injury to the head. Although the notion of "spontaneous origin" or arising from "minimal trauma" was claimed, an association with severe shaking injury occurring non-accidentally is now firmly established. Despite the evidence linking SDH and shaking injury, cases continue to be encountered where other non-abusive causes are questioned within both medical and legal contexts. Rare conditions reported to be associated with sub-dural haemorrhage in childhood include: *H.Influenzae* and pneumococcal meningitis, haemophilia, malignancy, A-V malformation/aneurysm, post cardiopulmonary bypass, glutaric acidaemia, Algelle's syndrome, disseminated intravascular coagulation, Menke's disease.

Descriptions of "the shaken baby syndrome" describe clinical findings including retinal haemorrhages, Subdural and/or subarachnoid haemorrhage, long bone metaphyseal avulsion and other skeletal injury including rib fracture and occasional vertebral injury and little or no evidence of external cranial trauma.

Difficulties in establishing the cause of SDH are more likely to be encountered in cases where there is no other evidence of trauma including those without retinal haemorrhages - estimated to be about 20 to 50% of cases. Examination of the fundi should ideally be undertaken by an ophthalmologist who frequently examines children using both direct and indirect ophthalmoscopy in accordance with recent guidelines (The Ophthalmic Child Abuse Working Party (D. Taylor, Chairman) Child Abuse and the Eye. Eye 1999; 13:3-10).

Methods

When a case was reported, the paediatrician or pathologist was asked to complete a questionnaire.

The Office of National Statistics reporting scheme will also report fatal cases and approaches made to the coroner involved for information. A questionnaire will be sent to the pathologist who completed the post-mortem examination.

Further patient details were sought by questionnaire. The information required was routinely available from medical records and case conference minutes. The information was handled anonymously and individual children not identified within the study. No contact with patient or family was made.

Case definition

Any child under 2 years of age with fatal and non-fatal subdural haemorrhage, haematoma or hygroma (collection of protein rich fluid in the subdural space) of any severity, arising from whatever cause and diagnosed on CT, MRI or ultrasound scan or at post-mortem examination.

Duration of study

Initial data collection from 1st April 1998 to 30th April 1999. Follow up data collection was undertaken six months from date of diagnosis.

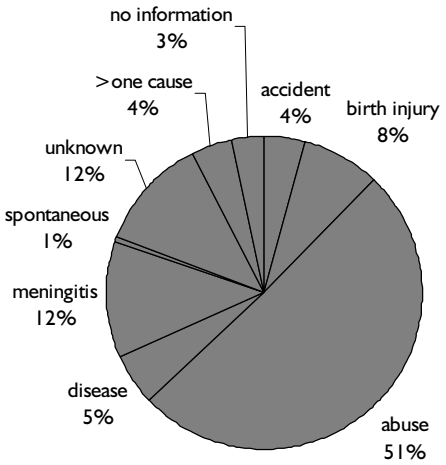
Results

- Confirmed cases 186 (50%)
- Duplicate notifications 78 (21%)
- Outside case criteria 49 (13%)
- Unaccounted for 56 (15%)

Total notifications received 369

Of 186 infants who fulfilled the criteria, there were 64 girls and 122 boys, average age 17.5 weeks (range 0 - 82), mean birth weight 2.95kg (164 infants), 26% were of low birth weight. There were 33 deaths. Preliminary aetiology is as shown in Figure 13.

Figure 13 *Aetiology of SDH/E*



The calculated incidence of SDH/E is 10.9/100,000 infants aged 0-2, and 20.8/100,000 infants aged 0-1. This compares closely with the only previous study (Jayawant et al "Severnside study" BMJ 1998: 317) where figures were 12.8/100,000 aged 0-2 and 21.0/100,000 aged 0-1.

Six month follow up information: information has been received for 149 children. Table 16 presents what was found:

Table 16 *Six Month Follow-up Information*

Condition number of children affected	
fits	20
cerebral palsy	29
hydrocephalus	15
microcephaly	19
normal neurologically	80
normal developmentally	76

Conclusion

SDH is a significant morbidity and mortality in childhood. Much of it is due to abuse although it is likely that this is a minimum estimate due to under-diagnosis.

Funding

Hospital Funds.

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6 New studies for 2000

Group B streptococcus disease (GBS)

Background

Group B streptococcus 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 an incidence of 0.3/1000 live births (< 2 months of age). There have been four published studies from England from the 1980s and 1990s which estimate incidence rates of between 0.6-1.2 / 1000 (average 0.7). A retrospective series from the Northern Region calculated a mortality from EOGBSD of 0.08 / 1000 live births. 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 thought to be about 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. It is conceivable that the burden of disease in the UK/ROI may be so low that a strategy of no intervention would be the most cost effective one.

