Royal College of Paediatrics and Child Health
British Paediatric Surveillance Unit

Annual Report 1998/99

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. Enquiries should be directed to our office.

The Unit positively encourages recipients to copy and circulate this report to colleagues, junior staff and medical students. Additional copies are available from our office, to which any enquiries should be addressed.

IN MEMORIAM

Professor John David Baum

All those associated with the BPSU deeply mourn the sudden unexpected death of David Baum, President of our College and Professor of Child Health in Bristol.

We have lost a good friend who has supported and encouraged the work of the Unit for many years. David was a founding member of the BPSU Executive Committee, set up in 1986 and he was the Chair of the Committee from 1988 to 1990. During that time he provided the inspirational leadership that was characteristic of him. When he became the Director of the Research Unit of the College he remained committed to the work of the BPSU and this continued during his time as President.

We will greatly miss the intelligence and verve of his ideas and the warmth of his personality.

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British Paediatric Surveillance Unit
A unit within the Research Division of the Royal College of Paediatrics and Child Health
50 Hallam Street
London
W1N 6DE
Telephone: 44 (0) 207 307 5680
Facsimile: 44 (0) 207 307 5690
E-mail: bpsu@rcpch.ac.uk
Registered Charity No. 1057744
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Compiled and edited by Richard Lynn, Angus Nicoll, Jugnoo Rahi and Chris Verity, September 1999
Typeset by Philippa Davies, Royal College of Paediatrics and Child Health

Membership of Executive Committee 1998-99

Dr Christopher Verity	Chairman
Dr Angus Clarke	Co-opted
Professor Richard Cooke	Royal College of Paediatrics and Child Health Research Division
Professor Peter Kearney	Faculty of Paediatrics, Royal College of Physicians, Ireland
Dr Margaret Guy	Medical adviser *(resigned September 1998)*
Mrs Linda Haines*	Royal College of Paediatrics and Child Health Research Division
Dr Patricia Hamilton	Co-opted
Dr Ian Jones	Scottish Centre for Infection and Environmental Health
Dr Christopher Kelnar	Co-opted
Dr Gabrielle Laing*	Co-opted
Mr Richard Lynn	Scientific coordinator
Dr Angus Nicoll	Medical adviser
Professor John Osborne	Royal College of Paediatrics and Child Health
Professor Catherine Peckham	Institute of Child Health (London)
Dr Jon Pollock	Royal College of Paediatrics and Child Health Research Division *(resigned September 1998)*
Dr Jugnoo Rahi*	Medical adviser
Professor Colin Roberts	Public Health Laboratory Service
Professor Euan Ross	Royal College of Paediatrics and Child Health
Professor Brent Taylor	Co-opted
Dr Roderick MacFaul*	Department of Health (observer)

** from September 1998*

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Foreword

Facilitation or competitive inhibition?

One of the benefits of having an epidemiological surveillance unit is that it saves effort. Coordination of activity facilitates the collection of information about conditions of public health importance. Investigators can be given help in formulating and organising surveillance projects. The centralisation of surveillance projects means that clinicians are approached from one centre and they are not inhibited by being sent questionnaires from many different sources.

When the British Paediatric Surveillance Unit (BPSU) was set up in 1986 it was to facilitate the surveillance of conditions that affected the health of children. Clearly the Unit has been successful in carrying out this aim - 37 surveillance projects were completed by the end of 1998, resulting in over 90 publications in peer review journals. The monthly orange surveillance card goes to over 1800 paediatricians each month and last year 93% of the cards came back completed.

The BPSU relies on collaboration. The Unit could not function without the active participation of the paediatricians who complete and return the orange surveillance card. The Executive Committee therefore tries to ensure that the conditions selected for surveillance are important to paediatricians. The Committee also tries to avoid overloading paediatricians by encouraging surveillance groups to make their questionnaires simple and by avoiding surveillance for conditions that are too common. There may be a dozen conditions on the card at any time: 300-400 notifications a year for one of those conditions is the maximum tolerated dose!

The work of the BPSU facilitates other College activities. This was shown in the quality of practice session at the College spring meeting in York this year, which was organised jointly by the Research Division of the College and the Quality of Practice Committee. The session included a brief review of the impact of BPSU studies on the quality of care. If paediatricians are to be helped by guidelines these must be based on good evidence. Surveillance Unit studies have provided evidence. For example studies of congenital infections have been relevant to the determination of appropriate antenatal screening strategies. The data suggested the following: ***don't start screening*** for neonatal herpes or toxoplasmosis because there are insufficient cases to justify maternal screening; in contrast ***don't stop screening*** for congenital syphilis or rubella because there are sufficient cases to justify continuation. Also there is a good case to ***start screening*** for HIV during pregnancy. This comes from the BPSU study of HIV and AIDS in children which showed that more than 80% of the infections were not identified before birth. There are now drugs which reduce the risk of maternal to fetal transmission in pregnancy and so there is a strong argument for identifying affected mothers in order to improve the outlook for their children. This annual report provides many more examples of BPSU studies that will help paediatricians and policy-makers to make rational decisions about measures to improve the health of children.

Information from Surveillance Unit studies must be disseminated and this annual report provides an important means of communicating the data as widely as possible. In addition the quarterly newsletter keeps paediatricians informed about Surveillance Unit activities. A joint meeting of the Royal College of Physicians of Edinburgh and the Royal College of Paediatrics and Child Health has been organised in the Edinburgh College on the 5 November this year. This will concentrate on the activities of the BPSU and set some of the Surveillance Unit studies in context. There will be sessions on infectious diseases, progressive neurological disorders, diabetes, international child health surveillance and the causes of cerebral palsy. We hope that this meeting will attract paediatricians from Scotland and the north of England and that it will be a successful part of our drive to communicate the importance of epidemiological surveillance as widely as possible. We are keen to get the message over to paediatricians, but in addition we target other health professionals and policy makers. Also it is very important that parents and parent support groups know about the work of the BPSU - some of these contacts are listed in the report.

The BPSU methodology has been so successful that it has been copied in the UK and world-wide. This is very flattering and is in itself a major achievement. Richard Lynn, BPSU Scientific Coordinator, has been involved in giving support and advice to many of the groups who have set up their own surveillance units. These include the adult neurologists, the gastro-enterologists and the ophthalmologists. In addition there is now a Welsh Paediatric Surveillance Unit and an Irish Paediatric Surveillance Unit. Cooperation between these units can facilitate surveillance activities - but there is the danger that there will be competitive inhibition. There are recent examples of fruitful collaboration. When the paediatric gastroenterologists were planning their surveillance study of inflammatory bowel disease it was recognised that many older children or adolescents would be seen by adult gastroenterologists. The BPSU study was therefore postponed until the British Society of Gastroenterology started to distribute its own card, which allowed surveillance to be carried out using both systems. Another example of helpful collaboration was the decision of the Welsh Paediatric Surveillance Unit to interrupt its own study of non-

accidental injury at the commencement of the BPSU study of subdural haemorrhage and effusion. It was agreed that it would confuse things if Welsh paediatricians simultaneously received cards from two surveillance units which asked for information about the same thing!

The Welsh Paediatric Surveillance Unit has become the latest member of the newly established **International Organisation of Paediatric Surveillance Units (INoPSU)**, making 10 members in all. The aim of this group is to maintain contact via the internet and have occasional meetings linked to international paediatric conferences. Many thanks to Richard Lynn, our Scientific Coordinator, and Angus Nicoll, BPSU Medical Adviser, for their hard work in helping to establish this international collaboration and thanks also to David Baum, our President, for his active support in taking the project forward.

The BPSU continues to thrive because its work is facilitated by so many people and so many institutions. The Executive Committee meets monthly and the members are to be thanked for all their hard work. The Committee includes representatives from the RCPCH, 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. We were very pleased to welcome Dr Roderick MacFaul to the Committee as Department of Health observer when Dr Ian Lister Cheese retired last year. At present the Department of Health makes a significant and much appreciated contribution to the funding of the BPSU. Last year we were fortunate to be able to appoint Dr Jugnoo Rahi as a Medical Adviser. Dr Rahi is a clinical lecturer in ophthalmic epidemiology at the London Institute of Child Health.

She joins Dr Angus Nicoll, the other Medical Adviser, who continues to work extremely hard for the BPSU despite his major commitments at the CDSC, Colindale. The work of the two Medical Advisers is essential to the running of the unit and this work is supported financially by their employers, the Institute of Child Health and the Public Health Laboratory Service. As always Richard Lynn, Scientific Coordinator, and his assistant Myra Schehtman have ensured that the BPSU runs as smoothly as possible and they deserve many thanks for their work, which provides the firm base for all BPSU activities. The Surveillance Unit is part of the Research Division of the College and we receive excellent support from Linda Haines, Principal Research Officer and Richard Cooke, College Vice-President.

The BPSU is fortunate in receiving so much support from so many different sources, however the key to its success is the continuing enthusiasm and support of its main collaborators - the paediatricians who return the report cards and complete the questionnaires. The response continues to be tremendous and we hope that all paediatricians will continue to be proud of their key role in facilitating the work of the BPSU.

Dr Christopher Verity,
Chairman, BPSU Executive Committee

1 Introduction

In July 1986 the British Paediatric Surveillance Unit (BPSU) was set up to enable paediatricians in the United Kingdom and the Republic of Ireland 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 monthly 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 1998. Reference is also made to studies and activities which have commenced in 1999.

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. Though priority is given to studies of importance to public health, 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 12-14 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.

For a number of reasons it may be considered that the BPSU system is not best suited for answering the study protocol. 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 and research; 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.

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 and aims of the study along with the practicalities of how the study is to be administered. Factors which 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 research methods.

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. Though this is the responsibility of the investigators, the BPSU urges that there is compliance with the Caldecot Report (Report on the Review of Patient-Identifiable Information, NHSE, December 1997) on data confidentiality and information flow.

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.

In recent years, consultants working in a number of other specialties have also been invited to participate in the scheme to help ascertain cases of conditions being surveyed which are also seen by them. 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 preceeding 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.

Figure 1 *BPSU orange card*

British Paediatric Surveillance Unit Report Card

June 1999 [9906]

NOTHING TO REPORT ☐ **CODE No [ ]**

If case(s) seen, identify how many

1. HIV & AIDS ☐
2. *Haemophilus Influenzae* infections 01865 221068/01865 220859 ☐
3. Haemolytic uraemic syndrome 0208 200 6868 ext 4551(E/W, Eire) 0141 300 1180 ext 1227 (Scotland) ☐
4. Progressive intellectual & neurological deterioration ☐
5. Fatal/severe allergic reactions to food ingestion ☐
6. Subdural haematoma/effusion in under two year olds ☐
7. Inflammatory bowel disease in under 20 year olds ☐
8. Encephalitis in under 3's 0207 504 9134 ☐

9. Congenital Rubella ☐ 10. Reye's Syndrome ☐ 11. SSPE ☐

Figure 2 *Clinicians section - BPSU orange card*

Clinicians Section - **Please keep if necessary**

British Paediatric Surveillance Unit Report Card

for cases seen in June 1999

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

When cases are reported, the BPSU informs the relevant research 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 researchers 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.

This completeness of reporting is known as the 'completion rate'. Table 1 (page 10) shows the number of cases reported to the BPSU from its inception until the end of 1998 for all the conditions under surveillance during 1998. 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 1998, only 419 (8%) of the 5339 case reports had yet to be followed-up. As a study nears completion this figure will fall. The final completion rate will average between 90-95%. In the past, studies requesting pathological specimens have a lower completion rate, though this has not been seen in the current encephalitis and *Haemophilus influenzae* surveys.

Table 2 (page 10) summarises the outcome of the follow-up of all cases reported to the BPSU by the end of 1998 and provides evidence for the high level of accuracy of reporting by participating clinicians. By the end of June 1999, 887 (28%) 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 June 1999).

Difficulties in case reporting

Though the BPSU has many strengths its Executive Committee is aware that reporting is never complete, and like any reporting or surveillance system some under-reporting always occurs, reasons for which are listed in the box overleaf. 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 underascertainment. Some researchers 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 (ie. producing quite a few false positives). Secondly, an analytic case definition which 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 3 overleaf). The first complementary data sources to be used were laboratory reports to the PHLS of infectious disease. In the past year the *Haemophilus influenza,* HIV/AIDS and SSPE studies have included this additional ascertainment. Other sources which have been used include death registration (Reye's syndrome), hospital episode data (insulin dependent diabetes, congenital dislocation of the hip) and birth registrations (higher order births). In order to increase ascertainment of subdural haematoma forensic and paediatric pathologists were involved in surveillance. The use of multiple sources of data has shown to improve case ascertainment, the completeness of which varies between studies and conditions, according to the ease of case ascertainment and the availability of complementary data sources.

The unit uses a number of 'rates' in assessing the BPSU performance and that of an individual study, and these are highlighted in the box opposite.

BPSU assessment rates

Reporting rate	Percentage of orange cards returned each month.
Report completion rate	The proportion of cases reported to researchers where an outcome has been reached, ie valid, invalid etc.
Ascertainment rate	A more abstract rate indicating the proportion of all true cases (meeting the surveillance case definition) that are estimated to have been reported.

Figure 3

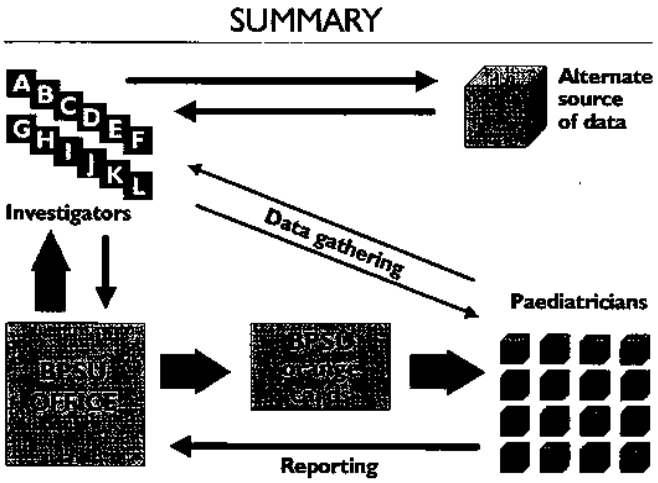
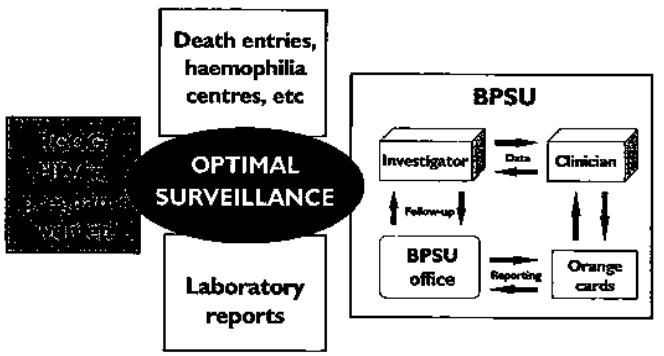


Figure 4



Funding

For a three year period commencing in September 1998 the Department of Health agreed to 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 1998 the minimum sum was £210 per month. In 1998 the Unit saw the receipt of the final installment of a grant from an anonymous donor.

Further non-cost support is received from the Royal College of Paediatrics and Child Health, Public Health Laboratory Service, Brent and Harrow Health Authority, Scottish Centre for Infection and Environmental Health, Institute of Child Health (London) and Radcliffe Interactive who helped develop the web-site.

3 Surveillance activities in 1998

During 1998 four major surveys each of public health importance were commenced. The first in March, was to identify the incidence and examine the causes of congenital brachial palsy. This was followed in April by studies on subdural haematoma and effusion (SDHE) and fatal and severe reaction to food ingestion. The former has been much in the public eye due to the association of SDHE with child abuse. This is a multi-disciplinary project involving not only paediatricians but also pathologists and neurosurgeons. Much publicity has also surrounded the latter condition particularly when deaths have followed anaphylaxis secondary to nut ingestion. Finally, in June a study examining the incidence of inflammatory bowel disease in under 20 year olds commenced. This project has been ascertaining cases from paediatricians and adult gastroenterologists through collaboration with the British Gastroenterology Research Unit.

Thirteen further study applications were received for consideration. September 1999 will see the commencement of a study of visual impairment and blindness. A further three studies have been provisionally approved; vitamin K deficiency bleeding, stroke in childhood and venous/arterial thrombosis excluding cerebrovascular disease.

October 1998 saw the completion of the cerebral odema following diabetic ketoacidosis survey, whilst 1999 saw the completion of the hepatitis C infection survey (March) and the aforementioned surveys on congenital brachial palsy (March), subdural haematoma (April) and inflammatory bowel disease (June). Forty studies have now been completed since the BPSU began in June 1986 - those completed prior to 1998 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 1998/99 relating to these studies and the unit's work, totalled 33 and are listed in Appendices B and C.

Other activities within the Unit include advising other medical societies in the development of their own surveillance systems and alliance liaising with parent support groups such as Contact a Family (CAF) as a part of the UK Rare Disease Alliance and the European Organisation of Rare Disease. This year has also seen the development of the BPSU web-site <http://bpsu.rcpch.ac.uk> with the support of Radcliffe Interactive.

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 international scene is described more fully in Chapter 8.

Participation in the scheme during 1998

The BPSU ascertains the names of new consultants primarily through the RCPCH advisory appointment committees, membership office, BMJ adverts or through personal communication. The number of consultant paediatricians participating in the scheme during 1998 rose to 1836, an increase of over 5% compared with the previous year. It should, however, be noted that some paediatricians who hold consultant status are excluded as they do not undertake relevant clinical work, or else colleagues report on their behalf. The BPSU mailing list also includes selected groups of consultants other than paediatricians ie. cardiologists, clinical geneticists and pathologists. In order to help in the ascertainment of cases of subdural haematoma this past year has also seen the inclusion of forensic pathologists, and our thanks are extended to the Royal College of Pathologists for supporting this initiative.

