Royal College of Paediatrics and Child Health
British Paediatric Surveillance Unit

16th Annual Report 2001-2002

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British Paediatric Surveillance Unit – Annual Report 2001-2002

Compiled and edited by Richard Lynn, Hilary Kirkbride, Mike Preece, and Jugnoo Rahi, September 2002

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Dr Simon Lenton	Department of Health (observer)

* retired in 2001

** Retired April 2001

September 2001

++ April 2001

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Foreword

This is my first Foreword for the Annual Report and the past year has seen a number of changes and innovations. Chris Verity has stepped down as Chairman and I succeeded him last November. Already I have discovered what a hard act he is to follow. The past five years under his Chairmanship has been a particularly successful period for the BPSU, but they have also seen a number of significant challenges. I will discuss some of the more notable issues later.

A number of other stalwarts have also left the Executive Committee. Richard Cooke has come to the end of his term as Vice-President (Research) and is succeeded by Neil MacIntosh. I thank Richard for his support in past years. Ian Jones, who represented the Scottish Centre for Infection and Environmental Health (SCIEH), Rodderick MacFaul from the Department of Health (DH), Peter Kearney representing the Royal College of Physicians of Ireland (RCPI), Angus Clarke, Chris Kelnar, and Brent Taylor all leave the committee and deserve thanks for their support over the years. Their places have been taken by Clare Bramley from SCIEH, Simon Lenton from DH, Denis Gill for the RCPI, Martin Richardson, William McGuire, and Allan Colver; to them all, welcome.

In April the BPSU successfully hosted the second International Network of Paediatric Surveillance Units (INoPSU) conference, held over two days at York University, in conjunction with the Annual Scientific meeting of the College. The first day brought together 20 representatives from 12 of the 14 national surveillance units. Dr Chris Verity, Richard Lynn and I represented the UK. Countries represented at the meeting were Germany, Netherlands, Australia, New Zealand, Republic of Ireland, Wales, Switzerland, Canada, Malaysia, Portugal and Greece. The aims of INoPSU are to facilitate communication between existing units; encourage the sharing of information between researchers and to assist in the development of new units. With the final aim in mind the Portuguese and Irish Paediatric Surveillance Units were accepted as full INoPSU members whilst the Greece/Cyprus Unit was accepted as an affiliate until such time as it has fulfilled the requirements for entry. Topics discussed included funding problems, the difficulties with data collection and handling and the need for multi-national rare disease surveillance.

A series of lectures on the second day demonstrated the work of the INoPSU; around 100 paediatricians attended the open session. Following an introduction by Professor Elizabeth Elliott of the Australian Paediatric Unit on the workings of the INoPSU the session continued with seven more specific presentations of various projects run through the BPSU. It was a very interesting and stimulating session endorsed from the feedback received by delegates.

There is an increasing anxiety concerning confidentiality and consent. In the past the BPSU has carried out, with ethics approval, its surveillance, in most cases, without prior consent from patients or their families. Great care is taken that the data collected is managed in an appropriate manner and that minimal identifying data is retained. Ideally it should be completely anonymised, but sometimes it is necessary to keep minimal identifiers to avoid duplication when data comes from multiple sources. If prior consent were needed it would seriously hamper the Units work (in that the reporting process would become more complex and prolonged); in one study undertaken by a similar surveillance system where consent was sought (because there was a need to approach families with a questionnaire) the whole project was significantly hampered. There is also the fear that failure to give consent, if asked, might lead to biased ascertainment that would undermine the validity of the whole surveillance process. This issue was the subject of a highly relevant publication in the BMJ in May (C. M. Verity and A. Nicoll, Consent, confidentiality, and the threat to public health surveillance. *Br.Med.J.* 2002; **324**:1210-1213).

Recent legislation that bears upon the handling of patient identifiable data places the BPSU's activities at risk and this has been further threatened by statements from the General Medical Council on confidentiality and consent. One possible way forward lies in the Health and Social Care Act 2001, which contains a facilitating clause (Section 60) that would allow certain specified surveillance activities to be continued, under closely regulated conditions, if an adequate case can be made in terms of public health benefit. We are studying this with care. Over the past nine months the Nuffield Trust have sponsored an extensive consultation on the issues of confidentiality and secondary use of health data and the outcome of this will be presented at a joint meeting with the Royal Society of Medicine on 28th November 2002. This will be an important occasion for the future working of the BPSU.

One ongoing concern is the completeness of ascertainment and some study investigators in this Report have voiced anxieties about this. Contributing factors that might reduce ascertainment are: low returns of the orange cards; delays in following-up positive reports by the investigators; poor returns of completed questionnaires; and situations when children with the condition

of interest are seen by professionals outside the orange card mailing list. At present the return rate of cards remains high at over 90%, and though it has fallen slightly in recent years, we make regular efforts to maximize returns. Delays in the follow-up of positive case reports can only be managed by the investigators, but there are several ways in which they can maximize returns: prompt contact with informants and clear and unambiguous case definitions and questionnaires are the most important. The fourth problem, where cases are not seen by paediatricians, is more difficult. The Executive Committee actively encourage the use of alternative sources of data such as, microbiologists, pathologists and other specialty groups and the involvement in recent studies of other surveillance systems e.g. ophthalmologists. This not only improves ascertainment, but also allows for validation of ascertainment by capture-recapture analysis. This greatly improves the security of the study conclusions, but increases the need for retention of a minimal set of patient identifiers to avoid double counting. They can of course be removed once the data set is complete and validated.

Recent innovations include changes to the BPSU web site (http://bpsu.inopsu.com/) and to the mailing list for the quarterly bulletin. The web site has been extensively revised with the help of the Australian surveillance unit. Apart from a smart new appearance it now includes the protocols for all current studies, study application guidelines, and access to all past published papers of BPSU studies. To improve communications we are now mailing the quarterly bulletin and information on new studies to all career grade doctors.

To finish, I would like to thank all those that make the BPSU work: the members of the Executive Committee; the RCPCH; the investigators who initiate and carry through the studies; but most of all the more than 2000 paediatricians who complete the cards every month.

Professor Mike Preece

Chairman of the BPSU Executive Committee

1 Introduction

Rare diseases and infections are, paradoxically, a numerically important cause of morbidity and mortality in childhood. Individually uncommon, together they number thousands, and many result in severe sequelae. Many are characterised by chronicity and by high rates of disabling sequelae or death. Most pose a large financial and emotional burden for affected children, their families, and health systems.

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

The Unit's main concern is that of epidemiological surveillance. This is defined as "the collection, analysis and dissemination of high quality data relevant to the understanding, prevention and control of medical conditions of public health importance so as to satisfy the needs of health care professionals, science, government, voluntary organisations and the public at large". (Adapted from: Bulletin of the World Health Organisation, 1994; 72).

Several agencies collaborate in the BPSU: the Royal College of Paediatrics and Child Health (RCPCH), the Public Health Laboratory Service (PHLS), the PHLS Communicable Disease Surveillance Centre (CDSC), the Centre for Paediatric Epidemiology and Biostatistics at the Institute of Child Health, London (ICH), the 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 attends the BPSU's Executive Committee, which meets every eight weeks to consider individual applications and the progress of studies.

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 – 2001/2002

The BPSU's key challenges are to:

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

2 How the surveillance system works

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

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

Selection of studies for inclusion in the scheme

The BPSU application procedure consists of two phases. In phase one, a short study protocol is requested covering no more than two sides of A4 paper. This should include the background to the proposed study, a case definition, the 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 8 weeks, is comprised of consultant paediatricians (general and specialist), epidemiologists, and specialists in public health.

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

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

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

Finally, all studies must have ethical approval from a Multi Research Ethics Committee (MREC). Though this is the responsibility of the investigators, the BPSU insists that there is compliance with the principle of Caldicott Report (Report on the Review of Patient-Identifiable Information, NHSE, December 1997) on data confidentiality and information flow and procedures that come from it. The BPSU Executive Committee has produced a document that outlines its position on ethics and confidentiality in relation to surveillance, and this is available from the BPSU office or can be viewed on the BPSU website at http://bpsu.inopsu.com/ethics.html.

Factors that favour acceptance by the British Paediatric Surveillance Unit

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

The reporting system

Those participating in the reporting system include consultant paediatricians who are either members of the RCPCH or the Faculty of Paediatrics of the Royal College of Physicians of Ireland. Mailing lists are regularly updated by the BPSU office, which monitors new consultant appointments, retirements etc.

Where necessary to improve case ascertainment, consultants working in a number of other specialties have been invited to participate in the scheme. For example, since 1992, pathologists who are not members of the RCPCH have also been included in

the reporting scheme. In addition, most studies of infections use laboratory reports to microbiologists e.g. HIV/AIDS and congenital rubella. Other current studies that are benefiting from such multiple ascertainment include cerebrovascular disease/stroke and thrombosis studies who are also ascertaining cases through members of the National Haematology Forum.

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

July 2002 [2-207]

NOTHING TO REPORT ☐ **CODE No [ ]**

If case(s) seen, identify how many

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

Figure 2 *Clinicians section - BPSU orange card*

Clinicians Section **- Please keep if necessary**

British Paediatric Surveillance Unit Report Card

for cases seen in July 2002

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

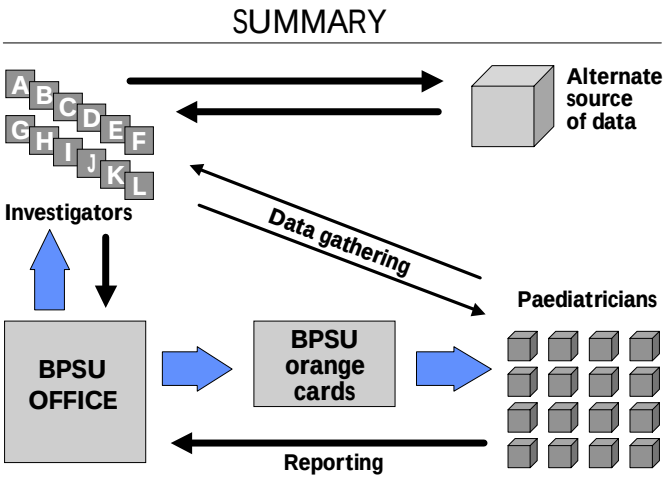
CONDITION	PATIENT	HOSPITAL NO

Detach this section before posting

Follow-up and confirmation of case reports

On receiving a case report, the BPSU informs the relevant investigating team who contact the reporting clinician for further information about the case in accordance with the agreed protocol for the particular study (Figure 3). Particular care is taken to ensure that questionnaires sent to reporting clinicians are as short as possible, clear, straightforward, and not excessive in their demands. The amount of patient-identifiable data collected is strictly limited, though not to an extent which would compromise study aims. The investigators subsequently report back to the BPSU on the outcome of each case follow-up, indicating when cases have been confirmed as meeting the case definition and identifying duplicate case reports. Duplication of reporting is most likely to occur when the condition requires referral to a tertiary unit, but this is encouraged, as it is better to receive duplication than miss the chance of receiving a report.

Figure 3



The extent to which investigators receive survey data, identifying incorrect reports and duplicates and the speed with which this is done is known as the **'completion rate'**. Table 2 (page 10) shows the number of cases reported to the BPSU from its inception until the end of year 2001 for all the conditions still under surveillance during year 2002. 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 current conditions under surveillance during the year 2001, only 229 (5%) of the 4878 case reports had yet to be followed-up. As a study draws to a close this completion rate figure will rise. The final completion rate normally averages average between 90-98%. There may however be delays in reporting outcomes to the BPSU office when there is the need for the collection of pathology specimens.

Table 3 (page 10) summarises the outcome of the follow-up of all cases reported to the BPSU by the end of year 2001 and provides evidence for the level of accuracy of reporting by participating clinicians.

Classification of case reports

Valid reports:

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

Invalid reports:

These include:

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

  and

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

Outcome not yet known:

Outcome of follow-up not yet received by BPSU (by July 2002).

Difficulties in case reporting

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

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

Reasons for incomplete case reporting

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

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

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

The use of complementary data sources

A distinctive and powerful feature of the BPSU system is the ability to use data from complementary sources to validate the surveillance system, to increase case ascertainment and to increase the accuracy of data (Figure 4). The first complementary data sources to be used were laboratory reports to the PHLS of infectious disease. In the past year, studies on HIV/AIDS, and encephalitis in childhood have included this additional ascertainment. Other sources which have been used include death registration (Reye's syndrome), hospital episode data (congenital brachial palsy and fatal/severe allergic reactions to food ingestion) and 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 been shown to improve case ascertainment, demonstrated through the inflammatory bowel disease (IBD) study which identified cases through the BPSU, adult gastroenterologists and the IBD register. However, it is known that completeness varies between studies and conditions, according to the ease of case ascertainment and the availability of complementary data sources.

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

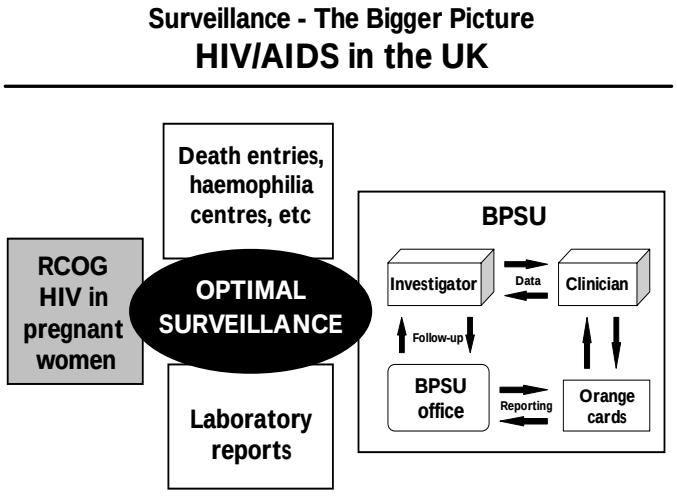
Funding

For the three-year period to September 2001 the BPSU has been in receipt of a grant from the Department of Health (DH). Through the willingness of the DH to extend the grant for a further three years to September 2004, the BPSU's work continues to be recognised as an effective way of contributing towards improved child health in the UK. This contribution will support a substantial percentage of the Unit's running costs. In addition, the BPSU asks surveillance teams to contribute a sum to cover the printing/distribution of the orange cards, and where possible the administrative costs of co-ordinating the study. In the year 2001 this sum was £7,000 per annum, though a lower rate of £3,600 exists for those who are applying for funds from small local sources. These funding sources manage to cover the day-to-day costs of running the Unit.

Further non-cost support is received from the Royal College of Paediatrics and Child Health, the Public Health Laboratory Service and its Communicable Disease Surveillance Unit, the Scottish Centre for Infection and Environmental Health and the Institute of Child Health (London). Assistance with the re-development of the BPSU website was received from the Australian Paediatric Surveillance Unit.

The Unit was also in receipt of donations from the Wellcome Trust and Wyeth Vaccines who contributed towards the costs of the second conference of the International Network of Paediatric Surveillance Units, held in April 2002.

Figure 4



3 Surveillance activities in 2001

Five studies commenced in 2001. January saw the start of a 13-month study into cerebrovascular disease/stroke and stroke-like illness and a third BPSU survey of vitamin K deficiency bleeding. February saw the start of the thrombosis in childhood and congenital cytomegalovirus studies and March saw the start of a survey on severe internal abdominal injuries due to child abuse. Both the cerebrovascular disease and thrombosis studies have utilised the National Haematology Forum in order to ascertain paediatric cases likely to be seen by adult haematologists.

Several studies ended in 2001. February saw the completion of surveys on Group b streptococcal disease and haemolytic uraemic syndrome and in July after 16 years on the orange card, surveillance of both Reye's syndrome and subacute sclerosing panencephalitis ended. October saw the completion of the three-year surveillance of encephalitis in children. Three studies had their period of surveillance extended for a further year: HIV/AIDS, congenital rubella and progressive intellectual and neurological deterioration (PIND). By December 2001, forty-six studies had been completed since the BPSU started in June 1986 - those completed prior to the year 2001 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 2001/2002 relating to these studies and the Unit's work totaled 46 and are listed in Appendices B and C.