The risk factors on which current interventions are based are derived mostly from data from the USA. These include maternal age (under age 20), black ethnic group, prolonged rupture of membranes, prematurity and low birth weight. Such factors may not necessarily apply outside the USA. In addition to cost, increased exposure to antibiotics has other possible implications such as anaphylaxis as well as encouraging antibiotic resistance and the emergence of other pathogens.

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 has been prioritised by a working group convened by the Public Health Laboratory Service which includes all relevant professional groups including the British Association of Perinatal Medicine. Only with a national study will data be generated of sufficient size 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 will be asked to report all cases meeting the case definition by indicating on the orange card that they have seen a case. Telephone reporting is not necessary. A 2 page questionnaire will then be sent to the paediatrician seeking brief clinical and outcome details. Questionnaires will be sent back to the coordinator in a pre-paid return envelope. The data will be coded so as to preserve confidentiality.

To ensure as complete ascertainment as possible Microbiologists and Consultants in Communicable Disease Control are 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 will be valuable for designing future serotype based conjugate vaccines. In the Republic of Ireland, microbiology laboratories will be contacted by telephone every 2 weeks.

Case definition

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

Cases will subsequently be classified as early onset (< 7 days) and late-onset (7-90 days of age).

Study duration

February 2000-February 2001

Coverage

United Kingdom and Republic of Ireland

Ethical approval

The study has received ethical approval from the Wandsworth Local Research Ethical Committee.

Funding

Meningitis Research Foundation.

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Cerebrovascular disease, stroke and stroke-like illness

Background

The aetiology of stroke 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 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.

Methods

All cases of cerebrovascular disease and/or stroke or stroke-like illness presenting to British and Irish pediatricians in children aged between birth (>37 weeks gestation) and 16 years will be identified using the BPSU. The aim is to be over-inclusive, so previous infection, epilepsy or trauma, will not be *automatically* excluded. All British Neurosurgeons, cardiothoracic surgeons, cardiologists, paediatric radiologists and haematologists/oncologists will be surveyed regularly independently for any cases presenting to them. Mortality statistics will also be reviewed.

Details on all patients will be sought through a brief questionnaire. A separate questionnaire will be sent for cases of Sturge-Weber syndrome. All the information sought from the reporting paediatrician will be routinely available from medical records. No special investigations are sought. The patient or family will not be contacted. Reporting clinicians will be sent a follow up questionnaire in one year's time to see how the patient has fared.

Case definition

Any child from birth (>37 weeks gestation) and the 16th birthday with cerebrovascular disease and/or stroke or stroke-like illness. The WHO definition of stroke is: "A clinical syndrome of rapidly developing 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 eg.

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

This does not automatically exclude prior illness eg. 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

Study duration

Autumn 2000 for 13 months

Coverage

United Kingdom and the Republic of Ireland

Ethical approval

The project has been approved by North Thames MREC

Funding

Stroke Association

Reference

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7 RCPCH/RCPE Joint Symposium – Key Issues in Child Health

The BPSU was particularly proud to be the theme for the second Joint symposium of the Royal College of Paediatrics and Child Health and the Royal College of Physicians, Edinburgh. Held on the 5th November 1999 at the RCPE this was the third meeting to showcase the work of the BPSU, and the first to be held outside of London. Over a hundred paediatricians, researchers, nurses and epidemiologists attended. There were also representatives from our sister paediatric units from Australia, Canada and Latvia; the British Ophthalmological Surveillance Unit, the British Gastroenterology Research Unit. Representatives also attended from Belgium, Italy and Portugal.

The morning session chaired by the RCPE President Professor James Petrie opened with Dr Angus Nicoll outlining the BPSU mechanism and its impact on public health. Dr David Goldberg of the Scottish Centre for Infection and Environmental Health discussed the impact infectious disease has had on the Scottish population from the polio outbreak in 1900 through to the typhoid epidemic in 1968 and the Lanarkshire *E.coli* O157 outbreak in 1996. Taking surveillance of HIV and AIDS as an example, emphasis was placed on the need for multi-ascertainment. Such ascertainment helped confirm that nationally, two thirds of mothers born with HIV infected infants were unaware of their infectious status. Knowledge of this could have allowed appropriate therapy that may have prevented vertical transmission to the newborn. Highlighting the current haemolytic uraemic syndrome study Dr Bob Adak presented the latest surveillance data. It was stated that since the Lanarkshire *E.coli* O157 outbreak there have been additional smaller outbreaks leading in several cases to the death of children due to HUS. 193 cases have been confirmed in the two years to Feb 1999 of which five have died. On examining the outbreaks it was clear that food contamination was not the only route of infection, environmental contamination and person to person contact were others. The importance of making information available to the public was also emphasised.