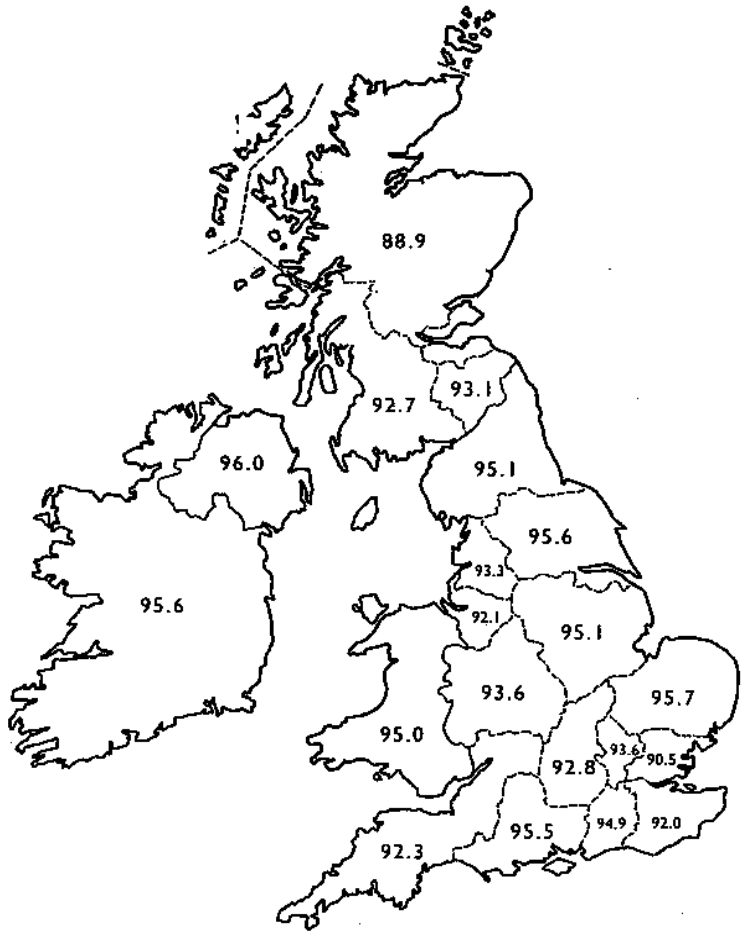
Reporting rates for returning the orange cards remains high - the overall response rate for 1998, calculated as a proportion of orange cards returned, was 93.6%, slightly up on 1997 (93.4%). Monthly response rates ranged from 89.9% in September to 96.8% in January, with a median of 93.7%. Respondents 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. Paediatricians in Northern Ireland achieved the highest average yearly response rate - 96.0% and lowest being Northern Scotland at 89.1%. With regard to rank order, Northern Ireland, North West Thames and South West Thames rose by 14 and 10 places respectively, while North Scotland and West Scotland fell by 12 and 11 places respectively.

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-two percent (1023) of participants reported no cases in 1998, slightly down on 1997 (54%). Forty-three percent (846) reported between one and four cases and only 5% (91) reported five or more cases. The greatest number of cases reported by a single paediatrician was 28. Specialties that had a particularly high level of reporting were the paediatric neurologists (PIND, encephalitis, SSPE, Reye) and gastroenterologists (IBD).

Figure 5 *Average orange card return rate (%) by area, 1998*



Overall average orange card return rate = 93.6%

Table 1 *Cases reported from June 1986 - December 1998 of conditions under surveillance during 1998 (cases confirmed by July 1999 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 1997	1998
HIV/AIDS	1986	137 (90)	495 (386)	359 (214)	314 (193)	174 (124)
Reye's syndrome	1986	149 (76)	71 (31)	57 (20)	22 (16)	9 (4)
SSPE	1986	84 (50)	55 (29)	28 (14)	17 (6)	10 (5)
Congenital rubella	1991	– –	43 (27)	29 (12)	33 (15)	7 (2)
Hi infection	1992	– –	25 (20)	146 (105)	136 (92)	64 (40)
DKA	1995	– –	– –	25 (9)	63 (37)	41 (24)
Hepatitis C infection	1997	– –	– –	– –	451 (360)	105 (72)
HUS	1997	– –	– –	– –	176 (104)	157 (91)
PIND	1997	– –	– –	– –	327 (242)	285 (188)
Congenital brachial palsy	1998	– –	– –	– –	– –	352 (258)
Fatal/severe allergic reactions	1998	– –	– –	– –	– –	122 (84)
Subdural haematoma/effusion	1998	– –	– –	– –	– –	263 (26)
Inflammatory bowel disease	1998	– –	– –	– –	– –	453 (133)
Encephalitis (2-36 months)	1998	– –	– –	– –	– –	55 (247)
Total		**370 (216)**	**689 (493)**	**644 (374)**	**1539(1539)**	**2097(1298)**

Tables exclude previously completed studies (see page 46).

AIDS/HIV 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.

DKA Cerebral oedema following diabetic ketoacidosis.

HUS Haemolytic uraemic syndrome.

PIND Progressive intellectual and neurological deterioration

Table 2 *Outcome of follow-up of the cases reported in 1998 of conditions under surveillance during 1998*

Condition under surveillance	Valid reports (%)	Invalid reports: Duplicates	Errors	(Total %)	Not yet known (%)	Total reports
HIV /AIDS	1007 (68)	210	234	(30)	28 (2)	1479
Reye's syndrome	147 (48)	43	111	(50)	7 (2)	308
SSPE	104 (54)	37	33	(36)	20 (10)	194
Congenital rubella	56 (50)	23	29	(46)	4 (4)	112
Hi infection*	257 (69)	18	88	(29)	8 (2)	371
DKA	70 (54)	29	24	(41)	6 (5)	129
Hepatitis C infection	432 (78)	39	50	(16)	35 (6)	556
HUS*	195 (59)	61	33	(28)	44 (13)	333
PIND	430 (70)	58	101	(26)	23 (4)	612
Congenital brachial palsy	258 (73)	19	32	(14)	43 (12)	352
Fatal/severe allergic reactions	84 (69)	0	15	(12)	23 (19)	122
Subdural haematoma/effusion	133 (51)	20	24	(17)	86 (33)	263
Inflammatory bowel disease	247 (55)	42	105	(32)	59 (13)	453
Encephalitis (2-36 months)	26 (47)	4	12	(29)	13 (24)	55
All	**3446 (65)**	**603**	**891**	**(28)**	**399 (7)**	**5339**

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

4 Main findings of studies undertaken in 1998

The survey of **cerebral oedema and death following diabetic ketoacidosis (DKA)** (page 12) found that this was a very serious condition with about 25% of children dying and 40% of the survivors being left seriously affected neurologically. Younger children and those with newly diagnosed diabetes were more at risk. A preliminary analysis suggested that the incidence of cerebral oedema following diabetic ketoacidosis in the UK (7 / 1000 cases of DKA) was similar to that observed in American studies, despite seeming differences in the fluid and electrolyte management between the two countries.

The study on **congenital brachial palsy** (page 14) has only just been completed but it found that the incidence of this condition was significant at approximately 0.5-1.0 per 1000 live births.

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 a substantial increase in cases in UK born women. This stemmed from a mini-epidemic of rubella transmission in the UK in 1996.

A new survey of **encephalitis in young children (2 months to three years)** (page 17) has only just begun and is finding cases attributable to Human Herpes Virus 6.

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 very uncommon.

The second survey of **haemolytic uraemic syndrome (HUS)** and E. *coli* O157 (page 20) through the BPSU has so far confirmed that most HUS in the UK are due to E. *coli* O157 and that it is commoner in children under age 3 but rare beyond age 11. The survey has also discovered peaks of HUS incidence in the autumn and seemingly poor laboratory reporting of E. *coli* O157 in London and the South East.

Another survey has found that most **hepatitis C infection (HCV)** in children (page 22) has been due to infection through contaminated blood products. Such transmission has been almost eliminated in the UK but smaller numbers of children are continued to be infected through mother to child (vertical) transmission with the children at risk of acquiring HCV being those born to women who have injected drugs. Reports of HIV infected children are increasing.

A BPSU survey of **HIV and AIDS** (page 24) 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 he greatest number of infections are in London but cases are occurring in all parts of the country.

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.

A new short-term survey of **inflammatory bowel disease (IBD)** in under 20 year olds (page 26) has found an annual incidence of IBD amongst children < 16 years of 3.9 - 4.8 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 different groups of clinicians.

Surveillance of **invasive *Haemophilus influenzae* b infection (Hib)** (page 29) 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 world-wide in only giving a primary vaccine course and not using a booster. There is no evidence from the survey that this policy results in any loss of protection.

A difficult survey of **progressive intellectual and neurological deterioration in children (PIND)** (page 31) 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) no cases of variant CJD have been diagnosed.

Results from long-term surveillance of **Reye's syndrome** (page 33) 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.

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) this year 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.

5 Surveillance studies undertaken in 1998

Conditions included in the scheme during 1998

During 1998, 14 conditions were the subject of surveillance. One study was completed and 4 studies commenced, congenital brachial palsy, fatal/severe allergic reactions in childhood, inflammatory bowel disease and subdural haematoma/effusion.

The studies are listed in Table 3 below. Several projects have been given approval but have yet to commence. These include visual impairment and blindness in children, vitamin K deficiency bleeding, stroke in childhood and venous/arterial thrombosis.

Table 3 Studies underway in 1998

Page	Study	Principal investigators	Research institutions
12	Cerebral oedema following DKA	J Edge, D Dunger, M Hawkins	John Radcliffe Hospital, Oxford
14	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
20	Haemolytic uraemic syndrome*	M Taylor, B Adak, S Locking, R Lynn	B'ham Children's Hospital, PHLS, SCIEH, BPSU
22	Hepatitis C infection	D Gibb, P Neave, P Tookey	ICH (London), SCIEH
24	HIV/AIDS infection in childhood*	P Tookey, A Nicoll, D Goldberg	ICH (London), PHLS, SCIEH
26	Inflammatory bowel disease	B Sandhu, A Sawczenko, R Logan	RHSC Bristol, BSG Research Unit
29	Invasive *Haemophilus influenzae* infection*	P Heath, M Slack, R Moxon, N Begg	PHLS, National Haemophilus Ref. Lab., Oxford
31	Progressive intellectual and neurological deterioration*	C Verity, G Devereux, A Nicoll, R Will	Addenbrookes, PHLS, National CJDSU
33	Reye's syndrome*	S Hall, R Lynn	Sheffield Children's Hospital/BPSU
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 September 1999.

Cerebral oedema and death following diabetic ketoacidosis

Background

Cerebral oedema is a devastating complication of diabetic ketoacidosis (DKA) in children, and appears to be sporadic and unpredictable. The most recent figures available show that between 10 and 15 children under 20 years of age die each year from DKA in Britain, and that 80% of the deaths in diabetic children under 12 are due to cerebral oedema. The incidence of non-fatal cerebral oedema in Britain is not known.

The aetiology of cerebral oedema is not understood. Even with optimum management by current standards, cases still occur. Retrospective studies suggest that cerebral oedema is more common in newly diagnosed diabetes, especially in children under five years of age. Possible contributory factors may be the severity of DKA, the rate and/or quantity of intravenous fluid administration, a fall in plasma sodium concentration and hypoxia from bicarbonate administration. Animal studies have suggested that insulin itself is required for cerebral oedema to occur. There have been no sizeable case-control studies to support any of these theories.

This study will compare the clinical course of cases of cerebral oedema with controls with DKA but without cerebral oedema, ascertained by a separate reporting mechanism, which we have developed. This is the first large prospective case-control study in this important complication of diabetes.

Objectives

1 To analyse all deaths attributable to DKA and all cases of cerebral oedema (whether fatal or not).
2 To establish an independent national procedure for the ascertainment of cases of DKA in the childhood population.
3 To estimate the absolute risk of cerebral oedema among children with diabetic ketoacidosis.
4 To identify factors in the clinical presentation and subsequent clinical course of the child with DKA which may influence the development of cerebral oedema.
5 To study the outcome of cerebral oedema in Britain in terms of mortality and morbidity.

Case definition

1 Sudden or unexpected deterioration in conscious level in a child with diabetic ketoacidosis.
2 Any death during assessment or management of DKA.

Study duration

October 1995 - September 1998.

Results

Cases of cerebral oedema - Collection of cases of cerebral oedema was completed in September 1998. From October 1995 until September 1998, 126 returns were made to the BPSU. Questionnaires have been returned on 116 of these notifications. Of these notifications 22 were reporting errors or non-cases and 26 were duplicate reports. Of the remainder, there were six deaths during ketoacidosis, which were not associated with cerebral oedema occurring after the start of hospital treatment for DKA. The causes of death are shown in Table 4.

There were 35 cases of cerebral oedema in 14 males and 21 females, age range 1-15, median 11 years.

Presentation - The 35 cases of cerebral oedema by definition presented with reduced level of consciousness and combinations of other signs of raised intracranial pressure; 14 (40% had hypertension and bradycardia, 13 (38%) had pupil abnormalities, 5 (15%) had decerebrate or decorticate posturing and 11 (33%) had a respiratory arrest. Twenty-two of the 35 had CT scan confirmation of cerebral oedema; one case had a normal CT scan but the timing is as yet uncertain.

Management - Twenty-seven (77%) of the 35 cases were treated with intravenous mannitol, three (<10%) with dexamethasone, 26 (75%) were intubated and ventilated and three (<10%) underwent intracranial pressure monitoring. Four patients received no specific treatment; all of these had alteration in conscious level together with hypertension and bradycardia only.

Outcome - Nine of the 35 children with cerebral oedema died (3 male, age 1-15, median 9yr; 26% mortality). There was no difference in the sex distribution or ages of those that died and survived. Of the 26 survivors, questionnaires have not yet been received on two, and 15 children have no obvious sequelae. The remaining nine children have a variety of new problems following the episode of cerebral oedema; motor (8), vision (6), memory (6), speech (4) and fits (2). These children also have a variety of learning and emotional problems including poor concentration, disinhibited behaviour and emotional lability. Thus 35-40% of survivors of cerebral oedema have long-term disabilities. Outcome was not related to treatment received, and in particular, all of those who died and all but one with neurological sequelae had received mannitol. However, the outcome was related to presentation in that all of those who had a respiratory arrest either died or had significant sequelae.

Table 4 *Causes of death in the six children who died from DKA but did not fit into the criteria of cerebral oedema during management of DKA*

Age	Sex	Cause of Death
12	F	death from DKA (new diabetes) before arrival at hospital
12	F	death from DKA at home (known diabetic), brain not examined
1	M	severe acidosis possibly due to another underlying metabolic disorder, new diabetic, no cerebral oedema
10	M	death from cerebral infarction, probably following cerebral oedema which developed at home before treatment
10	M	severe development delay, DKA (new diabetes) final event
1	F	severe retardation, hyperlipidaemia

In addition, there were 25 cases of unexplained deterioration of conscious level but without other definite signs of raised intracranial pressure, of these seven were male and 18 female, aged between 1-15 years, median eight years. There was no difference in sex distribution or ages of those who developed frank cerebral oedema and those who had a reduced level of consciousness alone. Seven of these children received mannitol treatment and seven were intubated and ventilated, but in five cases this was for transfer or respiratory difficulties. Five had CT scans although the scan was normal in three. Only one child has visual and motor sequelae; and was the only one treated with both mannitol and ventilation. The remaining 24 are entirely normal neurologically.

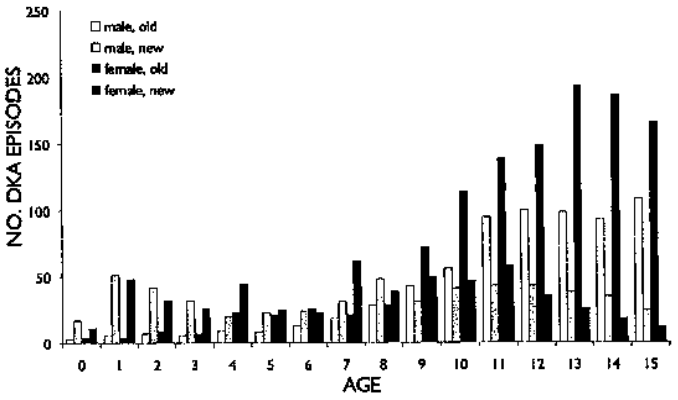
Control group with DKA - In order to obtain controls with DKA but without cerebral oedema, we also requested monthly notifications of all cases of DKA admitted in England, Scotland and Wales from 243 paediatricians in 231 hospitals between March 1996 and February 1998. The definition of DKA was "decompensated diabetes mellitus with evidence of ketoacidosis (pH < 7.3 or plasma bicarbonate level < 18 mmol/l or heavy ketonuria)". Information requested about each episode were; age, sex, hospital number and whether the child had newly diagnosed ('new') or known ('old') diabetes.

During the two-year period, 2949 episodes of DKA were reported. Of these, complete data were available on 2941 (99.7%). There were 1708 episodes in females (1154 old and 554 new diabetes), and 1233 episodes in males (691 old and 542 new diabetes) (Figure 6 overleaf). Of the known diabetics, 529 (30%) had more than one episode during the two year period; in these the number of episodes ranged from 2-37. Eleven percent of the patients who had more than four episodes over the two years, contributed 40% of the total number of episodes in the known diabetics.

The likelihood of developing cerebral oedema was 7.1 per thousand episodes of DKA overall. The risk was higher in males (8.9/1000) than females (5.9/1000) and in new (11.9/1000) than old (4.3/1000) diabetes. The risk of cerebral oedema was greatest in younger children (Figure 7 overleaf).

Future plans - The investigators have matched six controls from this group to each case of cerebral oedema and have appointed a research assistant to examine the medical records of cases and controls. It is the aim to compare factors in the presentation and clinical course of cases and controls, and determine factors that may predispose to the development of cerebral oedema.

