Surveillance Unit

10th Annual Report

College of
Paediatrics
and Child Health

1995-1996

The Surveillance Unit always welcomes invitations to give talks describing the work of the Unit and makes every effort to respond to these positively. Enquiries should be directed to the Surveillance Unit office.

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

The College of Paediatrics and Child Health received its Royal Charter in July 1996. Consequently in this publication, which relates to the work of the BPASU for the year 1995, the text and name of the Surveillance Unit have been changed to conform with the nomenclature of the new College.

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Surveillance Unit of the College of Paediatrics and Child Health
5 St Andrews Place
Regent's Park
London NW1 4LB
Telephone: 0171 935 1866
Facsimile: 0171 224 2038
Registered Charity No. 1057744

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Compiled and edited by Margaret Guy and Richard Lynn, September 1996
Typeset by Philippa Davies, College of Paediatrics and Child Health, Publications Department

Membership of Executive Committee 1995-96

Dr Christopher Verity	Chairman *(from Jan 96)*
Professor David Baum	College of Paediatrics and Child Health Research Unit
Dr Angus Clarke	Co-opted
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Dr Angus Nicoll	Medical adviser
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Dr Jon Pollock	College of Paediatrics and Child Health Research Unit
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Dr Ian Lister Cheese	Department of Health (observer)

*Dr Ralph Counahan 1946-96

We are sad to report the sudden and untimely death of Dr Ralph Counahan (Consultant Paediatrician, Waterford Regional Hospital) in May 1996. From 1987 to 1992 he served on the Surveillance Unit Joint Committee of Management and from 1993 its Executive Committee. Ralph was a great supporter of the Surveillance Unit and all that it stood for. He was effectively the face of the Unit to Eire and to the Faculty of Paediatrics, Royal College of Physicians, Ireland. He will be sadly missed by those who knew and worked with him.

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Acknowledgements

As in previous years the Surveillance Unit thanks the Children Nationwide Medical Research Fund for its continued and generous core financial support. We thank the Muirhead Trust for supporting the development costs of new computer equipment and Allen and Hanburys for supplying the protocol booklets.

In 1995, the Surveillance Unit held its first scientific seminar; we extend our thanks to the Sir Jules Thorne Trust, Serono, Roche, and Pasteur Mérieux MSD for their support.

We particularly thank members of the College of Paediatrics and Child Health, the Faculty of Paediatrics of the Royal College of Physicians of Ireland, and the many other clinicians and pathologists who have contributed reports and data to the Surveillance Unit, and through it to the researchers who use the Unit. Without these contributions the Surveillance Unit would not be the world leader that it is.

Surveillance Unit Executive Committee
September 1996

Foreword

'British and Irish paediatricians can therefore feel justly proud of themselves as pioneers and key enactors of this unique reporting system'

Sir Cyril Clarke, Chairman of BPSU Management Committee (1991)

This quotation is from the sixth annual report of the British Paediatric Surveillance Unit. The message seems particularly relevant now, as we celebrate ten years of Surveillance Unit activity. The active cooperation of individual paediatricians has been of fundamental importance in those ten years. Indeed **paediatricians *are* the Surveillance Unit** - without them surveillance could not take place. It is clear that most paediatricians already know this. If they did not feel part of the Unit and did not recognise the importance of its work they would not support it by completing and returning over 90% of the report cards every month - a fantastic achievement.

The basic idea behind the Surveillance Unit is simple enough. However, until 10 years ago there was no such coordinated activity anywhere. It took vision and hard work to translate a good idea into an organisational network that runs smoothly. The history of this process is summarised by Richard Lynn, the Surveillance Unit Scientific Coordinator, in his article, Paediatric Surveillance - the first ten years (page 5). The great thing is that **the Unit brought people together right from the start.** The key participants in planning the British Paediatric Surveillance Unit were: the British Paediatric Association, the Communicable Disease Surveillance Centre and the rest of the Public Health Laboratory Services, the Institute of Child Health (London), the Royal College of Physicians (Ireland) and the Scottish Centre for Infection and Environmental Health. Representatives from all these organisations - and others - have remained in active contact by attending the monthly meetings of the Surveillance Unit Executive Committee at the College of Paediatrics and Child Health (CPCH) headquarters. The past and present members of the Committee should be congratulated and thanked for all the time and effort that they have put into the work of the Unit, thereby strengthening the close working relationships that are essential for the Unit to flourish.

The efficient running of the Unit depends on continued cooperation between agencies. Richard Lynn, Scientific Coordinator and Myra Schehtman, his assistant, are the core of the Unit - they are employees of the College of Paediatrics and Child Health (formerly the British Paediatric Association). The two Medical Advisers, Margaret Guy and Angus Nicoll, provide essential expertise. The sessions they work for the Surveillance Unit are funded by their employers - the Brent and Harrow Health Authority and the Public Health Laboratory Service. When the BPSU became part of the BPA Research Unit, not only did it take on a new name - the BPASU - but also it was provided with extra help and support, in particular from David Baum, Director of the Research Unit and Jon Pollock, Principal Research Officer. This was in addition to help that it was already receiving from other personnel within the BPA. This happy arrangement continues in our new College.

Whilst the Surveillance Unit could not have functioned at all without the BPA and its members, it would not have got off the ground and continued to fly without the generous funding that it has received from the Medical Research Fund of Children Nationwide. Much support has come from the BPA, but **the running costs of the Surveillance Unit have been mainly covered by external funding, together with fees charged to investigators for their place on the monthly report card.** As Catherine Peckham pointed out in her Chairman's review last year, financial responsibility for the Surveillance Unit now lies with the College through its Research Unit. However, the aim is still to obtain external sources of funding for Surveillance Unit activity. The members of the Executive Committee are keen to work closely with Jon Pollock of the Research Unit to secure funds for the future.

Much of the above is about organisation, but **it is the content of the Surveillance Unit's work that is so exciting.** Surely that is why paediatricians are interested enough to tick boxes and fill in questionnaires and why Executive Committee members are prepared to travel long distances every month to join in discussions about research proposals. The scientific work of the Unit is a continuing source of interest to all those involved - the diversity of the research workers and their projects continues to excite, as can be seen in Margaret Guy's review of Surveillance Unit activity in 1995 (page 12).

The excitement of the scientific work has stimulated others to set up their own surveillance units, in the British Isles and elsewhere in the world. Already this

year the Executive Committee has been host to representatives from the Australian Paediatric Surveillance Unit and the Canadian Paediatric Surveillance Programme. At the request of the Canadian Unit, and with its support, Angus Nicoll visited Ottawa in the Spring to give advice and support on the basis of his considerable experience as Medical Adviser to the British Unit. We in turn have been able to learn from the work being carried out in Australia and Canada. This is a small example of the sort of interaction that has been made possible by the world wide spread of surveillance activity based on the original BPSU model.