In promoting the work of the BPSU, representatives of the Unit have been invited to give talks at various events and meetings. Once again the Unit was involved in the RCPCH Research Division session at the RCPCH scientific meetings.

Through the convening of an annual discussion forum, the Unit has strengthened its links with other college surveillance units and national epidemiological institutions. At the most recent forum the matter of how to improve case ascertainment was discussed. Ethics and confidentiality were once again also considered. The BPSU chairman Professor Mike Preece continues to represent the group in discussion with the DH over these issues.

The BPSU continues to disseminate information on its activities to clinicians and the public alike. This is achieved mainly through this report, the quarterly bulletin and increasingly through the BPSU website. This site (http://bpsu.inopsu.con) was re-launched in October 2001 following an extensive re-design and thanks go to the Australian Paediatric Surveillance Unit for making this possible. The site is also accessible through the new RCPCH website at www.rcpch.ac.uk/research/bpsu.htm.

Through its position as "server" the BPSU continues to contribute to the work of the International Network of Paediatric Surveillance Units (INoPSU). Following a similar meeting in Ottawa two years ago, in April 2002 the BPSU hosted the second, very successful INoPSU conference. This was held over two days at York University, in conjunction with the Annual Scientific meeting of the RCPCH and is described more fully with news on the international scene in Chapter 7.

Participation in the scheme during the year 2001

The BPSU ascertains the names of new consultants primarily through the RCPCH Advisory Appointment Committees, the membership office, BMJ adverts, personal communication and through the ongoing College manpower census. During the year, 211 consultants were placed on the mailing list whilst 84 were removed, ostensibly following retirement. The number of consultant paediatricians participating in the scheme by the end of 2001 therefore rose to 2204, an increase of 5.1% on the previous year. It should, however, be noted that some paediatricians who hold consultant status are excluded, as they do not undertake relevant clinical work, or else colleagues report on their behalf. The BPSU mailing list also includes selected groups of consultants other than paediatricians - for instance, cardiologists, clinical geneticists and pathologists. In order to help in the ascertainment of cases pathologists continue to be included in the surveillance system, and our thanks are extended to the Royal College of Pathologists for supporting this initiative.

Reporting rates for returning the orange cards remains high - the overall card return compliance rate for the year 2001, calculated as a proportion of orange cards returned, was 92.7 % (23,088/24,905), a similar rate to 2000. Monthly response rates ranged from 89.3% in December to 94.3% in January, with a median of 92.8%**.** The overall response rate remains above 90.0% and the downward trend from a high of 95.0% in 1996 has ceased. To maintain this excellent compliance rate, respondents who have not returned cards for two consecutive months are sent letters, as much to verify postal address as to act as a reminder. Of those responders not returning cards less than 2% could be considered as persistent non-responders. The return rate is considerably higher than any equivalent UK scheme and ranks sixth of the 13 other national paediatric units (table 16 page 44).

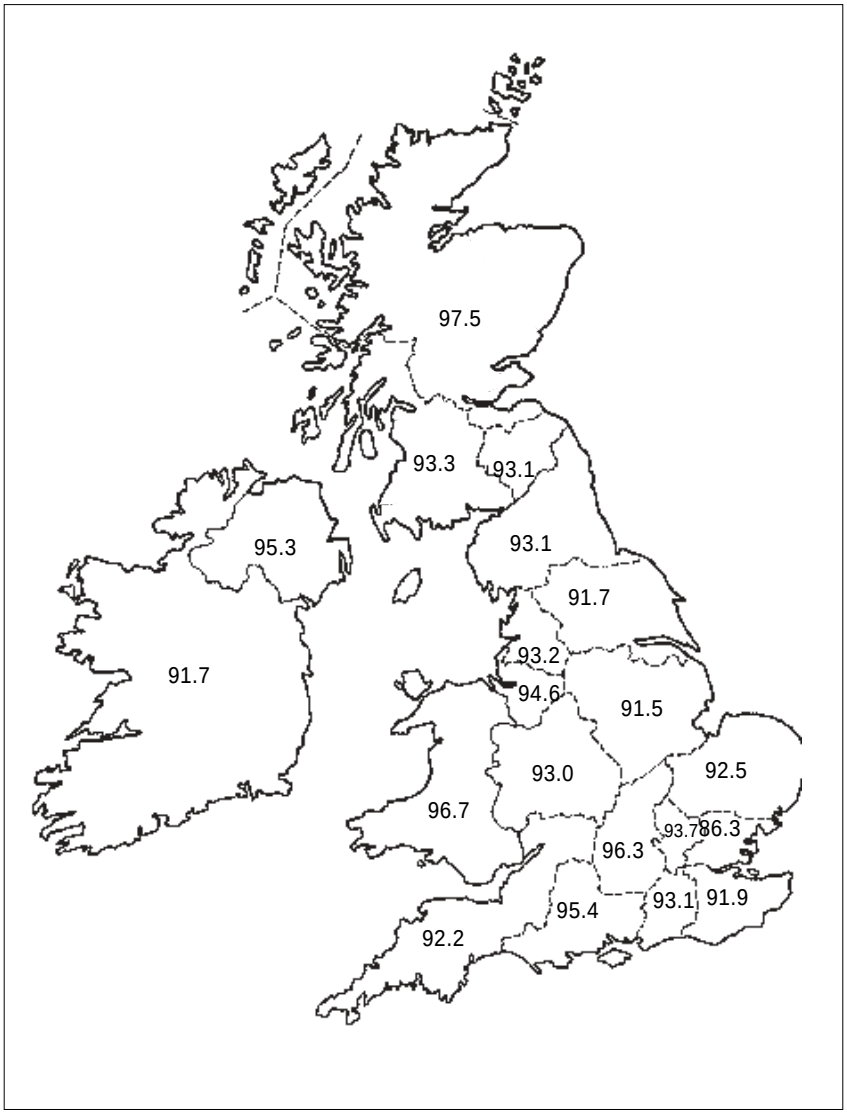
As in previous years, reporting rates varied considerably across the country, as is shown in Figure 5. North Scotland achieved the highest average yearly response rate – 97.5%, with Wales a close second (96.7%). The Thames area showed a cumulative response rate of 91% with North East Thames returning just

86.3% of cards. With so many teaching hospitals in London, there is concern that cases may be going unreported. However, it should be recognised that there are many paediatric specialists in London who receive the orange card but are never likely to see the conditions and thus may be less likely to return the cards on a regular basis. With regards to rank order over the year, North West Thames rose 13 places and Wessex 8 places, while Trent and South Scotland fell 14 and 11 places respectively. From a rank high of 1 in 1997 the Republic of Ireland now lies just 18th in rank order. (Table 1).

Table 1
Regional ranking 2000 and 2001

Region	Rank 2001	Rank 2000
Northern	10	9
Yorkshire	17	18
Trent	19	3
E Anglia	14	14
NWT	7	19
NET	20	20
SET	16	17
SWT	11	11
Wessex	4	12
Oxford	3	4
SWest	15	16
WMids	13	10
Mersey	6	7
NWest	9	13
Wales	2	2
NScot	1	5
SScot	12	1
WScot	8	5
NIre	5	8
RIre	18	15

Figure 5 *Average orange card return rate (%) by area 2001*



Overall average orange card return rate = 92.7%

Workload of those reporting in the scheme

The BPSU continually monitors the workload of participants in the scheme in terms of the number of cases reported. 67 % (1478) of participants reported no cases in 2001, more than in 2000 (57%). 31% (686) reported between one and four cases and only 1.8% (40) reported five or more cases. The greatest number of cases reported by a single paediatrician was 85. Specialties that had a particularly high level of reporting were, paediatric neurologists (PIND, encephalitis, SSPE, Reye's syndrome) and neonatologists (HIV/AIDS, encephalitis). Community paediatricians continue to make a significant contribution to the reporting and their continued involvement in the scheme is very much required. With the continuation of the PIND and HIV/AIDS studies and the commencement of the severe internal abdominal injury study we would expect this important contribution to continue in 2002.

Table 2 *Cases reported from June 1986 – December 2001 of conditions under surveillance during the year 2002 (cases confirmed by July 2001 shown in brackets)*

		Reports (confirmed cases)				
Condition under surveillance	**Date when reporting began**	**June 1986 to Dec 1995**	**Jan 1996 to Dec 1998**	**1999**	**2000**	**2001**
HIV/AIDS	Jun 86	991(691)	488 (329)	202 (134)	327 (226)	445 (314)
Congenital Rubella	Jun 90	72 (39)	40 (18)	2 (2)	7 (5)	12 (1)
PIND	May 97	– –	617 (385)	218 (133)	229 (133)	197 (129)
Encephalitis (2-36 months)	Oct 98	– –	56 (31)	138 (65)	122 (39)	85 (22)
CVD/S	Jan 01	– –	– –	– –	– –	298 (168)
VKDB	Jan 01	– –	– –	– –	– –	26 (5)
cCMV	Feb 01	– –	– –	– –	– –	135 (75)
Thrombosis	Feb 01	– –	– –	– –	– –	124 (67)
IAI	Mar 01	– –	– –	– –	– –	47 (14)
Total		**1063 (730)**	**1201 (763)**	**560 (334)**	**685 (403)**	**1369 (795)**

HIV/AIDS Acquired immune deficeiency syndrome/human immunodeficiency virus: reports of AIDS in June 1986 includes cases previously seen; case definition extended to include HIV infection in January 1990.
CVD/S Cerebrovascular disease, stroke and like illness includes Sturge-Weber and Vein of Galen
cCMV Congenital cytomegalovirus
IAI Internal abdominal injuries upto 14 yrs due to child abuse

Table 3 *Outcome of follow-up of the cases reported in 2001 of conditions under surveillance during the year 2002.*

	Valid reports (%)		**Invalid reports**			**Not yet**		**Total**
Condition under surveillance			**Duplicates**	**Errors**	**(Total %)**	**known (%)**		**reports**
HIV /AIDS	1,694	(69)	311	392	(29)	56	(2)	2453
Congenital Rubella	65	(49)	24	40	(48)	4	(3)	133
PIND	780	(62)	135	332	(37)	14	(1)	1261
Encephalitis*	157	(39)	33	165	(49)	46	(11)	401
CVD/S	168	(56)	12	40	(17)	78	(26)	298
VKDB	5	(19)	3	11	(54)	7	(27)	26
Thrombosis	67	(54)	17	32	(40)	8	(6)	124
cCMV*	75	(56)	15	31	(34)	14	(10)	135
IAI	14	(30)	13	18	(66)	2	(4)	47
All	**3025**	**(62)**	**563**	**1061**	**(33)**	**229**	**(5)**	**4878**

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

4 Main findings of studies undertaken in 2001

A 13-month surveillance of **cerebrovascular disease/stroke & like illness** (page 12) was completed in March 2002. To date 370 notifications have been received of which 223 cases have so far been confirmed. This includes five cases of Vein of Galen and four of Sturge-Weber. Seven deaths have already been identified, and this is concerning. An audit of two main centres suggests there is under-ascertainment with this study and this is something that needs to be addressed.

After the first year of **congenital cytomegalovirus** (page 14) surveillance 54 cases have been confirmed with a further 31 possible cases. Only 11 cases were identified antenatally. Over 50% of the confirmed cases have neurological signs (microcephaly, seizures, intracranial calcification), and sadly there have been five deaths to date.

Surveillance for **congenital rubella** (page 16) in the UK has been underway continuously since 1971. Eight infants born since 1999 have been reported; in five of these cases the maternal infection was acquired abroad. The current level of MMR uptake gives cause for concern, as it may not be enough to prevent circulation of rubella infection in the long-term.

The three-year surveillance of **encephalitis in children two months to three years** (page 18) ended in October 2001 and has to date reported 280 children most of whom presented between 10 and 21 months of age. HHV-6 and HHV -7 infections were identified as commonly as herpes simplex and varicella zoster virus infections.

The BPSU survey of **HIV and AIDS** (page 20) 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 although the greatest number of infections are in London, cases are occurring in all parts of the country. As a result of previous findings it is now professional and Department of Health policy to routinely offer and recommend HIV testing to all pregnant women. It has been known for several years that interventions such as antiretroviral therapy for the pregnant woman and newborn child, elective caesarean section, and avoidance of breast feeding substantially reduce mother to child transmission of infection. However, as many infected pregnant women were not aware of their HIV status, they could not take advantage of these interventions.

Surveillance of **internal abdominal injury due to child abuse** (page 22) commenced in March 2001 and continues to March 2003. Fifteen cases have been confirmed of which only five occurred during the surveillance period. Sadly, in six of the fifteen cases the child died from their internal abdominal injury. Preliminary findings also suggest that small bowel/duodenal injury is more common in non-accidental injury than accidental injury due to road traffic accidents and falls.

Despite the complexity of the conditions involved the survey of **progressive intellectual and neurological deterioration in children** (PIND) (page 25) has proved successful. It is being undertaken to identify any cases of variant Creutzfeldt-Jakob disease in UK children. Over 1200 cases of suspected PIND have been reported. Among them 535 cases are confirmed diagnoses, consisting of 93 different conditions. Six cases of vCJD have been identified.

The study into **thrombosis in childhood** (page 28) continued for a second year. During the first 12 months 68 confirmed cases have been received. The main risk factors were central venous/ femoral lines, infection and malignancy. Of these 52 achieved partial or complete resolution. Overall mortality was low (5.8%) with no death attributed to venous thromboembolism. The number of reports is less than expected and specialists will be more actively targeted during the second year surveillance.

The third BPSU survey of **vitamin K deficiency bleeding** (page 29) continues into its second year. To date, of the 25 reports, five fit the case definition. Three of the cases presented in the first week of life, the others at 39 and 63 days. Three had received no vitamin K, two had oral prophylaxis. In four cases the birth unit's policy for vitamin K prophylaxis had not been followed, in all because of parental refusal or indecision. In two cases underlying liver disease almost certainly contributed to the vitamin K deficiency; one was associated with cystic fibrosis and one with biliary atresia.

5 Surveillance studies undertaken in 2001

During the year 2001, 13 conditions were the subject of surveillance. Four studies were completed: haemolytic uraemic syndrome (HUS), Group B streptococcal disease (GBS), Reye's syndrome, and subacute sclerosing pan-encephalitis (SSPE). Five studies commenced: congenital cytomeaglovirus, cerebrovascular disease/stroke and like illness, thrombosis in childhood, vitamin K deficiency bleeding, and internal abdominal injury due to child abuse. The final reports on HUS, GBS, SSPE and Reye's syndrome are contained in the 15th BPSU Annual Report 2000, whilst the remainder undertaken in 2001 are listed in Table 3 below.

Four studies have or are due to commence in 2002: suspected fatal adverse drug reactions in childhood, congenital toxoplasmosis, severe reaction to varicella, and Langerhans cell histiocytosis. These are described in Chapter 6.

Table 3 Studies underway in the year 2001

Page	Study	Principal Investigators	Research Institution
12	Cerebrovascular disease/stoke & like illness	F Kirkham, A N Wi'liams	Southampton University Hospital, Birmingham Children's Hospital
14	Congenital rubella *	P Tookey, C Peckham	ICH (London)
16	Congenital cytomegalovirus*	P Tookey	ICH (London)
18	Encephalitis (2 months - 3 years)	K Ward, E Ro..	Kings College Hospital, London
20	HIV/AIDS in childhood *	P Tookey, A Nicoll, D Goldberg	ICH (London), PHLS, SCIEH
22	Internal abdominal injury due to child abuse*	Professor J Sibert	University of Wales
25	Progressive intellectual and neurological deterioration *	C Verity, G Devereux, A Nicoll, R Will	Addenbrookes Hospital, PHLS, CJDSU
28	Thrombosis in childhood*	B Gibson, D Henderson	RHSC Glasgow
29	Vitamin K deficiency bleeding*	J Tripp, A McNinch	Royal Devon & Exeter Hospital

*Studies still in progress to July 2002.