Figure 6 *DKA episodes by age*



Conclusions

The incidence of cerebral oedema in the UK (7.1/1000 episodes of DKA) is similar to that seen in the US, despite differences in the fluid and electrolyte management between the two countries. It is commoner in those with newly diagnosed diabetes than known diabetes, and is more likely to develop in younger children. The mortality in cerebral oedema is 25% in this study (lower than the previously reported 50-80%), although 35-40% of survivors are still left with significant neurological and neuro psychological sequelae. All of those children who had a respiratory arrest either died or were left with significant neurological problems, despite treatment with mannitol in the majority of cases. The significance of the group who had only a reduced conscious level is unknown: only a small proportion received mannitol and yet none went on to develop fulminant cerebral oedema. It is possible that these represent a different entity, this group will be analysed separately.

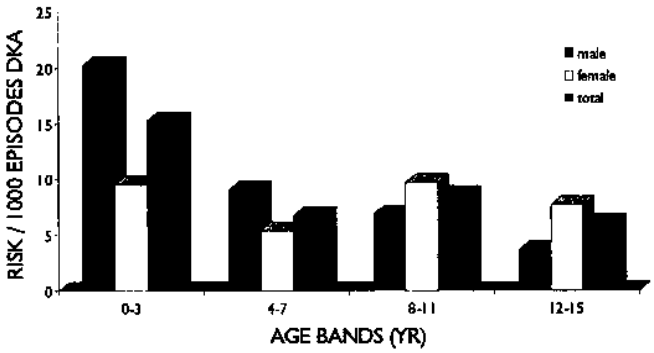
The investigators are most grateful to all those paediatricians who have notified cases and taken the time and trouble to complete our questionnaires.

Key points

Based on 35 confirmed cases for whom data are available so far:

- The incidence of cerebral oedema in the UK (7.1/1000 episodes of DKA) is similar to that seen in the US, despite differences in the fluid and electrolyte management between the two countries.
- The risk of risk of cerebral oedema is higher in younger children and those with newly diagnosed diabetes compared than established diabetes. Further analysis is being undertaken, using a case- control approach, to identify factors that predispose to the development of cerebral oedema.
- Mortality in cerebral oedema is 25% in this study, lower than the previously reported.
- About 40% of survivors have significant neurological and neuropsychological sequelae.

Figure 7 *Risk of cerebral oedema by age*



Funding

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Dr J Edge, Dr M Hawkins, Dr D Dunger, Dept of Paediatrics, John Radcliffe Hospital, Oxford OX3 9DU Tel: 01865 221488 Fax: 01865 220479

Congenital brachial palsy

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 declined in the 1950s and 1960s, with an annual incidence in one series which reviewed cases in New York between 1932 and 1962 of 0.39 per 1000 live births[1]. A recent audit at the hospital of one of the authors reported an annual incidence of 0.8 per 1000 live births (unpublished data), suggesting that the incidence may have increased in recent years. However, the true incidence in the UK is unknown.

The cause is commonly thought to be 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 brachial 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 syndrome. Between eight and 20% of cases of Erb's palsy have been reported as to be bilateral, almost exclusively associated with breech extraction. As well as breech presentation, shoulder dystocia and large fetal weight are significant common associations, but some cases are unexplained. The reported incidence of full muscle recovery varies widely from as little as 13% to 80% of cases. Similarly the onset of recovery is variable, ranging from two to fourteen weeks and may continue for up to 18 months. Severe cases with little recovery cause 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 residual impairment of shoulder movement only, 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 technique remains unproven[2]. It has been suggested that some infants who could benefit from surgery are not given the opportunity for early expert assessment and may be referred too late for surgery to be effective. It is argued that there is a 'window of opportunity' between successful surgical treatment at three to six months of age.

Many reported studies are of selected cases; this study will provide an opportunity to establish more accurate data about this important condition.

Case definition

Surveillance - A newborn presenting with a congenital 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.

Analytic - CBP occurs 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 eg. 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 (C) 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)

C5-7 as above, although the elbow may be slightly flexed. (Narakas' Group II)

C5-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 The natural history of CBP in the first year of life.

Study duration

March 1998 - March 1999

Results

Table 5 summarises the results of the survey from March 1998 to 28 February 1999 ie. 12 months including the March 'run-in' period, there being one further month to be completed. The figures are in keeping with the investigators estimate incidence of 0.5-1.0 per 1000 live births/per year. The returns from the Republic of Ireland are analysed separately, as there may be lower ascertainment from there for reasons that are currently being explored. Approximately 30% of cases reported are currently unconfirmed - that is, the respondents have not returned a completed first questionnaire. Therefore a great deal of effort is being made to chase these up. A second questionnaire to be completed at six months of age will provide information about natural history. It is expected that this will be the most comprehensive survey of CBP in the UK to date. All paediatricians and other clinicians involved in the management of these infants are encouraged to report all cases and complete the questionnaire in as much detail as is possible. The investigators are most grateful to you for all your support.

Table 5 *Incidence of cases reported March 1998 - 28 February 1999*

	UK	Rep of Ireland
Number of cases reported	370	53
Number of cases confirmed	215	34
Number of ineligible cases	28	4
Number of cases unconfirmed (%)	127 (34)	15 (28)

Key point

Based on 215 (UK) and 34 (Eire) confirmed cases for whom data are available to date:

- The incidence of Congenital Brachial Palsy is approximately 0.5-1.0 per 1000 live births/per year.
- Data regarding natural history of CBP in the first year of life are still being collated and analysed and should detailed information that has not been available previously.

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Dr G Evans-Jones (principal investigator), Countess of Chester Hospital, Liverpool Road, Chester CH2 1UL Tel: 01244 365059 Fax: 01244 365089

Mr S P J Kay, Consultant Plastic Surgeon, The Children's Hand Clinic &

Ms A Ward, Clinical Academic Assistant, Paediatric Surgery Dept, St James's University Hospital, Beckett St, Leeds LS9 7TF

Tel: 0113 2065265 Fax: 0113 2438162

Prof M Weindling, Dept of Child Health, Dept of Neonatology, University of Liverpool, Women's Hospital, Crown Street, Liverpool L8 7SS

Congenital rubella

Background

National surveillance of congenital rubella started in 1971 with passive reporting to the National Congenital Rubella Surveillance Programme (NCRSP) 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 a year in the period 1971-75 to an average 23 births a year in 1986-90. With fewer cases occurring, active surveillance was required, and congenital rubella first appeared on the orange card in January 1990. BPSU reports from Ireland are followed-up, but not normally included in the published figures.

The selective immunisation of all schoolgirls and of susceptible adult women, introduced in the early 1970s, was supplemented in 1988 with the introduction of the combined measles/mumps/rubella (MMR) vaccine for all children in the second year of life. In 1996 a pre-school MMR booster was added to the immunisation schedule. Antenatal screening with postpartum vaccination continues, but the schoolgirl programme has now ceased. Uptake of MMR vaccine by 24 months declined somewhat to 88% in the last half of 1998 (from about 93% in 1995), following a public concern about the safety of the vaccine. In 1998 about 75% of five year olds had received two doses of MMR.

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 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 are also now requested.

Study duration

Congenital rubella was included in the BPSU reporting scheme in January 1990. Reports were previously made directly to the NCRSP.

Analysis

Case classification - Cases of congenital rubella are registered with the NCRSP as congenital rubella infection (CRI only) if they have laboratory confirmation of infection without reported defects, and congenital rubella syndrome (CRS) if they have associated defects. CRS cases are classified as confirmed, compatible, possible or unclassified, depending on the laboratory and clinical data. Information is normally only published on the confirmed and compatible cases, currently numbering 871 (Table 6). The 245 possible and unclassified cases are mostly children born in the 1960s and 1970s who lacked laboratory evidence of congenital infection, but had symptoms suggestive of congenital rubella. Further details of case classification are available from the investigators.

Table 6 Current classification of cases registered with the NCRSP

	Confirmed/compatible	Other
CRI only	167	
CRS confirmed	551	
CRS compatible	153	
CRS possible		140
Unclassified		105
Total	**871**	**245**

CRI = congenital rubella infection; CRS = congenital rubella syndrome

BPSU notifications - Six previously unreported confirmed cases of congenital rubella were identified in a one-off BPSU survey in 1988. Since the beginning of active surveillance in 1990, 109 reports have been made through the BPSU (Table 7). Of the 95 reports from England, Scotland and Wales, 40 are confirmed or compatible, previously unreported cases of congenital rubella, two are possible cases, eight had already been reported from another source and four remain outstanding. The remaining reports were duplicates (18), reporting errors (21) and two where 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 7 Congenital rubella reports to BPSU 1990-1999

	England, Scotland and Wales	Ireland
Registered Cases	42	4
Already reported	8	2
Outstanding	4	0
Duplicate, error or lost	41	8
Total	**871**	**245**

Among the children born since the beginning of active surveillance in 1990, 32 (71%) of the 45 confirmed or compatible cases (Table 8) were first reported through the BPSU.

Recent reports - The incidence of congenital rubella in the British Isles is now very low.[1] Between 1991 and 1995, most of the 19 women giving birth to infected infants either came to Britain as susceptible adults (9), or having acquired rubella in early pregnancy abroad (6) (imported cases). However, in 1996, following a resurgence of rubella transmission in the community, mainly affecting young males, 12 confirmed cases were reported in England, Scotland and Wales, including eight infants born to British-born women. Only two cases were imported: one Asian woman arrived just two weeks before her baby was born, and one British-born woman acquired infection early in pregnancy while on holiday in Spain. Almost all of the 12 infants had multiple rubella defects. 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. No cases have yet been confirmed for 1997 or 1998.

Table 8 *Confirmed and compatible congenital rubella births reported to the NCRSP 1971-1998* (England, Scotland & Wales only)*

Year of birth	Primary source of notification		Total
	BPSU	Other	
1964-69	0	39	39
1970-79	1	453	454
1980-89	13	320	333
1990-98**	32	13	45*
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*
Total	**46**	**825**	**871**

* The data for recent years are provisional

** The data for 1990-1998 include 2 reported stillbirths

It is essential that case ascertainment is as complete as possible. Please notify 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

The surveillance of congenital rubella is funded by the PHLS.

Key findings

- The incidence of congenital rubella syndrome (CRS) in the UK and Republic of Ireland is generally low but preventable cases continue to occur.
- A resurgence of rubella transmission in the UK resulted in an increase in CRS in 1996.
- Girls and women coming into the UK from countries where immunisation is not routine or universal are at higher risk than UK women to have CRS. They should be immunised with MMR.
- Children with isolated sensorineural deafness due to congenital rubella are probably not being under-recognised.
- High levels of MMR vaccination are needed to prevent further CRS cases but also all women should be screened for rubella immunity in pregnancy and those found to lack immunity should be immunised after birth but before leaving hospital.

Reference

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Ms P Tookey, Professor C Peckham, Dept of Epidemiology and Public Health, Institute of Child Health, 30 Guilford St, London WC1N 1EH
Tel: 0171 905 2604 Fax: 0171 242 2723 E-mail: ptookey@ich.ucl.ac.uk
Dr E Miller, PHLS, Communicable Diseases Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ Tel: 0171 200 6868

Encephalitis in children two months to three years

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 National Childhood Encephalopathy Study (NCES), 1976-1979, suggested an unidentified viral illness as a likely cause (ie. an encephalitis) but the agents remain largely unknown due at least in part to lack of sensitive tests. Greater precision of diagnosis would help to curtail unnecessary investigation, rationalise treatment and improve reliability of prognosis. Fortunately, more accurate diagnosis of encephalitis has recently become possible with the availability of new, highly sensitive laboratory methods for detection of nucleic acid (PCR), antibody and antigen. Two newly discovered viruses, human herpesviruses-6 and -7 (HHV-6 and HHV-7), are obvious candidates for causal agents 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.

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.

Case definition

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

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

2 **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.

3 **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.

4 if in doubt please discuss with the investigators.

Duration

October 1998 for 13 months; extension subject to review.

Coverage

UK and Republic of Ireland.

Methods

Paediatricians are asked to report all cases promptly by telephone to Dr Ward (0171 504 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 CSF. 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 paediatrician and microbiologist.

A questionnaire is sent to the reporting paediatrician after about 3 months to allow sufficient time for follow-up. Completed questionnaires are used initially to identify those cases that meet the reporting case definition and those that do not. Due to the difficulties of diagnosing encephalitis, which is often a diagnosis of exclusion, a final decision will be based on a more detailed analytical case definition.

Analysis

At the end of April 1999 a total of 95 children had been reported. Of these :

1 Twenty five cases were classified as meeting the reporting case definition and are undergoing investigation and analysis.
2 Twenty cases did not meet the reporting case definition because of duplication or revised diagnosis (motor axonal form of Guillain-Barré -Syndrome, congenital immunodeficiency etc) or reporting error. The most common error was reporting of cases in children less than two months old and the orange card has now been modified to clearly state 'Encephalitis in children two months to three years'.
3. Follow-up has not yet been completed for the remaining fifty children.

As regards collection of specimens for HHV-6 and -7 testing the investigators have received at least some specimens (serum and/or saliva and/or CSF) from roughly nine out of every ten cases. Support from local microbiology laboratories has been excellent but CSF has been the most difficult specimen to obtain, and we have a sample from only about six out of every ten cases. CSF is of course the key specimen as testing of other samples can only provide coincidental evidence of possible CNS infection. The success rate with retrieval of CSF was highest when cases were reported early rather 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 despatch of specimens, especially CSF, therefore remain the most important ways in which paediatricians and microbiologists can contribute to the success of the survey and the full virological diagnosis of their patients.

Comment

The study is going very well but is still at an early stage and firm conclusions cannot yet be made. There is good geographical distribution of reports so far although none have been received from Northern Ireland. There is a slight preponderance of children aged between one and two years old which is at variance with the NCES findings where the peak presentation was in the first year of life. Nevertheless, it is difficult to draw any conclusions until the analytical case definition has been applied to all children.

Turning to infectious aetiology, the most commonly suspected cause was herpes simplex and almost all children received a course of acyclovir. However, in the majority of cases, herpes simplex infection of the CNS was not confirmed. A range of other infections has been identified, including HHV-6, but some may have been coincidental. It is certainly becoming clear that, aside from herpes simplex, HHV-6 and HHV-7, other possible causes are often not being investigated. Indeed, in many cases the aetiology remains uncertain; in part at least this may reflect difficulty in having laboratory tests carried out that are not freely available locally. Where this is a problem Dr Ward's laboratory can provide additional tests to detect, for example, other human herpesviruses and enteroviruses. From the good progress so far it looks as if this collaborative work between paediatricians and microbiologists will lead to a firmer scientific basis for the accurate diagnosis and perhaps prevention of childhood encephalitis.

The investigators are very grateful to all paediatricians for supporting this surveillance project. Grateful thanks are also due to microbiologists and virologists for their help and support with specimens.

Funding

Wellcome Trust.

Key points

- Between October 1998 and April 1999 95 children have been reported with encephalitis between 2 months and 3 years.
- Causes of the encephalitis being considered include HHV-6, HHV-7 and herpes simplex.

Dr K N Ward, Consultant Virologist, Dept of Virology, University College London, Windeyer Building, 46 Cleveland St, London W1P 6DB. Tel: 0171 504 9134 (24 hour cover) Fax: 0171 580 5896 E-mail: k.n.ward@ucl.ac.uk
Professor E M Ross, Professor of Community Paediatrics, Mary Sheridan Centre, Guy's, King's & St Thomas' School of Medicine, 405 Kennington Road London SE11 4QW

Fatal/severe allergic reaction to food ingestion

Background

A number of recent studies suggest 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. No population-based studies have been undertaken in the United Kingdom or North America. A preliminary search by the Office of National Statistics 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 be 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 - may need special training, reinforced each year.
- The prescription will 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.

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.

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.

Study duration

March 1998 - 2000.

Method

It is assumed that all children admitted to hospital for severe allergic reactions will come under the care of a paediatrician and that these cases will be identified through the BPSU. A questionnaire with covering letter and a summary of the study protocol is sent to reporting paediatricians.

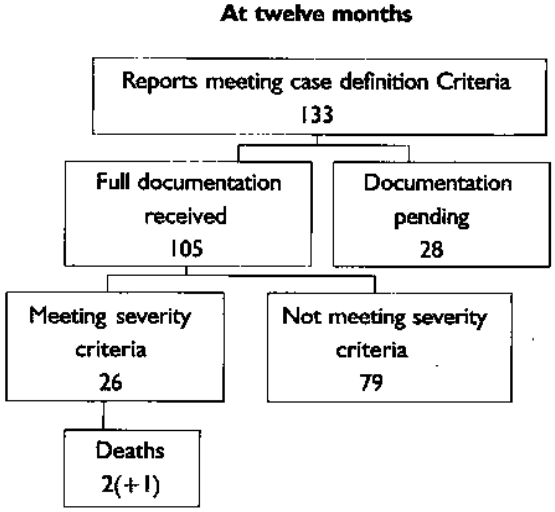
It cannot be assumed that paediatricians will be aware of all deaths due to severe allergic reaction; particularly if the child dies at home or in an A&E department. These cases will also be identified through the Offices of National Statistics in the United Kingdom and Republic of Ireland. For the very small number of children who die (we expect one or two per year), a member of the research team may need to visit the parents for more details. This would only be undertaken if the parents have given written consent following a discussion with the reporting clinician and their family doctor.

Analysis

The following represent the interim results for the first year, being March 1998 to the end of February 1999. This information was compiled at the end of April 1999. After exclusion of reports withdrawn after notification, and accepting that we can only confirm whether a case meets our case definition once full documentation is received, we currently have 133 reports logged (Figure 8).

Once full case documentation has been received the case is checked to confirm it meets our case definition and its severity is then assessed against a set of management based factors. Respondents report on the basis of our case definition and not on our criteria, to avoid them having to apply a series of complex criteria. Of the 133 currently logged, full documentation is available on 105, 26 of these meet our severity criteria. A further 79 are within the scope of our case definition but do not meet our severity criteria. Three children are known to have died. One of these deaths, however, has a number of unresolved issues concerning aetiology, which could, potentially, put it outside our study.