Research fostered by the Unit has had more than theoretical interest. It has influenced the work of paediatricians. With this in mind, members of the Surveillance Unit Executive Committee have planned a second scientific meeting entitled '***Paediatric Surveillance in Practice***' which will take place at the ***Royal College of Physicians on 4 December 1996.*** The hope is that many of you who have completed Surveillance Unit cards over the years will come and participate. The programme looks excellent.

The members, the officers and the staff of the BPA have given great support to the work of the Surveillance Unit over the last ten years. I am particularly grateful to members of the Executive Committee who so generously give their time to attend frequent meetings and to work between meetings. I am sure that all those who are part of the College of Paediatrics and Child Health will continue to be proud of the British Unit and support it, not just because it is a College activity but because it provides such important links with other organisations that are working for improvements in child health both in the British Isles and throughout the world.

Dr Christopher Verity,
Chairman Surveillance Unit Executive Committee

1 Introduction

It is now ten years since the British Paediatric Surveillance Unit was set up to enable paediatricians in the United Kingdom and the Republic of Ireland to participate in the surveillance and further study of uncommon disorders affecting children. The aims of the Surveillance Unit are summarised in the box below.

Several agencies collaborate in the Surveillance Unit: the College of Paediatrics and Child Health (CPCH), the Public Health Laboratory Service (PHLS), the PHLS Communicable Disease Surveillance Unit (CDSC), the Department of Epidemiology at the Institute of Child Health, University of 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 Surveillance Unit monitors conditions of public health importance, observers from the Department of Health and the Office for National Statistics also attend meetings of the Surveillance Unit's Executive Committee.

This report begins with a review of the Surveillance Unit's first ten years and then mainly focuses on activities undertaken during 1995. Reference is also made to studies and activities which have commenced in 1996.

Aims of the 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

2 Paediatric surveillance - the first ten years

June 1996 marked the completion of ten years of surveillance by the Unit. In this time the Surveillance Unit has grown from a small base into an internationally renowned surveillance system, which has provided the model for similar units throughout the world.

History

The Surveillance Unit (SU) developed from the collaboration between the then British Paediatric Association (BPA), and the Public Health Laboratory Service Communicable Disease Surveillance Centre (PHLS CDSC) to improve the surveillance of infectious diseases and associated conditions that could not be monitored through existing data collection systems. Surveillance began in 1981 with Reye's syndrome and later extended to include haemolytic uraemic syndrome, Kawasaki disease, and haemorrhagic shock encephalopathy syndrome. This was initially a voluntary and passive reporting system, ie. BPA members were asked to report cases as they occurred, but they were not prompted (there were no regularly revised orange cards) and it was realised that not all cases were being reported. However, the success and enthusiasm expressed by clinicians suggested that an active case gathering system could be implemented to achieve the higher levels of case ascertainment necessary for assessing trends in rare disorders. Such a system would reduce the number of requests received by clinicians from individual researchers for data on rare disorders.

In response to this the British Paediatric Surveillance Unit was set up in July 1985, following consultation between the BPA, the PHLS, the Institute of Child Health (London), the Royal College of Physicians of Ireland and the Scottish Centre for Infection and Environmental Health, and became operational a year later. The aims of the Unit (see page 4) were to provide a method of nationwide disease surveillance orientated to the study of rare childhood disorders, including infections or infection-related conditions of uncertain aetiology or epidemiology. The two principal objectives were firstly to involve paediatricians in the reporting and surveillance of uncommon childhood conditions of importance to public health and secondly to provide a unified reporting scheme that was simple and flexible, involving minimal paperwork, and yet capable of rapid response to an 'epidemiological emergency'.

In order to monitor the system and consider research applications, an Executive Committee was set up, originally chaired by Sir Peter Tizard. Still in existence, and now chaired by Dr Chris Verity, the Committee includes representatives from each of the 'parent' bodies, general and specialist paediatricians, epidemiologists and an observer from the Department of Health. Care is taken to co-opt paediatricians who are active in practice and research and represent a broad range of sub-specialists.

The first mailing card included seven disorders: AIDS, Lowe syndrome, haemolytic uraemic syndrome, neonatal herpes, subacute sclerosing panencephalitis (SSPE) and X-linked anhydrotic ectodermal dysplasia (XLAED). The card was sent to 800 consultant paediatricians in the UK and the Republic of Ireland. There are now approximately 1500 clinicians participating in the mailing scheme. The initial response rate was around 80%. Over the years this has increased and now stands at 94%.

Study Profiles

A total of 40 studies have been undertaken during the first ten years - 31 have now been completed and nine are currently in progress. Twelve studies have involved the surveillance of infections and eleven have predominantly involved the reporting of cases occurring in infants. There have been three main categories of research question: 1) what is the size of the problem and is it changing over time? 2) what are its epidemiological and pathological characteristics? and 3) what is the natural history?

On average 35 cases are identified per month. Fewer than five cases per year have been reported for some conditions, such as transient neonatal diabetes, subacute sclerosing panencephalitis and congenital syphilis, whereas more than 200 cases per year have been reported for other conditions including congenital dislocation of the hip, type 1 diabetes and Rett syndrome. In total over 5,000 cases have been reported since the Unit's inception in 1985.

The period of surveillance varies. Seven conditions have been monitored over a long period, including HIV/AIDS, SSPE, congenital rubella and Kawasaki disease. Just over half of the studies have lasted for one to two years. Three conditions were included on the reporting card for four months

or less: congenital dislocation of the hip, long term parenteral nutrition and Rett syndrome. This was due either to the relatively common nature of the disorder (congenital dislocation of the hip) or because a sample prevalence "snapshot" (long term parenteral nutrition, and Rett syndrome) rather than incidence, was required.

The types of data sought by investigators have also varied. Some studies have asked for information about clinical management, referral patterns, and outcome. Most have sought demographic characteristics. The response to the follow up questionnaires has been high - over 92% of questionnaires have been completed and returned. Seven studies have requested specimens as part of the protocol. Of these seven, three employed initial telephone reporting in order to obtain specimens during the acute phase of illness.

Several of the studies extended their enquiries beyond paediatricians to include microbiologists, pathologists, obstetricians and midwives. Eleven involved contacting general practitioners and in eight studies parents were contacted. In at least 18 studies cases have been followed-up for at least one year, usually via the initial reporting clinician, thus enabling an evaluation of management or a description of the natural history of the disorder. Some surveys have effectively developed into a register. This is the case for congenital rubella, galactosaemia, HIV and AIDS, Rett and Reye's syndromes.

Ascertainment

During the first decade of activity under-ascertainment has emerged as one of the most prominent concerns. However, it should be acknowledged that, in many cases, complete ascertainment is not always required to answer the more important research questions.