Cerebrovascular Disease, stroke and like illness in childhood

Key Points

- **370 notifications have been received of which 223 have so far been confirmed.**
- **Of these five were cases of Vein of Galen and four of Sturge Weber.**
- **There have been 7 deaths.**
- **An audit of 2 main centres suggests a degree of under - ascertainment and this needs to be addressed.**

Background

Cerebrovascular disorders in childhood are associated with significant mortality and considerable residual handicap, both physical and cognitive. For the United Kingdom, however, the actual numbers of children affected annually by stroke remains unknown. This 13 month study is a prospective observational study of one year's cases with independent surveying of British neurosurgeons, cardiac surgeons, cardiologists, paediatric radiologists and haematologists/oncologists.

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

Objectives

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

Surveillance period

January 2001- January 2002

Case definition

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

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

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

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

To Exclude:

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

Multiple ascertainment

As well as using the infrastructure of the BPSU orange card case ascertainment will be achieved through parallel surveillance involving paediatric cardiologists, radiologists, neurosurgeons and haematologists. Monthly contact has been maintained with these groups throughout the study period.

Preliminary Analysis

By nine months there were 273 notifications, of which 223 cases were confirmed to April 2002.[1] The BPSU identified 200 (86%) of the cases. Overall, this provides an estimated incidence of 2.5 cases per 100,000 per annum and a calculated yearly estimate of 297 cases, which is in line with the Birmingham pilot regional study.[2] To date 370 notifications have been reported. From the 103 cases for which data are available, 53% were male, the mean age was 6.1 years and the median age was 3.5 years (range one day–16 years).

Interestingly only 13 cases were neonates and five of those were from one centre. From clinical experience and recent evidence from the US[3] this suggests an under-ascertainment in reporting.

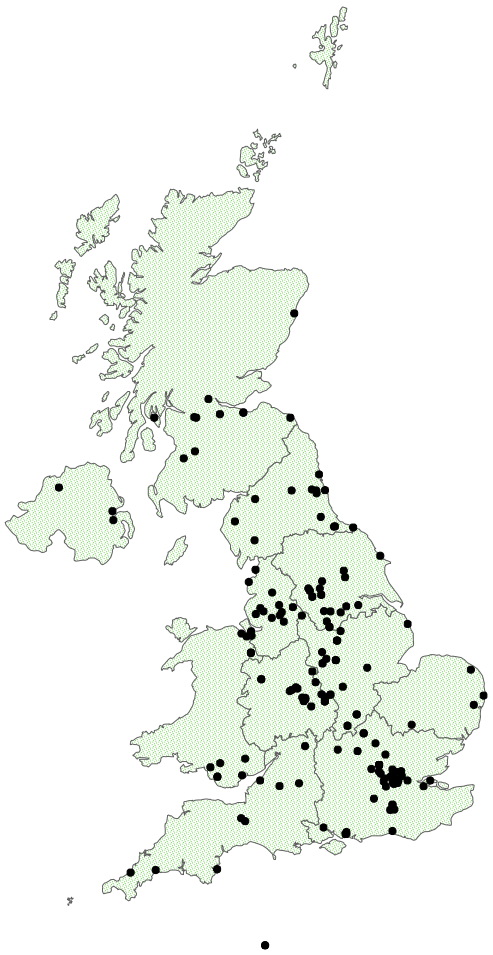
For this nine-month period there has been seven deaths which is a concern. The number of confirmed cases is likely to rise still higher when the Office of National Statistics mortality data becomes available.

There were also five cases of Vein of Galen and four of Sturge-Weber syndrome, which are being separately surveyed, as there has been no surveillance undertaken before to define their incidence.

Regional reporting

Cases have been reported from across the country (Figure 6) and these are reflected in the reports received into the major specialist centres (Table 4 overleaf).

Figure 6 *UK Stroke cases on basis of patient postcode*



A variation in reporting across these main specialist centres has been noticed. A review of referrals from two centres was therefore undertaken. In both centres only five cases were initially reported. However in one the total including haemorrhage was 16 and in the other the total ischaemic strokes was also 16, suggesting that more than half the cases were not being reported of cases. This is a concern, if reflected in other centres.

Table 4 *BPSU Notifications from major medical centres*

Centre	Reports	Centre	Reports
Birmingham	9	Cambridge	4
Cardiff	9	Dublin	9
Dundee	1	Edinburgh	12
GOS	5	Guys	1
Glasgow	7	Leeds	10
Leicester	7	Liverpool	16
Manchester	14	Newcastle	11
Nottingham	11	Oxford	12
Southampton	13		

Comment

The study has so far raised some interesting questions regarding childhood cerebrovascular disease in the United Kingdom and Republic of Ireland. Possible under-reporting is a concern and recently De Veber albeit in Canada demonstrated an incidence of six per 100,000 per annum.[4]

It is hoped that the data obtained from this study will assist in the development of a national consensus regarding management and making a case for the development of appropriate services. Of course, it will also lay the groundwork for the UK participation in international multicentre interventional trials that are presently being planned which might include the establishment of a childhood stroke registry.

Funding

Stroke Association

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Congenital cytomegalovirus (cCMV)

Key points

- **In the first year there have been 54 confirmed and 31 possible reports.**
- **In 11 cases maternal CMV was diagnosed antenatally.**
- **Five infants have died.**
- **One year outcome follow-up will be undertaken.**

Background

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

Objectives

Surveillance of clinically recognised, confirmed and suspected, congenital cytomegalovirus (cCMV) infection in infants born in the British Isles, to ascertain the population prevalence of cCMV disease, current management strategies, and the clinical disease outcome. A further objective is to explore the feasibility of using routinely collected neonatal dried blood spots to confirm or exclude a diagnosis of cCMV infection in infants who present after three weeks of age.

Surveillance Period

April 2001-April 2003

Case definition

Any infant with confirmed or suspected cCMV infection born in the UK or Republic of Ireland since 1 January 2001. When reporting twins, two reports are required even if one of the twins is uninfected.

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

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

Analysis

By the end of March 2002, 167 reports had been made through the BPSU (Table 5). Of the 167 reports, 48 were confirmed and 26 possible cases (diagnosis after three weeks of age). Eleven BPSU reports were for another six confirmed and five possible cases which had already been reported from another source. The remaining reports included 19 duplicates and 34 reporting errors. Twenty-nine reports are currently outstanding.

Among the 54 confirmed cases reported through the BPSU (whether as primary or secondary reports), 45 were from England (including 15 from London), seven from Scotland, and two from the Republic of Ireland. There were another 11 confirmed cases which have so far only been reported through the laboratory reporting system, and for which there are therefore few details as yet.

Preliminary observations

Among the 54 infants with confirmed cCMV for whom information is available, there were three twin pairs where both infants were infected, and another two infants who each had an uninfected twin. The twins were delivered at between 28 and 35 weeks. The mean gestation of the 46 singleton infants was 36 weeks (median 37), and mean birthweight was 2290gms (median 2260). In eleven of the 51 pregnancies maternal CMV infection in pregnancy had been diagnosed antenatally, usually following the investigation of flu-like illness in the mother, or abnormal findings at ultrasound. Over 50% of the confirmed cases have neurological signs (microcephaly, seizures, intracranial calcification), and about one third of those were treated with gancyclovir. Those without neurological signs were generally diagnosed following an antenatal diagnosis, or investigation of non-specific symptoms in the neonatal period. Five infants are known to have died, one at birth, three in the first month and one at six weeks. Outcome at one year will be sought for the survivors through the notifying paediatrician. Among the 31 infants reported with possible cCMV, 42% were born at between 26 and 32 weeks gestation (and three of these have died). Most of the other infants presented with problems after the neonatal period. A substantial proportion are likely to have acquired perinatal or postnatal infection, and we intend to try to clarify the timing of infection by testing dried blood spots collected at birth. Please continue to notify all diagnosed or suspected cCMV cases. The investigators are grateful to all notifying paediatricians for their co-operation.

Funding

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Table 5 *Reports made through the BPSU to March 2002*

	Confirmed	Possible	Already reported	Duplicate or error	Outstanding	Total
England	39	22	11	44	20	136
Wales				3	3	6
Scotland	7	2		6	2	17
NI		1			1	2
RoI	2	1			3	6
Total	**48**	**26**	**11**	**53**	**29**	**167**

Congenital rubella

Key Points

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

Background

Surveillance of congenital rubella in Scotland, Wales and England started in 1971 with passive reporting by audiologists, paediatricians, and microbiologists. Following the introduction of vaccination for schoolgirls (1970) and susceptible women post-partum (1972) the number of reported congenital rubella births and rubella associated terminations declined from an average 50 births and 740 terminations a year in 1971-75 to an average 22 births and 54 terminations a year in 1986-90. Since there were so few cases, active surveillance was required, and congenital rubella first appeared on the orange card in January 1990. BPSU reports from Ireland are also followed up, but are not normally included in published figures.

Since 1988 the combined MMR vaccine has been offered to all children in the second year of life. In 1994, as part of an attempt to avert a predicted measles epidemic, all 5-16 year olds were offered combined measles/rubella vaccine. In 1996 a second dose of MMR was introduced for four year olds, and the schoolgirl rubella vaccination programme was discontinued. As a consequence of these changes in the vaccination strategy, the circulation of wild rubella virus has been at extremely low levels in the UK in recent years, and an increasing proportion of individuals are protected by vaccine-induced immunity. In the early 1990s, uptake reached 92% in children at 24 months. However adverse publicity about unproven associations between MMR, bowel disease and autism led to a decline in uptake, and although coverage stabilised at about 88% in 1998-2000, in 2001 it dropped again to under 85%.[1] This is not sufficient for the long-term maintenance of a herd immunity level of 85-88% which is required to prevent transmission of rubella virus, particularly since few children now acquire natural infection. It is possible that rubella could once again start to circulate in the UK, as it does in many other parts of the world. Awareness of rubella infection and congenital rubella among paediatricians, and health professionals looking after pregnant women must be maintained. Continued surveillance of congenital rubella is vital.

Objectives

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

Surveillance period

Surveillance began in January 1990 and is reviewed annually.

Case definition

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

Analysis

BPSU notifications

Since the beginning of active surveillance in 1990, 131 reports have been made through the BPSU (Table 6 below). Of the 116 reports from England, Scotland and Wales, 44 are confirmed or compatible, previously unreported cases of congenital rubella, four are possible cases, and 13 had already been reported from another source. The remaining reports were duplicates (19), reporting errors (32) and four where further information could not be obtained. Fifteen reports were from the Republic of Ireland or Northern Ireland, and included three children with confirmed congenital rubella (one born in 1989 and two in 1996), and a fourth possible case (born in 1983). One report from the Republic of Ireland is currently outstanding.

Congenital rubella 1990-2001

Fifty-three confirmed or compatible congenital rubella births have been recorded since the beginning of active surveillance in 1990; 37 of these cases (70%) were first reported through the BPSU (Table 7). In the last decade most reported cases ofcongenital rubella were identified close to the time of birth because of abnormal signs in the infant. Hardly any children with

Table 6 *Congenital rubella reports to BPSU 1990-2001*

	England, Scotland & Wales	**Ireland**
Registered Cases	48	4
Already Reported	13	2
Outstanding	0	1
Duplicate, error or lost	55	8
Total	**116**	**15**

isolated hearing loss due to congenital infection are now reported; any such children would probably remain undiagnosed as they have vaccine induced antibodies following MMR in early childhood. The diagnosed reported cases therefore probably represent only a proportion of the true cases. There have also been 75 terminations for rubella disease or contact in pregnancy recorded by ONS in England and Wales during the period 1990-2000.[2] Overall, about a quarter of the 53 infants born since 1990 had mothers whose infection was acquired abroad. Another third were born to women who, although they acquired infection in the UK, had only arrived in the country relatively recently. Three women had confirmed reinfection in pregnancy.

Recent reports

Eight infants born between 1999 and 2001 have been reported (Table 7). Although five cases were imported, with women acquiring infection in their countries of origin (Bangladesh, Pakistan, Sri Lanka, Nigeria and Zambia) three infants were born to women whose infection occurred in the UK.[3,4] One UK-born woman acquired her infection in Scotland, although it was epidemiologically linked to an outbreak in Greece in 1999.[5,6] The remaining two maternal infections were acquired in London, one by a UK-born woman, and the other by a Sri Lankan woman who had been in the UK for several years.

While rubella infection is currently rare in the UK, women who travel abroad during early pregnancy may come into contact with infection. Results from antenatal rubella testing 1996-1999 in the (former) North West Thames region show that rubella susceptibility in pregnant women continues to vary considerably by ethnic group, with women from many parts of Asia and Africa having particularly high rates.[7] Women who have come to the UK from countries with less successful, or disrupted vaccination programmes are likely to be at higher risk if there is renewed circulation of rubella here.

The BPSU's orange card has proved to be a rapid and effective reporting system for congenital rubella and was particularly quick to identify the increase in cases in 1996, when all but two of the BPSU reports were made within two months of the infant's birth. These cases were associated with a resurgence of rubella infection in the UK in the spring of 1996, mainly affecting young men.[8] It is essential that case ascertainment is as rapid and complete as possible, both for imported cases and those where infection was acquired in the UK. Please notify to the BPSU all infants with suspected congenital rubella, whether or not they have the associated typical defects. The investigators are extremely grateful to all participating paediatricians, especially those who have notified cases and completed questionnaires.

Table 7 *Confirmed and compatible congenital rubella births reported to the NCRSP 1971-2001* (England, Scotland & Wales only)*

	Primary source of notification		
year of birth	BPSU	Other	Total
1964-69	0	39	39
1970-79	1	453	454
1980-89	13	320	333
1990-2001~	37	16	53*
1990	8	4	12
1991	2	1	3
1992**	5	2	7
1993	2	1	3
1994	5	2	7
1995	1	0	1
1996	9	3	12
1997	0	0	0
1998	0	0	0
1999	0	1	1
2000	4	0	4
2001	3	0	3
Total	51	828	879

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

Funding

The PHLS makes a contribution towards the costs of the surveillance.

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Encephalitis in children two months to three years

Key points

- **Between October 1998 and September 2001, 280 children meeting the surveillance case definition were reported to the BPSU.**
- **Sixty percent of confirmed cases (i.e. fulfilling the analytical case definition) presented aged between 10 and 21 months which is the most frequent age at which primary human herpesvirus-6 and -7 (HHV-6 and HHV-7) infections occur.**
- **In confirmed cases (i.e. fulfilling the analytical case definition) primary HHV-6 and HHV-7 infections were identified as commonly as herpes simplex and varicella zoster virus infections combined.**

Background

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

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.

Figure 7
Electron micrograph of a group of human herpesvirus-6 particles in a negative contrast preparation showing mature intact virions and naked nucleocapsids.

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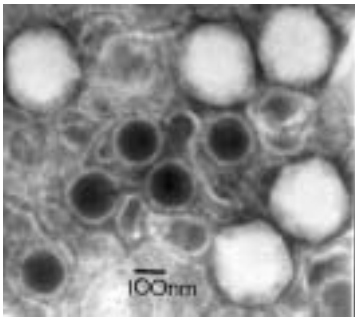


Surveillance case definition

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

- **include:** encephalitis of *known* infectious or post-infectious aetiology (*unless* due to pyogenic infection)
- **also include:** convulsions in a *febrile* child:
  (i) with a total duration of more than half an hour;
  or (ii) followed by coma lasting 2 hours or more;
  or (iii) followed by paralysis or other neurological signs not previously present and lasting 24 hours or more.
- **exclude:**
  (i) viral (aseptic) meningitis without encephalopathy;
  (ii) the following confirmed causes: pyogenic infections, hypoxic/ischaemic, vascular, toxic, metabolic, neoplastic;
  (iii) uncomplicated fits/convulsions or a series of fits convulsions lasting less than half an hour.
- if in doubt please discuss with the investigators.