Figure 8 *Fatal/severe allergic reaction to food ingestion, interim results for March 1998 - February 1999*



Retrospective and prospective deaths search - The Offices of National Statistics have run preliminary searches for deaths for the United Kingdom and the Republic of Ireland. The Office of National Statistics (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 (eg. 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. The timetable of future searches has been set. Three probable deaths have been identified in the 1993-98 period. Preliminary searches in Scotland and Ireland (where searches are limited to code searches) have revealed no further cases. These will be repeated using information on possible additional codes gained during the England and Wales searches.

Plans for contacting the parents of reported children who have died have been confirmed in accordance with the provisions mentioned above, including seeking of permission to contact.

Interim conclusions

The overall reporting rate has been encouraging and we are grateful for the interest shown. The range of severity being reported to us (66 cases meeting our case definition but falling short of our severity criteria) is very suggestive that clinicians are following our reporting instructions correctly. It cannot be guaranteed that we will be informed about all cases at the milder end of the spectrum but it is likely that we will ascertain almost all of the severe cases.

Incidence - Early analysis seems to support our original hypothesis that truly severe allergic reactions to food in childhood are rare. Most strikingly, the number of deaths is very small. This underlies both the need to continue into a second year and the vital importance of continued vigilance.

Circumstance and clinical management - Given the number of cases reported, the descriptive part of our work (on circumstances, clinical course and associations such as asthma) will be undertaken after the full two years as we would be reluctant to draw conclusions about the relatively small numbers we currently have.

Previous reactions - Again this work will be undertaken at the end of the reporting period. 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 - Presuming the reporting rate continues as currently, our conclusions are likely to be very controversial. We therefore have to be very confident about case assertainment. We have explored other channels of information (including the Anaphylaxis Association) which have so far yielded no new cases. The investigators are dependent, however, on the ongoing vigilance of clinicians and would like to underline the need to report all cases that meet our case definition to ensure high ascertainment through the BPSU.

Key points

Based on 26 severe (using study severity criteria) and 2 fatal confirmed cases with available data:

- Severe allergic reactions to food in childhood are rare.
- Severe allergic reactions to food leading to childhood deaths are very rare.

** References (1-12) available from principal investigators on request*

Dr A Colver, Dr A Cant, Dr C Macdougall, Donald Court House 13 Walker Terrace, Gateshead NE8 3EB Tel: 0191 477-6000 Fax: 0191 473 0370
E-mail: allan.colver@ncl.ac.uk or c.f.macdougall@ncl.ac.uk

Haemolytic uraemic syndrome

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 Vero cytotoxin-producing *E. coli* O157 (O157 VTEC)[1,7,8,9,10]. O157 VTEC is an emerging infection, 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.

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 will explore the effect of this increase in the VTEC 0157 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

Start February 1997. For three years with annual reviews.

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 Department of Medical Microbiology in Aberdeen. 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: 0181 200 6868 ext 4551) and in Scotland to SCIEH (tel: 0141 300 1100 ext 1118). Initial summary details will then be taken and recorded. A structured questionnaire designed to collect specific epidemiological and clinical data will then be sent to the reporting paediatricians. The paediatricians will be asked to complete the questionnaires and return them to the BPSU scientific coordinator (Mr R Lynn) or SCIEH (Ms L Browning) 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. Follow-up questionnaires will be sent to all paediatricians who have reported twelve months after their initial report of a case in order to obtain information on longer term morbidity. All data analysis will be conducted by CDSC and SCIEH.

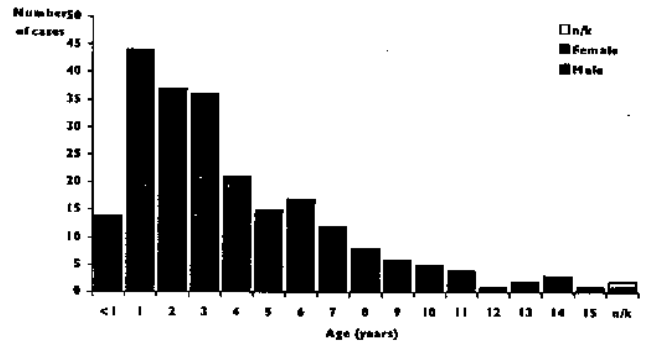
4 **Birmingham Children's Hospital NHS Trust:** Drs C M Taylor and D V Milford advise on clinical aspects of the study on behalf of the British Association for Paediatric Nephrology.

Results and discussion

In the period February 1997 to February 1999 the BPSU, PHLS and SCIEH received 386 reports of suspected HUS cases from paediatricians in the United Kingdom and Republic of Ireland. After de-duplication and verification it was established that 228 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. However in order to maintain high levels of case ascertainment it is essential that reporting from both local hospitals and specialist centres continues.

The age and sex distribution of clinically confirmed cases of HUS is shown in Figure 9. It can be seen that most reported cases are children of three years of age and below and cases became rare after age 11. The high number of female cases in the age group one to two years is also striking.

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 overleaf). In both 1997 and 1998 sharp peaks in reporting were recorded in late summer.

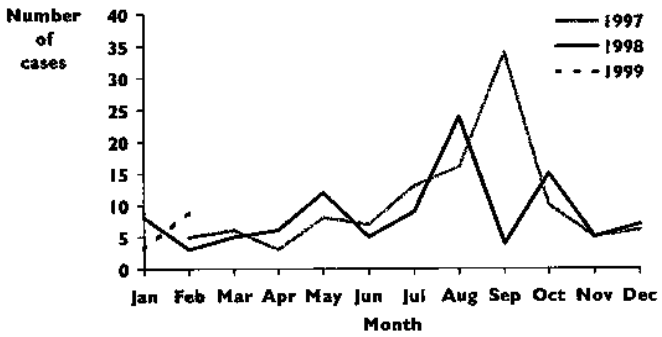
The geographical distribution of cases in the UK is shown in Figure 11 overleaf. Clinically confirmed cases were mapped according to their post code of residence. The Republic of Ireland does not operate an equivalent post coding system therefore it was not possible to plot the geographical distribution of disease in this part of the study area.

Disparities have been identified between the geographical distribution of clinically confirmed cases of HUS and microbiologically confirmed cases of verocytotoxin producing Escherichia coli O157 (VTEC O157) infection. The most striking of these disparities relates to the higher than expected ratio of HUS to VTEC O157 infection in the regions of North and South Thames. The clustering of cases residing in London and the South East of England is surprising given that the regions of North and South Thames have consistently reported the lowest rates of VTEC O157 infection. This might reflect poor ascertainment of laboratory confirmed VTEC O157 infection in these regions or from geographical differences the aetiology of HUS. More sophisticated analyses will be conducted in order to characterise in greater detail the relationships between the geographical, seasonal, age and sex distributions of VTEC O157 infection and HUS.

It can be seen that cases are clustered in particular parts of the country, most notably in London, South East Lancashire, South Yorkshire and Nottinghamshire. By contrast relatively few cases were reported to reside in Wales, Northumberland and Cumbria.

The researchers would like to thank all of the paediatricians who have reported cases.

Figure 10 *Seasonal distribution of confirmed cases of HUS*



Key points

- Most cases of HUS in the UK are due to E. *coli* O157.
- HUS is commoner in children under age 3 and rare beyond age 11 years.
- There seems to be poor laboratory reporting of E. *coli* O157 in London and the South East.
- There are peaks of HUS incidence in the autumn.
- When clusters and outbreaks of HUS/E *coli* O157 occur they require urgent investigation to determine if there is ongoing risk to children.

Figure 11 *HUS confirmed cases reported February 97 - February 99 for the United Kingdom*

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

Dr C M Taylor, Dr D V Milford, Birmingham Children's Hospital NHS Trust, Laboratory of Enteric Pathogens, Ladywood Middleway, Birmingham B16 8ET Tel: 0121 454 4851 ext 6120
Dr G K Adak*, Dr S O'Brien, Central Public Health Laboratory, 61 Colindale Avenue, London NW9 5HT Tel: 0181 200 6868 ext 4551 Fax: 0181 200 7868 E-mail: BAdak@phls.co.uk*
Ms L Browning*, Scottish Centre for Infection and Environmental Health, Clifton House, Glasgow G3 7LN Tel: 0141 300 1100 ext 1118*
Professor T H Pennington, Dept of Medical Communicable Disease Microbiology, Aberdeen Royal Hospitals NHS Trusts, Forester Hill, Aberdeen AB9 2ZB

Hepatitis C virus (HCV) infection

Background

HCV is the major cause of post-transfusion and community acquired nonA- nonB hepatitis. Infection in HCV has the ability to persist in the host in the majority of cases, it may lead to chronic liver disease and hepatocellular carcinoma. However, there is little information on the natural history of HCV infection in children.

HCV can be transmitted from mother to child, but the risk of vertical transmission appears to be low (1-10%) unless there is co-infection with HIV. The main recognised routes of transmission are transfusion of infected blood or blood products, organ transplantation, intravenous drug use and other situations where percutaneous inoculation may occur (needlestick injuries, tattoos). Transmission between family members has been reported, and sexual transmission may occur, though conclusive evidence of this is lacking. Viral inactivation of clotting factor concentrate started in the UK in 1984, but did not extend to all blood products; routine screening of blood, blood products and organ donors for HCV started in September 1991. Children at high risk of being infected with HCV prior to 1991 include those who received bone marrow transplants or multiple blood transfusions, and those with haemophilia. Screening all children at risk has not been undertaken systematically, and

paediatricians from a range of specialities may be involved in the management and follow-up of children who have been identified.

Objectives

1 To estimate the prevalence and distribution of known paediatric HCV infection in the UK and Republic of Ireland;
2 To look at patterns of presentation according to mode of transmission (infected blood products/organ transplantation or mother to child);
3 To describe the current management by risk group;
4 To investigate the natural history of HCV infection in children with a known date of infection.

Case definition

1 Any child who is HCV antibody positive (including any child under 18 months of age born to an HCV infected woman and any older child with definitive HCV infection).
2 Any child who is positive for HCV by RNA PCR.

In 1998 the surveillance strategy changed, since then only children infected with HCV need to be reported and it was not necessary to report children born to HCV infected mothers.

Study duration

March 1997 - March 1999.

Methods

Reporting paediatricians are asked to complete a surveillance form shortly after the reporting card is received by the BPSU, and a follow-up form will be sent annually thereafter.

Surveillance of paediatric HCV is running in parallel with surveillance of paediatric HIV and is conducted by the same group of investigators. If a paediatrician has already reported a child with HIV infection who also has HCV, a new report should be made for the HCV. For new cases of dual infection, both boxes on the orange card should be ticked. Once it is established that the child has been reported to both studies, follow-up will be coordinated to avoid duplication.

Results

By the end of March 1999 there had been 807 notifications. After excluding 60 duplicates, 98 notifications made in error and 65 outstanding reports there remained 584 confirmed cases. Four hundred and forty were of children born to HCV positive mothers and in 352 of these the mother's HCV status was known before the child's birth.

For just over 80% of vertically exposed children the mother's most likely risk factor was injecting drug use. Vertically exposed children were reported from all over the UK and Republic and Irish Republic, with 111 reports from Dublin, 91 from the Thames regions and 80 from the North West.

As of December 1998 there were 182 reports of children with definitive HCV infection. One hundred and thirty-four children had received infected blood or blood products, two received organ transplants, 40 were infected through mother to child transmission and six were infected through other routes (four needlestick injuries and two unknown). Infected children were reported from 54 centres spread throughout all parts of the UK and Republic of Ireland (Table 9 for current residence) and over 80% were of white ethnic origin. The median estimated time for acquisition of HCV for all children was 6.7 (range 0.04-15.6) years. Six centres were caring for ten or more children whilst 34 centres reported only one child. The majority of respondents were general paediatricians, with reports from nine other paediatric specialists.

Twelve children were co-infected with HIV (six received contaminated blood products and six were vertically infected children). Liver function tests were more likely to be abnormal on children co-infected with HIV. Only one child had any symptoms of clinical significance. Thirty-one children had received interferon therapy including three vertically infected children.

Conclusions

Children are reported from all over the UK and Irish Republic, with large numbers of children in Dublin, Liverpool and London. Most infected children received contaminated blood products and the majority of vertically exposed children were born to drug using women. Long term follow-up of children with a known date of infection is planned through the Communicable Disease Surveillance Centre.

A paper describing the infected children has been submitted for publication. Data on prospectively followed children is currently being analysed and papers on mother to child transmission are also being planned.

Key points

- Most children diagnosed with HCV are those infected through contaminated blood products.
- A small group are children infected through mother to child (vertical) transmission.
- Children now at risk of acquiring HCV are those born to women who have injected drugs.
- The risk of a baby acquiring HCV from an infected mother is greater if the mother is also infected with HIV than if the mother has HCV infection alone.

Dr D Gibb, Ms P Neave, Ms P Tookey Department of Epidemiology & Public Health, Institute of Child Health, 30 Guilford St, London WC1N 1EH.
Tel: 0171 813 8396 Fax: 0171 242 2723
Collaborators: Dr M Ramsey, PHLS, Communicable Disease Surveillance Centre, National Blood Authority, Dr D Goldberg, Scottish Centre for Infection and Environmental Health/Scottish National Blood Transfusion Service

Table 9 *Current residence of infected children (n=182)*

	Blood product recipient	Organ transplant recipient	Other	Vertically infected	Total (%)
Current residence					
Thames regions	29	1	2	11	43 (23.7)
Rest of England and Wales	72	1	2	17	92 (50.5)
Scotland	19	0	1	3	23 (12.6)
Republic of Ireland	14	0	1	9	24 (12.6)
Total	**134 (74%)**	**2 (1%)**	**6 (3%)**	**40 (22%)**	**182**

HIV/AIDS infection in childhood

Background

National surveillance of paediatric 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 and 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. At present (1997) less than a third of infected pregnant women are identified before their baby is born and paediatric HIV in the UK is still most commonly recognised only when the child, or a member of their family, becomes ill (Figure 12). However, following the publication of intercollegiate guidelines[1] in April 1998, there are early signs of an improvement in the offer and uptake of antenatal HIV testing[2]. 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 1999 there had been 1460 reports through the BPSU. Eight hundred and eighty-five children born to HIV infected women, and therefore at risk of vertical transmission, were reported (Table 10), together with 48 children who were infected in the course of treatment for haemophilia, 23 infected through blood or tissue transfer and five for whom the transmission route cannot be established. Two hundred and forty-two of the remaining reports were duplicates, and there were 234 reporting errors. Twenty-three reports are still being investigated.

Table 10 Infants born to HIV infected women, and confirmed cases of paediatric HIV infection (notified by 31 January 1999)

Transmission route (actual or potential)	BPSU Reports	Reports from other sources	Total
risk of vertical transmission	885	670	1555
haemophilia treatment	48	219	267
blood transfusion/products	23	16	39
other/not yet established	5	14	19

A further 919 reported cases have been identified from other sources (see Endnote) including 670 children born to HIV infected women, 219 children with haemophilia, 16 infected through blood transfusion and 14 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).

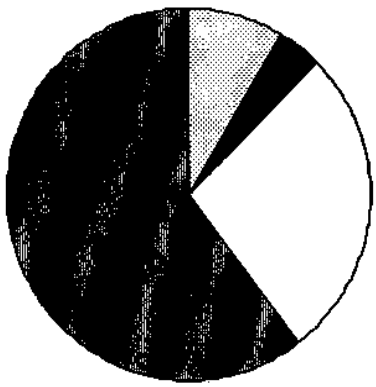
All reporting is voluntary and confidential. Almost all of the surviving young people infected during the course of treatment for haemophilia are now over 16 years old, and their follow-up is undertaken by the UK Haemophilia Centre and the PHLS AIDS and STD Centre. All other children are followed-up 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 1999, among the 1555 children born to HIV infected mothers (Table 11), 590 had confirmed infection, 329 were then of indeterminate status and 636 were known to be uninfected. Transmission rates cannot be estimated from these data as there is a bias towards the reporting of symptomatic

Table 11 Infection status of children born to HIV infected women (notified by 31 January 1999)

Region of first report	Infected	Indeterminate	Not Infected	Total
Thames regions	428	230	333	991
Rest of England, Wales & Northern Ireland	90	46	76	212
Scotland	35	31	133	199
Republic of Ireland	37	22	94	153
TOTAL	**590**	**329**	**636**	**1555**

Figure 12 Vertically infected children born in the UK and developing AIDS: data to January 1999

For children with AIDS born in the UK, at what stage were maternal infections diagnosed?



Mother's HIV infection diagnosed:

before pregnancy:	19	(8.5%)
during pregnancy:	9	(4.0%)
after child's birth but before AIDS developed:	61	(27.2%)
when child developed AIDS:	135	(60.3%)

TOTAL 224 CHILDREN

CDSC, SCIEH & ICH(L)

Source: Voluntary confidential reporting by Obstetricians (RCOG), Paediatricians (BPSU/RCPCH) and laboratories (CDSC/PHLS)

children. One hundred and fifty-three (10%) of these children had been reported from the Republic of Ireland, 199 (13%) from Scotland, 991 (64%) from the Thames regions and 212 (14%) 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.

Key points

- Reports of HIV infected children are increasing.
- Almost all new infections are now acquired through mother to child transmission.
- The greatest number of infections are in London but cases are occurring in all parts of the country.
- Vertical transmission risk can be reduced to under 5%. Many of the children's infections could have been prevented as mothers were not aware of their infection.
- It is now national policy to offer and recommend HIV testing to pregnant mothers as an integral part of antenatal care[3].

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.

References

1 Intercollegiate Working Party for Enhancing Voluntary Confidential HIV Testing in Pregnancy (Royal Colleges of General Practitioners, Midwives, Nursing, Obstetricians & Gynaecologists, Pathologists, Paediatrics & Child Health and Physicians; Public Health Laboratory Service; Faculty of Public Health Medicine, Directorates of Public Health for North & South Thames). Reducing mother to child transmission of HIV infection in the United Kingdom. Royal College of Paediatrics and Child Health 1998.