The next pair of presentations examined the rise of BSE in the cattle population and its relation to new variant Creutzfeldt Jacob Disease (vCJD). Professor Rob Will of the CJD surveillance unit reported on the current status of the infection in the UK. It was stated that though current vCJD incidence levels are low as yet not enough data is available to assess whether this will remain the case. To date the youngest confirmed case was that of a 15-year-old. Dr Chris Verity followed with an update of the BPSU progressive and intellectual neurological degeneration study (PIND). So far 700 cases have been reported representing over 10 disorders. At that time, no cases had yet to be identified as vCJD. Disorders that have been identified include neuronal ceroid lipofuscinose (40), mitochondrial encephalomyelopathies (27).

The Charles McNeil lecture given by Dr Chris Kelnar opened the afternoon session. A brief history of the recognition and treatment of diabetes was followed by the main theme of the lecture that of the need for 'diabetic control'. It was reported how lack of glucose control leads to the inevitable complications in children. Teenagers have the most difficulty in maintaining diabetic control. Mention was made of an audit evaluating agreed standards was to be undertaken through the RCPCH in collaboration with the British Diabetic Association. Dr Kelnar also highlighted the need for quality evidence based guidelines and it is hoped that this can be addressed in future. On the theme of diabetes Dr Julie Edge presented the data collected during surveillance of Cerebral Oedema (CO) and death in diabetic coma. She said that over three-year period 34 cases were identified. There were 6 deaths during ketoacidosis not associated with CO occurring after the start of hospital treatment for DKA. Dr Edge also reported on the case control study that is still underway. During a two-year period 2941 episodes of DKA were reported. The risk of CO was 6.8/1000 episode of DKA overall, there being a trend for increased risk in younger children.

The last session from Professor Elizabeth Elliott of the Australian unit highlighted the proposed activities of the International Surveillance Network. Finally Professor Karen Nelson (NIH Bethseda, USA) gave the RCPCH endowed lecture on possible causes of cerebral palsy (CP). Professor Nelson presented evidence to support the view that it was wrong to presume that cerebral palsy is caused by birth asphyxia alone. Other factors that have been shown links with CP include maternal infection, and raised cytokine levels and fetal stroke.

We would like to express our thanks to the RCPE for hosting the symposium and the administrative support from Eileen Strawn and from Serono Laboratories for their financial support. Abstracts from the meeting are available on request.

9 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 put in place the administration to set up a unit, and is expected to pilot surveillance in 2001. Interest has also been shown in Belgium, the Czech Republic and Greece. 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 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 by the units 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 to be known as the Amsterdam-Ottawa Note detailing the functions and structure of the network has been agreed and will posted on the INoPSU website which is currently under development (www.inopsu.org).

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 and Ottawa:

- facilitating 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 Programme (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.

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 Marchessault (Canada), Dr Chris Verity and Richard Lynn (BPSU). The British Paediatric Surveillance Unit will continue to act as server until the summer of 2001.

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 1000 clinicians in child health on a monthly basis, covering a child population of 3.9 million.[1] The overall response rate was 98% in 1999. APSU introduced email reporting in 1997 and currently 42% (417) of clinicians have elected to use this service. Workload for the individual clinician was generally low for 1998 with 16% of clinicians reporting one case, 9% reporting between two and three cases and less than 3% reporting four or more cases. Seventy-five percent clinicians did not report a case of any condition under surveillance and hence were not required to complete a questionnaire.

Conditions surveyed in 1999, include, acute flaccid paralysis, congenital cytomegalovirus, congenital and idiopathic nephrotic syndrome, congenital rubella, haemolytic uraemic syndrome, Hirschsprung disease, HIV/AIDS, invasive haemophilus influenzae infection, neonatal herpes simplex virus infection, Prader-Willi syndrome and vitamin K deficiency bleeding. The year 2000 has already seen the commencement of three studies, charge association, Munchausen by Proxy Syndrome and Rett syndrome.

The recent evaluation of the APSU[2] indicated that paediatricians perceive the APSU to be educationally useful particularly in the provision of diagnostic criteria for conditions studied. It was perceived to be a simple and flexible scheme and acceptable in terms of workload. APSU was found to fulfil most of its objectives and meets CDC criteria in this respect.