Like any national multi-respondent surveillance scheme, the SU recognises that it will not achieve 100% ascertainment of cases. This can be for a variety of reasons - participants in the reporting scheme may fail to return their card, under-diagnose or forget to report cases. Participants may also withhold from reporting, perhaps because of concerns about confidentiality or additional paperwork. The easiest response to the orange card is to tick the 'nothing to report' box. Some cases may be managed by junior hospital doctors who are unaware of the surveillance scheme or by non-paediatricians or may die suddenly at home. Other causes of under ascertainment include confusing case definitions, the incompleteness of the reporting base and cases that may have been seen by clinicians apart from paediatricians. Investigators using the Surveillance Unit are therefore encouraged to use other sources of case reports in order to optimise ascertainment, provide validation and improve the accuracy of information. At least 20 studies have used additional sources of data and on average these have contributed 20-30% of the total cases ascertained (range 5-80%). Other notification sources have included death certificates, laboratory reports, registers, hospital episode data and other reporting systems modelled on the Surveillance Unit. Obstetricians, orthopaedic surgeons, neurologists and ophthalmologists have all set up such systems. The relative level of case ascertainment varies substantially from study to study. Studies of infectious diseases and those involving telephone reporting and/or specimen collection are affected by under-reporting. In the case of *Haemophilus influenzae* following Hib immunization, 36% of cases were neither reported by telephone by paediatricians nor reported subsequently on the report card. Only 45% of cases of SSPE were identified via the SU: although once removed from the reporting card passive case ascertainment from other sources dried up. As a result SSPE was placed back on the report card.

Those investigators employing other sources to ascertain cases have begun to use statistical techniques to estimate the "true" incidence or prevalence. However, such techniques rely on the independence of the various reporting sources, which may not be easy to achieve. When such techniques have been applied, the SU has faired well suggesting that 80-90% of cases have been identified by the Unit.

Achievements

The Unit has been a great success in meeting its original aims. Additional achievements have been in three main areas:

1) education
2) dissemination
3) public health impact

Through the production of study protocol cards the SU has

raised the profile of rare disorders and the general diagnostic awareness of such conditions. Over sixty papers utilising surveillance data have been published: additionally many presentations on its methodology and on the findings of its studies have been presented. A quarterly newsletter provides an update of Surveillance Unit activities and the Annual Report is distributed worldwide. The SU has had a considerable impact on public health. For instance, the Unit monitored the effects of warnings about the association between Reye's syndrome and aspirin. The Unit has kept under surveillance diseases targeted by vaccination programmes as well as the late sequelae of vaccination. Examples include the surveys on congenital rubella, SSPE, meningoencephalitis after MMR vaccine, acute flaccid paralysis and Hib vaccine failures. The Unit has provided the base for reporting of HIV and AIDS in children in the UK and Eire. To achieve this it has combined with reporting by obstetricians, laboratories and others to give surveillance which achieves 98% completeness. It has become even more powerful when combined with unlinked anonymous HIV surveillance ascertaining that surprisingly few HIV infections in pregnant women are detected prior to birth leading to Department of Health initiatives to change this situation. This makes the crucial point that the value of surveillance by paediatricians is greatly enhanced by joining with other sources and specialties.

One of the aims of the Unit is to have a 'rapid response' to emergencies. For instance the Unit has helped to assess the impact of changing the route of administration of vitamin K in newborn infants, following concern about a possible link between vitamin K injections and the subsequent development of childhood cancers. Another 'rapid response' was to study the risks of labour or delivery in water.

Conclusions

The above achievements demonstrate the impact which the Surveillance Unit and its surveys have had on public health not only in the British Isles but internationally. Over the first decade of its operation the Surveillance Unit has met and exceeded the aims set by its founders. Simply by having cases on the orange card have informed paediatricians and assisted in making diagnosis that otherwise would have been missed or delayed. By facilitating research into less common disorders, knowledge has increased. The presentation and publication of the results of surveillance studies have led to the improved diagnosis and management of individual patients. The methodology used by the Surveillance Unit breaks new ground and many lessons have had to be learned. As a model for similar work in other countries and with its committed participants, the future success of the Surveillance Unit should be guaranteed.

Richard Lynn
Scientific Coordinator

3 How the Surveillance Unit works

The surveillance scheme involves the active reporting by paediatricians of children affected by any of the conditions currently included in the reporting scheme. To be eligible for inclusion in the scheme, the condition under study must be sufficiently rare to require the ascertainment of cases at a national level.

Any researcher may apply to use the Surveillance Unit to identify cases of a particular condition. However, before a condition can be included in the scheme, the study must be approved by the Surveillance Unit's Executive Committee. The number of conditions under surveillance at any one time is usually limited to twelve and priority is given to the study of conditions of particular public health importance.

Selection of studies for inclusion in the scheme

A study is eligible for participation in the scheme if its 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. Particular priority is given to studies of importance to public health but 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 SU with or through a paediatrician or paediatric department.

The number of conditions under surveillance is usually limited to 12 and there is keen competition for places on the SU card. Occasionally, the capacity of the reporting card has been increased to accommodate 14 rather than 12 conditions. The Unit receives an average of 30 general enquiries about potential studies each year; only a minority of which are eventually incorporated into the reporting card. About 25 studies are currently in various stages of development.

The SU has recently adopted a procedure to process applications with minimal delay. The Executive Committee meets monthly or six weekly to achieve this and the Scientific Coordinator, the Medical Advisers and individual committee members work in between meetings to assist applicants. The Unit sees itself as having a particular responsibility to assist paediatricians in producing good, high quality and practical studies. The procedure consists of two phases: in phase one, a short study protocol is submitted, covering no more than two sides of A4 paper. This should include the background to the proposed study, a case definition, 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 SU Executive Committee.

Many studies are found to be unsuitable at phase one for a number of reasons. The condition may be too common and therefore place too great a burden on paediatricians for reporting or follow up; there may be no suitable case definition; the aim of the study may constitute audit rather than surveillance and research; or data obtainable more appropriately elsewhere. In addition some studies present insuperable practical difficulties. Once the Executive Committee agrees that the protocol is suitable, a phase two application is requested. This should provide full details of the methodology and aims of the study. The applicant presents the details to the Executive Committee which comprises consultant paediatricians (general and specialist) and epidemiologists. Factors which increase the likelihood of a study being accepted are listed in the box.

Factors that favour acceptance by the Surveillance Unit

- rarity but short term or geographically limited studies of commoner disorders are considered.
- proposals with outcomes of clear importance to public health.
- scientific importance.
- uniqueness, priority will not be given if similar studies have recently been undertaken or if other data sources are readily available (although the Surveillance Unit encourages the use of alternative data sources for validation and completeness of reporting).
- attention to detail, in terms of clear achievable objectives, practicability, patient confidentiality, and resources.
- practicality and limited workload placed on the reporting paediatricians.
- ethical approval if appropriate.