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

3 Reducing mother to baby transmission of HIV. Health Services Circular (HSC 1999/183), NHS Executive (August 13 1999)

Ms P Tookey, Ms J Masters, Miss T Duong, Department of Epidemiology & Public Health, Institute of Child Health, 30 Guildford St, London WC1N 1EH Tel: 0171 829 8686 Fax: 0171 242 2723 E-mail: p.tookey@ich.ucl.ac.uk

Dr A Nicoll, PHLS CDSC, 61 Colindale Avenue, London NW9 5EQ
Tel: 0171 200 6868 E-mail: Anicoll@phls.co.uk

Dr D Goldberg, SCIEH, Clifton House, Glasgow G3 7LN Tel: 0141 300 1100

Inflammatory bowel disease in under 20 year olds

Background

Whilst the incidence of ulcerative colitis (UC) appears static or falling, some recent reports suggest an increase in the incidence of Crohn's disease (CD) in the industrialised countries. If these findings are confirmed their reason will remain uncertain but they would 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 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 part probably reflects the lack of specificity in presenting symptomatology which prevents 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 rises 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 and this collaboration, including raising the reporting age to 20 years, should ensure optimal reporting of adolescent cases.

Basic and epidemiological data from 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, a collection of cases will be required, the planning of which depends on good data on incidence and prevalence. This data will be obtained in the course of this study.

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/adolescents (under 20 years of age).
2 The mean 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).

Interim analysis

The following analysis is based on data collected during the first 9 months of the study through the BPSU. Data collected through the BSG has yet to be incorporated thus all findings are provisional.

During this period of the study there were 379 confirmed cases, with 95 questionnaires still to be returned and 141 invalid reports, mostly duplicates. The median time from notification to return of questionnaires was 5 weeks, with 75% of questionnaires being returned within 9 weeks.

Incidence - Cases appear to be evenly distributed throughout the UK and Ireland having been reported from 198 different institutions.

Using the latest available population estimates (for England, Scotland, Wales, Northern Ireland mid-1997 and for the Republic of Ireland mid-1996). A preliminary estimate of the overall incidence of inflammatory bowel disease in children aged less than 16 years is 3.9-4.8 cases/100,000/year.

Disease type - Crohn's disease predominates (Table 12). In addition, there have been 8 (2%) cases of orofacial granulomatosis (OFG) which represent a well defined IBD sub-group. However, in Table 12 they have been combined with cases of Crohn's disease.

Table 12 *Clinical diagnosis of inflammatory bowel disease*

	n	
Crohn's disease*	232	61%
Indeterminate colitis	48	13%
Ulcerative colitis	99	26%
Total	**379**	**100%**

* includes 8 cases of orofacial granulomatosis

Table 13 Historical diagnosis

	n	
Crohn's disease*	232	61%
Indeterminate colitis	48	13%
Ulcerative colitis	99	26%
Normal bowel	12	3%
Histology not taken	17	4%
Results not available	29	8%
Uncertain	6	2%

* includes 8 cases of orofacial granulomatosis

Clinicians - Most cases were cared for, or initially investigated by, two or more clinicians. Overall 72% of children were seen by a paediatric gastroenterologist, 21% by an adult gastroenterologist, 9% by a paediatric surgeon, 8% by an adult surgeon and 57% by a paediatrician. Disease type did not seem to influence the clinicians involved.

Presenting symptoms - Weight loss, lethargy ($p=0.02$) and anorexia ($p<0.01$) were reported more commonly in Crohn's patients compared to other IBD patients (Table 14). Overall 9% of all IBD patients had oral symptoms (eg lip swelling, cracked lips), 8% joint symptoms (mainly pain) and 3% had nausea or vomiting as a major presenting symptom. 3% of IBD patients had growth failure or (primary) amenorrhea as a major presenting symptom. 1% presented with acute appendicitis, 1% had liver involvement and 2% had erythema nodosum or a rash.

Age at diagnosis - The mean age at diagnosis was 11.7 years (range 0.4-16 years) with no significant difference between the 3 main disease groups (Table 15 overleaf). Three percent of children were aged less than five years at diagnosis. Children whose care involved a paediatric gastroenterologist were diagnosed significantly earlier than other children (11.4 versus 12.3 years, $p=0.006$). However, the onset of symptoms was also significantly earlier in this group, the mean delay between the onset of symptoms and diagnosis remained the same, at 0.5 years.

Cases of orofacial granulomatosis formed a sub-group with a higher proportion of males (88%) who were diagnosed at a significantly younger age (mean 8.7 years). If excluded from the Crohn's group then the mean age of the Crohn's patients at diagnosis rose to 12.0 years, still older than the ulcerative colitis and indeterminate colitis groups though differences did not reach conventional levels of significance ($p=0.08$).

Height, weight and sex - At diagnosis children with inflammatory bowel disease were shorter (mean -0.38 SD) and lighter (mean -0.77SD) than would be expected. Thirty-eight percent of Crohn's patients had a weight less than 2 standard deviations below the mean and 10% had a height less than 2 standard deviations below the mean. The comparative figures for the ulcerative colitis group were 8% and 3% respectively.

Family history - In 15% of cases there was a family history of inflammatory bowel disease. There was no difference in disease type, mean age of onset of symptoms or mean age at diagnosis in this group compared to those without a family history.

Ethnic background - Seventy-eight percent of parents were recorded as white, 4.8% as black (Caribbean 3.2%, African 0.8%), 8.9% as Asian (Indian 6.3%, Pakistani 1.8%, Bangladeshi 0.8%) and 0.4% as 'other'. This is a higher proportion of ethnic minority groups than expected. In 8% of cases the ethnic background of parents was not reported.

Investigation - Overall 86% of children had a colonoscopy and/or sigmoidoscopy and 42% an oesophagoduodenoscopy (OGD). Fourteen percent of children had both a sigmoidoscopy and a colonoscopy. A child was more likely to have had a sigmoidoscopy if seen by an adult gastroenterologist or surgeon (both $p=0.005$) but more likely to have had an OGD if seen by a paediatric gastroenterologist ($p<0.001$). 39% of Crohn's patients had both an OGD and a colonoscopy.

A radio-labeled white cell scan was more likely to have been undertaken if a child had been seen by an adult gastroenterologist ($p=0.04$). Fourteen percent of children had both a radio-labeled white cell scan and barium meal and follow through and this combination was significantly more likely if children had been seen by an adult surgeon ($p=0.02$). A barium enema was significantly more likely to have been performed if a child had been seen by a paediatric gastroenterologist ($p=0.026$).

Treatment - Overall 93% of children were reported as receiving one or more therapies including 3% who underwent surgery. Systemic steroids (alone or in combination) were used in 47% of Crohn's (CD) patients, 45% of indeterminate colitis (IC) patients and 70% of ulcerative colitis (UC) patients. Dietary therapy (alone or in combination) was used in 43% of CD, 25% of IC and 6% of UC patients. Polymeric feeds were used more frequently than elemental or semi-elemental feeds and exclusion diets (eg milk free) were used in a several patients with colitis. 59% of CD patients, 79% of IC patients and 80% of UC patients were treated with systemic 5-ASAs.

Nine percent of children received immunosuppression; 26 children received azathioprine, 1 6MP, 6 cyclosporin and 1 tacrolimus. 14% of children received antibiotics with metronidazole being most commonly used (44/53 patients).

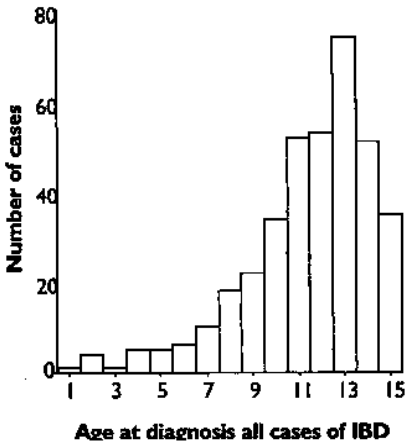
Table 14 Common presenting symptoms

	Weight loss	Pain	Bleeding	Lethargy	Anorexia	Diarrhoea
All cases of IBD	48%	71%	45%	23%	17%	64%
Crohn's disease*	59%	73%	24%	28%	23%	59%
Indeterminate colitis	38%	81%	69%	15%	15%	72%
Ulcerative colitis	32%	61%	85%	15%	6%	71%

* includes 8 cases of orofacial granulomatosis

Table 15 *Age at diagnosis*

	Symptoms		Diagnosis	
	yr (mean)	*n*	*yr (mean)*	*n*
All cases of IBD	11.1	351	11.7	371
Crohn's disease*	11.2	218	11.9	228
Indeterminate colitis	10.8	44	11.5	47
Ulcerative colitis	11.1	89	11.3	96
* includes 8 cases of orofacial granulomatosis				
** anova	p=0.8**		p=0.16**	



Administration of a diet (+/- ASA) was more likely in Crohn's patients if their care involved a paediatric gastroenterologist (p=0.003). However, the involvement of a paediatric gastroenterologist did not appear to reduce the use of systemic steroids in Crohn's patients. Similarly the involvement of a paediatric gastroenterologist did not appear to significantly alter the treatment of patients with indeterminate colitis or ulcerative colitis.

Discussion

This is the largest prospective survey of IBD to date. These interim data suggest that the incidence of IBD in the UK and Ireland in children <16 years is 3.9- 4.8 cases/100,000/year. Reports from the British Society of Gastroenterology (BSG) may increase this rate somewhat (through cases under 16 seen by adult physicians).

The overall incidence of IBD appears to be higher than noted in the Welsh (Cosgrove) and Scottish (Barton) retrospective surveys (Table 17). It is not clear whether these higher figures reflect a true increase in incidence or better case ascertainment. It was found that 2% of IBD cases were orofacial granulomatosis and that the incidence of Crohn's disease appears to be twice that of ulcerative colitis.

The mean age of children at diagnosis was 11.7 years and this is lower than in most other series. After examining the preliminary BSG data we found no evidence that the marked drop in incidence amongst 15 year olds was because children of this age were being missed by the BPSU survey. A similar peak in incidence at around 13 years was found in both the Norwegian and French studies. The preponderance of males has been reported in other studies. Fifteen percent of cases had a family history of IBD, but this did not seem to influence the age of diagnosis or disease type. This is the first study to examine the ethnic breakdown of children, and it has been confirmed that children from Asian and African backgrounds are affected by IBD.

The mean delay between symptoms and diagnosis in Crohn's patients was 0.5 years and this had not changed significantly from Barton's Scottish survey undertaken 15 years ago. There was no evidence to suggest that the delay in diagnosis was greater if care had not involved a paediatric gastroenterologist.

The investigators found that at diagnosis children with both ulcerative colitis and Crohn's disease were lighter and shorter than their peers. Preliminary investigation has not suggested that this finding was because of any systematic error (ie month of diagnosis being later than the date of measurement of height and weight).

Overall 72% of children had some input from a paediatric gastroenterologist during their initial diagnosis and/or treatment. 56% of children were cared for by either a paediatric gastroenterologist alone, or in combination with a paediatrician. Ten percent of children

Table 16 *Selected incidence studies*

				Incidence/100,000/year			
				Crohn's	UC	IC	All IBD
PROSPECTIVE STUDIES			*Ages*				
BPSU	**1998**	**UK & Ireland**	***0-16***	**2.4-2.9**	**1-1.3**	**0.5-0.6**	**3.9-4.8**
Hildebrand	1983	Sweden	*0-16*	1.7	1-1.1	1.4	3.1
Hildebrand	1983-7	Sweden (SW)	*0-16*	2.7	1.9	0.7	5.3
Gottrand	1991	France (N)	*0-17*	2.1	0.5		2.6
Olafsdottir	1984	Norway (W)	*0-15*	2.5	4.3		6.8
RETROSPECTIVE STUDIES							
Cosgrove	1993	Wales (S)	*0-16*	3.1	0.7		3.8
Cosgrove	1983-8	Wales (S)	*0-16*	1.3	0.7		2.0
*Barton***	1983	Scotland	*0-16**	2.3	1.6		2.3
*Barton***	1968	Scotland	*0-16**	0.7	1.6		2.3
** only inpatients		* Crohn's disease only age 5-16					

were cared for either by a paediatrician alone or in combination with an adult surgeon.

The investigators also found a relationship between the type of clinicians involved in care and the investigations undertaken, in particular upper GI endoscopy was more common if Crohn's patients were seen by a paediatric gastroenterologist. This probably accounts for the frequent finding of upper GI disease activity in the Crohn's patients. Similarly the management of Crohns disease was also found to vary, with paediatric gastroenterologists prescribing more dietary therapy (polymeric feeds being used more commonly than elemental feeds). Dietary therapy may account, in part, for the lower overall use of systemic steroids in Crohn's patients compared to the data of Barton (47% versus 74%) as we did not find an increased use of immunosuppressive therapy.

Reference

1 Inflammatory bowel disease incidence: up, down, or unchanged? Logan R. 1998 Gut:1 42: 309-311

Key findings

- Incidence of IBD amongst children < 16 years is 3.9 - 4.8 cases 100,000/year.
- The incidence of Crohn's disease appears to be twice that of ulcerative colitis.
- Children from African and Asian backgrounds are affected by IBD.
- There seems to have been little change in the presenting features of IBD during the last 15 years, with a mean time from the onset of symptoms to diagnosis of 0.5 years in both Crohn's and ulcerative colitis patients.
- Most children have some input from a paediatric gastroenterologist.
- Management varies between different groups of clinicians.

Dr B Sandhu, Dr A Sawczenko, Royal Hospital for Sick Children, St Michael's Hill Bristol BS2 8BJ Tel: 0117 9285445 Fax: 0117 9285701
In collaboration with Professor R Logan, British Society for Gastroenterology Research Unit and the IBD Working Committee of the British Society of Paediatric Gastroenterology and Nutrition.

Invasive Haemophilus influenzae infection

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 *H. influenzae* 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 aims in 1995 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.

Analysis

By March 1999, 499 reports that met the case criteria had been made including 363 cases in vaccinated and 136 in unvaccinated children. One hundred and twenty-six cases represented true vaccine failures (TVF), 74 apparent vaccine failures and 13 were possible vaccine failures (course of vaccination received, isolate of *H. influenzae* obtained but not typed). Amongst vaccinated children there were 117 with invasive disease due to non capsulate strains of *H influenzae* and 33 with non b capsulate strains, mostly type f.

One hundred and seventeen of the 126 TVF were vaccinated in the first year of life: 106 received three doses and 11 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, 17 developed disease between five and 11 months of age, 36 between 12 and 23 months of age, 26 between 24 and 35 months of age, eleven between 36 and 47 months of age, five between 48 and 59 months of age and one 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% (94-98%) between 24-35 months of age, 97% (95-99%) between 36-47 months of age, 93% (84-98%) for those aged 48-59 months of age and 97% (84-100%) for those 60-71 months of age. For the whole period from five to 71 months of age, the estimate is 98% (98-99%).

In the Republic of Ireland (ROI) (to 31.12.98), numbers of cases in each age class together with point estimates of efficacy (for three doses) and 95% CI (assuming 75% vaccine coverage) are as follows: 8-11 months of age - 0 (100%, 95-100%), 12-23 months of age - 4 (96%, 90-99%), 24-35 months- 5 (83%,61-95%) 36-47 months of age - 1 (92%, 54-100%) and 48-59 months of age - 0 (100%, 8-100%). For the whole period the estimate is 96% (92-98%).

The modes of presentation and associated medical and immunological conditions amongst the cases of TVF are detailed in Table 17. Overall 45 (36%) were shown to have an associated condition. Among TVF there have been 4 deaths.

Convalescent sera were available in 107 cases of TVF. Thirty-four (32%) 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 (84/136) with a predominance of neonatal disease, especially in premature infants. Hib has been isolated from 46 children.

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. In the ROI accurate vaccine coverage figures are not available and the relatively small population size results in wide confidence intervals around estimates. It is generally believed that vaccine coverage in the ROI is only moderate (eg. 75%) yet the decline in disease incidence has been dramatic (>92%), illustrating the impact of Hib conjugate vaccines on herd immunity.

Should vaccine protection wane due to the absence of a booster dose together with the reduction in boosting by pharyngeal carriage of Hib, an excess of cases should become apparent in older children. Currently, point estimates of efficacy remain very high up to and including the sixth year of life, although the point estimate for those 48-59 months of age seems lower (93%) this represents only five cases. Surveillance must continue to ensure that a booster dose will not be required.

Type b disease continues to occur however. In 1997 there was a total of 29 cases in vaccinated and unvaccinated children <5 years of age in the UK and 22 in 1998, this represents incidence rates of 0.8 and 0.6/100,000/year respectively which compares with 2/100,000 in 1993-4 and 31/100,000 in 1991-2. Amongst 39 unvaccinated Hib cases, there were three deaths. Six of 39 had associated risk factors including prematurity, hypogammaglobulinaemia, malignancy and neutropenia and five were children recently arrived from countries where Hib is not routinely given. After excluding those not eligible because of age, birth outside the UK or risk factors that may have impaired their response to vaccination, it is apparent that 14/39 (36%) were eligible for a complete course of vaccination. Timely vaccination and high vaccine uptake remains vital if this disease is to be eliminated.

In terms of clinical practice it is reasonable to seek an underlying host abnormality in cases of vaccine failure and measurement of

Table 17 *Presenting illness and associated conditions of true vaccine failures (TVF) Sept 1992 - April 1999*

Presenting Illness		Associated condition	
Meningitis	75	Prematurity	18
Epiglottitis	22	Chromosomal abnormality	4
Bacteremia	10	(includes 3 Down's syndrome)	
Pneumonia	7	Malignancy	5
Cellulitis	5	Dysmorphic	4
Septic arthritis	3	Cyclical neutropenia	1
		Immunoglobulin deficiency	34

convalescent Hib antibody levels following vaccine failure provides guidance on further doses of vaccine. The most frequently identified associated clinical condition has been prematurity. Immunogenicity studies of Hib vaccines in those born prematurely suggest that indeed this group might be at greater risk of vaccine failure. However, this study has shown that as a group they are not represented in excess of the numbers expected. These data are very important, as they do not support a change in vaccination policy for these specific individuals, a conclusion one might otherwise draw from the immunogenicity studies.