Studies through the APSU have given rise to more than 50 publications and a wide range of presentations that have informed the general public and the wider medical community.

APSU collaborates closely with the New Zealand Paediatric Surveillance Unit, sharing study protocols as well as having representation on each other's scientific panels. APSU is a founding member of INoPSU and has recently established a web-site (www.racp.edu.au/apsu/) that will be linked to the INoPSU web-site.

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2 Gazaian M, Williams K, Elliott E et al. Evaluation of a national surveillance unit. Arch. Dis. Child. 1999; 80:21-27.

Contacts

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Canadian Paediatric Surveillance Programme (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 an anticipated 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 1999, the overall initial response rate to the monthly card was 83%, with an overwhelming 95% voluntary completion rate for follow-up detailed reports.

Conditions surveyed in 1999 include acute flaccid paralysis (AFP), cerebral oedema in diabetic ketoacidosis, congenital rubella syndrome, Creutzfeldt-Jakob disease (CJD) /progressive intellectual and neurological deterioration, hemorrhagic disease of the newborn and subacute sclerosing panencephalitis (SSPE). Early in the year 2000, paediatric sub-specialists in allergy, medical genetics and intensive care were added to the surveillance database to accommodate the introduction of new studies on anaphylaxis, Smith-lemli-Opitz and hemolytic uremic syndrome. In the fall of 2000, neonatal herpes 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, one CJD case and two SSPE cases were detected, when none were anticipated. Of particular note, the CPSP received international recognition from the Pan American Health Organisation (PAHO) for its AFP study which met the internationally targeted rate of one case per 100,000 in children under 15 years of age expected to occur in the absence of wild polio.

In the coming year, serious consideration will be given to new studies on hepatitis C, lead toxicity, and child and youth maltreatment, and to the introduction of e-mail response as requested by 20-25% of participants in a recent survey.

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

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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.

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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 however good at 90%. 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).

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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.

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Netherlands Paediatric Surveillance Unit (NSCK)

The Netherlands Paediatric Surveillance Unit started surveillance in October 1992. Around 390 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 1999. 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 three 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 1999 the conditions under surveillance were: acute flaccid paralysis (27 reports), coeliac disease (204 reports), insulin dependent diabetes mellitus (406 reports), group B streptococcal infections (276 reports), HIV/AIDS (40 reports), neural tube defects (78 reports), hospital admissions due to pertussis (207 reports), congenital adrenal hyperplasia (23 reports) and inflammatory bowel disease (86 reports).

In 2000 surveillance for neonatal allo-immune thromobocytopenia commenced.

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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 160 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. Ten conditions are currently being surveyed. These are acute flaccid paralysis, congenital rubella, neonatal herpes simplex infection, perinatal HIV exposure, haemolytic uraemic syndrome, vitamin K deficiency bleeding, subdural haemorrhage under the age of 2, retinopathy of prematurity (Grade III and above), diabetes mellitus, and fetal alcohol syndrome.

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.

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Papua New Guinea Surveillance Unit (PGNSU)

This unit began in 1996 and is closely associated with the Paediatric Association of PNG. 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 1999 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.

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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 five conditions under surveillance in 1999 were: acute flaccid paralysis (8 cases), congenital rubella syndrome (1 case), haemolytic uraemic syndrome (24 cases) and vitamin K deficiency bleeding (5 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. In 2000, varicella zoster infections, tick borne encephalitis and acute rheumatic fever was included in the surveillance.

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Welsh Paediatric Surveillance Unit

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 which 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 134. This covers a child population of 650,000. The overall response rate for 1999 was over 95%. The coordinators are delighted to observe that the Welsh system appears to have enhanced the Welsh response to the BPSU (97.6%) currently ranked first.

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 iInflammatory 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 physical abuse, the critically ill child, coeliac disease, inflammatory bowel disease, congenital adrenal hyperplasia. Two studies were unsuccessful and were withdrawn:- ingestion of household products and haemoglobinopathies.

Current studies include newly diagnosed malignant disease, newly diagnosed diabetes, subdural haemorrhages, Marfan's syndrome, childhood tuberculosis, children in housefires and facial palsy. A study on splenectomy in children is currently being considered.

The unit looks to providing 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.