If necessary the Surveillance Unit will help potential investigators, especially those with less experience in research methods, to develop potentially valuable studies. If a study is not accepted, the Executive Committee always tries to advise the applicant on alternative means of undertaking the study.

The reporting system

Participants in the reporting system include consultant paediatricians who are members of the College of Paediatrics and Child Health and the Faculty of Paediatrics of the Royal College of Physicians of Ireland. Particular care is taken to ensure that questionnaires sent to reporting doctors are clear, straightforward and not excessive in their demands. Mailing lists are regularly updated by the SU office by monitoring new consultant appointments.

Recently, consultants working in a number of other specialities have also been invited to participate in the scheme to help ascertain cases of conditions which are also seen by other specialists. For example, since 1992 pathologists who are not members of the BPA have also been included in the reporting scheme. This has improved the level of ascertainment of cases of biliary atresia and haemophagocytic lymphohistiocytosis.

Each month, all those participating in the scheme are sent an orange card listing the conditions currently under surveillance and a set of instructions for completing the card, including case definitions of the conditions listed on the card. When a new study begins, the mailing also includes a study protocol and information about the study.

Respondents are asked to return the card to the Surveillance Unit office, indicating the number of cases of each condition on the card which they have seen during the preceding calendar month. Scottish paediatricians return their completed cards through the Scottish Centre for Infection and Environmental Health.

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 and followed up - reminders are sent to all participants in the scheme who have not returned their card for three consecutive months. Overall response rates are continually monitored.

Follow up and confirmation of case reports

When cases are reported, the Surveillance Unit informs the relevant research team who contact the reporting clinician for further information about the case, in accordance with the agreed protocol for the particular study. The researchers subsequently report back to the Surveillance Unit on the outcome of follow up, indicating when cases have been confirmed as meeting the case definition and identifying duplicate case reports - this is particularly likely to occur when the condition requires referral to a tertiary unit.

Table 1 (page 10) shows the number of cases reported to the surveillance unit from its inception until the end of 1995 for all the conditions under surveillance during 1995. The number of cases which were 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 rate of follow up is high. For example, by the end of July 1996, only 87 (4%) of the 2164 cases reported up to the end of 1995 had yet to be followed up. The final proportion of case reports which are successfully followed up averages between 95% and 100%.

Table 2 (page 10) summarises the outcome of the follow up of all cases reported to the Surveillance Unit by the end of 1995 and provides evidence for the high level of accuracy of reporting by participating clinicians. By the end of July 1996, only 454 (21%) of the 2164 cases reported had been classified as reporting errors - details of the system used to classify case reports are set out in the box below.

Classification of case reports

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

Invalid reports:
These include:

- **duplicate reports** of cases already reported to the Surveillance Unit, 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 Surveillance Unit (as at July 1996).

Table 1 Cases reported from June 1986 - December 1995 of conditions under surveillance during 1995 (cases confirmed by July 1996 shown in brackets)

Condition under surveillance	Date when reporting began	Reports (confirmed cases) June 1986 to Dec 1988	Jan 1989 to Dec 1990	Jan 1991 to Dec 1992	Jan 1993 to Dec 1994	1995
AIDS/HIV	June 1986	107 (73)	239 (185)	286 (220)	218 (139)	137 (74)
Reye's syndrome	June 1986	127 (63)	41 (21)	52 (23)	34 (8)	23 (10)
SSPE	June 1986	63 (38)	46 (25)	31 (17)	25 (12)	4 (0)
Congenital rubella	Jan 1991	– –	22 (14)	21 (13)	21 (11)	8 (1)
Hib	Sept 1992	– –	– –	26 (20)	81 (56)	65 (49)
Biliary atresia	March 1993	– –	– –	– –	162 (80)	18 (7)
Congenital syphilis	July 1993	– –	– –	– –	10 (9)	8 (5)
MCAD	March 1994	– –	– –	– –	49 (27)	44 (24)
Water births	April 1994	– –	– –	– –	30 (23)	36 (27)
TPND	April 1994	– –	– –	– –	9 (1)	8 (1)
Pyridoxine dependency	Sept 1995	– –	– –	– –	– –	15 (8)
Congenital cataract	Sept 1995	– –	– –	– –	– –	75 (46)
DKA	Oct 1995	– –	– –	– –	– –	23 (5)
Total		**297 (174)**	**348 (245)**	**416 (293)**	**639 (366)**	**464 (257)**

Tables exclude previously completed studies (see page 36).

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

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

Hib *Haemophilus influenzae* b vaccination, from Oct 1995 **includes all cases of Hib infection.**

MCAD Medium chain acyl-CoA dehydrogenase.

Water births Adverse effects on the infant of labour/birth in water.

TPND Transient and permanent neonatal diabetes.

DKA Cerebral oedema following diabetic ketoacidosis.

Table 2 Outcome of follow up of the cases reported up to December 1995 of conditions under surveillance during 1995

Condition under surveillance	Valid reports (%)	Invalid reports: Duplicates	Invalid reports: Errors	Invalid reports: (Total %)	Not yet known (%)	Total reports
AIDS/HIV	691 (70)	128	159	(29)	9 (1)	987
Reye's syndrome	125 (45)	39	102	(51)	11 (4)	277
SSPE	92 (54)	23	29	(31)	25 (15)	169
Congenital rubella	39 (54)	15	17	(45)	1 (1)	72
Hib*	125 (73)	14	31	(26)	2 (1)	172
Biliary atresia	87 (48)	32	45	(43)	16 (9)	180
Congenital syphilis	14 (78)	0	3	(17)	1 (6)	18
MCAD	51 (55)	18	15	(35)	9 (10)	93
Water births	50 (66)	9	6	(23)	1 (2)	66
TPND	2 (12)	2	13	(88)	0 (0)	17
PDS	8 (53)	2	4	(40)	1 (7)	15
Congenital Cataract	46 (61)	0	23	(31)	6 (8)	75
DKA	5 (22)	6	7	(57)	5 (22)	23
All	**1335 (61)**	**288**	**454**	**(47)**	**87 (4)**	**2164**

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

The use of complementary data sources

A distinctive and powerful feature of the Surveillance Unit system is the ability to use data from complementary sources both to validate the surveillance system and to increase case ascertainment. The first complementary data source to be used was laboratory reports of infectious diseases to the PHLS. Other sources which have been used include birth registrations, death registrations and hospital episode data. The use of multiple sources of data improves case ascertainment, the completeness of which varies between studies and conditions, according to the ease of case ascertainment and the availability of complementary data sources.

Funding

The Surveillance Unit asks research teams to contribute a sum of money each month to cover the printing and distribution of the orange cards and the other administration costs of coordinating the study. In 1995, the sum was £185 per month. Contributions from researchers met 35% of the Surveillance Unit's total running costs in 1995. The remainder of the Unit's costs were met through a grant from the Children Nationwide Medical Research Fund and an anonymous donor. Support is received from the College of Paediatrics and Child Health, the Public Health Laboratory Service, Brent and Harrow Health Authority and the Scottish Centre for Infection and Environmental Health.