Suveillance Period

October 1998 - September 2001

Coverage

UK and Republic of Ireland.

Methods

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

A questionnaire was sent to the reporting paediatrician after about 3 months to allow sufficient time for follow-up. Due to the difficulties of diagnosing encephalitis, which is often a diagnosis of exclusion, a final decision as to whether the case is included in the survey is based on a detailed analytical case definition. A Working Party judges difficult cases and comprises Professor Euan Ross, Dr Chris Verity and Dr Kate Ward.

Analysis

The survey ended in September 2001 at which point 402 cases had been reported to the BPSU (134/annum); twenty seven from the Republic of Ireland and the remainder from the UK (Table 8). Reports have been received from all regions but tended to come from the hospital where the child first presented rather than the Paediatric Intensive Care Unit (PICU) to which they were transferred.

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

Of the 402 cases reported:

- 122 were invalid because of duplication or reporting error (including misdiagnosis and children who were either too old or too young). In 16 cases we did not receive a reply to our request for further information despite reminders.

Of the remaining 280 cases that met the surveillance case definition:

- 149 cases fulfilled the analytical case definition and were confirmed
- 66 cases did not fulfil the analytical case definition and were not confirmed
- Follow-up has not yet been completed for 65 of the most recently reported cases. As explained previously, questionnaires are not sent immediately so as to allow the paediatrician time to confirm the initial diagnosis. Of the 65 cases, 38 difficult cases await a decision from the Working Party and questionnaire replies are yet to be received from 27 paediatricians.

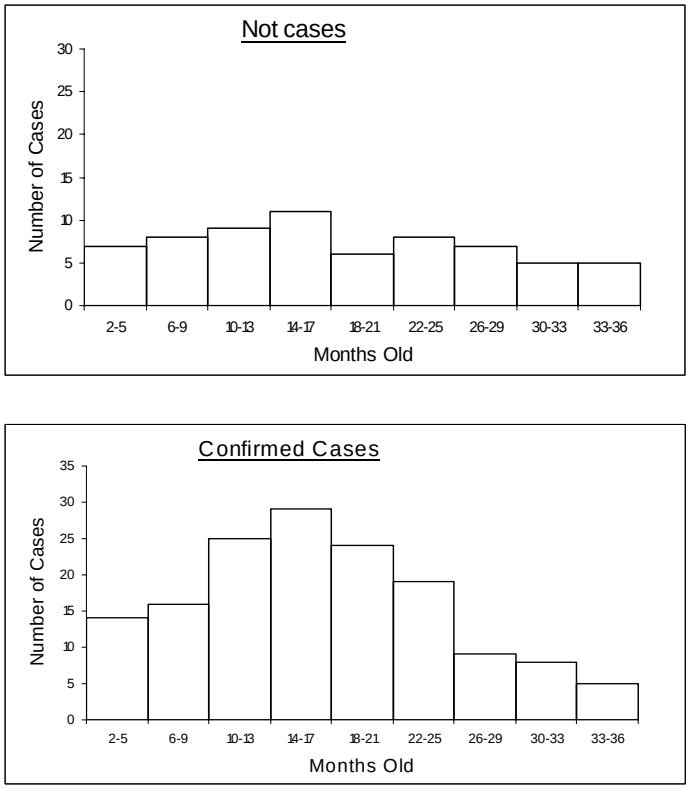
From the above analysis, it can be estimated that the final number of confirmed cases per annum will be about 64. This is less than the original estimate of 200 cases per annum which was based on the number of reports received by the NCES. Since the latter was undertaken, measles, mumps, rubella (MMR) vaccination has almost abolished measles and mumps encephalitis which may partly explain the lower number of encephalitis cases reported to the present survey. Moreover, although the surveillance case definition is very similar to that of the NCES, there are important differences. The present survey definition omits infantile spasms but includes convulsions in a *febrile* child, i.e. severe febrile convulsions, whereas the NCES definition includes both severe febrile convulsions and 'other' severe convulsions. In addition, only 70% of cases meeting the surveillance case definition are confirmed cases when the analytical case definition is used; this is probably due to the difficulty of diagnosing encephalitis.

Table 8 *Regional distribution of reports.*

REGION	Total	REGION	Total
East Anglia	14	NE Thames	42
Mersey	12	NW Thames	23
North	10	SE Thames	29
North West	24	SW Thames	28
Oxford	16		
South West	19	Wales	20
Trent	39		
Wessex	17	North Scotland	2
West Midlands	34	South Scotland	8
Yorkshire	22	West Scotland	11
		Northern Ireland	5
		Republic of Ireland	27
TOTAL			402

Figure 8 compares the age distribution of the 180 cases that met the analytical case definition with that of the 66 cases that did

Figure 8



not fulfil the definition. The most frequent age of presentation of the confirmed cases is between 10 and 21 months old. This is also the most frequent age for primary HHV-6 and -7 infections in children. In this context the Survey has identified 14 children with primary HHV-6 infection and 17 children with primary HHV-7 infection. Notably no similar evidence for HHV-6 or -7 infection has been found so far in the cases that did not meet the definition.

Comment

The study has gone very well; both primary HHV-6 and -7 infections have been found and the investigators are now in a position to begin looking at the clinical picture, outcome of these infections and possible temporal coincidence with vaccination especially MMR.

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

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

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

Funding

Wellcome Trust.

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HIV/AIDS infection in childhood

Key points

- **Most new infections are acquired through mother to child transmission.**
- **Interventions can reduce vertical transmission of infection from mother to child to less than 2%. HIV testing should be offered and recommended to all pregnant women as an integral part of antenatal care.**
- **A significant number of older symptomatic children, often recently arrived from endemic areas, continue to be reported.**
- **Annual follow-up of infected and indeterminate children through contact with the appropriate paediatrician continues. Follow-up of uninfected children to identify any adverse effects of exposure to prophylactic antiretroviral therapy is currently being piloted.**

Background

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

Most children living with HIV in the UK and Republic of Ireland (RoI) acquired their infection through mother to child transmission. A small number probably acquired infection as a result of nosocomial transmission outside the UK, and in very few sexual transmission or injecting drug use was the likely source of infection. Children known to have acquired infection during the course of treatment for haemophilia were all born before 1984.

Antiretroviral treatment for the pregnant woman and her newborn infant, delivery by elective caesarean section and the avoidance of breastfeeding have dramatically reduced vertical transmission rates in the British Isles, and it is now rare for a woman whose infection is diagnosed prior to delivery to have an infected infant. Pregnant women should now be offered and recommended an HIV test as a routine part of antenatal care in most parts of the UK and RoI. National targets have been set in England for the uptake of antenatal testing (90% by end 2002), and detection of infection in pregnancy (80% by end 2002) in order to reduce the proportion of infected infants.[1] There have been substantial improvements in antenatal detection of infection.[2] Combined with an increase in the number of women already aware of their infection status who are becoming pregnant, this has led to a considerable increase in the number of infants born to diagnosed women and reported through the surveillance systems.

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. 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.

Surveillance Period

Surveillance began in June 1986 and is reviewed annually.

Analysis

By the end of December 2001 there had been 2330 reports through the BPSU. One thousand four hundred and twelve children born to HIV infected women, and therefore at risk of vertical transmission, were reported (Table 9), together with 48 children who were infected in the course of treatment for haemophilia, 27 through blood or tissue transfer and 12 for whom the transmission route could not be established. Of the remaining 831 reports, 85 are still under investigation, 373 were duplicates, and there were also 373 reporting errors. A further 1690 cases have been reported from other sources (see Endnote) including 1418 children born to HIV infected women, 219 children with haemophilia, 19 infected through blood transfusion and 34 where the route of transmission remains unclear. The increase in the number of cases (reported through all sources) where the route of transmission cannot be established reflects an increase in the reporting of older, symptomatic children, recently arrived from areas where HIV infection is endemic. In many of these cases the HIV status of the mother at the time of the child's birth is unknown.

Data from all sources are combined each quarter and form the basis of the national surveillance of paediatric HIV infection, with UK summary tables appearing on a quarterly basis in the Communicable Disease Report (England, Wales and Northern Ireland) (available at www.phls.co.uk) and the SCIEH Weekly Report (Scotland).

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

By the end of December 2001, 2830 children born to HIV infected women had been reported (Table 10), about 11% of whom had been born abroad. Transmission rates cannot be estimated from these data as there is a bias towards the reporting of symptomatic children, but 865 had confirmed infection, 710 were of indeterminate status and 1255 were known to be uninfected. Two hundred and eighty (10%) children were reported from the Republic of Ireland, 244 (9%) from Scotland, and 2306 (81%) from England, Wales and Northern Ireland (see footnote). About 15% of indeterminate and infected children were known to have died.

A growing number of children, most of whom are uninfected, have been exposed to antiretroviral therapy in fetal or early life.

Table 9 *Infants born to HIV infected women, and confirmed cases of paediatric HIV infection (notified by 31 December 2001)*

Likely transmission route	BPSU reports	Reports from other sources	TOTAL
Risk of vertical transmission	1412	1418	2830
Haemophilia treatment	48	219	267
Blood transfusion/products	27	19	46
Other/not yet established	12	34	46

Table 10 *Infection status of children born to HIV infected women (notified by 31 December 2001)*

Region of first report	**Infected**	**Indeterminate**	**Not infected**	***Total***
England, Wales & N Ireland*	776	624	906	2306
Scotland	43	41	160	244
Republic of Ireland	46	45	189	280
Total	865	710	1255	2830

* Over 80% reported from former Thames regions, <2% from Wales and NI combined

Mechanisms are being established for on-going follow up of these children, so that any unexpected or unusual sequelae of treatment can be recognised as early as possible. A pilot study to assess the most appropriate way to follow up the uninfected children is currently underway in five London units.

We would like to thank all members of the RCPCH, particularly those paediatricians who have reported cases and completed questionnaires, for their continued support and diligence.

Funding

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Endnote

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

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Internal abdominal injury due to child abuse

Key Points

- **Internal abdominal injury (IAI) due to child abuse is rare.**
- **Preliminary analysis suggests that small bowel/ duodenal injury may be an important diagnostic feature.**
- **Six of the 15 reported cases died of their internal abdominal injury.**

Background

Non-accidental injury in childhood is sadly not an uncommon occurrence in today's society. In the UK, according to a recent NSPCC survey, 7% of young adults have experienced serious physical injury at the hands of their carers during their childhood. On average four children died each week in the UK as a result of child abuse in 1997.

The skeletal and intra-cranial manifestations of physical child abuse are well described in the medical literature, with head injuries being the leading cause of death in children injured non-accidentally.[1]

Internal abdominal injuries due to child abuse are also described but are thought to account for less than 2% of all non-accidental injuries.[2] However this type of injury is the second commonest cause of death following child abuse with mortality rates as high as 40-50% reported in the USA.[3] Child abuse has been identified along with motor vehicle trauma as the major aetiological factors in childhood internal abdominal injury.[4]

There is only a small body of UK literature available on the subject of internal abdominal injury due to child abuse. Clinicians involved in analysing a suspected case as part of a child protection investigation may be faced with real difficulties if looking for information. In the USA, it has been suggested that hollow viscous injury is the most commonly identified internal abdominal injury seen as a result of abuse whereas accidental injury is more likely to be associated with injury to solid organs within the abdomen, for example the spleen or kidney.[5] However, it is clear from available case reports that any intra-abdominal organ can be injured following abuse.

In view of this paucity of information in the UK, an epidemiological study of internal abdominal injury due to child abuse would be important and informative. There are a number of important questions to consider. For example, how common is this condition in the UK and which children are commonly affected? How do children present and what is their eventual clinical outcome? What associated signs or injuries should be looked for in addition? Is there a pattern of injury that is more likely to indicate a non-accidental rather than an accidental cause? Are there any pointers to prevention?

This background formed the basis of a two-year study, which is currently ongoing in the Academic Department of Child Health in

Cardiff. Some important messages seem to be emerging at the end of the first year of the study, and these are described.

Objectives

- What is the incidence of abdominal injury due to abuse?
- What organs are involved?
- What are the key diagnostic features in the differential diagnosis of abuse versus accident and the diagnosis of injury?
- Were there factors prior to diagnosis that could have prevented the abuse?
- What was the Child Protection outcome?

Case Definition

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

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

Exclude - abdominal bruising alone

Study Duration

March 2001 to March 2003

Methodology

All consultant paediatricians across the UK and the Republic of Ireland since March 2001 have been asked to report cases of suspected internal abdominal injury due to child abuse. Cases are reported on the basis of the case definition described above and following consideration of the circumstances at a multidisciplinary meeting (such as a strategy meeting, case-conference or part VIII review).

A questionnaire which has been designed to collect information about the demographic details of the case child, mode of presentation and any previous child protection concerns prior to this particular injury is then dispatched. The exact nature of the internal abdominal injury, along with other associated injuries such as fractures, burns and bruises – particularly of the external abdominal wall, is enquired about. Information is sought on the diagnostic investigations undertaken, as well as the treatment and outcome in each case. Finally information about the family make-up (including information about the alleged perpetrator, where known) and also the child protection investigation and outcome is collected.

Working in collaboration with Professor David Yates in Manchester who is conducting the 'UK Major Trauma Outcome Study', information about accidental internal abdominal injury in childhood has been obtained. This study has collected information for over a decade from over half of the A&E departments in the UK. Road traffic accidents and falls from over two metres are two of the commoner causes of accidental injury seen in this study, and details have been obtained regarding the pattern of internal abdominal organ injury seen as a result of accidents. A comparison with these accidental injury patterns and those seen in the abused children will be made, analysing differences by employing odds ratio / chi squared test.

Analysis

In the first year of the study, 49 notifications have been received from consultants in the UK and Ireland, through the BPSU.

However, 16 notifications were made in error (for example, accidental injuries or external abdominal bruising alone), and 14 duplicate notifications have been received. At present four replies are still awaited (it is known that these include two fatal cases of internal abdominal injury due to abuse).

Of the 49 reports, 15 cases have met the case inclusion criteria in the first 12 months. However seven of these cases were injured prior to March 2001, but the child protection investigation was ongoing in most when the study started and might account for the notification being made. The important findings are presented for all 15 notifications received.

The mean age of cases was three years 11 months (range three months – 14 year 9 months) of these 46% were males.

In nine of 15 (60%), child protection concerns were evident before the current episode of abuse resulting in internal abdominal injury. Eleven of 15 (73%) case children lived with a single biological parent – always the mother, and in all but one of these cases the alleged perpetrator was a male cohabiter, other than the father.

In eight of 15 (54%) cases, there were new or recent fractures found in association with the internal abdominal injury.

In four of 15 (27%) cases, NO external abdominal bruising was reported despite serious internal abdominal injury.

Sadly in six of the 15 cases notified (40%), the child died from their internal abdominal injury.

The cases seem to present in one of three ways; with either acute abdominal symptoms and signs, being referred to hospital by a GP (27%); in a shocked / collapsed state presenting to hospital / A&E and requiring fluid resuscitation (33%) or alternatively they are discovered or brought to hospital already dead, and beyond medical help (33%).

In 11 of 15 cases notified (73%), small bowel injury (including duodenum) was reported and in nine of these rupture of small bowel / duodenum was evident (60% of all cases). Excluding the

notifications whose injury preceded the date of study onset, similar percentage figures (63% and 50% respectively) for this pattern of small bowel injury are seen.

All but one death was associated with the presence of small bowel injury.

Data for accidental internal abdominal injury in children shows that 978 injured in a road traffic accident, only 76 (7.8%) had evidence of small bowel injury (including duodenum) and for 181 children who had fallen over two metres to sustain an internal abdominal injury, this injury was seen in only seven children (3.8%).