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Table 17 *National paediatric surveillance units status circa end 1999*

Country	Child population *(10^6- aged 0-15 years)*	Established	Respondents	Reply paid	Response rate **(E-mail reporting)*	Fee for study
Australia	1.5	1992	934	Yes	96%*	No
UK/Rep of Ireland	12.8	1986	2005	No	93%	Yes
Canada	6.3	1996	2212	Yes	83%*	No
Germany	14.0	1992	468**	No	94%	Yes
Latvia	0.4	1996	22	No	90%	No
Malaysia	7.7	1994	395	Yes	75%	No
Netherlands	2.9	1992	432	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	1995	134	No	95%	No

** *Heads of paediatric centres*

Table 18 *Conditions currently under surveillance worldwide 2000*

Condition	Unit performing surveillance
Acute flaccid paralysis	Australia, Canada, Netherlands, New Zealand, Papua New Guinea, Switzerland
Anaphylaxis	Canada
Aseptic meningitis following MMR vaccination	Germany
Atresia (stomach, esophagus)	Latvia
Celiac disease	Netherlands
Cerebral oedema in diabetic ketoacidosis	Canada
CHARGE association	Australia
Congenital adrenal hyperplasia	Netherlands, Wales
Congenital cytomegalovirus infection	Australia
Congenital hypothyroidism	Papua New Guinea
Congenital laryngeal stenosis	Latvia
Congenital nephrosis, Finnish type	Latvia
Congenital rubella	Australia, Britain, Canada, New Zealand, Switzerland
Congenital syphillis	Latvia
Diabetes mellitus	Germany, Netherlands, New Zealand, Papua New Guinea, Wales
Duchenne muscular dystrophy	Malaysia
Encephalitis 2-36 months	Britain
Eosinophilic granuloma	Latvia
Fetal alcohol syndrome	New Zealand
GMUT-1 deficiency	Germany
Group B streptococcal infections	Britain, Netherlands
Haemophilus influenzae infections	Australia, Britain, Germany
Hemolytic ureamic syndrome	Australia, Britain, New Zealand, Switzerland
Haemorrhagic disease of the newborn (vitamin K deficiency bleeding)	Australia, Canada, Germany, New Zealand, Switzerland
Hirschsprungs disease	Australia
Histiocytosis	Latvia
HIV/AIDS	Australia, Britain, Latvia, Malaysia, Netherlands, New Zealand, Papua New Guinea
Household fires	Wales
Idiopathic and congenital nephrotic syndrome	Australia
Inflammatory bowel disease	Netherlands
Invasive pneumococcal infections	Germany
Ischaemic stroke in infants	Germany
Leukemia (acute lymphoblastic, acute myeloblastic, chronic myeloblastic)	Latvia
Lymphogranulomatosis	Latvia
Malignant disease	Papua New Guinea, Wales
Marfan's syndrome	Wales
Medullary sponge kidney	Latvia
Multiple sclerosis	Germany
Munchausen by proxy syndrome	Australia
Neurologic endemic cretinism	Papua New Guinea
Organoaciduria and fatty acid oxidation defects	Germany
Neonatal herpes simplex	Australia, New Zealand
Neonatal fungal septicemia	Germany
Neural tube defects	Netherlands
Cystic fibrosis	Latvia
Pertussis	Germany, Netherlands
Pigbel	Papua New Guinea
Polycystic kidney disease	Latvia
Prader-Willi syndrome	Australia
Primary immunodeficiency disorders	Australia
Progressive intellectual and neurological deterioration/Creutzfeldt-Jakob disease	Britain, Canada
Renal tubular acidosis	Papua New Guinea
Retinopathy of prematurity	New Zealand
Rett syndrome	Australia
Reye's syndrome	Britain
Severe bronchial asthma	Latvia
Severe/Fatal allergic reactions to food ingestion	Britain
Severe visual impairment and blindness	Britain
Smith-Lemli-Opitz syndrome	Canada
Subdural haemorrhage	Britain, New Zealand, Wales
Subacute scerosing panecephalitis	Britain
Tuberculosis	Latvia, Wales
Tracheomalacia	Latvia
Transient myeloproliferative syndrome	Germany
Vitamin C deficiency bleeding	Switzerland
Williams-Campbell syndrome	Latvia

Appendix A Completed studies prior to 1999

By mid 1999 the British Paediatric Surveillance Unit had completed thirty-six 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. London 1987

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: *Haemolytic Uraemic Syndrome in the British Isles 1985-88; Association with Verocytotoxin-Producing E.coli.* Milford DV, Taylor CM, Guttridge B, Hall SM, Rowe B, Kleanthous H. Arch Dis Child 1990; **65**: 716-72

Kawasaki disease
Completed: June 1986 – December 1992
Investigator: Dr S Hall
Published Paper: *Kawasaki Disease in the British Isles. A survey of management.* Dhillon R, Newton L, Rudd PT, Hall SM Arch Dis Child1993. **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. London 1987

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
I*nvestigator: 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: *Congenital Toxoplasmosis.*Hall S. BMJ 1992*; **305**: 291-7*

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

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

Non-accidental poisoning and suffocation/ 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
Vitamin K Deficiency Bleeding. McNinch A, Tripp J.
Published paper: 9th BPSU Annual Report 1993/94. 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, Professor D Harvey
12th BPSU Annual Report 1997/8. London. 1998.