4 Review of activities in 1995

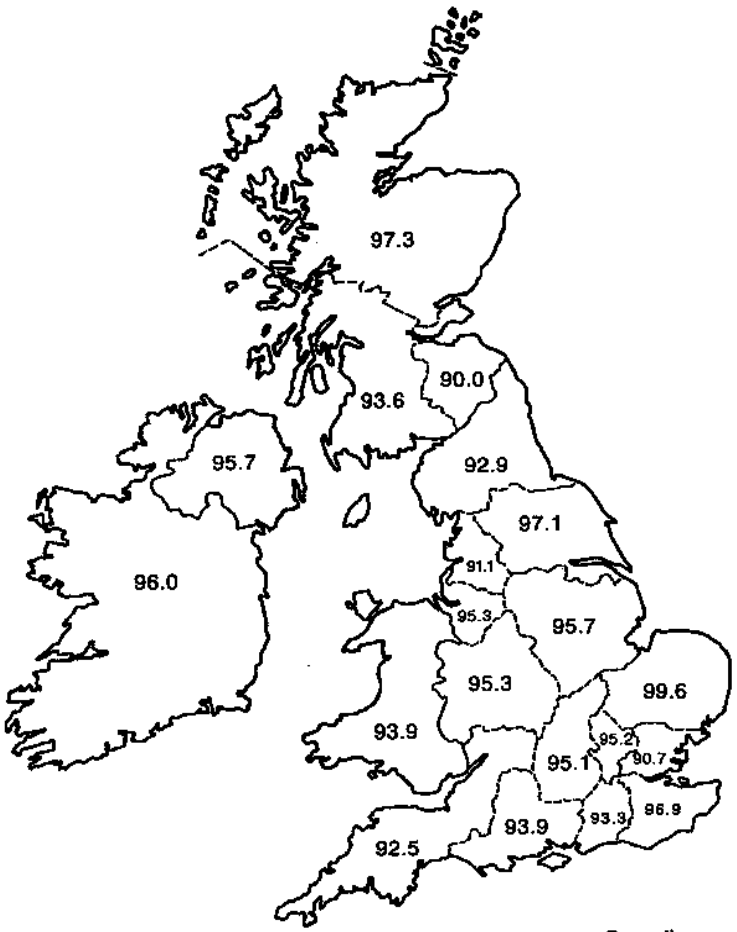
1995 was a productive year for the Surveillance Unit. Thirteen conditions were the subject of surveillance for all or part of 1995. By the end of 1995, 23 studies had been completed since the Surveillance Unit began its work in 1986 - those completed prior to 1995 are listed at Appendix A. Publications and presentations in 1995 relating to these studies and the unit's work are listed in Appendices B and C. However, the highlight of the year was the Unit's first Scientific Seminar, held in June 1995 to herald the Surveillance Unit's tenth year.

Participation in the scheme during 1995

The number of paediatricians participating in the Surveillance Unit scheme rose from 1372 to 1444 by December 1995, an increase of 5% over the year. Response rates remained high - the overall response rate for 1995, calculated as the proportion of orange cards returned within sixty days of mailing, was 94.4% (15,918/16,866), the same as in 1994. Monthly response rates ranged from 92.8% (1271/1370) in February 1995 to 95.5% (1346/1410) in August 1995, with a median of 94.0%.

As in previous years, response rates varied considerably across the country, as is shown in Figure 1. East Anglian paediatricians achieved the highest response rate - 99.6%. Response was lowest in South Scotland and North East Thames - only 90.0% and 90.7% respectively.

***Figure 1** Average response rate (%) by area, 1995*



Overall average response rate = 94.4%

Workload of those participating in the scheme

The Surveillance Unit continually monitors the workload of participants in the scheme in the terms of the number of cases reported. Figure 2 demonstrates that 78% of participants reported no cases in 1995, 20.3% reported between one and four cases and only 0.5% reported five or more cases.

Conditions included in the scheme during 1995

During 1995, thirteen conditions were the subject of surveillance. Two surveillance studies were completed during 1995 and four new studies commenced. The studies are listed in Table 3. The main findings of the studies, which are described in full in Chapter 5, are summarised below.

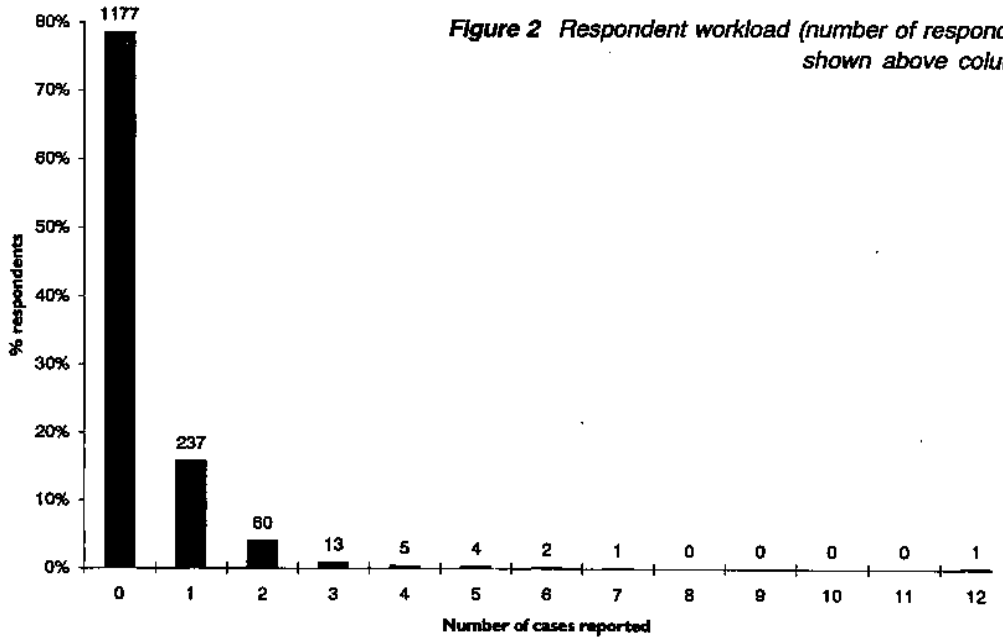


Figure 2 Respondent workload (number of respondents shown above columns)