Thus although a direct comparison is not possible, these preliminary findings support that small bowel/duodenal injury is more common in non-accidental injury than accidental injury or road traffic accident and falls.

Conclusions

Internal abdominal injury due to child abuse seems to be a rare occurrence based on the small number of notifications received during the first year of this study.

Initial findings in the very small numbers to date suggest that small bowel injury (including duodenum) is by far the commonest organ involved resulting from abuse, and usually perforation is evident. This type of injury is much less common than other significant but accidental forms of trauma such as road traffic accidents, and the findings regarding this pattern seem to mirror closely those reported in a US series by Ledbetter[5] (65% of abusive internal abdominal injuries were hollow viscous injuries, compared to only 8% of the internal abdominal injuries sustained accidentally).

The absence of external bruising despite the presence of serious internal abdominal injury in 27% of this study population is similar to the 35% figure reported by Ledbetter.[5] Children who present with shock and abdominal symptoms or shock and who are non-specifically unwell may have suffered an internal abdominal injury due to abuse yet have no external markers would suggest that NAI should be considered as part of the differential diagnosis list in such cases (with CT scanning the diagnostic method of choice suggested in the literature[6]).

Mortality in our series seems to be high as reported by others.[3] Co-existent injury, particularly skeletal, seems to be common and should be looked for in all cases.

It is important to note that to date the investigators have only a small number of cases on which to be able to report findings and that some of these are strictly speaking historical notifications. Also it is important to consider that only the most severe cases, where the diagnosis is obvious, are being reported, and that other perhaps less severe cases with different patterns of internal abdominal injury may not have abuse considered as a possible cause. It is reassuring to note that duplicate notifications are being received, which indicates that cases are being picked up through the BPSU.

Although the number of cases is small at present the emerging pattern is that small bowel / duodenal injury, more than any other internal abdominal injury should raise suspicions that the injury is non-accidental. It will be of interest to see if this is borne out in the final analysis.

Surveillance is now entering its second year and case notifications continue (an additional four cases have been notified in March and April 2002).

Funding

Local hospital funds

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Progressive Intellectual and Neurological Deterioration in Children (PIND)

Key Points

- **We want to hear about all children with progressive intellectual and neurological deterioration even if you have already made a diagnosis! This is important because we want to ensure that ascertainment is as complete as possible.**
- **Six cases of variant Creutzfeldt-Jakob disease (vCJD) have been reported to the study since December 1998. Of these four have been classified as "definite" and two "probable" according to the National Creutzfeldt-Jakob Disease Surveillance Unit.**
- **The clinical presentation of the six cases of vCJD in the PIND study has been similar to that in adults. However, the youngest of the PIND cases developed symptoms at the age of 12 years. It is possible that younger children with vCJD might present with a different clinical picture. This is why it is so important to review all children with progressive intellectual and neurological deterioration in the UK and not just those already thought to have vCJD.**
- **Over the five-year study period 1299 children have been notified. 936 cases have been discussed by an Expert Neurological Advisory Group of six paediatric neurologists. 535 have a definite diagnosis (which is not vCJD), and these comprise 93 known degenerative conditions.**
- **The most commonly occurring diagnoses are the neuronal ceroid- lipofuscinoses (64 cases), the gangliosidoses (60 cases) and the mucopolysaccharidoses (57 cases)**
- **There are districts with considerably higher rates of incidence of PIND. In some of these areas there are high consanguinity rates and a heterogeneous mixture of diagnoses.**

Background

Active prospective surveillance of UK children with progressive intellectual and neurological deterioration (PIND) commenced in May 1997. Funded by the Department of Health, it is being carried out via the BPSU in coordination with the National Creutzfeldt-Jakob Disease Surveillance Unit in Edinburgh (NCJDSU) and the Public Health Laboratory Service (PHLS). It is hoped to extend this until October 2005 (including an 18 month writing up period).

The main aim is to determine whether or not any children in this group have developed variant Creutzfeldt-Jakob disease (vCJD). The appearance of vCJD in patients as young as 16 years of age[1] first suggested the possibility that it might occur in younger children. The detection of vCJD in UK children has important implications for both paediatrics and child health and there was a call for further epidemiological surveillance to investigate this issue[2] The presentation of vCJD is different from that of classical CJD. It is possible that young children with vCJD might present with a clinical picture different from that already described in adults with vCJD. The strategy is to detect suspected vCJD cases by looking at a broader group of conditions causing progressive intellectual and neurological deterioration in children (PIND). In this way, not only are vCJD cases detected, but also unique epidemiological data on a variety of PIND conditions are obtained.[3]

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

Objectives

- To carry out active prospective surveillance of UK children with paediatric neurological conditions (including those with specific diagnoses) defined by their common presentation - Progressive Intellectual and Neurological Deterioration (PIND) - to determine the incidence and distribution of PIND.
- To evaluate cases presenting with PIND in order to classify them and investigate the possibility that vCJD is occurring in children.

Surveillance Period

Surveillance commenced in May 1997 and is reviewed annually.

Case Definition

Any child under 16 years of age at onset of symptoms who fulfils all of the following three criteria:

- Progressive deterioration for more than three months

With

- Loss of already attained intellectual/developmental abilities

And

- Development of abnormal neurological signs.

Excluding: Static intellectual loss, e.g. after encephalitis, head injury or near drowning.

Including: Children who meet the case definition even if specific neurological diagnoses have been made.

- Metabolic disorders leading to neurological deterioration.
- Seizure disorders if associated with progressive deterioration.
- Children that have been diagnosed as having neurodegenerative conditions but who have not yet developed symptoms.

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

Analysis

By the beginning of April 2002 a total of 1299 children had been reported via the BPSU (Figure 9). Of these the Expert Neurological Advisory Group has classified 936 cases according to various study groups. The 460 "No Cases" include those who do not fulfil the criteria for PIND, reporting errors and duplicate notifications. The 79 outstanding cases include 24 due for discussion at the May 2002 Expert Group meeting and 55 awaiting data collection.

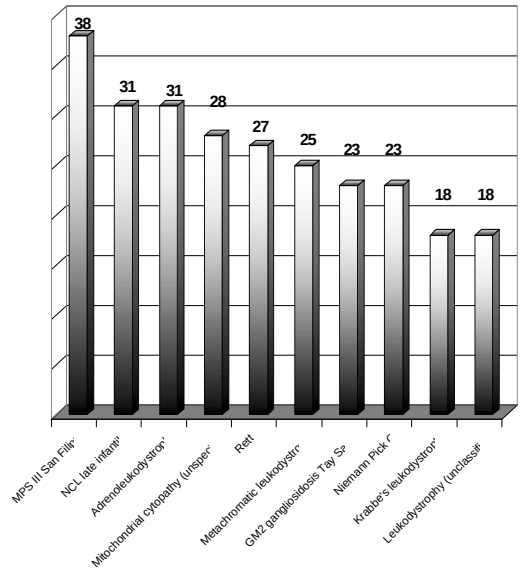
Definite/Probable Cases of vCJD

Six cases of vCJD have been notified - the youngest was a girl aged 12 years at onset. The other five were three girls (two aged 14 years and one aged 13 years at onset) and two boys aged 15 years at onset. One child was notified in 1998, two in 1999, one in 2000 and two in 2001. Four have died and neuropathology has confirmed vCJD (classified as definite cases), and two are still alive (classified as probable cases).

Children who have definite PIND diagnoses other than vCJD

The study is producing unique population-based data on the causes of PIND. The majority of children with PIND have a known degenerative diagnosis or a likely underlying diagnosis which is not vCJD. In the 535 children with a confirmed diagnosis other than vCJD there were 93 different neurodegenerative conditions. The ten most commonly occurring diagnoses are shown in Figure 10.

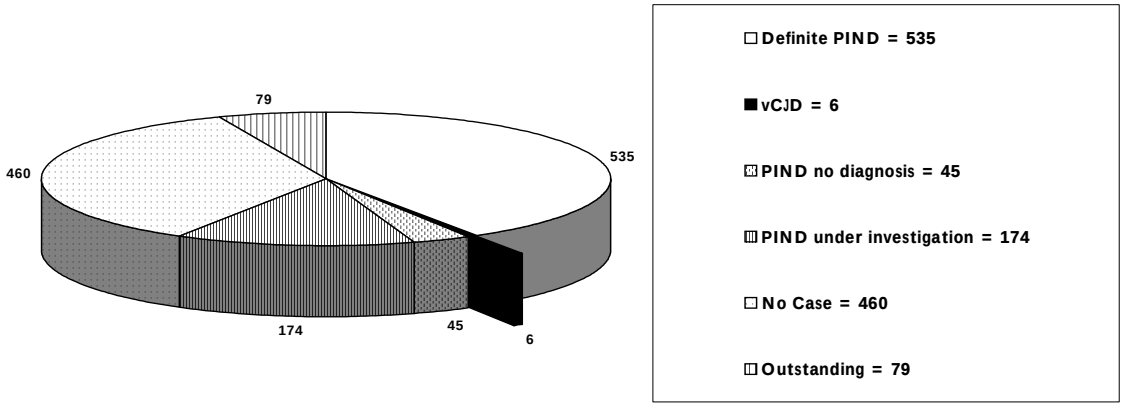
Figure 10 *Ten most commonly reported PIND diagnoses*



Variation in reporting by district

Geographical analysis by hospital of report and by residence reveals significant variations. A few hospitals have not reported any cases. There are some areas with considerably higher numbers of children with PIND. Yorkshire remains the highest reporting BPSU region (166 cases) with North East Thames next (144 cases), followed by West Midlands (137 cases).

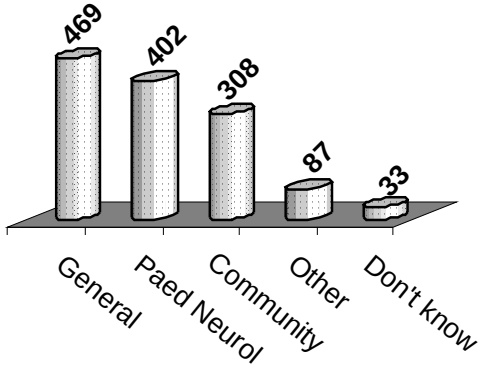
Figure 9 *PIND Study Status*



Variation in reporting by category of referring paediatrician

Most children were notified by general paediatricians followed by paediatric neurologists then community paediatricians.

Figure 11 *Category of Referring Paediatrician*



Interim Conclusions

PIND surveillance has been running for five years now. Paediatricians are still responding enthusiastically with a median number of 20 notifications per month (Figure 12). Six cases of vCJD in children under 16 years of age at first presentation have been notified to the studv. There were four cases of definite

The PIND surveillance team is very grateful to the members of the Expert Neurological Advisory Group (Prof J. Aicardi, Dr P. Baxter, Dr S. Green, Prof. R. Robinson, Dr R. Surtees and Dr J. Wilson) for all their work in classifying cases and for the cooperation of UK paediatricians in support of this surveillance project.

Funding

Dept of Health

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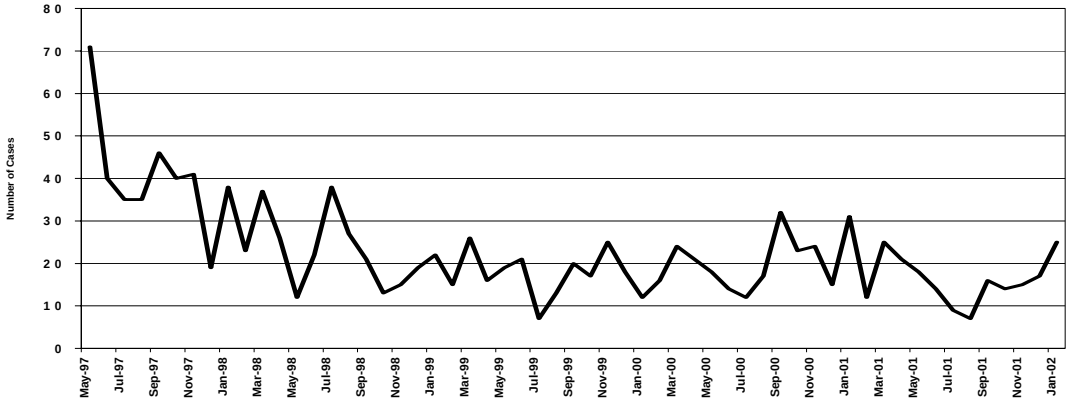
Figure 12
Reporting Rates May 1997 - January 2002



Thrombosis in childhood

Key Points

- **Sixty eight cases have been reported in the first year - less than had been expected.**
- **Overall mortality was low (5.8%) with no death attributed to venous thromboembolism.**
- **The main risk factors were central venous/femoral lines, infection and malignancy.**
- **Concern over under ascertainment has led to a more active targeting of specialists known to caring for such cases.**

Background

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

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

DVT involves the upper system in between 26-36% of children (due to the use of central venous catheters) compared to 1-2% of DVT in adults. Idiopathic DVT is rare (4% in the Canadian Registry and 2% in the literature) in contrast to approximately 30% of adult DVT. More than 95% of children with DVT/PE have one or more predisposing factors. The role of acquired and inherited thrombophilia in children remains unclear.

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

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

Objectives

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

Study duration

February 2001 – February 2003

Case definition

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

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

Analysis

During the first 12 month period 138 thrombotic episodes have been reported and data collection forms sent to reporting clinicians. 112 forms have been completed and returned and of these 68 fit the criteria for the study. 44 (39.3%) were excluded for the following reasons – duplicate reporting, events occurred in neonatel period, fitting the criteria of the Stroke Study and the actual event occurred before February 2001, when the study started.

Site of Thrombus: Of the 68 cases analysed 59 (87%) were venous related. Four patients also had pulmonary embolism. Five cases were cardiac related. 61% occurred in the lower limbs, 29% in the upper limbs, jugular and subclavian veins and 10% in various other sites.

Risk Factors: The main risk factors were – central venous/femoral lines (38%), infection (29.5%) and malignancy (26.5%). Other risk factors included renal disease/nephrotic syndrome, surgery and family history.

Diagnostic Investigations: Doppler ultrasound, echocardiogram, venogram, CT and MRI scans were the main method of diagnosis, with ultrasound being the most common at 79%. In over 32% of cases more than one diagnostic investigation proved to be abnormal.

Management: More than 61% of cases were treated with Heparin/LMWH followed by Warfarin. 25% received Heparin alone. Central venous/femoral lines were removed in 20% of cases

Outcome: Of the 68 first mailing forms analysed 52 cases (76.5%) had achieved complete or partial resolution at the time the forms were completed. In 16 cases (23.5%) resolution had either not been achieved or this was unknown. However, the time between the thrombotic event and completion of the form may have a bearing on this figure. The six-month follow up mailing forms will give a more accurate picture of the incidence of complete resolution. Bleeding complications in only four cases were noted, and these were all minor. The overall mortality is low in these patients (5.8%) with no death attributed to venous thromboembolism.

Comment

The study was initially intended to run for a period of 13 months during which it was anticipated that data, suitable for analysis, would be collected on at least 100 cases fitting the criteria of the study. At the end of the first year recruitment to the study was less than anticipated which could be due to an over-estimation by study investigators, or the under-reporting of actual thrombotic events. As a result the ascertainment period has been extended for a further year. Existing clinicians reporting via the orange card system are encouraged to do so, and other clinical groups most likely to be involved in the management of thromboembolic episodes in children will more actively targeted. These include paediatric anaesthetists, paediatric intensivists, paediatric cardiac and general surgeons.

For the study to give realistic and accurate data on which to base future diagnostic and therapeutic practice, it is important to collect information on as many thrombotic episodes as possible. To this aim clinicians are urged to report any episode of thrombosis fitting the criteria of this study.