Following the impressive reduction in Hib disease the majority of cases now reported to the study are due to non type b *H. influenzae* i.e. not vaccine preventable, a distinction important in maintaining public confidence in this vaccine. There is no evidence of an increase in non type b *H. influenzae* as a result of widespread Hib vaccination.

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

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.
- Children who present as a true vaccine failure deserve further investigation as to the underlying cause.
- Despite the UK and Republic of Ireland not using a booster dose there is no evidence of immunity waning with age.

Dr P Heath, St George's Hospital, London SW17
E-mail: paul.heath@sghms.co.uk
Professor R Moxon, Dr M Slack, Oxford Vaccine Group and PHLS Haemophilus Reference Laboratory, John Radcliffe Hospital, Oxford OX3 9DU Tel: 01865 221068/220859 Fax: 01865 220479
Dr J Fogarty, Dept of Public Health Medicine, Merlin Park Hospital, Galway, Republic of Ireland Tel: 00353 91 751131
Dr M Ramsay, PHLS Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ Tel: 0181 200 6868
Scottish Centre for Infection and Environmental Health, Clinton House, Glasgow G3 7LN

Progressive intellectual and neurological deterioration in children

Background

Surveillance for progressive intellectual and neurological deterioration (PIND) in children (including Creutzfeldt-Jakob Disease) through the BPSU began in May 1997. Paediatric PIND covers an important group of conditions, which have not previously been investigated epidemiologically in the UK. The recent appearance of new variant CJD (nvCJD) in patients as young as 16 years of age[1] suggested the possibility that nvCJD is occurring in children. The detection of nvCJD in UK children would have important implications for paediatrics and public health. The presentation of nvCJD differs from classical CJD, and therefore the clinical presentation of any cases in children is difficult to predict.

The strategy is to detect suspected cases by looking at a broader group of conditions. This group needs to be large enough to include all possible cases of nvCJD, hence surveillance is being undertaken for a range of presentations under a combined term - progressive intellectual and neurological deterioration. An Expert Neurological Advisory Group consisting of six senior paediatric neurologists supports the research team by meeting quarterly, discussing the anonymised details of all newly notified cases, and classifying them according to study categories. The investigation is being coordinated with the National CJD Surveillance Unit in Edinburgh and the Public Health Laboratory Service.

Objective

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 nvCJD is occurring in children.

Study duration

May 1997 to April 2000 (three 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, eg. after encephalitis, head injury or near-drowning.
Including:

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

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

Current status

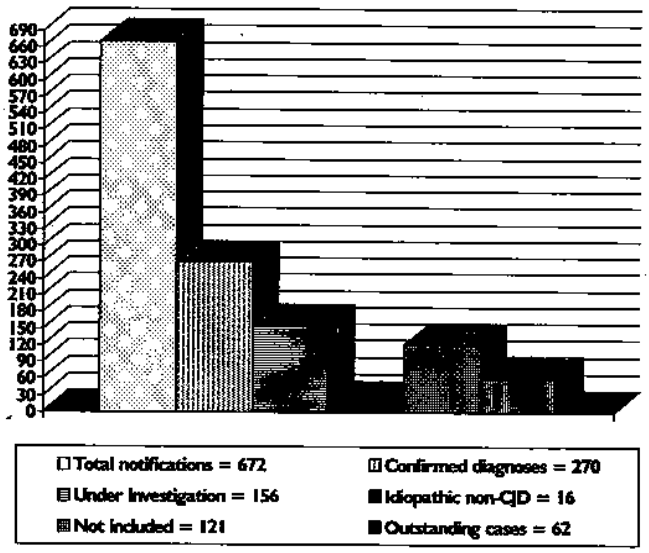
By the end of April 1999 a total of 672 children had been reported via the BPSU. Of these the Expert Group has discussed 489 cases. Of these 270 have been classified as having a recognised cause of PIND; 156 have been classified as meeting the surveillance case definition and are still under investigation; 47 did not strictly fulfil the study criteria for PIND and were not included; 16 have been classified as Idiopathic Non-CJD. No cases have been classified as definite nvCJD.

Of the remaining 183 notifications not yet discussed by the Expert Group: 62 are currently in the process of being followed-up (33 'no replies', 12 'to arrange interview or visit', nine 'awaiting further information', eight 'awaiting return of self-completed questionnaire'); 121 were not included for various reasons - ie. child too old for study, reported in error or duplicate report.

Important regional differences have been noted in the incidence of PIND cases. Yorkshire has notified the highest number of cases to date (96), and West Midlands the second highest (77)[2]. The reasons for this are now being investigated.

Sixty-three different conditions have been reported which are included in the 270 cases classified by the Expert Group as having a recognised cause of PIND (in other words, a definite diagnosis). These include the neuronal ceroid-lipofuscinoses (33 cases), MPSIIIA San Filippo (23 cases), GMI gangliosidosis (Tay Sachs) (15 cases), adrenoleukodystrophy (15 cases) and Niemann Pick Type C (14 cases).

Figure 13 *Current status*



Comments

PIND surveillance has been running for almost two years now and is planned to continue until at least April 2000. The median number of notifications per month between May 1997 and December 1998 is around 30, which is in line with our initial estimation of 350 cases per annum. There are interesting variations in reporting rates between paediatric centres. Although in general there has been an excellent response to the study, geographical analyses have revealed considerable under-reporting of patients in a few places.

The main aim of the study is to investigate whether or not children are developing new variant Creutzfeldt-Jakob disease (nvCJD), and, in the light of this, our most important finding to date is that no cases have been classified as definite nvCJD. However, the study is also producing unique national population-based data on the causes of PIND.

Surveillance for PIND is working satisfactorily, thanks to the active cooperation of UK paediatricians, and the investigators remain very grateful to all paediatricians for supporting this research and for sharing information about their patients.

Key points

- Surveillance of PIND through the BPSU has proved successful.
- A few centres seem not to be reporting fully.
- By the end of April 1999 489 cases had been reported and classified.
- Over 60 different conditions have been found that meet the case definition.
- To date (April 1999) no cases of new variant CJD have been diagnosed but surveillance and investigations are continuing.

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2 'Yorkshire' and 'West Midlands' are BPSU regions.

(first contact) Ms G Devereux, Research Nurse; Mrs L. Stellitano, Research Administrator, c/o Paediatric Administration Office, Box 45, Addenbrooke's NHS Trust, Hills Road, Cambridge, CB2 2QQ
Tel: 01223 216299 Fax: 01223 217253 Email: gilliandev@yahoo.com
Dr C Verity, Consultant Paediatric Neurologist (Principal Investigator), Addenbrooke's NHS Trust, Hills Road, Cambridge, CB2 2QQ
Tel: 01223 216662 Fax: 01223 242171
Dr A Nicoll, PHLS Communicable Disease Surveillance Centre, London, NW9 5EQ Tel: 0181 200 6868 Email: Anicoll@phls.co.uk
Dr R Will, The National Creutzfeldt-Jakob Disease Surveillance Unit, Western General Hospital, Edinburgh, EH4 2XU

Reye's syndrome

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 Surveillance Unit in June 1986 and from CDSC to the Department of Paediatrics at Sheffield in 1995. In the early years, the results of surveillance showed that the incidence of Reye's syndrome in the British Isles was similar to that in the USA but 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 study of risk factors mounted on to the surveillance database showed an association between Reye's syndrome and consumption of aspirin. In response to this and 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 under 12 years. Since then, products that contain aspirin have been required to carry warning labels.

There is increasing recognition that a number of inherited metabolic disorders - most notably those affecting fat oxidation and ureagenesis, may present as a 'Reye-like' illness, 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 and by 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-specifity 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; it has been granted a further one year extension to July 2000.

Analysis

Between August 1981 and July 1998 a total of 614 suspected cases of Reye's syndrome were reported to the surveillance unit (Table 18), but the diagnosis was subsequently revised in 156 (25%). Seventy-six (49%) of the revisions were to one of the 'Reye-like' inherited metabolic disorders. Two hundred and thirty-five (53%) of the total 444 cases compatible with a diagnosis of Reye's syndrome died.

In the year to July 1998, eleven reports of new cases were received and further information was provided on all of them. Three of the 11 diagnoses had subsequently been revised, leaving eight cases whose clinical and pathological features were compatible with the case definition of Reye's syndrome. All the cases were first reported via the BPSU. Death entries were subsequently received for all five of the cases of Reye's syndrome who died.

Cases compatible with a diagnosis of Reye's syndrome (N=8): year to July 1998

There were four males and four females; the ages ranged between 10 months and 13 years with a median of 4 years and 9 months. Six lived in England, one in Wales and one in Northern Ireland. Two were ill in August; five, between September and March; and one in June.

Only two children survived normal, outcome was unclear at the time of reporting in the other survivor. Among the five patients who succumbed, there were two sudden unexpected deaths (these children were aged four and a half years and 10 months) and in these cases the diagnosis was first made at post mortem. A third child who died had a pre-existing chronic neurodegenerative disorder of unknown cause, but was reported to have had the characteristic hepatic histological appearance of Reye's syndrome as well as the biochemical features. Two cases had had no pre-admission medications; four had received paracetamol, one, the patient with a neurological disorder, was on long term benzhexol; the eighth, a child aged 12 years seven months, had been given aspirin.

Seven of the eight patients had had a pre-encephalopathic viral-type prodrome - flu-like in three, gastroenteritis in three, and varicella in one. This last case was confirmed serologically and influenza A was isolated from on other patient; 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, although in two the reporting paediatrician referred only to those for medium chain acyl coA

dehydrogenase deficiency (MCADD). In two cases this information was unavailable; the other patient was not investigated. This was the 10 month old infant who had died suddenly and unexpectedly.

The 'Reye Score' (possible range 1-25) ranged between 11 and 16 with a mean and median of 13. The median compares with 12, 12, and 13 in the previous three years respectively. One patient, the child who had received aspirin, could not be scored because of missing information; however, she was described as a 'classic' case of Reye's syndrome associated with an influenza-like prodrome.

Revised diagnosis cases (N=3)

One patient was a two year old male who survived the encephalopathic episode and was subsequently found to have a carnitine transport defect. Another, a four year old boy, had two episodes of a Reye-like encephalopathy within a short interval; detailed investigations suggested the presence of a metabolic disorder, the precise nature of which is as yet undetermined. The third case was a 10 year old female with cerebral palsy associated with birth asphyxia. She developed an acute encephalopathy and Reye's syndrome was a provisional diagnosis made at autopsy, because of the histological changes in the liver. However, these were not typical of classical Reye's syndrome, no cerebral oedema was noted and hepatic transaminases were not raised antemortem, so although no obvious alternative diagnosis was reported, this case did not satisfy the criteria for inclusion.

Comment

The surveillance findings in 1997/98 were similar to those of the past five years - annual totals remain very low compared to those seen before 1986, the year when warnings about the association between aspirin and Reye's syndrome were first publicised by the Committee on Safety of Medicines. The trends also mirror those in the USA described earlier this year[2]. It appears that the trend is continuing into 1999 - by the end of June a total of only seven reports had been received. The diagnosis was subsequently revised in two of these and a further case was highly atypical.

As was the case last year, none of the 1997/98 patients, with one possible exception, could be described as having classical 'North American-type' Reye's syndrome[1]. This is reflected in the relatively low median 'Reye score'. That Reye's syndrome was the final diagnosis reflects the fact that no alternative was found and that the case definition is non-specific. The most likely alternative diagnosis is one of the 'Reye-like' inherited metabolic disorders, the detection of which may be extremely difficult. The design of our standard surveillance proforma, which is intended to be as short as possible for busy clinicians, means that we cannot determine the extent to which each patient is investigated in detail for inherited metabolic disorders. However, it is our impression from volunteered information that the tendency is toward simply ruling out the relatively common fat oxidation defect, MCADD. For the third year in succession

Table 18 *Reye's syndrome surveillance 1981/82 - 1997/98*

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	3	(2)	8	5
TOTAL	614	156	(76)	444	235

* *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

there was a case with a particularly high likelihood of having had an inherited metabolic disorder, who nethertheless was not investigated.

Although it is apparent that primary prevention of Reye's syndrome in children is continuing effectively, we reiterate our concern expressed last year, that aspirin-associated cases are continuing to occur in children over 12, the upper age limit on the warning. The one aspirin-associated case in 1997/98, a child who died, was over 12 as were two or three such cases reported to date in 1998/99 (they all survived). This brings the total aspirin-associated cases since the 1986 warning to 17, 10 of whom were over 12. In the USA series, 8% of cases were aged 15 and over and we suspect that we underascertain Reye's syndrome in this age group in the UK as they maybe admitted to adult intensive care units, where Reye's syndrome is unlikely to be as high on the agenda as it is in the paediatric setting.

We are most grateful to all the paediatricians who report cases and who provide further information.

Key points

- Children presenting with Reye-like encephalopathy may not always be receiving optimum investigation for inherited metabolic disorders:
- The age limit on the aspirin warning may need amending upwards.

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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Dr S M Hall Department of Paediatrics Sheffield Children's Hospital, Sheffield S10 2TH Tel: 0114 271 7344 Fax: 0114 755 364
Mr R Lynn BPSU, RCPCH, London W1N 6DE
Tel: 0171 307 5680 Fax: 0171 307 5690 E-mail: rlynn@rcpch.ac.uk

Subacute sclerosing panencephalitis

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 passive reporting was employed, 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 late. 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.

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) is analysed using the polymerase chain reaction and direct sequencing to detect and classify viral genome. Serum and CSF samples are also examined for evidence of intrathecal measles antibody production.

Case definition

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

1 raised measles antibody titres in the serum and CSF indicative of intrathecal antibody production and a higher level in the CSF compared to serum.
2 typical EEG changes.
3 typical brain histology or other evidence of measles virus in brain tissue.

a definitive case requires the presence of 1 and 2.

Cases identified as SSPE should also be reported to the PIND surveillance project see page 31.

Study duration

Continuation through the BPSU is reviewed on an annual basis and an application for extension until summer 2000 has been granted.

Recent results and progress

Within the last few years it has been repeatedly proposed that measles vaccination could either cause or precipitate SSPE. So far follow-up of the 1994 MR campaign, when millions of UK children received vaccinations with measles rubella (MR) combined vaccine, has revealed no evidence of an increase in cases. However, the best response to these concerns is to demonstrate that active surveillance is in place whereby any potential delayed effects may be detected and investigated in SSPE cases that do occur. Moreover, now that a genotyping system for the characterisation of measles virus strains has become established in the Enteric and Respiratory Virus Laboratory at Colindale (a WHO accredited Global Reference Laboratory for Measles), it is possible to distinguish between wild-type strains and between wild-type and vaccine strains. Hence, with an appropriate diagnostic specimen, not only can a causative strain be identified, but also the frequency of association with SSPE of particular strains be noted.

Clearly, the progress of this vital research depends on the availability of suitable fresh specimens, and so the complete and timely cooperation of clinicians with the Enteric and Respiratory Virus Laboratory at Colindale is of crucial. Since new cases now are very likely to have been vaccinated, either through the routine primary vaccination programme or during the 1994 MR mass school vaccination campaign, further investigations in current or any new SSPE cases will be able to evaluate/exclude the role of measles vaccine in the aetiology of SSPE.

Four new cases have been reported with onset in 1998, two from England, and one from Scotland and one from Northern Ireland. The ages at onset were 15 years, 11 years, six years and five years. All four have a history of probable measles infection and all four have also been vaccinated. Sequence analysis of the H-gene from one fresh frozen brain specimen detected a D-related genotype; genotype D being one of the currently predominant wild types of measles virus in the UK and throughout Europe. The vaccine-like strain (genotype A) was not detected. 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.

Key points

- Four new cases were reported in 1998.
- None of the four showed virological evidence of being vaccine-related.
- Wild virus not measles vaccine causes SSPE.

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Dr E Miller, Consultant Epidemiologist, PHLS Communicable Disease Surveillance Centre, 61, Colindale Avenue, London NW9 5EQ.
Tel: 0181 200-6868 Fax: 0181-200 7868 Email: emiller@phls.co.uk

Subdural haematoma/effusion (SDHE)

Background

SDHE is an important cause of death and neurological disability in childhood. Over half the cases of SDHE 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 proposed 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, Alagelle'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 SDHE 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 ocular fundi should be undertaken using both direct and indirect ophthalmoscopy through a dilated pupil and ideally by an ophthalmologist who frequently examines children.

Methods

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

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

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

NB. The child's initials only (with date of death & date of birth) are used to identify duplicate reports.

Case definition

Any child under two 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.

Study duration

Initial data collection from 1 April 1998 to 30 April 1999. Follow-up data collection from 6 months of date of diagnosis. Data collection should be completed by end 1999.

Results

To date over 150 questionnaires have been returned on 369 cases notified. The gender ratio is 2:1, boys: girls. The mean age is four months. The cases include 28 deaths, many from abusive head trauma. There are still a significant number of outstanding questionnaires to be returned. Follow-up questionnaires to establish short-term outcome continue to be sent out to reporting clinicians. The aetiology of the subdural haematoma or effusion was predominantly trauma - abusive, birth or occasionally accidental.

Other disease states accounted for the remainder although a significant number of cases were reported where the cause was stated to be unknown.

Call for continued response - The response to this study has in general been excellent. If anyone has not returned their questionnaire then do not feel embarrassed - it's always better late than never. Not all the cases are solved and we are short of post-mortem reports. Infants presenting with large heads are less often resolved diagnostically. Thank you also for the follow up information. Medico-legal cases take a long time and we may be missing important outcomes. If you do hear of any significant outcome then a brief note is very welcome.

Conclusions

The study is not yet complete and data is still being collected and analysed. The diagnosis of abusive head trauma remains difficult (Jenny et al 1999). This study should help to describe in more detail this diagnosis which is often missed or mis-diagnosed.