Cerebral oedema and death following diabetic ketoacidosis
Completed: October 1995 – September 1998
Investigator: Dr J Edge, Dr M Hawkins
Published paper: 13th BPSU Annual Report 1998/99. London 1999

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

Appendix B Published papers 1999-2000

AIDS and HIV Infection in the United Kingdom: monthly report. Communicable Disease Report CDR Weekly 1999; 9:45-48

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

Rubella infection. Logan S, Tookey PA. Oxford Textbook of Medicine 1999, Oxford Medical Press: 409-12

National cross sectional study of detection of congenital and infantile cataract in the United Kingdom: role of childhood screening and surveillance. Rahi J, Dezateux C. BMJ 1999; 318: 362-365

Capture-recapture analysis of ascertainment by active surveillance in the British congenital cataract study. Rahi J, Dezateux C. IQVS 1999; 40: (1): 236-239

Case-control study of thermal environmental preceding HSES. Bacon CJ, Bell SA, Gaventa J, Greenwood DC. Arch. Dis. Child. 1999; 81: 155-158

Perinatal mortality and morbidity among babies delivered in water: surveillance study and postal study. Gilbert RE, Tookey PA. BMJ 1999; 319: 483-7

Falling HIV vertical transmission rates in the British Isles: estimates based on surveillance data. Duong, T Ades A E, Gibb DM, Tookey PA, Masters J. BMJ 1999; 319: 1227-1229

Cost effectiveness analysis of antenatal HIV screening in United Kingdom. Ades AE , Sculpher M J, Gibb D M, Gupta R, Ratcliffe J. BMJ 1999; 319: 1230-1234

The disappearance of Reye's syndrome – A public health triumph. Letter of response. Hall SM, Lynn R.
The New Engl J Med 1999; 341, No. 11: 845

Epidemiology of pyridoxine dependent and pyridoxine responsive seizures in the UK. Baxter P Arch Dis Child. 1999; 81(5):431-3

HUS Surveillance – What Does it Tell Us About VTEC? – Adak GK, Lynn R & 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. Arch Dis Child 2000 82(4):286-91

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

Clinical and Immunological risk factors associated with Hib conjugate vaccine failure in childhood: Heath P T, Booy R, Slack M P E, Foggarty J, Moloney AC, Moxon ER. Clin Infect Dis 2000; in press.

Incidence, presentation, management and outcome of cerebral oedema associated with diabetic ketoacidosis (DKA) in Great Britain. Edge J, Hawkins MM, Winter DL, Dunger DB. (submitted)

An international network of paediatric surveillance units - a new era in monitoring uncommon diseases of childhood. Elliott E, Nicol A, Lynn R et al. (in press) 2000

Appendix C Recent presentations

RCPCH Annual Scientific Meeting 1999 & 2000

Impact of the BPSU on clinical practice. Verity C. 1999.

Six year outcome for the BPSU galactosaemia cohort.
Marlow N, Wadsworth EJ, Holton JB, MacDonald A, Shield JPH, Tyfeild L. 1999.

Incidence, presentation, management and outcome of cerebral oedema associated with diabetic ketoacidosis (DKA) in Great Britain.
Edge J, Hawkins MM, Winter DL, Dunger DB. 1999.

Cost-effectiveness of antenatal HIV screening in the UK.
Gibb D, Sculpher M, Ades AE, Gupta R, Ratcliffe J. 1999.

Falling HIV vertical transmission (VT) and progression rates: estimates from surveillance data in the UK and Eire.
Gibb D, Duong T, Ades AE, Tookey PA, Masters J. 1999.

The global HIV epidemic: implications for UK paediatricians.
Tudor Williams G, Nicoll A, Tookey PA. 1999.

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). 2000.

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

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

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

RCPE/RCPCH Symposium 1999

The British Paediatric Surveillance Unit – past achievements and future challenges. Edinburgh 1999.
Dr A Nicoll.

New facts about haemolytic uraemic syndrome Edinburgh 1999.
Adak G K, Lynn R, Locking M, Taylor C M.

Are children developing new variant CJD? The PIND study. Edinburgh 1999.
Verity C.