Funding

Local hospital research fund

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Vitamin K Deficiency Bleeding

Key points

- **Five cases have been identified in the first year.**
- **Three were early onset and two were late onset.**
- **Three had received no vitamin K, two had oral prophylaxis.**
- **In four cases the birth unit's policy for vitamin K prophylaxis had not been followed, in all because of parental refusal or indecision.**

Background

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

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

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

Vitamin K is now given in four common but very different regimens. In 1993 one or two units gave no routine prophylaxis, some gave a single oral dose, some gave multiple oral doses and some gave intramuscular vitamin K to all infants.[4] The relative risk of bleeding

in infancy is maximum in the first and minimum in the last of these groups with dramatic differences across the groups; babies given no prophylaxis (including those whose parents have refused it) are eighty times more likely to bleed than those given intramuscular prophylaxis.[5] Errors in administration of the planned regimen or parental refusals would tend to mask these differences.[5]

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

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

Surveillance Period

January 2001 - January 2003

Objectives

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

Case definition

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

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

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

Analysis

In the first full year of the study 25 notifications were returned and 18 completed questionnaires have so far been received (seven are outstanding), in relation to 15 infants (three were reported in duplicate). One was for a confirmed case which predated the study and so is not included below.

Further information has led to reclassification in some cases. Nine reports are now classified as "no case"; five, all relating to term infants, are classified as "confirmed" (three reported in duplicate). Three cases presented in the first week of life (classical VKDB), the other two at 39 and 63 days (late onset VKDB). Four were exclusively breastfed and one soy formula fed. Two presented with bruising (one with nosebleed in addition), three with gastrointestinal bleeding (one associated with campylobacter infection; one also had umbilical bleeding). Three had received no vitamin K, two had oral prophylaxis. In four cases the birth unit's policy for vitamin K prophylaxis had not been followed, in all because of parental refusal or indecision. In two cases underlying liver disease almost certainly contributed to the vitamin K deficiency; one was associated with cystic fibrosis and one with biliary atresia.

Discussion

In the four years of the previous studies the average prevalence was about 15-confirmed/probable cases/ year, including five with intracerebral bleeding. These preliminary results from the current study show no increase in prevalence; they allow the possibility that there has been significant reduction but emphasise that parental anxiety leading to refusal of prophylaxis is now an important factor.

The investigators are repeating their survey of vitamin K prophylaxis policies, as was carried out in association with the two previous BPSU surveys.

The investigators would like to thank all those who have notified cases (including doubtful cases) and spent time and effort collecting data for this study.

Funding

Department of Health

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6 New Studies 2002

Suspected fatal adverse drug reactions in children

Background

The Yellow Card Scheme, set up in 1964, the UK's spontaneous reporting scheme is the mainstay of drug safety monitoring in the UK. It is perceived that there may be under-reporting of suspected adverse drug reactions (ADRs) in children. Medicines in children are frequently prescribed "off-label" and therefore have not been formally evaluated for safety and efficacy in that age group. It is particularly important to report and detect potential drug safety issues in children. This prospective study will for the first time allow us to document with a degree of certainty whether fatal adverse drug reactions are a problem in children.

Objective

To study the frequency and nature of suspected adverse drug reactions with a fatal outcome in children below the age of 16 years.

Sureveillance Period

June 2002 - June 2003

Methodology

All cases meeting the case definition will be identified using the BPSU Orange card. Details of the case will be sought through a written questionnaire. If necessary, a further follow-up letter will be sent. The patient, family or other health professional involved with the care for the child will not be contacted. A causality assessment will be undertaken.[1] An expert panel will be convened to discuss individual cases.

Case Definition

Any child below the age of 16 years with a suspected adverse drug reaction with a fatal outcome. ADRs include suspected reactions to vaccines. Importantly clinicians are also asked to report cases seen through the MCA Yelllow Card scheme.

Ethical Approval

London MREC

Funding

The Medicines Control Agency, UK

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Congenital Toxoplasmosis

Background

When toxoplasma infection is acquired for the first time in pregnancy, foetal infection occurs in about 25% of women.[1] One in six infected infants have lesions to the brain or eye, which may result in long term impairment. Up to date information on the birth prevalence and severity of CT is required to inform prevention strategies such as neonatal screening in the UK, which is already carried out in the US and Europe.[2, 3, 4] This study will determine birth prevalence of symptomatic CT detected by clinicians in the British Isles and the severity of clinical manifestations. Results will be compared with findings from a similar study conducted 12 years ago.[5] Since then, changes in travel and diet may have led to an increase in the incidence of maternal infection.[6] The study will also investigate the feasibility of testing stored Guthrie card blood spots to confirm a suspected case of CT.[3]

Objective

Surveillance of clinically recognised, confirmed and suspected, congenital toxoplasmosis (CT) infection in children under 16 years in order to ascertain birth prevalence in a one year period, severity of clinical manifestations and age at first diagnosis. This information will aid decision-making about appropriate prevention measures such as neonatal screening. A further objective is to determine the feasibility

of using stored neonatal dried blood spots to confirm or exclude a diagnosis of CT infection in childrenprevention measures such as neonatal screening. A further objective is to determine the feasibility of using stored neonatal dried blood spots to confirm or exclude a diagnosis of CT infection in children.

Surveillance Period

July 2002 – July 2003

Case Definition

Respondents are asked to report all stillbirths or under under 16 seen in the last month where CT is ***suspected***. CT may be suspected in any of the following:

1. toxoplasma specific IgM/IgA antibodies under two years of age in peripheral blood (or cord blood)
2. any child with toxoplasma IgG detected between approximately 6-18 months
3. any child with toxoplasma DNA or parasite detected in body tissues or placenta
4. any child with unexplained retinitis and toxoplasma IgG antibodies
5. any infant (<12 months) with unexplained hepatosplenomegaly or lymphadenopathy and toxoplasma IgG antibodies or serological results compatible with maternal toxoplasma infection during pregnancy
6. any child with unexplained hydrocephalus, intracranial calcification, microcephaly or micropthalmia and toxoplasma IgG antibodies or serological results compatible with maternal toxoplasma infection during pregnancy.

Methodology

Reporting clinicians will be sent a brief questionnaire asking for demographic information about the child and mother, including where the mother lived for most of her pregnancy and her ethnic group. Clinicians will be asked to report a history of squint, episodes of visual loss or ocular pain, and afebrile convulsions. Data will be requested for clinical findings from the general examination (hepatosplenomegaly, lymphadenopathy, microphthalmia, microcephaly, abnormal neurology, cerebral palsy), ophthalmoscopy and assessment of visual acuity, and results of intracranial imaging.

Results of tests for specific toxoplasma antibodies in the child (IgG, IgM, IgA) and the mother during pregnancy will be requested to confirm the diagnosis. Testing for congenital toxoplasmosis is best performed by a reference laboratory.

The study will examine the feasibility and usefulness of testing stored Guthrie card bloodspots to detect toxoplasmosis specific IgM/IgA antibodies in children with suspected CT infection.

Ascertainment of cases will also be achieved through the British Ophthalmological Surveillance Unit.

Clinicians will be asked to forward a brief questionnaire to the parents requesting consent for retrospective testing of stored Guthrie card blood spots

Ethical Approval

London MREC

Funding

Local hospital funds

References

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Severe complications to varicella

Background

Varicella zoster is a highly contagious and infectious virus, causing varicella upon primary infection and herpes zoster upon subsequent reactivation.[1] Approximately 90% of varicella cases occur in children less than 15 years of age with the highest incidence of infection in the one to four year age group.[2,3] Varicella is generally a mild disease in healthy children. Nevertheless, some severe complications may occur even in previously healthy children, including secondary bacterial infections, central nervous system manifestations, and death.[4]

There are few data on complicated varicella cases in the UK. Routine hospital discharge records and mortality data in the UK have been analysed previously [3,5,6], but cannot provide data with sufficient detail or accuracy due to the problems inherent in retrospective studies.

This study aims to identify hospitalised children with severe complications of varicella. It is acknowledged that there is a larger group of children in hospital with varicella, either for specific treatment, or with co-incidental infection. These patients are an important group, but are too numerous to be included in this study.

A live-attenuated vaccine developed in Japan in the early 1970s has been shown to be safe and effective and is now recommended for routine use in all healthy children in several countries, including the United States and Canada.[7] The vaccine prevents varicella in 85% of immunised children, with 97% protection against moderately severe and severe disease. [8]

Currently, there is no immunisation programme against varicella in the UK, or Ireland and a policy decision on its possible introduction has yet to be taken. More information is required to inform this process, including epidemiological data such as disease incidence, trends, complications and case fatality, as well as other issues such economics and professional and parental acceptability. Data provided by this study on severe varicella complications in the UK and Ireland will, therefore, contribute to the epidemiological and economic information available and help to determine the advisability of an immunisation programme. If a vaccination programme is established the data will provide one baseline against which its impact can be evaluated.

Objectives

Primary

- To estimate the annual incidence of complicated varicella in hospitalised children less than 16 years of age living in United Kingdom, the Channel Islands and the Republic of Ireland.

Secondary

- To characterise severe varicella complications.
- To describe the characteristics (age, underlying medical conditions) of these children.
- To estimate the annual financial cost of hospitalisation for severe varicella.
- To estimate the annual mortality from varicella in children.

Surveillance Period

Autumn 2002 - Autumn 2003

Case definition

Any child less than 16 years hospitalised with complicated varicella, as defined by list of clinical conditions*, or admitted to a paediatric ICU or HDU with varicella or one of its complications.

*Bacteraemia / septic shock, toxic shock syndrome / toxin-mediated disease; necrotising fasciitis; encephalitis; purpura fulminans / disseminated coagulopathy; pneumonia (abnormal x-ray); neonatal varicella; fulminant varicella; Reye's syndrome; ataxia; admitted into ICU / HDU; death due to varicella.

Virological testing

All reporting clinicians wishing virological testing for severe cases of varicella are encourage to submit throat swabs and/or vesicle fluid samples for molecular analysis at no charge. Please contact Dr Judy Breuer, Consultant in Virology, St Barts and The London. Tel: 020 7 377 7141.

Ethical Approval

Scotland MREC

Funding

Through Scottish Centre for Infection and Environmental Health

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Langerhan Cell Histiocytosis

Background

Langerhans Cell Histiocytosis (LCH), previously known as Histiocytosis X, is a disease in which cells ('LCH cells') with the characteristics of epidermal Langerhans cells (a form of dendritic cell) accumulate with other immune cells in various parts of the body and cause tissue damage by the release of cytokines.[1] In health, Langerhans cells recognise foreign antigens including bacteria and stimulate the immune system to react to them. Langerhans cells are normally found only in the skin, lymph nodes, and main airways. In disease, LCH commonly affects skin (rash), bone (single or multiple lesions) and the pituitary gland (diabetes insipidus) and may also affect the lungs, intestines, spleen, bone marrow and brain. The disease is therefore not confined to areas where Langerhans cells are normally found. The disease is more common in children than adults and tends to be more severe in very young children, especially when several organs are affected.[2] Why cells accumulate (particularly within those tissues, such as CNS from which they are normally absent), why 'LCH cells' proliferate (little or no proliferation is detected in normal Langerhans cells) and what role they play in pathogenesis are all unknown.

The cause of LCH is unknown. It may be triggered by an unusual reaction of the immune system to something commonly found in the environment. It is not a known infection or a cancer and, although there may be a more than one patient in certain families[3], it is usually not hereditary.

Around 10-20% of patients, usually infants, die. In other patients the disease usually burns itself out, but there may be long term sequelae due to damage caused by the disease process.[4,5] Not all children require specific treatment. Quality of life in survivors is often poor[6] and chronic sequelae are a constant drain on health care resources.

Objectives

1. To describe the epidemiology of LCH in the UK, Eire, Canada and Netherlands. In particular;
- to describe the incidence of LCH in boys and girls by age and extent of disease at diagnosis
- to study variation between ethnic groups
- to determine whether or not there are international differences in LCH incidence
- within each country to describe regional differences in incidence rate to assess geographic variation eg north/ south or urban/rural. There would be too few cases and too short a timescale of ascertainment for cluster analysis.
- to assess the frequency of familial LCH.

2. To document patterns of presentation. In particular;
- to describe the interval between the onset of symptoms and diagnosis
- to describe early exposures which may be associated with LCH.

Surveillance Period

Autumn 2002 - Autumn 2003 in the first instance.

Case Definition

Children of any age newly diagnosed with either (a) or (b)

a) biopsy-proven LCH; lesional cells (LCH cells) must contain Birbeck granules or be CD1a positive or S100 positive with characteristic H&E morphology. Central review of histopathology slides is available and desirable.

b) Lytic bone lesion or pituitary/hypothalamic abnormality with the characteristics of LCH but not biopsied whether
i) because clinical features suggest spontaneous resolution or
ii) because the risk of the biopsy procedure in view of the location on the lesion (eg cervical vertebra, pituitary mass), is considered too great

Clinical features of LCH include: otherwise unexplained bone pain with/without overlying soft tissue swelling, especially in the skull and jaws (floating teeth); proptosis; recurrent otitis with otorrhoea; maculo-papular rash resembling seborrhoeic dermatitis and in the same distribution (especially scalp and flexures) but resistant to topical treatments; interstitial pneumonitis; unexplained colitis; sclerosing cholangitis; diabetes insipidus; unexplained hypothalamic-pituitary dysfunction

Ethical Approval

To be sought through Northern MREC

Funding

Histiocytosis Research Trust

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7 The International Perspective

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

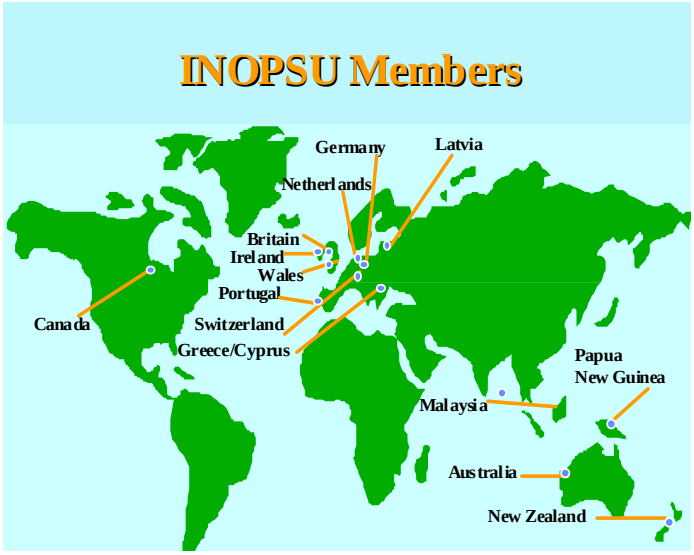
The European initiative was also the stimulus for the development in 1992 of an Australian unit and later the Malaysia unit (1994) to be followed more recently by units in Canada (1996), Papua New Guinea (1996), New Zealand and Latvia (1997). Portugal (2001) is the latest country to develop a surveillance unit and Greece/Cyprus has recently put in place the administration to set up a unit, and is expected to pilot surveillance in 2002. Wales (1995) and Republic of Ireland (1997) developed surveillance units using a similar methodology to the BPSU, though they are concentrating on less rare disorders.

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

The director of the Australian unit keeps in contact with those of units in Papua New Guinea, New Zealand and Malaysia. Given the existence of at least ten national paediatric surveillance units undertaking similar work and this level of informal contact it was accepted 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) was accepted in principle by all units existing at that time. Now all the units contact each other for results, sharing of protocols, putting researchers in touch with each other and a common international report is shared as part of national reports.

International Network of Paediatric Surveillance Units (INoPSU)



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

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. A document known as the Amsterdam-Ottawa Note detailing the functions and structure of the network has been agreed and posted on the INoPSU website.

Following the first INoPSU conference in 2000 the Welsh Paediatric Surveillance Unit was accepted into the Network. The Portuguese and Irish Units were accepted as full members of the Network in 2002.