Key points

- Based on about 150 confirmed cases with data currently available which include 28 deaths:
- There is a male preponderance with a gender ratio of 2 boys to 1 girl. The mean age is four months.
- The aetiology of the subdural haematoma or effusion was predominantly trauma - abusive, birth or occasionally accidental. Other disease states accounted for the remainder although a significant number of cases were reported where the cause was stated to be unknown.

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Dr C Hobbs, Community Paediatrics, St James' University Hospital, Leeds LS9 7TF Tel: 0113 2064327 Fax: 0113 2064877
E-mail: cjhobbs@netcomuk.co.uk
Dr J Wynne, Dr J Livingston, Leeds General Infirmary, Belmont House, 3/5 Belmont Grove Leeds LS2 9NP Tel: 0113 2926106
Dr AM Childs, Dr A Seal, Leeds, General Infirmary Clarendon Wing, Leeds LS2 Tel: 0113 2432799

6 New studies for 1999

Severe visual impairment and blindness

Background

Knowledge of the incidence, mode of detection and causes of severe visual impairment and blindness is essential for developing and evaluating preventive strategies, for monitoring secular trends and for aetiological research. It is also important for provision and evaluation of health, educational and social services for children with isolated visual loss and those with other impairments. However, there is no reliable routine source of national information about severely visually impaired or blind children and there has been no recent national study of affected children. Thus the available information about severe visual loss in childhood in the UK remains limited in scope, completeness and generalisability[1,2]. A national study is proposed which should provide information that has previously not been available about the burden and impact of severe visual impairment and blindness in childhood.

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.

Methods

Active surveillance for all eligible cases (defined below) will be undertaken simultaneously but independently through the BPSU and the British Ophthalmological Surveillance Unit to ensure high ascertainment, particularly of children with multiple impairments. Information about each child will be sought from notifying paediatrician using questionnaires. This will include details of presentation or detection of visual loss, disorder(s) giving rise to visual loss and their underlying or associated cause(s), any non-ophthalmic disorders or impairments, and any assessment of special needs or provision of special services. All information should be available from the clinical records and no special investigations are sought. The child and family will not be contacted and measures in line with current guidelines will be taken to ensure confidentiality.

Case definition

It is intended to capture all children with impairment of vision which is sufficient to interfere significantly with development and/or have serious educational implications.

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[5]

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

Study duration

13 months from September 1999.

Geographic area

United Kingdom and Republic of Ireland

Ethical approval

Approved by the local research ethics committee at Great Ormond Street/Institute of Child Health.

Selected references

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Ms Jugnoo Rahi [1,2] (principal investigator), Ms Clare Gilbert [3], Miss Isabelle Russell Eggitt [1], Mr David Taylor [1] and Professor Catherine Peckham [2] on behalf of the Childhood Visual Impairment/Blindness Study Group
[1] Dept of Ophthalmology, Great Ormond Street Hospital, London
[2] Dept of Epidemiology and Public Health, Institute of Child Health, London WC1N 1EH
[3] Dept of Preventive Ophthalmology, Institute of Ophthalmology, London
Tel: 0171-905-2250 Fax: 0171-242-2723 email j.rahi@ich.ucl.ac.uk

7 Past studies re-visited

Pyridoxine dependency

Background

Pyridoxine dependency is a rare, but treatable, recessively inherited cause of seizures starting in early childhood. Since its description in 1954 less than 50 definite cases have been described in the published literature, all in case reports or small hospital based series. No large scale or population based study has ever been reported and the incidence and prevalence of the condition are essentially unknown.

Objectives

The aims of this study, whose surveillance covered the period October 1995 - October 1997, were to:

a) determine the prevalence of definite or possible pyridoxine dependent seizures in children under 16 years of age,
b) to prospectively study the incidence in children under 5 years of age, and to define the clinical presentation, natural history, and clinical management of pyridoxine dependency.

Results

1 Notifications. Cases born during the study period continued through 1998 to be notified to the investigator, Dr P Baxter. Some cases were redefined into different categories. Amended and updated epidemiological data, which can be used for public health purposes, have now been submitted for publication. Result details are also available in the 12th Annual Report of the BPSU.

2 Including all sources and ages, 14 definite, nine probable and ten possible cases were notified. The point prevalence of definate and probable cases in children less than 16 years of age at the end of the study was 1:687,000 and the birth incidence 1:783,000. With the inclusion of possible cases these become 1:441,000 and 1:313,000 respectively. When all forms of pyridoxine responsive seizures are included the prevalence becomes 1:317,000 and the birth incidence 1:157,000.

3 Analysis of the clinical data is still underway but the main messages for clinical management are the high percentage of children with atypical presentations and the number of neonates presenting with features of birth asphyxia/hypoxic-ischaemic encephalopathy. Both of these could result in underdiagnosis.

4 Pyridoxine is an effective anticonvulsant in a small group of neonates and young children without pyridoxine dependency, including some with infantile spasms.

Key findings

- There was an increased incidence of diagnoses during the study. This suggests that there is an indirect effect of the BPSU on paediatric practice even while surveillance is in progress.
- **Notifications:** Sixty-three percent of all notifications were made via the BPSU, 20% directly and 17% were children seen personally. For those with pyridoxine dependency, the figures are 49%, 27% and 24%. Some of the late direct notifications were made when the child came into contact with another consultant.
- **Geographical variation:** There was a marked lack of patients from Greater London and the West Midlands: most of those notified did not come through the BPSU itself. When analysed by current NHS regional populations, one entire region had no cases, which remains unexplained but suggests that some paediatricians do not notify cases to the BPSU. Encouraging paediatricians to participate remains essential to the success of the BPSU.

Future

Collaboration has begun with a project to identify the gene responsible for pyridoxine dependency. Linkage studies support previous reports excluding the favoured candidate gene, glutamic acid decarboxylase. A new linkage is being explored. Definition of the gene will allow better diagnostic precision and further understanding of mechanisms behind epilepsy.

A pilot study of the optimal dose of pyridoxine in terms of IQ has been completed and it is hoped to extend this to patients in a national study.

Dr Peter Baxter, Ryegate Children's Centre, Sheffield Children's Hospital S10 2TH Tel: 0114 267 0237 Fax: 0114 267 8296
E-mail: p.baxter@sheffield.ac.uk

8 The international perspective

Background

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, through the Public Health Laboratory Service, Institute of Child Health (London), the RCPCH and the Faculty of Paediatrics Royal College of Physicians Ireland initiated the British Paediatric Surveillance Unit (BPSU) in 1986. 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). Interest in developing similar units has also been shown in Portugal, Belgium and the Czech Republic. Wales (1995) and Republic of Ireland (1997) developed surveillance units using a similar methodology to the BPSU, though they are concentrating on less rare disorders.

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

The director of the Australian unit has met 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 has come to formalise these links into a network. In 1996 the proposal to form an International Network of Paediatric Surveillance Units (INoPSU) within and outside Europe 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. A pre-circulated document detailing the functions and structure of the network was agreed at that meeting. It was also agreed that the British Paediatric Surveillance Unit would, in the first instance, act as the server for such a network.

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:

- 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.

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).

In order to carry out the aims and direct the activities of INoPSU a secretariat has been set up. This consists of representatives from UK, Netherlands, Canada, and Australia.

One of the first activities of this new network is to set up a website <www.inopsu.org> and this is expected to be active by September 1999. Two meetings have been arranged to allow discussion on methodologies and work underway, these will be held in Edinburgh, Scotland (5 Nov 1999) and in Ottawa, Canada (15 June 2000).

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 894 clinicians in child health on a monthly basis, covering a child population of 2 million[1]. The overall response rate was 96% in 1998. APSU introduced email reporting in 1997 and currently more than 15% of clinicians have elected to use this service. A recent survey identified that a further 22% clinicians who now wish to report by e-mail. Workload for the individual clinician was generally low for 1997 with 15% of clinicians reporting one case, 7% reporting between two and three cases and less than 2% reporting four or more cases. Seventy-six percent clinicians did not report a case of any condition under surveillance and hence were not required to complete a questionnaire.

Twelve conditions, including a number of infectious and vaccine-preventable diseases were surveyed in 1998. New studies for 1998 included idiopathic and congenital nephrotic syndrome, invasive *H. influenzae* infection and Prader-Willi syndrome. Continuing studies include congenital rubella, vitamin K deficiency bleeding (inc. haemorrhagic disease of the newborn), HIV/AIDS (including perinatal exposure for HIV), neonatal herpes simplex virus infection, primary immunodeficiency disorders (inc. severe combined immunodeficiency), Hirschsprung disease, haemolytic uraemic syndrome, acute flaccid paralysis. Studies of arthrogryposis multiplex congenita and subacute sclerosis panencephalitis were completed in 1998. Congenital cytomegalovirus infection commenced in 1999.

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 is currently establishing a web-site that will be linked to the INoPSU web-site.

1 Williams K, Elliott E. Role of the Australian Paediatric Surveillance Unit in monitoring communicable diseases in childhood. CDI 1998; **22(13)**: 283-287

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

Contacts

Dr Elizabeth Elliott (Director), Dr Katrina Williams (Assistant. Director), Dr Greta Ridley (Scientific Officer), Ms Diana Redmond (Research Assistant), Ms Gabrielle Williams (Administrator), and Ms Jennifer Fowler (Administrator) APSU, New Children's Hospital, PO Box 3315, Parramatta, NSW 2124 Australia. Tel: ++61 2 9845 3005/2200, Fax: ++61 2 9845 3082. E-mail: apsu@nch.edu.au

Canadian Paediatric Surveillance Programme (CPSP)

Under the auspices of the Canadian Paediatric Society and funded by the Laboratory Centre for Disease Control (LCDC), the CPSP was established in January 1996. Beginning with three conditions in the pilot year of the program, the CPSP increased surveillance in 1997 and 1998 to include six studies: acute flaccid paralysis (AFP), congenital rubella syndrome (CRS), Creutzfeldt-Jakob disease (CJD), hemorrhagic disease of the newborn (HDNB), neural tube defects (NTD) and subacute sclerosing panencephalitis (SSPE). The NTD study concluded in December 1998.

Response rates over the past few years have increased steadily towards the goal of 90%. With more than 2100 paediatricians enrolled in the program, making the CPSP the largest paediatric surveillance unit in the world, the initial response rate continued to climb from 82% in 1997, to 86% in 1998. In addition, detailed reporting forms were received for 93% of the 258 cases reported in 1998.

There was an overwhelming response last summer to the CPSP Steering Committee's *Call for New Studies*. Protocols for six exciting new studies, including anaphylaxis, cerebral oedema in diabetic ketoacidosis, idiopathic interstitial lung disease, perinatal hemochromatosis, pyridoxine dependent status epilepticus and vitamin D-deficiency rickets, were approved by the committee and will commence once organizational arrangements and funding are in place. To act as a control for one of the British Paediatric Surveillance Unit studies, the CPSP agreed to expand the CJD study, late in the spring of 1999, to include cases of progressive, intellectual and neurological deterioration (PIND).

Contacts

Ms Jo-Anne Doherty, MSc, A/Chief, Division of Disease Surveillance, Bureau of Infectious Diseases, Laboratory Centre for Disease Control, Health Canada, Tunney's Pasture, 0603E1 Ottawa ON K1A 0L2 Tel: ++613 946 2328 Fax: ++613 998 6413 E-mail: jo-anne_doherty@hc-sc.gc.ca

Dr. Richard Stanwick, Chair, CPSP Steering Committee, Canadian Paediatric Society, 100-2204 Walkley Rd, Ottawa ON K1G 4G8 Tel: ++ 613 526 9397 Fax: ++613 526 3332 E-mail: cpsp@cps.ca

German Paediatric Surveillance Unit (ESPED)

Encouraged by the success of the BPSU, a German adaptation of the surveillance scheme called the ESPED was initiated in July 1992 to cover the country which has one of the largest child populations of any of the units (around 12 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 1998, 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. In 1998 the conditions under surveillance were: fatal and near fatal asthma; 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 neonatal infections due to fungi (candida); aseptic meningitis following MMR vaccination and haemolytic uraemic syndrome. In 1999 it is planned to add surveillance for transient myeloproliferative syndrome in newborns with Down syndrome; organoacidopathia and fatty acid oxidation defects, glucose transporter defect (GLUT1).

Contacts

Professor R Von Kries, Institute for Social Paediatrics and Adolescent Medicine, Ludwig-Maximilians University Munich, Germany
Tel: 89 71009 314 Fax: 89 71005 315 E-mail: ag.epi@lrz.uni-muenchen.de
Beate Heinrich, ESPED Office, Universitats-Kinderklinik, Moorenstrasse 5, 40225 Duesseldorf, Germany E-mail: heinrich@med.uni-duesseldorf.de

Latvian Paediatric Surveillance Unit

The Latvian paediatric surveillance system began in 1997. Though currently not using a card mailing system all rare disease are reported to the Children's Hospital in Riga. In 1997 there have been two cases of congenital hypothyroidism, one nesidioblastosis, salt losing congenital adrenal hyperplasia, 38 primary diabetes (type 1), 17 cases of luekaemia (myeloleucosis-three), 16 cases of coeliac disease (primary diagnosed) in the age group one to 16 years and one Reye's syndrome.

For 1998, 6 cases of cystic fibrosis, 12 leukaemia (myeloblastic 4, lymphoblastic 8), 1 case of ulcerative colitis, 3 cases of herpes progenitalis, 2 cases of HIV/AIDS and 3 of Hodgkins disease.

Contact

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

Malaysian Paediatric Surveillance Unit (MPSU)

The MPSU was established in December 1993 and surveillance began in September 1994 under the auspices of the Malaysian Paediatric Association. It covers all of Malaysia with a child population of 7.6 million. The Unit has adopted the classical BPSU methodology with cards being circulated to around 340 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. During 1998 surveillance for Duchenne muscular dystrophy commenced.

Contact

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

Netherlands Paediatric Surveillance Unit (NSCK)

The Dutch Paediatric Surveillance Unit started surveillance in October 1992. Around 380 paediatricians in general hospitals receive the monthly card. The child population is 2.8 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 has risen from 83% in 1992 to 91% in 1998. The follow-up rate is also high at over 93%. In 1997, 18% of the clinicians reported one case, 11% reported 2 cases, 40% reported 3 or more cases while 32% 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.

In 1998 the conditions under surveillance were: acute flaccid paralysis (26 reports), coeliac disease (229 reports), insulin dependent diabetes mellitus (431 reports), group B streptococcal infections (299 reports), HIV/AIDS (37 reports), neural tube defects (84 reports), venous thromboembolic complications (55 reports), hospital admissions due to pertussis (56 reports), congenital adrenal hyperplasia (45 reports) and hospital admissions due to rotavirus infections (1028 reports).

In 1999 surveillance for inflammatory bowel disease was added.

Contact

Professor S P Vanloove-Vanhorick, Dr. R.A. Hirasing, TNO Prevention and Health, Postbus 2215, 2301 CE Leiden, Netherlands, Tel.: ++ 31 71 518 16 53 Fax:++ 31 71 518 19 20 E-mail: RA.hirasing@pg.tno.nl

New Zealand Paediatric Surveillance Unit (NZPSU)

The NZPSU, established in 1997, is co-directed by Professor Barry Taylor and Dr Nigel Dickson and receives financial support from the New Zealand Ministry for Health. Covering a child population of 0.8 million, each month over 160 clinicians are circulated with a surveillance card. The response rate is excellent at 96%. Nine studies are currently being surveyed. These are acute flaccid paralysis, congenital rubella, perinatal HIV exposure, neonatal herpes simplex infection, haemolytic uraemic syndrome, vitamin K deficiency bleeding, subdural haemorrhage, retinopathy of prematurity and diabetes mellitus under the age of 10.

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. In 1999, NZPSU added studies initiated by New Zealand clinicians. It is hoped that more New Zealand-initiated studies can be introduced in the future.

Contact

Professor B Taylor, Dr N Dickson, Ms N Dow, University of Otago, Dept of Paediatrics and Child Health, Dunedin School of Medicine, PO Box 913, Dunedin, New Zealand
Tel: 03 474 7825 Fax: 03 474 7817 E-mail: nzpsur@gandolf.otago.ac.nz

Switzerland 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 hospital or clinic-based paediatricians (ie. not to those delivering primary care). There are approximately 500 respondents in 41 clinics, covering a total child population of 1.3 million children. The most recent response rate was 98%. The five conditions under surveillance in 1998 were: acute flaccid paralysis, congenital rubella syndrome, congenital toxoplasmosis, haemolytic uraemic syndrome and haemorrhagic disease of the newborn. The study on cystic periventricular leukomalacia has been completed in December 1997. The study on congenital toxoplasmosis ended December 1998.

Contact

Dr. H.P. Zimmermann, Swiss Paediatric Surveillance Unit, Swiss Federal Office of Public Health, 3003 Bern, Switzerland Tel: ++4131 323 8710 Fax: ++4131 323 8795 E-mail: hans-peter.zimmermann@bag.admin.ch

Welsh Paediatric Surveillance Unit

Set up in 1995 to monitor less rare disorders seen in Wales. The WPSU covers a population of 0.65 million. Over 130 respondents are sent a monthly mailing with a respondent rate of over 91%.

Disorders currently being surveyed include congenital adrenal hyperplasia, childhood tuberculosis, Marfan's syndrome, children in housefires, newly diagnosed diabetes and newly diagnosed malignant disease.

The WPSU will be liaising with the BPSU in order that disease surveillance is not duplicated. The unit will be concentrating on more common disorders in children.