Cerebral oedema and death in diabetic coma – the BPSU Diabetic Ketoacidosis Project. Edinburgh 1999.
Edge J.

An international network for studying diseases in children – INoPSU. Edinburgh 1999.
Elliott E (on behalf of the INoPSU secretariat).

Other conferences

Methodology for the surveillance of rare disease internationally.
Niklos Symposium, Athens, Greece, 1999.
Lynn R.

Interim results of the British Paediatric Surveillance Unit 1998/ 1999 survey on the incidence of inflammatory bowel disease.
European Society for Paediatric Gastroenterology and Nutrition, Warsaw, Poland 1999.
Sawczenko A, Sandhu B.

HUS Surveillance – What Does it Tell Us About VTEC? -
Scottish Centre for Infection and Environmental Health/Scottish Veterinary Medical Consortium E. coli O157 Update Glasgow 1999.
Adak GK, Lynn R & O'Brien SJ.

HUS surveillance- what does it tell us about VTEC PHLS Annual Scientific Warwick, Meeting. 1999.
Adak B, Smith H, Lynn R England.

PIND Project. Hong Kong Society of Child Neurology and Developmental Paediatrics Annual Scientific Meeting. Hong Kong 1999.
Verity C.

British Paediatric Surveillance Unit . Hong Kong Society of Child Neurology and Developmental Paediatrics Annual Scientific Meeting. Hong Kong 1999.
Verity C.

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

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

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 Rd, 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

Crohn's disease and ulcerative colitis
Mrs Margaret Lee, Crohn's in Childhood Research Association, Parkgate House, 356 West Barnes Lane, Motspur Park, New Malden KT3 6NB

National Association for Crohn's and Colitis Disease, 4 Beaumont House, Sutton Road, St Albans AL1 5HH

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

Erb's palsy
Erb's Palsy Support Group, 2 Willoughby Close, Coventry CV3 2GS

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

Haemolytic uraemic syndrome
HUSH, PO Box 1303, Sheffield S6 6LY

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, Gloucs.

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/strokelike illness
The Stroke Association, CHSA House, Whitecross St, London EC1Y 8JJ

Different Strokes, 162 High Street, Watford WD1 2EG

Sturge-Weber Foundation (UK), Burleigh, 348 Pinhoe Rd, Exeter EX4 8AF

Visual impairment/blindness
LOOK, Queen Alexandra College, 49 Court Oak Rd 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'

170 Tottenham Court Road, London W1P 0HA Tel: 020 7383 3555

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.ons.gov.uk/dbank_f.htm

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

Dr A Cant, Royal Victoria Infirmary, Queen Victoria Road, Newcastle upon Tyne NE1 4LP

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

Professor R Cooke, Institute of Child Health, Liverpool Children's Hospital, Eaton Road, Liverpool L12 2AP

Dr P Davis, Department of Community Child Health, Lansdowne Hospital, Sanatorium Road, Cardiff CF1 8UL

Dr S Devane, Department of Child Health and Community Paediatrics, King's College School of Medicine and Dentistry, London SE5

Ms G Devereux, Paediatric Administration Office, Box 45, Addenbrooke's NHS Trust, Hills Road, Cambridge CM2 2QQ

Dr C Dezateux, Department of Paediatric Epidemiology, Institute of Child Health, 30 Guilford Street, London WC1N 1EH

Dr R Dhillon, Department of Cardiology, Hospital for Sick Children, Great Ormond Street, London WC1

Dr R Dinwiddie, Institute of Child Health, 30 Guilford Street, London WC1N 1EH

Dr J Doherty, Bureau of Infectious Diseases, Laboratory Centre for Disease Control, Ottawa, Ontario, K1A 0L2

Professor D Dunger, University of Cambridge School of Clinical Medicine, Addenbrooke's Hospital, Cambridge CB2 2QQ

Dr J Edge, Department of Paediatrics, John Radcliffe Hospital, Headington, Oxford OX3 9DU

Dr E Elliott, Australian Paediatric Surveillance Unit, PO Box 3315, Parramatta, NSW 2124 Australia

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 D Goldberg, Scottish Centre for Infectious & Environmental Health, Clifton House, Glasgow G3 7LN

Professor P Goodfellow, Department of Genetics, University of Cambridge School Medicine, Addenbrookes Hospital, Cambridge CB2 2QQ

Dr S Hall, c/o BPSU office, 50 Hallam Street, London W1W 6DE

Dr M Hawkins, Department of Paediatrics, John Radcliffe Hospital, Headington, Oxford OX3 9DU

Dr P Heath, Immunology/Infectious Disease, Dept of Child Health, St Georges Vaccine Institute, Tooting London, SW17 0RE