The activities of the INoPSU are coordinated by a secretariat, with Professor Elizabeth Elliott (APSU) as convenor. The secretariat from 2002 includes from Canada Professor Victor Marchssault (convenor elect), Dr Rudi von Kries (Germany), Dr Nigel Dickson (New Zealand), Dr Mario Coelho (Portugal) and Richard Lynn (BPSU). The BPSU will continue to act as server until April 2003 from which time the representatives of the Canadian Surveillance Programme will take over as convenor and Network server.

Following the second INoPSU conference held in 2002 at York University, UK, it was agreed a further conference would be held in Portugal in 2004.

Report on the 2nd INoPSU Conference

Following a similar meeting in Ottawa two years ago, the British Paediatric Surveillance Unit has hosted a second successful INoPSU conference. This was held over two days at York University, in conjunction with the Annual Scientific meeting of the College. The first day brought together 20 representatives from 11 of the 14 national surveillance units. Professor Mike Preece, Dr Chris Verity and the BPSU Scientific Co-ordinator, Richard Lynn represented the UK. Countries represented at the meeting included Germany, Netherlands, Australia, New Zealand, Republic of Ireland, Wales, Switzerland, Canada, Malaysia, Portugal and Greece. The aims of INoPSU were reiterated, to facilitate communication between existing units; encourage the sharing of information between researchers and to assist in the development of new units. With the final aim in mind the Portuguese and Irish Paediatric Surveillance Units were accepted as full INoPSU members whilst the Greece/Cyprus Unit was accepted as an affiliate until such time as it has fulfilled the requirements for full membership. The British Opthalmological Surveillance Unit continues as an associate member.

Topics discussed included funding problems, the difficulties with data collection and handling and the need for multi-national rare disease surveillance. To this end several disorders were considered for such targeting, including haemolytic uraemic syndrome, and congenital toxoplasmosis. Ways in which communications can be improved by national research teams were also proposed and it is hoped that this will stimulate the use of multi-national surveillance protocols.

A series of lectures on the second day demonstrated the work of INoPSU. Around 100 paediatricians attended the open session. Following an introduction by Professor Elizabeth Elliott on the working of INoPSU, the session continued with a presentation by Dr Jodie McVernon of the Oxford Vaccine Group on *Haemophlus* b vaccination strategies (Hib). Particular concerns were raised over the recent increase in Hib vaccine failures. Several theories for this have been proposed which will require further study and the question arose about the need for placing Hib back onto the BPSU orange card. This was followed by a telling presentation from Dr Elizabeth Miller of the PHLS on how the hypothesis linking MMR with a myriad of disorders including, Crohn's colitis, and autism has continually evolved to try and fit with new evidence. However there continues to be no evidence to show any causal associations. This was followed by Dr Marie Louise Newell of the ICH (London) talking on HIV mother to child transmission rates in the UK and worldwide and how effective screening and appropriate interventional procedures can help to reduce such rates.

The fifth lecture presented by Professor Bhupinder Sandhu of the RHSC Bristol outlined the BPSU survey of inflammatory bowel disease proposing that this may be increasing in the paediatric population. Dr Sarah Muirhead outlined the Canadian surveillance on cerebral oedema following DKA. Dr Chris Verity then presented results from the BPSU study of progressive intellectual and neurological deterioration. Effectively being used to identify paediatric vCJD in the UK it was reported that 1299 cases of suspected PIND had been reported; of these six (four confirmed, two probable) have been identified as vCJD. Finally to put rare disease into context the audience heard a talk from Ms Carol Youngs of the European Organisation for Rare Disease, an umbrella organisation for parent support groups. The importance of appropriate communication with parents when treating such disorders were emphasised as well as bringing to attention the difficulties faced by the family once a child has been diagnosed with a rare disease.

The meeting was considered a great success and will be repeated in 2004 in Portugal. Copies of the abstracts are available via the BPSU office, Tel: (020) 7307 5671, Email: bpsu@rcpch.ac.uk or online at <http://bpsu.inopsu.com/Whatsnew.htm>, where information on the BPSU can also be found. Further information on INoPSU is available online at <http://www.inopsu.com>.

Reports from the National Paediatric Surveillance Units

Australian Paediatric Surveillance Unit (APSU)

The APSU commenced surveillance in May 1993 and currently surveys approximately 1042 clinicians in child health on a monthly basis, covering a child population (<15 years) of 3.9 million. The current return rate for monthly report cards is 96% and for completed questionnaires is 86%. APSU introduced email reporting in 1997 and currently 52% (538) of clinicians have elected to use this service.

Studies that commenced in 2001 include adverse effects from complimentary or alternative medicine, fetal alcohol syndrome and hospitalised pertussis in infancy. Studies that were completed in 2001 include haemolytic uraemic syndrome (December 2001), Congenital and idiopathic nephrotic syndrome (June 2001), severe combined immunodeficiency syndrome (December 2001) and hospitalised pertussis in infancy (December 2001). Other studies currently under surveillance include acute flaccid paralysis, CHARGE association, congenital cytomegalovirus infection, congenital rubella, HIV/AIDS, Munchausen by proxy Syndrome, neonatal herpes simplex virus infection, Rett syndrome and vitamin K deficiency bleeding. Conversion disorder was approved for study in 2002.

In 2001, the APSU provided clinical and diagnostic information to a number of Public health related organisations. This included participation by investigators of the FAS study in a national review of FAS research conducted by the National Expert Advisory Committee, Curtin University of Technology, Western Australia. Investigators of the Hospitalised pertussis in infancy study contributed to the Pertussis in Adolescents and Adults workshop in Sydney which was also attended by public health personell, and data from the primary immunodeficiency disorders study has been included in the national Primary Immunodeficiency Register.

Studies through the APSU have given rise to more than 108 publications including peer-reviewed articles, research reports and published abstracts and a wide range of presentations (102) that have informed the general public and the wider medical community. The APSU's most recent publication, "The Australian Paediatric Surveillance Unit - Progress report" which is currently in press in the Journal of Paediatrics and Child Health, provides a surveillance overview of the APSU and discusses study results to date.

The APSU updates paediatricians with quarterly bulletins that include current study profiles and also provide the Royal Australasian College of Physicians bulletin (RACP news) with regular updates. Information on the ASPU may be accessed through the APSU website (http://apsu.inopsu.com). APSU personnel have also developed websites for INoPSU (http://www.inopsu.com) and assisted in the development of the BPSU website (http://bpsu.inopsu.com).

The APSU currently receives its major funding from the Federal Department of Health and Aged Care. Individual studies have also received sponsorship from Roche (vitamin K deficiency bleeding), GlaxoSmithKline (hospitalised pertussis in infancy) and Healthways (fetal alcohol syndrome).

APSU continues to maintain close links with INoPSU members: currently, Associate Professor Elizabeth Elliott is the convenor of INoPSU.

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Canadian Paediatric Surveillance Program

The Canadian Paediatric Surveillance Program (CPSP) started in 1996 as a joint project of the Canadian Paediatric Society (CPS) and Health Canada's Centre for Infectious Disease Prevention and Control. From three studies in the inaugural year to nine studies in 2001, today nearly 2350 paediatricians and paediatric sub-specialists participate monthly and achieve a 95% response rate for completing detailed case questionnaires. The Canadian paediatric population under the age of 18 years is 6.3 million.

Three studies concluded in 2001 – anaphylaxis, cerebral oedema in diabetic ketoacidosis and progressive intellectual and neurological deterioration, and two were added – CHARGE association/syndrome and necrotising fasciitis. Other current studies included – acute flaccid paralysis, congenital rubella syndrome, haemolytic uraemic syndrome, hepatitis C infection, neonatal herpes simplex virus infection, neonatal liver failure/ perinatal haemochromatosi and Smith-Lemli-Opitz syndrome. In total 19 studies have been facilitated through the Program.

For 2002, the CPSP Steering Committee approved new studies on vitamin D dependent rickets and severe hyperbilirubinemia in the newborn and is considering proposed studies on severe adverse drug reactions, autism and Prader-Willi syndrome.

No surveillance programme would be complete without timely feedback to its participants. So in 2001, the CPSP concentrated on promoting the programme and increasing communication to its participants and the general public. A series of publications followed including educational resources, abstract and poster presentations, updates in the CPS News, monthly highlights in the CPS Journal: Paediatrics & Child Health, culminating with the

May/June issue dedicated to surveillance. The bilingual CPSP website was updated in-house and was up and running early in 2002. The CPSP also continues to participate actively in INoPSU.

The CPSP is most encouraged by the recent trend of an increased level of support from CPS expert committees, national paediatric sub-speciality associations, chronic-disease family support groups, various departments within Health Canada and paediatric hospital research foundations. This is a manifestation of how the CPSP is building recognition within the Canadian research community.

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German Paediatric Surveillance Unit

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 452 groups of clinicians have risen significantly from 55% in 1992 to 98% in 2001, with the follow-up rate of completion of questionnaires in the range of 47 to 100%.

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

In 2001 the conditions under surveillance were:
Diabetes mellitus under 5 years / insulin-dependent diabetes mellitus, steroid-resistent nephrotic syndrome, invasive group B streptococcal disease, invasive *Haemophilus influenzae* infections (all types), idiopathic juvenile osteoporosis, kernicterus, imported tropical diseases (malaria, schistosomiasis, leishmaniasis), neonatal sinus venous thrombosis, ingestion of lamp oil (intoxications), pneumococcal sepsis/Meningitis, RSV disease requiring intubation and artificial ventilation, intersexuality and severe genital malformations, Transient myeloproliferative syndrome in neonates with Down-Syndrome, haemorrhagic disease of the newborn (vitamin K deficiency bleeding), glucose transporter defect (GLUT1)

The *haemophilus influenzae* type b disease study demonstrated the impact and effectiveness of diphteria-tetanus toxoids-acellular pertussis (inacitvated poliovirus)/*H. influenzae* type b combination vaccines

Schmitt H-J, von Kries R, Hassenpflug B, et al. Haemophilus influenzae type b disease: impact and effectiveness of diphtheria-tetanus toxoids-acellular pertussis (-inactivated poliovirus)/H. influenzae type b combination vaccines. Pediatr Infect Dis J 2001;**20**(8):767-774.

New studies for 2002 include inherited hypocalemic salt-losing tubulopathies/Bartter-like syndromes and narcolepsy

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Irish Paediatric Surveillance Unit

Set up in 1996 by the Faculty of Pediatrics of the Royal College of Physicians (Ireland) in cooperation with the Ulster Paediatric Society, the IPSU compliments the work of the British Paediatric Surveillance Unit by survey for more common disease in Ireland, North and South. Covering a child population of around 1.3 million, surveillance is achieved through a monthly prepaid postcard circulated to around 150 members of the Irish Paediatric Society. The response rate is currently around 80%. Studies undertaken in 2001 include tuberculous meningitis, status epilepticus, coeliac disease, nephrocalcinosis, diaphragmatic hernia and neural tube defects.

The IPSU application to join INoPSU was approved at the 2nd INoPSU conference.

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Latvian Paediatric Surveillance Unit

The Latvian paediatric surveillance system began in 1997. The active mailing of a surveillance card has recently been adopted. Lativa has a child population of 429,000 and there are only two major children's hospitals in Latvia cards have been sent to a comparatively few clinicians. Response rates in the past year are currently around 70%. In 2001 the following were reported congenital syphilis (4), Hodgkin's disease (10), Non-Hodgkin's lymphoma (7), diabetes mellitus (47), histocytosis X (2), aplastic anaemia (1), PKU (2), leukemias (24) and Reye's Syndrome (1),

In 2000 2 cases of haemolytic uraemic syndrome was seen but none in 2001.

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Malaysian Paediatric Surveillance Unit (MPSU)

The MPSU was established in December 1993 and surveillance began in September 1994 under the auspices of the Malaysian Paediatric Association. It covers all of Malaysia with a child population of 7.6 million. The unit has adopted the classical BPSU methodology with cards being circulated to around 400 paediatricians and surgeons. The initial response rate was encouraging at 75%, having risen as the system becomes more familiar to respondents. Initially four conditions were under surveillance, paediatric HIV and AIDS, neonatal meningitis, acute fulminant liver failure and death from asthma. 1998 saw commencement of surveillance for Duchenne muscular dystrophy and in 1999 for neonatal congenital heart disease. However since then there have been financial problems that led to the system being suspended. The management of the Unit has recently under gone re-organisation and it is hoped to re-commence surveillance soon.

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New Zealand Paediatric Surveillance Unit (NZPSU)

The NZPSU, established in 1997, is co-directed by Professor Barry Taylor and Dr Nigel Dickson. From the beginning the NZPSU has received financial support from the New Zealand Ministry for Health to provide active surveillance of acute flaccid paralysis as part of WHO's polio eradication initiative. Covering a child population of 0.83 million, each month over 180 paediatricians are circulated with a surveillance reply-paid card or email (depending on their preference). The response rate and completion rate of questionnaires has remained high at 90%.

Ten conditions are currently being surveyed. These are acute flaccid paralysis, congenital rubella, perinatal HIV exposure, haemolytic uraemic syndrome, vitamin K deficiency bleeding, subdural haemorrhage (<2 years), kawasaki disease, bronchiectasis, idiopathic nephrotic syndrome and childhood inflammatory bowel disease.

Studies on fetal alcohol syndrome, childhood diabetes (types 1 & 2) and retinopathy of prematurity (stage III) have already been completed since the NZPSU's inception.

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Netherlands Paediatric Surveillance Unit (NSCK)

The Dutch Unit started surveillance in October 1992. It consists of a scientific board of eight clinicians, one co-ordinating paediatrician (0.2 FTE) and secretarial assistance (0.3 FTE). It started following approval of the Dutch Paediatric Society and all 932 clinically working paediatricians participate, whether personally or represented by a colleague.

Every month the Unit sends "blue cards" with 10 condition to 410 paediatricians in general hospitals, 30 cards to representatives of paediatric departments (covering 125 paediatricians) and to 53 cards to contact persons for a specific disease in the 8 academic hospitals (covering 397 academic paediatricians). Child population under 15y is about 3 million.

Following the report of a case a questionnaire is sent by post from the NSCK office. Since January 2002 about 30% of the paediatricians receive an "electronic blue card" and after reporting back if they have reported a case they receive automatically a questionnaire, that they have to send to the investigators. The response rate in 2001 was 87% (89% for general hospitals and only 77% for academic hospital contact persons). Where possible full case ascertainment by other sources is pursued.

To date 16 conditions have been completed, 10 are under surveillance and there are three conditions that have to be approved for next year.

The following studies have now been completed: sickle cell disease, thalassemia major; postneonatal mortality in pre-dysmature children; haemolytic disease of the newborn (non ABO, non Rh D); haemorrhagic disease of the newborn; invasive *H. inflenzae*; congenital rubella; venous thromoembolic complications; hospital admissions from Rota virus; group A streptococcal infection and coeliac disease.

Data for those completed in 2001 is as follows (between brackets the 2001 reports) neonatal alloimmune thrombocytopenia (30), diabetes mellitus (473), neonatal group B streptococcal disease (240), inflammatory bowel disease (82), adrenogenital syndrome (34).

Studies currently under surveillance are: acute flaccid paralysis (30), HIV/AIDS (97), neural tube defects (72), hospital admissions

Pertussis (182), severe complications of medical therapy (32), atypical mycobacterial infections (25)

Thanks to the surveillance unit the adrenogenital syndrome (AGS) screening proved to be 100% reliable and was implemented nationwide.

Again the reports of diabetes showed that there was a strong rise, especially in children under 5 (doubled in 5 years) and in immigrants. Further studies are urgently needed to clarify this increase.

Three studies were approved for 2002: Idiopathic thromobocytopenia (ITP), acute ataxia, ALTE, medium chain aceyl dehydrogenase deficiency (MCADD).

Studies under consideration include influenza hospital admissions, Erb paralysis, and TPN due to bowel insufficiency.