Table 3 Studies underway in 1995

Page	Study	Principal researchers	Research Institutions
17	AIDS/HIV infection in childhood*	P Tookey, A Nicoll, D Goldberg	ICH (London), PHLS, SCIEH
18	Reye's syndrome*	M Catchpole, L Newton†	PHLS
20	Congenital rubella*	G Jones, P Tookey, C Peckham	ICH (London)
21	Subacute sclerosing panencephalitis	E Miller, N Begg	PHLS
22	Congenital syphilis*	A Nicoll, T Lissauer	PHLS, St Mary's Hospital (London)
23	*Haemophilus influenzae* type b	P Heath, M Slack, R Moxon, N Begg	PHLS, National Haemophilus
24	Biliary atresia	J P McKiernan, D Kelly, A Baker	Birmingham Children's Hospital, King's College Hospital
25	Medium chain acyl-CoA dehydrogenase*	R Pollitt	Sheffield Children's Hospital
26	Adverse effects of birth/delivery in water*	P Tookey, R Gilbert	ICH (London)
27	Transient and permanent neonatal diabetes	J Shield, J D Baum	ICH (Bristol)
28	Pyridoxine dependency	P Baxter	Sheffield Children's Hospital
29	Cerebral oedema following DKA	J Edge, D Dunger	John Radcliffe Hospital
30	Congenital cataracts	J Rahi	Great Ormond Street/ICH (London)

* Studies still in progress to September 1996.

† Since 1996 this study has been administered by S Hall and R Lynn

Main findings of studies undertaken in 1995

Ongoing studies

Paediatric HIV infection and AIDS

The SU has contributed to the national surveillance of paediatric HIV infection and AIDS since the inception of the Unit in June 1986. Although cases are also ascertained from other sources, the Surveillance Unit remains the most important source of case reports, particularly for infants born to HIV infected women - by 31 January 1996, 596 of the 972 total cases reported had been notified through the Surveillance Unit. During 1995 there was a substantial increase in the number of affected children identified in London, emphasising again the importance of making antenatal HIV testing routine in London.

Reye's syndrome

Surveillance of Reye's syndrome began in August 1981 as a shared venture between the British Paediatric Association (BPA) and the Communicable Disease Surveillance Centre (CDSC). Responsibility for surveillance was transferred to the SU when it was set up in June 1986. Cases are also ascertained via death certificates and via laboratory reports to CDSC.

In the year to 31 July 1995, 17 cases were reported, the lowest number of cases to be reported in any year since surveillance commenced.

As well as the link between Reye's syndrome and the consumption of aspirin, it is increasingly being recognised that a number of inherited metabolic disorders, such as medium chain acyl-CoA dehydrogenase deficiency, may present as a "Reye-like" illness indistinguishable from Reye's syndrome. As part of the follow up of notified cases, reporters of cases are therefore now also asked whether patients have been investigated for these conditions. One of the cases notified in 1994/95 was subsequently found to have medium chain acyl-CoA dehydrogenase deficiency. This condition is now also under surveillance.

Medium chain acyl-CoA dehydrogenase (MCAD) deficiency

Medium chain acyl-CoA dehydrogenase (MCAD) deficiency was included on the orange card between March 1994 and March 1996. By the end of December 1995, 47 cases had been identified, including ten children who had been diagnosed because an older sibling was already known to have MCAD deficiency. Although 80% of the 37 index cases were diagnosed after only one episode, six died following an initial attack and a further six have some degree of neurological impairment. The data from this study will be used to help make the case for introducing a neonatal screening programme for MCAD deficiency.

Congenital rubella

The National Congenital Rubella Surveillance Programme (NCRSP) was established in 1971 to monitor the effectiveness of rubella immunisation in reducing the incidence of congenital rubella. Since January 1990, congenital rubella has been included in the SU scheme - all cases were previously reported directly to the NCRSP. The level of case ascertainment through the Surveillance Unit is high - 23 of the 33 children born with congenital rubella since 1 January 1990 were first reported to the Surveillance Unit.

The incidence of congenital rubella is now very low - only one case was notified in 1995. Most affected infants are born to women who come to the UK as adults and have therefore not been covered by the schoolgirl immunisation programme. Ways of offering immunisation to recent immigrants should therefore be considered.

Haemophilus influenzae infections in childhood

The SU system is also being used to evaluate the effectiveness of the Hib vaccination programme. Invasive *Haemophilus influenzae* infection occurring after Hib vaccination has been included on the orange card since the introduction of the Hib vaccination programme in October 1992. This surveillance has confirmed that Hib vaccination results in high levels of protection up to at least three years of age - continued surveillance is required to establish the duration of protection provided by primary immunisation. Many of those who do develop infections despite vaccination have either been infected with non vaccine preventable strains or have an underlying immunological deficiency or other medical problem.

In November 1995 the case definition was widened to include all cases of invasive *Haemophilus influenzae* infection, regardless of vaccination status, thereby enabling pockets of continuing transmission to be identified. This information will inform the development of future vaccination strategies.

Congenital syphilis

Congenital syphilis was included on the orange card over a three year period, ending in July 1996. Of the sixteen confirmed cases reported between July 1993 and May 1996, all but one came to medical attention as a result of maternal screening. The results of the survey will contribute to an evaluation of the antenatal screening programme.

Adverse neonatal outcomes of delivery or labour in water

Surveillance of adverse neonatal outcomes of delivery or labour in water began in April 1994 and continued until April 1996. Paediatricians were also asked to retrospectively report cases occurring between October 1993 and March 1994. Over the study period 79 cases were reported through the SU of which 60 have so far been confirmed as satisfying the case definition. These cases are being scrutinised for possible risk factors and mechanisms. The total number of deliveries in water is being ascertained by the National Perinatal Epidemiology Unit. This will enable the incidence of adverse neonatal outcomes to be estimated.

Studies completed in 1995

Biliary atresia

Cases of biliary atresia were ascertained over a two year period ending in February 1995. During this time, 90 confirmed cases were reported, giving an annual incidence of 1:18,000 live births in the British Isles. The study confirms that many children are being operated on too late to obtain maximum benefit. There is often an unacceptable delay in referral - three children were referred too late for surgery - and too many surgical units are operating on children with biliary atresia resulting in a dilution of surgical and medical expertise - time between referral and surgery was significantly shorter in the two centres which operated on more than five children each year.

The results of this study will contribute to the debate about the advisability of introducing postnatal screening for jaundice and the need to restrict the number of surgical units undertaking surgery for biliary atresia.

Transient and permanent neonatal diabetes

Surveillance of neonatal diabetes ended in August 1995. During the fourteen month surveillance period, two new cases were notified giving an incidence of one per 400,000 births. The investigation of these cases, as well as a further thirteen cases which have also been notified, suggests a genetic basis for these disorders.

New studies commenced in 1995

Pyridoxine dependency

Surveillance of pyridoxine dependency began in September 1995 to enable the incidence, presentation, natural history and clinical management of pyridoxine dependent seizures to be defined.