Contact

Dr John Morgan, Children's centre, East Glamorgan Hospital, Church Village, Pontypridd, Mid Glamorgan. CF38 1AB Tel: 01443 216211 Fax: 01443 217775
Professor J Sibert, Dept of Child Heath, Llandough Hospital, Penarth, South Glamorgan CF64 2XX. Tel: 01222 716906 Fax: 01222 350140

Table 19 National paediatric surveillance units status circa end 1998

Country	Child population (10^6 - aged 0-15 years)	Established	Respondents	Reply paid	Response rate *(E-mail reporting)	Fee for study
Australia	2	1992	928	Yes*	93%	No
UK/Rep of Ireland	12.8	1986	1925	No	92%	Yes
Canada	6.0	1996	2125	Yes	86%	No
Germany	11.0	1992	496**	No	95%	Yes
Latvia	0.5	1996	7	No	n/a	No
Malaysia	7.6	1994	340	Yes	75%	No
Netherlands	2.8	1992	416	Yes	92%	Yes
Papua New Guinea	1.8	1996	40	Yes	73%	No
New Zealand	0.8	1997	163	Yes	96%	No
Switzerland	1.2	1995	41**	Yes	98%	No
Wales	0.65	1995	134	No	91%	No

** Heads of paediatric centres

Table 20 Conditions currently under surveillance by national paediatric surveillance units in 1998

Condition	Unit performing surveillance	
	Current studies	*Specimens requested*
Acute flaccid paralysis (AFP)	*APSU, CPSP, NSCK, NZPSU, PNGPSU, SPSU*	*APSU, CPSP, NZPSU, PNGPSU, SPSU*
Aseptic meningitis following MMR-vaccination	*ESPED*	
Chronic inflammatory bowel disease[†]	*BPSU*	
Coeliac disease (CD)	*LPSU, NSCK*	*LPSU*
Congenital adrenal hyperplasia (CAH)	*NSCK*	
Congenital brachial palsy	*BPSU*	
Congenital heart disease	*MPSU*	
Congenital hypothyroidism	*PNGPSU*	
Congenital rubella	*APSU, BPSU, CPSP, NZPSU, SPSU*	*CPSP, SPSU*
Cystic fibrosis	*LPSU*	
Duchenne muscular dystrophy	*MPSU*	
Encephalitis (3-36 months)	*BPSU*	*BPSU*
Fatal/near fatal asthma	*MPSU*	
Group B streptoccal infection	*NSCK*	
Haemolytic uraemic syndrome (HUS)	*APSU, BPSU*, ESPED, NZPSU, SPSU*	*APSU, BPSU, NZPSU*
Haemorrhagic disease of the newborn (inc. vit K deficiency bleeding)	*APSU, CPSP, ESPED, NZPSU, SPSU*	*CPSP, SPSU*
Hirschsprung disease	*APSU*	
HIV/AIDS	*APSU, BPSU, LPSU, MPSU, NSCK, PNGPSU*	*BPSU, LPSU*
Hospitalised pertussis	*ESPED, NSCK*	
Idiopathic thrombocytopenia (ITP)	*ESPED*	
Insulin-dependent diabetes mellitus	*ESPED, LPSU, NSCK, PNGPSU*	*LPSU*
Invasive *Haemophilus influenzae* infection	*APSU, BPSU, ESPED*	*APSU, BPSU*
Ischaemic stroke in infants	*ESPED*	
Leukaemia	*LPSU*	*LPSU*
Lues congenita	*LPSU*	*LPSU*
Multiple sclerosis in infants	*ESPED*	
Neonatal fungal septicaemia	*ESPED*	
Neonatal herpes simplex virus infection (HSV)	*APSU, NZPSU*	
Neonatal meningitis	*MPSU*	
Neural tube defects	*CPSP, NSCK*	*CPSP*
Neurological endemic cretinism	*PNGPSU*	
Organic and fatty acid oxidation defects	*ESPED*	
Paediatric malignancies [‡]	*PNGPSU*	
Pneumoccoccal sepsis/meningitis	*ESPED*	*ESPED*
Prader Willi syndrome	*APSU*	
Primary immunodeficiency disorders (PID)[§]	*APSU*	
Progredient subacute neurologic diseases	*LPSU*	*LPSU*
Progressive intellectual and neurological deterioration (PIND), including CJD	*BPSU, CPSP*	*CPSP*
Renal tubular acidosis	*PNGPSU*	
Reye's syndrome	*BPSU*	
Rotavirus infection	*NSCK*	
Severe combined immunodeficiency (SCID)	*APSU*	
Subacute sclerosing panencephalitis (SSPE)	*APSU, BPSU, CPSP, PNGPSU*	*CPSP, PNGPSU*
Subdural haematoma/effusion (<2years)	*BPSU*	
Transient myeloproliferative syndrome in new-borns with Down syndrome	*ESPED*	
Venous thromboembolic complaints	*NSCK*	

**Previously studied by the BPSU in 1986-9. † ulcerative colitis, Crohn's disease and intermediate colitis. ‡Wilm's tumour, Burkitt's lymphoma, leukaemia, neuroblastoma, lymphoma (non-Burkitt's), other. § Predominantly antibody defects (eg X-linked agammaglobulinaemia, IgA deficiency, IgG subclass deficiency); Combined immunodeficiencies (eg severe combined immunodeficiency, common variable immunodeficiency); Immunodeficiencies with other major defects (eg Wiscott-Aldrich syndrome, Di George syndrome, ataxia telangiectasia); Complement deficiencies, including C1 esterase inhibitor deficiency (eg hereditary angioneurotic oedema); Defects of phagocytic function (eg chronic granulomatous disease, leukocyte-adhesion deficiency, Schwachman's syndrome); other.*

Appendix A Completed studies prior to 1998

By mid 1998 the British Paediatric Surveillance Unit had completed thirty-four studies. Information about these studies has been included in previous annual reports of the BPSU, which are available from the BPSU office. The studies and their principal investigators are listed below. For addresses see the list at the end of this report.

1. **X-linked anhydrotic ectodermal dysplasia**
(June 1986 – August 1986)
Dr A Clarke

2. **Lowe syndrome**
(June 1986 – February 1988)
Dr C McKeown

3. **Insulin dependent diabetes in under 15s**
(January 1988 – December 1988)
Professor J D Baum

4. **Drowning and near drowning**
(January 1988 – December 1989)
Professor J Sibert

5. **Higher order births**
(January 1989 – December 1989)
Professor M Levene

6. **Haemorrhagic disease of the newborn**
(March 1988 – February 1990)
Dr A W McNinch, Dr H Tripp

7. **Haemorrhagic shock encephalopathy syndrome**
(June 1986 – December 1988)
Dr S Hall

8. **Haemolytic uraemic syndrome**
(June 1986 – December 1989)
Dr S Hall

9. **Neonatal herpes**
(June 1986 – Dec 1991)
Ms P A Tookey, Professor C S Peckham, Dr R Dinwiddie

10. **Kawasaki disease**
(June 1986 – December 1992)
Dr S Hall

11. **Galactosaemia**
(January 1988 – September 1991)
Mrs A Green, Dr J Holton, Dr M Honeyman, Professor J Leonard

12. **Congenital toxoplasmosis**
(June 1989 – May 1990)
Dr S Hall

13. **Acute rheumatic fever**
(January 1990 – December 1990)
Dr C Boyd-Scobie, Dr S Hall

14. **Rett syndrome**
(April 1990 – June 1990)
Dr A Kerr

15. **Measles, mumps, rubella/meningococcal meningitis**
(January 1990 – December 1991)
Dr N Begg

16. **Chemistry set poisoning**
(January 1991 – April 1992)
Dr E Mucklow

17. **Androgen insensitivity syndrome**
(September 1991 – August 1993)
Professor I A Hughes

18. **Acute flaccid paralysis**
(July 1991 - June 1994)
Dr N Begg

19. **Long term parenteral nutrition**
(February 1992 – April 1992)
Professor D Candy, Professor E Ross, Dr S Devane

20. **Insulin dependent diabetes**
(January 1992 – December 1992)
Professor J D Baum, Ms E Wadsworth

21. **Juvenile dermatomyositis**
(June 1992 – December 1993)
Dr D Symmons, Dr A Sills

22. **Congenital dislocation of the hip**
(April 1993 – July 1993)
Dr C Dezateux, Dr S Godward

23. **Haemophagocytic lymphohistiocytosis**
(September 1991 - August 1994)
Professor S Strobel, Dr J Pritchard, Dr M Leyton

24. **Non-accidental poisoning/Munchausen Syndrome by proxy**
(September 1992 - August 1994)
Dr P Davis, Professor J Sibert, Professor S R Meadow

25. **Neonatal necrotising enterocolitis**
(October 1993 - October 1994)
Professor A Lucas, Ms R Abbott

26. **Vitamin K deficiency bleeding**
(January 1993 - December 1994)
Dr A McNinch, Dr J Tripp

27. **Biliary atresia**
(March 1993 - February 1995)
Dr J P McKiernan, Dr D Kelly

28. **Congenital syphilis**
(July 1993 - July 1996)
Dr T Lissauer, Dr A Nicoll

29. **Medium chain acyl-CoA dehydrogenase**
(March 1994 - March 1996)
Dr J Pollitt, Professor J V Leonard

30. **Transient and permanent neonatal diabetes**
(July 1994 - August 1995)
Dr J Shield, Professor J D Baum

31. **Adverse neonatal outcomes of delivery or labour in water**
(April 1994 - April 1996)
Ms P Tookey, Dr R Gilbert

32. **Congenital cataract**
(October 1995 - October 1996)
Ms J Rahi

33. **Pyridoxine dependent seizures**
(October 1995 - October 1997)
Dr P Baxter

34. **Neonatal meningitis**
(July 1996 - December 1997)
Dr D Holt, Mrs S Halket

Appendix B Published papers 1998-1999

The British Paediatric Surveillance Unit - a pioneering method for investigating the less common disorders of childhood. Report of a seminar held in June 1995: Hall SM, Nicoll A. Child: Care, Health and Development 1998; **24**: 2: 129-143

Epidemiology and detection of HIV-1 among pregnant women in the United Kingdom: results from national surveillance 1988-96: Nicoll A, McGarrigle C, Brady AR, Tookey P, et al. BMJ 1998; **316**: 253-258

Intercollegiate Working Party for Enhancing Voluntary Confidential HIV Testing in Pregnancy (Royal Colleges of General Practitioners, Midwives, Nursing, Obstetricians & Gynaecologists, Pathologists, Paediatrics & Child Health and Physicians; Public Health Laboratory Service; Faculty of Public Health Medicine, Directorates of Public Health for North & South Thames). Reducing mother to child transmission of HIV infection in the United Kingdom. Royal College of Paediatrics and Child Health 1998.

Factors affecting uptake of antenatal HIV testing in London: results of a multicentre study. Gibb DM, MacDonagh SE, Ramyani G, Tookey P, Peckham CS, Ades AE. BMJ 1998; **316**: 259-61

Procedures, placement, and risks of further abuse after Munchausen syndrome by proxy, non-accidental poisoning, and non-accidental suffocation: Davis P, McClure RJ, Rolfe K, Chessman N, Pearson S, Sibert JR, Meadow R. Arch. Dis. Child. 1998; **78**: 217-221

Prospective surveillance study of medium chain acyl-CoA dehydrogenase deficiency in the UK: Pollitt RJ, Leonard JV. Arch. Dis. Child. 1998; **79**: 116-119

Plans for future influenza pandemics must raise awareness of Reye's Syndrome. Hall SM, Lynn R. BMJ 1998; **317**: 284

Bedford H, et al. Autism, inflammatory bowel disease and MMR vaccine (Letter). Lancet 1998; **351**: 907

Advice from CMO/CNO: McNinch AW, Tripp JH. DoH 1998

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

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

Falling HIV vertical transmission rates in the British Isles: Estimates based on surveillance data. Doung T, Ades AE, Gibbs DM, Tookey PA, Masters J. BMJ - in press 1999

The disappearance of Reye's syndrome - A public health triumph. Letter of response. Hall SM, Lynn R. New. Eng. Journ. Med - in press 1999

Appendix C Recent presentations

2nd RCPCH Annual Scientific Meeting 1998

Patterns of presentation of children with congenital/infantile cataract in Britain.
Rahi JS, British Congenital Cataract Interest Group.

National surveillance of paediatric hepatitis C.
Neave PE, Tookey PA, Gibb DM.

Pyridoxine dependent seizures in the UK: the BPSU Study.
Baxter P.

Malignancies occurring in children with vertically acquired HIV infection in the UK.
Evans JA, Holland, FJ; Tynan, DG; Novelli, V; Sharland, M; Berry, T; Tookey, PA; Gibb, DM.

3rd RCPCH Annual Scientific Meeting 1999

Impact of the BPSU on clinical practice.
Verity C.

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

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

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

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.

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

Conferences

Congenital rubella births: changing patterns in Britain.
EUROCAT-ICBDMS, Copenhagen, Denmark, 1998.
Tookey PA, Peckham CS.

Report of the BPSU PIND survey.
British Paediatric Neurology Association, Belfast, N Ireland 1998.
Verity C.

Surveillance of congenital rubella in Britain.
British Isles Network of Congenital Anomaly Registers (BINOCAR), Liverpool 1998.
Tookey PA.

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

Interim results of the British Paediatric Surveillance Unit 1998/9 survey on the incidence of inflammatory bowel disease.
European Society for Paediatric Gastroenterology and Nutrition, Warsaw, Poland 1999.
Sawczenko A, Sandhu B.

Appendix D Support groups and contacts

Anaphylaxis

The Anaphylaxis Campaign, PO Box 149, Fleet GU13

Congenital Rubella

SENSE (Deaf/Blind Rubella Handicaps) 31 Grays Inn Road, London WC1X 8PT

Crohn's Disease and Ulcerative Colitis

Mrs Margaret Lee, Crohn's in Childhood Research Association, Parkgate House, 356 West Barnes Lane, Motspur Park, New Maiden KT3 6NB

Encephalitis Effects

Encephalitis Support Group, Pasture House, Normanby, Sinnington, York YO6 6RH

Erb's Palsy

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

Haemolytic Uraemic Syndrome

HUSH, PO Box 1303, Sheffield S6 6LY

HIV/AIDS

Barnardos Positive Orphans, Unit 22, Angel Gate, City Road, London EC1V 2PT

Positively Women, 347-349 City Road, London EC1V 1LR

Meningitis

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

Meningitis Research Foundation, 13 High Street, Thornbury, Bristol BS35 2BS

Reye's Syndrome

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

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: 0207 383 3555

Useful web-site addresses

Communicable Disease Surveillance Centre of the Public Health Laboratory Service
http://www.open.gov.uk/cdsc/

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

Office of National Statistics
http://www.emap.com/ons97/

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 R Bartlett, Director, PHLS, Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ

Professor J D Baum, Institute of Child Health, Royal Hospital for Sick Children, St Michael's Hill, Bristol BS2 8BJ

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

Dr N Begg, PHLS Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ

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

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

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 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

Dr D Dunger, Department of Paediatrics, John Radcliffe Hospital, Headington, Oxford OX3 9DU

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

Mrs A Green, The Child and Family Centre, 142 Maas Road, Northfield, Birmingham B31 2PR

Dr S Hall, c/o Storrs House Farm, Storrs Lane, Sheffield, South Yorkshire S6 6GY

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

Dr P Heath, St Geroge's Hospital, London SW17

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

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

Dr D Holt, Karim Centre for Meningitis Research, Queen Charlotte's & Chelsea Hospital, Goldhawk Road, London W6 0XG

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

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

Dr T Lissauer, Department of Child Health, St Mary's Hospital, London W2 1NY

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

R Lynn, Scientific Coordinator, British Paediatric Surveillance Unit, Royal College of Paediatrics and Child Health, 50 Hallam Street London W1N 6DE

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

Dr R MacFaul, Paediatric & Child Health Services, Room 514 NHSE HQ, Dept of Health, Wellington House, 133-155 Waterloo Road, London SE1 8NG

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

Dr D V Milford, Birmingham Children's Hospital NHS Trust, Laboratory of Enteric Pathogens, Steelhouse Lane, B'ham B4 6NH

Dr E Miller, PHLS Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ

Dr A M Mott, Royal Hospital for Sick Children, St Michael's Hill, Bristol BS2 8BJ

Professor R Moxon, National Haemophilus Reference Laboratory, John Radcliffe Hospital, Oxford OX3 9DU

Dr E Mucklow, Keep Cottage, 5 Castle Lane, Carisbrooke, Isle of Wight PO30 1PH

Dr A Nicoll, PHLS, Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ

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 & Public Health, 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 Interactive, 18 Marcham Road, Abingdon, Oxfordshire OX14 1AA

Dr J Rahi, c/o Dept of Epidemiology & Public Health, Institute of Child Health, 30 Guilford Street, London WC1N 1EH

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

Professor C Roberts, Deputy Director, Public Health Laboratory Service, Headquarters, 61 Colindale Avenue, London NW9 5EQ

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 Gynaecologists, 27 Sussex Place, Regent's Park, London NW1 4RG

Royal College of Paediatrics and Child Health, 50 Hallam Street London W1N 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

Dr M Slack, National Haemophilus Reference Laboratory, John Radcliffe Hospital, Oxford OX3 9DU

Professor S Strobel, Institute of Child Health, 30 Guilford Street, London WC1N 1EH

Dr D P M Symmons, ARC Epidemiology Research Unit, Stopford Building, University of Manchester, Oxford Road, Manchester

Dr C M Taylor, Birmingham Children's Hospital NHS Trust, Laboratory of Enteric Pathogens, Ladywood Middleway, Birmingham B16 8ET

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

Ms P Tookey, Dept of Paediatric Epidemiology, Institute of Child Health, 30 Guilford Street, London WC1N 1EH

Dr P Verloove-Vanhorick, TNO Prevention and Health, P O Box 2215,2301 CE Leiden, Netherlands

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

Dr R Von Kries, Institute fur Social Paediatrie und Jugendmedizin der Ludwig-Maximimillian Universitat Munchen, Germany

Ms E Wadsworth, Institute of Child Health, Royal Hospital for Sick Children, St Michael's Hill, Bristol BS2 8BJ

Dr R Will, The National Creutzfeldt-Jakob Disease Surveillance Unit, Western General Hospital, Edinburgh

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

Dr J Wynne, Belmont House, Clarendon Wing, Leeds General Infirmary, 3-5 Belmont Grove, Leeds, West Yorkshire LS2 9NS

Dr H P Zimmerman, Swiss Paediatric Surveillance Unit, Federal Office of Public Health, Division for Epidemiology and Infectious Disease, CH-3003 Bern, Switzerland