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Papua New Guinea Surveillance Unit

This unit began in 1996 and is closely associated with the Paediatric Association of PNG. Covering a national child population of 1.92 million there are currently 40 respondents, including all paediatricians in the country and some general physicians in the more remote areas. Response rate for the year to June 1999 was 78.6%. Since 1996 surveillance has been undertaken for 11 conditions. Current studies are acute flaccid paralysis (57 cases); insulin dependent diabetes mellitus (8 cases); congenital hypothyroidism (41 cases) neurologic endemic cretinism (5 cases), renal tubular acidosis (27 cases); sub-acute sclerosing panencephalitis (112 cases); necrotising enterocolitis and HIV/AIDS (64 cases). It is hoped that this year will see the commencement of nephrotic syndrome.

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Portuguese Paediatric Surveillance Unit (PPSU)

Covering a population of 1.8 million children the PPSU is the newest of the active Units established in June 2000. Surveillance commenced in March 2001 with a circulation to over 2,000 paediatric members of the Portuguese Paediatric Society. To date the response has been good with an average monthly response rate of 30%, though this is expected to rise once the database has been verified and the system become familiar to the paediatricians. Studies currently under investigation include Group B streptococcal disease, Kawasaki disease, haemolytic uraemic syndrome and insulin dependent diabetes melitus in under fives.

The PPSU application to join INoPSU was approved at the 2nd INoPSU conference.

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Swiss Paediatric Surveillance Unit

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

Report cards are circulated to a willing paediatrician (45) at each of the 38 paediatric teaching clinics representing about 250 hospital or clinic-based paediatricians (i.e. not to those delivering primary care) and covering a total child population of 1.3 million children. The response rate for the initial cards was 100% in each year, and 96-98% for the complementary questionnaires.
The eight conditions under surveillance in 2001 were: acute flaccid paralysis (15 cases), congenital rubella syndrome (0 cases), haemolytic uraemic syndrome (24 cases), tick-borne encephalitis (10 cases), varicella/zoster (83 cases) and acute rheumatic fever (6 cases), neural tube defects (38 cases), severe RSV infections (12 cases). The study on cystic periventricular leukomalacia was completed in December 1997. The study on congenital toxoplasmosis ended December 1998, with a total of 21 confirmed cases. The study on vitamin K deficiency bleeding ended December 2000, with a total of 19 confirmed late-onset cases.

In 2002 a survey into neonatal herpes simplex commenced.

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Welsh Paediatric Surveillance Unit

The Welsh Paediatric Surveillance Unit (WPSU) was set up in 1994 as a joint venture between the University of Wales Departments of Public Health Medicine (Prof. S. Palmer) and

Child Health (Prof. J. Sibert). The management of the system was reorganised in 1996 in conjunction with the Welsh Paediatric Society, which supports the system. Funding has also been obtained from the Welsh Office for Research and Development and latterly the National Assembly for Wales.

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

Monthly green cards are distributed to consultant paediatricians and senior doctors of whom there are approximately 135. This covers a child population of 650,000. The overall response rate for 2001 was 100%.

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

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

The following studies have been completed successfully: acute and chronic renal failure, severe child abuse, the critically ill child, coeliac disease, inflammatory bowel disease, children in housefires, subdural haemorrhage(I), congenital adrenal hyperplasia. Two studies were unsuccessful and were withdrawn: ingestion of household products and haemoglobinopathy. Current studies include newly diagnosed malignant disease, newly diagnosed diabetes, Marfan syndrome, childhood tuberculosis, subdural haemorrhage(II) and facial palsy.

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

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Table 16

National paediatric surveillance units status circa end 2001

Country	Child population (10^6- aged 0-15 years)	Established	Respondents	Reply paid	Response rate **(E-mail reporting)	Fee for study
Australia	3.9	1992	1042	Yes	96%[1]	Yes
UK/Rep of Ireland	12.8	1986	2005	No	93%	Yes
Canada	6.3	1996	2294	Yes	82%	Yes
Germany	12.0	1992	468*	No	98%	Yes
Latvia	0.4	1996	22	No	70%	No
Malaysia	7.7	1994	395	Yes	75%[4]	No
Netherlands	2.9	1992	445	Yes	87%[3]	Yes
Papua New Guinea	2.0	1996	40	Yes	79%	No
New Zealand	0.8	1997	165	Yes	95%[2]	No
Switzerland	1.3	1995	40*	Yes	100%	No
Wales	0.65	1994	119	No	100%	No
Republic of Ireland	1.0	1996	135	Yes	85%	Yes
Portugal	1.8	2001	1500	Yes	30%	Yes

* Heads of paediatric centres

[1] 538 (52%) from a total 1042 clinicians reported to the APSU by email in 2001.

[2] Respondents reply either by reply-paid card (30%) or to an email (70%) depending on their preference. Telephone notification of AFP is also requested.

[3] Since January 2002, approximately 30% of paediatricians have received their card via email.

[4] MPSU is temporarily closed, due to recommence surveillance in June/July 2002

Appendix A Completed Studies 1986-2001

By mid-2001 the BPSU had completed forty-six studies. Information about these studies has been included in previous annual reports, which are available from the BPSU office. The studies, principal investigators and definitive papers are listed below. For addresses see the list at the end of this report.

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

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

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

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

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

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

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

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

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

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

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

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

Acute rheumatic fever
Completed: January 1990 – December 1990
Investigator: Dr C Boyd-Scobie, Dr S Hall
Acute Rheumatic Fever. Boyd-Scobie, Hall S.
Published paper: BPSU 5th Annual Report 1990. BPSU London 1990

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

Measles, mumps, rubella-meningococcal meningitis

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

Chemistry set poisoning

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

Acute flaccid paralysis

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

Androgen insensitivity syndrome

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

Long term parenteral nutrition

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

Insulin dependent diabetes in under fives

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

Juvenile dermatomyositis

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

Congenital dislocation of the hip

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

Haemophagocytic Lymphohistiocytosis

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

Non-accidental poisoning/Munchausen syndrome by proxy

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

Neonatal necrotising enterocolitis

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

Vitamin K deficiency bleeding II

Completed January 1993 – December 1994
Investigator: Dr A McNinch, Dr J Tripp
Published paper: Vitamin K in Infancy: International Symposium 1994 Ed. Sutor AM, Hathaway WE, Schattauer, Stuttgart New York 1994

Biliary Atresia

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

Transient and permanent neonatal diabetes

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

Adverse neonatal outcomes of delivery or labour in water

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

Congenital syphilis

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

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

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

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

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

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

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

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

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

Inflammatory bowel disease in under 20 year olds
Completed: June 1998 – June 1999
Investigator: Professor B Sandhu, Dr A Sawczenko
Published Paper: *Prospective survey of childhood inflammatory bowel disease in the British Isles*. Sawczenko A, Sandhu B K Logan, R F A, Jenkins H, Taylor C J, Mian S, Lynn R. Lancet 2001; **357**, 1095-96

Fatal/Severe allergic reactions to food ingestion
Completed: March 1998 – February 2000
Investigator: Dr A Colver, Dr A Cant, Dr C MacDougal
Published Paper: 14th BPSU Annual Report 1999/00. London 2000

Invasive Haemophilus influenzae infection
Completed: October 1992 - October 2000
Investigator: Dr P Heath, Dr J McVernon, Professor R Booy
Published Paper: *Vaccine failures after primary immunisation with Haemophilus influenza type-b comjugate vaccine without booster*.
Booy R, Heath PT, Slack MPE, Begg, N, Moxon ER.
Lancet,1997; **349**:1197-202

Severe Visual Impairment/Blindness
Completed: Sept 1999 - Dec 2000
Investigator: Dr J Rahi
Published paper: *15th BPSU Annual Report 2000/01*. London 2001

Haemolytic Uraemic Syndrome II
Completed: February 1997- February 2001
Investigator: Dr M Taylor, Dr D Milford, Dr B Adak, Mr R Lynn, Dr M Locking, Dr S O'Brien
Published Paper: *15th BPSU Annual Report 2000/01*. London 2001

Group B Streptococcal Disease
Completed: March 2000 - March 2001
Investigators: Dr P Heath
Published Paper: *15th BPSU Annual Report 2000/01*. London 2001

Reye's Syndrome
Completed: June 1986 - June 2001
Investigator: Dr S Hall, Mr R Lynn
Published Paper: 15th Annual Report 2000/01. London 2001

Subacute Sclerosing Panencephalitis
Completed: June 1986 - June 2001
Investigator: Dr E Miler
Published Paper: 15th Annual Report 2000/01. London 2001

Appendix B Published papers 2001-2002

Epidemiological surveillance of rubella must continue (letter). Rahi J, Adams G, Russell-Eggitt I, Tookey P.
BMJ 2001; **323**: 112

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

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

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

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

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

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

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

Ascertainment of children with congenital cataract through the National Congenital Anomaly System in England and Wales. Rahi JS, Botting B and the British Congenital Cataract Interest Group. *Br J Opthalmol* 2001; **85** (9) 1049-1051

Measuring and interpreting the incidence of congenital ocular anomalies: lessons from a national study of congenital cataract in the United Kingdom. Rahi JS, Dezateux C and the British Congenital Cataract Group.
Invest Opthalmol Vis Sci 2001; **42**: 1444-1448

How dangerous is food allergy in childhood? The incidence of severe and fatal allergic reactions acrossthe UK and Ireland. Macdougall CF, Cant AJ, Colver AF.
Arch Dis Child 2002; **86**:236–239

CDSC. Monitoring of antenatal screening for HIV in the United Kingdom. Commun Dis Rep Wkly [serial online] 2002 [cited 7 May 2002]; **12** (17): news. Available from www.phls.co.uk/publications/CDR%20Weekly/archive02/News/news1702.html#antenatal

PHLS. COVER programme: October to December 2001. Vaccination coverage statistics for children up to five years of age in the United Kingdom. Commun Dis Rep CDR Wkly [serial online] 2002 [cited 23 April 2002]; **12** (13): immunisation. Available from http://www.phls.co.uk/publications/CDR%20Weekly/pages/immunisation.html

Education and debate: Consent, confidentiality, and the threat to public health surveillance. Verity C, Nicoll A.
BMJ 2002; **324**: 1210-1213

The UK Hib vaccine experience. Heath P T, McVernon J.
Arch. Dis. Child. 2002; **86**: 396-399

Rubella susceptibility among pregnant women in London, 1996-1999. Tookey PA, Cortina-Borja M, Peckham CS.
Journal of Public Health Medicine, in press 2002

Congenital rubella: down but not out (letter). Tookey P. *Lancet*, in press 2002

MMR vaccine: review of benefits and risks. Miller E. *Journal of Infection*, in press 2002

Appendix C Presentations 2001-2

RCPCH Annual Scientific Meetings 2001 and 2002

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

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

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

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

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

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

Epidemiology of haemolytic uraemic syndrome, a worldwide perspective. Elliott E. York 2002

Vitamin K deficiency bleeding - international surveillance findings. Von Kries R. York 2002

Childhood cerebrovascular disease and stroke-like illness in the United Kingdom and Eire, a descriptive epidemiological study. Williams AN, Euson PD McShane MA, Lynn RM, Green S, Kirkham FJ. York 2002

The Canadian and British perspectives of paediatric intellectual and neurological deterioration; are the results comparable? Grenier D, Doherty J, Medaglia A. York 2002

Effects of antiretroviral therapy (ART) on Morbidity and Mortality of UK and Irish HIV infected Children. Duong T, McGee L, Sharland M, Tudor-Williams G, Novelli V et al. York 2002

Convalescent Serum Responses Following Invasive *Haemophilus influenzae* type b (Hib) Disease in Vaccinated and Unvaccinated Children: What is the Role of Immunological Memory? McVernon J, Johnson PDR, Pollard AJ, Slack MPE, Moxon ER. York 2002

INoPSU Conference York April 2002

Haemophilus b vaccination strategies - is their need for a booster? McVernon J.

Is there any danger associated with MMR vaccination? Miller E.

Reducing the risk of mother to child transmission of HIV worldwide. Newell M-L.

Is inflammatory bowel disease on the increase? Sandhu B.

Cerebral oedema and diabetic ketoacidosis. Muirhead S.

vCJD in UK children - implications for the world. Verity C.

European Organisation for Rare Diseases - A parental support perspective. Youngs C.

Other Conferences & Meetings

Group B streptococcal disease in infants < 90 days of age: a surveillance study. Heath P. European Society of Paediatric Infectious Diseases. May 2002

Interim Results of the BPSU childhood encephalitis survey. Ward K. Liverpool Paediatric and NorthWest Epidemiology Clubs. Liverpool 2002.

Interim results of the British Isles-wide Childhood Encephalitis Survey. Ward K. Oswaldo Cruz Foundation, Rio de Janeiro, Brasilia 2002.

HHV-6 AND -7 diagnosis and its relevance to measles notification. Ward K. Oswaldo Cruz Foundation, Rio de Janeiro, Brasilia 2002.

Aspects of Paediatric Surveillance. Lynn RM. RHSC Glasgow. Scotland June 2001

Interim Results of the BPSU childhood encephalitis survey. Ward K. PHLS Annual Virology Symposium. London 2001.

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

Measles vaccine, IBD and Autism. Miller E. Berzilius Symposium 55 Stockholm, Sweden. February 2001.

MMR: a cause of autism and inflammatory bowel disease. Miller E. Workshop on Safety of Vaccines. Leuven, Belgium. February 2002.

Appendix D Support groups and contacts

Congenital cytomegalovirus

Congenital CMV Association, 69 The Leasowes, Ford, Shrewsbury, SY5 9LU

Congenital Rubella

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

Encephalitis Effects

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

HIV/AIDS

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

Progressive Intellectual Neurological Degeneration

Adrenalleukodystrophy (ALD), ALD Family Support Trust, 30-32 Morley House, 320 Regent Street, London, W1R 5AB

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

Cerebrovascular disease/Stroke

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

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

'Contact a Family'

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

Useful web-site addresses

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

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

International Network of Paediatric Surveillance Units
http://www.inopsu.com

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

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

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

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

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

Pedinfo
http://www.pedinfo.org

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

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

Appendix E Contact addresses

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

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

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

Dr C Bramley, Scottish Centre for Infection & Environmental Health, Clifton House, Glasgow G3 7LN

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

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

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

Dr Allan Colver, Donald Court House, 13 Walker Terrace, Gateshead NE 8 1EB

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

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

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

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

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

Professor D Dunger, Addenbrooke's Hospital, Cambridge CB2 2QQ

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

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

Dr D Gill, Children's Hospital, Temple Street, Dublin 1, Republic of Ireland

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

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

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

Dr P Heath, Immunology/Infectious Disease, St George's Vaccine Institute, Tooting London, SW17 0RE

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

Dr R Modi Rawni, MPA Secretariat, Instiut Pedatrik, Hospita Kuala Lumpur, 5074 Kuala Lumpur, Malaysia

Professor I A Hughes, Addenbrooke's Hospital, Cambridge CB2 2QQ

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 H Kirkbride, PHLS Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ

Professor F Kirkham, Southampton University Hospital, Tremona Road, Southampton, Hampshire, SO16 6YD

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

Dr M Layton, Imperial College School of Medicine, Hammersmith Hospital, Du Cane Road, London W12 ONN

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

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

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

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

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

Dr W McGuire, Ninewells Hospital, Dundee, DD1 9SY

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

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

Dr D V Milford, Birmingham Children's Hospital NHS Trust, Laboratory of Enteric Pathogens, Steelhouse Lane, Birmingham B46NH

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

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

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, c/o BPSU, 50 Hallam Street, London W1W 6DE

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, Centre for Paediatric Epidemiology & Biostatistics, Institute of Child Health, 30 Guilford St, London WC11EH

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

Professor M Preece, Institute of Child Health, 30 Guilford Street, London WC1N 1EH

Dr J Rahi, c/o Centre for Paediatric Epidemiology & Biostatistics, Institute of Child Health, 30 Guilford Street, London WC1N 1EH

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

Dr Martin Richardson, Peterborough General Hospital, Thorpe Road, Peterborough, PE3 6DA

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

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