Dr C Hobbs, St James's Children's Hospital, Beckett Street, Leeds, West Yorkshire LS9 7TF

Dr J Ho, MPA Secretariat, Instiut Pedatrik, Hospita Kuala Lumpur, 5074 Kuala Lumpur, Malaysia

Professor J B Holton, Department of Child Health, Royal Hospital for Sick Children, St Michael's Hill, Bristol BS2 8BJ

Dr M Honeyman, The Child and Family Centre, 142 Maas Road, Northfield, Birmingham B31 2PR

Professor I A Hughes, University of Cambridge School of Clinical Medicine, Addenbrooke's Hospital, Cambridge CB2 2QQ

Dr I Jones, Scottish Centre for Infection & Environmental Health, Clifton House, Glasgow G3 7LN

Dr A M Kemp, Community Child Health, Community Health Headquarters, Landsdowne Hospital, Cardiff CF1 8UL

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

Professor F Kirkham, Consultant Paediatric Neurologist, Southampton University Hospital, Tremona Rd, Southampton, Hampshire SO16 6YD

Dr G Laing, Consultant Community Paediatrician, Child Health Unit, St Leonard's Hospital, Nutaal Street, London N1 5LZ

Dr M Layton, Department of Haematological Medicine, King's College Hospital, Denmark Hill, London SE5 8RX

Professor J V Leonard, Medical Unit, Institute of Child Health, 30 Guilford Street, London WC1N 1EH

Professor M Levene, Leeds General Infirmary, Belmont Grove, Leeds LS2 9NS

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Professor A Lucas, Infant and Child Nutrition Unit, Institute of Child Health, 30 Guilford Street, London WC1 1EH

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Professor V Marchessault, Canadian Paediatric Surveillance Programme, Canadian Paediatric Society, 100-2204 Walkley Road, Ottawa ON KIG G48, Canada

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Dr C McKeown, Department of Medical Genetics, St Mary's Hospital, Manchester M13 OJH

Dr A McNinch, Dept of Child Health, Postgraduate Medical School, Royal Devon & Exeter Hospital, Barrack Road, Exeter EX2 5DW

Professor Sir Roy Meadow, c/o Department of Paediatrics and Child Health, St James's University Hospital, Leeds LS9 7TF

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Dr J Morgan, Dept of Child Health, East Glamorgan General Hospital, Church Village, Pontypridd, Mid Glamorgan CF38 1AB

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Dr S O'Brien, PHLS Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ

Office of National Statistics, 1 Drummond Gate, London SW1V

Dr G Ogle, PNGSU, PO Box 3478, Boroko, NCD, Papua New Guinea.

Professor C S Peckham, Dept of Paediatric Epidemiology, Institute of Child Health, 30 Guilford St, London WC1 1EH

Professor T H Pennington, Department of Medical Communicable Disease Microbiology, Aberdeen Royal Hospital, Forester Hill, Aberdeen AB9 2ZB

Dr R Pollitt, Neonatal Screening Laboratory, Children's Hospital, Sheffield S10 2TH

Radcliffe-online, 18 Marcham Road, Abingdon, Oxfordshire OX14 1AA

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Dr M Ramsay, PHLS Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ

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Professor E M Ross, Mary Sheridan Centre, Guy's, St Thomas' & King's School of Medicine, 405 Kennington Road, London SE11 4QW

Royal College of Obstetricians and Gynecologists, 27 Sussex Place, Regent's Park, London NW1 4RG

Royal College of Ophthalmologists, 17, Cornwall Terrace, Regent's Park,London, NW1 4QW.

Royal College of Paediatrics and Child Health, 50 Hallam Street London W1W 6DE

Royal College of Pathologists, 2 Carlton House Terrace, London SW1Y 5AF

Royal College of Physicians (Ireland), Faculty of Paediatrics, 6 Kildare Street, Dublin 2

Dr B Sandhu, Institute of Child Health, Bristol Children's Hospital, St Michaels Hill BS2

Professor E Schmidt, Universitats-Kinderklinik, Moorenstrasse 5, 4000 Dusseldorf 1, Germany

Professor J R Sibert, Dept of Child Health, University of Wales College of Medicine, Llandough Hospital, Penarth, South Glamorgan CF64

Dr A J Sills, Royal Liverpool Children's Hospital NHS Trust, Alder Hey, Eaton Road, Liverpool L12 2AP

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Dr C Verity, Child Development Centre, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ

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UK Haemophilia Centre, Churchill Hospital, Headington, Oxford OX3 7LJ

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