Subacute sclerosing panencephalitis (SSPE)

As a result of the measles immunisation programme, the incidence of measles has declined but SSPE has not yet been eradicated. Surveillance of SSPE through the SU began in June 1986 but ceased in July 1994, when the CDSC again undertook passive surveillance. Subsequently, no new cases were reported and, as it was important to know whether there really had been no new cases, it was decided to reinstate SSPE on the orange card in the autumn of 1995 with a request for back reports of any new cases in the previous year. As a result, two new cases were identified with onset during 1995, demonstrating the effectiveness of the SU system.

Members of the Association of British Neurologists have now also been asked to notify any cases presenting to them since 1990 to ensure that any cases referred directly to neurologists are also identified.

Cerebral oedema and death following diabetic ketoacidosis

Cerebral oedema is a devastating complication of diabetic ketoacidosis (DKA) in children and is responsible for approximately ten deaths in children each year. The surveillance of cases of cerebral oedema and deaths due to DKA, which began in October 1995, will enable the incidence of cerebral oedema to be established. It is also planned to undertake a case control study in order to identify factors in the clinical presentation and subsequent clinical course which predispose to the development of cerebral oedema. Controls with DKA who did not develop cerebral oedema are being identified through a separate reporting mechanism.

Congenital cataract

Surveillance of congenital cataract through the SU began for a one year period in October 1995. The aims of the study are to estimate the prevalence of congenital and infantile cataract, to determine the aetiology and presentation of cases and the factors associated with good visual outcome.

Priorities agreed for 1996

The Surveillance Unit's priorities for 1996 are to:

- continue to provide a high quality surveillance service to CPCH members and other investigators using the Surveillance Unit
- continue to disseminate information about the Surveillance Unit to the wider scientific community
- validate the surveillance system
- further develop links with other national and international units involved in the surveillance of rare conditions
- ensure the future funding of the Surveillance Unit.

These are encapsulated in a workplan agreed by the Executive Committee and progress is reviewed regularly. In addition, a second Scientific Seminar is planned for December 1996.

5 Surveillance studies undertaken in 1995

AIDS and HIV infection in childhood

Background

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

Most cases of paediatric HIV infection and AIDS are children born to women infected with HIV. In Europe it is estimated that 15% to 20% of babies born to HIV infected mothers, and not breast fed, are infected themselves, and 25% of these develop AIDS within 12 months. With new laboratory tests HIV infection can usually be diagnosed by three to four months of age.

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, PCR or antigen detection, or any other laboratory marker of HIV infection. Also any child born to a woman known to be HIV infected at the time of that child's birth, regardless of the child's infection status.

Study duration

The survey began in June 1986.

Analysis

By the end of January 1996 there had been 974 reports through the SU. Five hundred and ninety-six children born to HIV infected women were reported; these included 254 children with confirmed infection, 235 who have lost maternal antibody and are now known to be uninfected, and 107 whose infection status is still indeterminate. Forty-eight children were infected in the course of treatment for haemophilia, a further 21 through blood transfusion, and in once case the transmission route cannot be established. Sixteen of the remaining reports are still being investigated, 136 were duplicates and there were 156 reporting errors.

A further 629 reported cases have been identified from other sources including 376 children born to HIV infected women (114 with confirmed infection, 102 uninfected and 160 indeterminate), 222 children with haemophilia, 17 infected through blood transfusion, and 14 where the route of transmission is at present unclear. These include reports

Table 4 Infants born to HIV infected women and confirmed cases of paediatric HIV infection (notified by 31 January 1996)

Transmission route	SU Reports	Reports from other sources	Total
risk of vertical transmission	596	376	**972**
haemophilia treatment	48	222	**270**
blood transfusion/products	21	17	**38**
other/not yet established	1	14	**31**

Infection status of children born to HIV infected women (notified by 31 January 1996)

HIV infection status	SU Reports	Reports from other sources	Total
AIDS	148	56	**204**
HIV infection (not AIDS)	106	58	**164**
indeterminate	107	160	**267**
uninfected	235	102	**337**
TOTAL	**596**	**376**	**972**

by obstetricians to the Royal College of Obstetricians and Gynaecologists (through a reporting scheme similar to the SU), reports to the UK Haemophilia Centre, and reports made directly to the coordinating centre at the Institute of Child Health (ICH) in London, the Public Health Laboratory Service (PHLS) AIDS Centre at the Communicable Disease Surveillance Centre, or the Scottish Centre for Infection and Environmental Health (SCIEH).

All reporting is voluntary and confidential. Children are followed up yearly to monitor their clinical and immunological status and to determine their infection status. Children born to HIV infected women who are subsequently found to be uninfected themselves are not followed up further. Most of the surviving young people infected during the course of treatment for haemophilia are now over 16 years old and their follow-up is undertaken by the UK Haemophilia Centre and CDSC.

Data from the various sources are combined each quarter and form the basis of the national surveillance of HIV infection and AIDS in children. These data are used to describe the current status of the epidemic in the UK and appear on a quarterly basis in the Communicable Disease Report and ANSWER (SCIEH publication). An important finding in 1995/96 was a substantial increase in the number of children in London requiring care because of their HIV infection. Data are also used to monitor the clinical spectrum of disease in children, estimate the vertical transmission rate, predict the future extent of vertically acquired HIV infection and to contribute to European global estimates of paediatric AIDS.

We would like to thank all members of the CPCH, particularly those paediatricians who have reported cases and completed questionnaires.

Funding

This study is funded by AVERT AIDS Education & Research Trust), and additional support is received from the collaborating institutions. Routine collation of data each quarter and transfer to national surveillance centres is funded by the Medical Research Council.

Ms P Tookey, Miss T Duong, Ms T Berry, Department of Epidemiology and Biostatistics, Institute of Child Health, 30 Guilford St, London WC1N 1EH Tel: 0171 829 8686.
Dr A Nicoll, PHLS CDSC, 61 Colindale Avenue, London NW9 5EQ Tel: 0171 200 6868
Dr D Goldberg, SCIEH, Ruchill Hospital, Glasgow G20 9NB Tel: 0141 946 7120.

Reye's syndrome

Background

Surveillance of Reye's syndrome began in August 1981 as a venture shared between the BPA and the CDSC. Responsibility for case ascertainment was transferred to the Surveillance Unit in June 1986. In the early years, the results of surveillance showed that the incidence of Reye's syndrome in the British Isles was similar to that in the United States although cases occurred at a younger mean age, there was no clear seasonal (winter) peak, no obvious association with influenza and chickenpox, and there was a higher case fatality rate.

In 1984/85 a study of risk factors mounted on the surveillance database showed an association between Reye's syndrome and consumption of aspirin. In response to this and similar findings in the United States, the Committee on Safety of Medicines issued public and professional warnings in 1986 about the use of aspirin in children under 12 years. Since then, products that contain aspirin have been required to carry warning labels.

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

In addition to SU reporting, cases were also ascertained via death entries provided by the Office for National Statistics and the Northern Ireland Statistics and Research Agency, and via laboratory reports to the PHLS, Communicable Disease Surveillance Centre.

Objectives

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

Case definition

A child under 16 years old with:

- unexplained non-inflammatory encephalopathy, and *one or more* of:
- serum hepatic transaminases elevated to at least three times the upper limit of normal;

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

Since this case definition is relatively non-specific, cases reported from surveillance year (1994/5 onwards have been allocated a 'Reye-score'.[1]

Study duration

The SU involvement with this study began in June 1986; it has been granted a further one year extension to July 1997.

Analysis

Between August 1981 and July 1995 a total of 579 suspected cases of Reye's syndrome were reported. In 145 cases (25% of the total) the diagnosis has subsequently been revised. Nearly half (48%) of the revisions were to one of the 'Reye-like' inherited metabolic disorders. In the year to July 1995, 17 reports were received and follow up was complete on 14 at the time of writing. Three of the 14 diagnoses had subsequently been revised leaving 11 cases whose clinical and pathological features were compatible with Reye's syndrome. Among the three cases on whom further information is pending there were two ascertained via death entries alone. They were aged 10 months and 23 months and both died at home.

Cases compatible with a diagnosis of Reye's syndrome: year (12 months) to July 1995

There were five males and six females; the ages ranged between two months and thirteen years with a median of fourteen months. Nine lived in England, one in Wales and one in the Republic of Ireland. Two were ill in Autumn; four had their onsets between December and March, two in April and three in July. Of the nine survivors, six were normal, two had neurological sequelae and the outcome was unclear in one. Five patients had received no pre-admission medication, three had received paracetamol plus an antibiotic, one had been given paracetamol and aspirin, one had been given penicillin and one had been on antiepileptic treatment.

Four patients were reported to have had no podromal illness, five had had upper respiratory tract infections and two had had non-specific pre-admission symptoms such as lethargy and feeling cold. An enterovirus was recovered from faeces in one patient and campylobacter jejuni from a rectal swab in another; none of the others had microbiological confirmation of infection. Eight patients were reported to have been investigated for inherited metabolic disorders; three (aged 11 weeks, 14 months and eight years) had not. The 'Reye Score' (possible range: 1-25) ranged between 6 and 21 with a median of 13.

Revised diagnosis cases

Of the three cases, one female aged six months had a confirmed inherited metabolic disorder, medium chain acyl-CoA dehydrogenase deficiency; she had had previous 'Reye-like' illnesses and a sibling had died during a similar episode. In another, a male aged 18 months, an inherited metabolic disorder was considered by the clinician to be more likely than Reye's syndrome because of pre-existing developmental delay and spasticity, although a definitive diagnosis had not yet been made. In the third, aged five months, the revised diagnosis was haemorrhagic shock encephalopathy syndrome associated with cytomegalovirus infection.

Comment

Surveillance year 1994/5 saw the lowest annual total reports to the Reye's syndrome surveillance scheme since it began in August 1981. The annual totals for 1992/3 and 1993/4 reported previously were spuriously low because of the delay in obtaining death entry data. This also accounts for most of the cases awaiting further information. It is noteworthy that, between 1992/3 and 1994/5, ten of the total 58 reports were death entries of patients not ascertained via the SU. These are currently the subject of a follow up study.

The continuing problem with surveillance of Reye's syndrome is the non-specificity of the case definition. Thus, unlike many other disorders surveyed by the SU, a case of Reye's syndrome can rarely, if ever, be described as 'confirmed'. Confirmation requires ultrastructural examination of the liver cells during the acute stage of the illness. However, this investigation has been undertaken in only a handful of reported cases since surveillance began. This probably reflects a combination of caution in undertaking liver biopsy in patients with disordered clotting and restricted availability of electron microscopy.

In 1994/5 the number (3) and proportion (21%) of revised diagnosis cases was lower than in any year since 1984/5; the same applies to those with a definite or suspected inherited metabolic disorder. As knowledge of these conditions increases this trend is to be expected. Nearly 75% of the non-revised cases were reported to have been investigated for inherited metabolic disorders. However, it is not known how complete the investigations were as the proforma does not seek this information. The lack of seasonality, young median age and atypical features such as absent or non-specific prodrome and absent or minimal

vomiting, suggests that some may have had unrecognised inherited metabolic or other Reye-like disorders, especially those with low Reye scores. Two of these 11 patients whose diagnosis was not revised by the clinician nevertheless may not have satisfied that part of the case definition which requires the encephalopathy and disordered liver function to be 'unexplained'. One did have unexplained encephalopathy but had had a cardiac arrest before the liver function tests were performed; the other, a child with pre-existing cerebral palsy and epilepsy, had been treated with sodium valproate, although there was uncertainty as to whether it had been given prior to the onset of the 'Reye-like' illness.

Just under half the patients had received pre-admission medication for prodromal symptoms but only one, a 13 year old, had received aspirin. This patient, who was extensively investigated for an inherited metabolic disorder, also had the highest Reye score (21) which is in keeping with recent observations on the relationship between the score and aspirin exposure.[1]

Reference

1 Hardie RM, Newton LH, Bruce JC, Glasgow JFT, Mowat AP, Stephenson JBP, Hall SM. The changing Clinical Pattern of Reye's Syndrome 1982-1990. Arch. Dis. Child. 1996; 74: 400-405

Dr S Hall, c/o PHLS Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ Tel: 0181 200 6868
Mr R Lynn, Surveillance Unit, College of Paediatrics and Child Health, 5 St Andrews Place, Regent's Park, London NW1 4LB
Tel: 0171 935 1866

Congenital rubella

Background

The National Congenital Rubella Surveillance Programme (NCRSP) was established in 1971 to monitor the effect of immunisation in reducing the incidence of congenital rubella. A selective immunisation programme was introduced in 1970 for all schoolgirls and for susceptible adult women. In 1988 the combined measles/mumps/rubella (MMR) vaccine was introduced for all children in the second year of life. In November 1994, as part of an attempt to avert a predicted measles epidemic, all 5-16 year olds were offered combined measles/rubella (MR) vaccine. Antenatal screening with postpartum vaccination continues, as does mass immunisation of young children, but the schoolgirl programme has now ceased.

Objectives

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

Case definition

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

Study duration

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

Analysis

A one-off SU survey in 1988 yielded twenty reports, six of which were previously unreported confirmed cases of congenital rubella. Since the beginning of active surveillance in 1990, 75 reports have been made through the SU. Of these 75, three reports were of children born in Eire or Northern Ireland who are followed up but not included in the NCRSP registry figures, and another six were children already reported via another source (audiologists, virologists and CDSC). Twenty-nine reports were confirmed, previously unreported cases of congenital rubella, two were possible cases which could not be confirmed because laboratory information was lacking; three reports are still under investigation. The remaining 32 reports were duplicates (15), reporting errors (16), and one where further information could not be obtained.

Altogether 858 children with confirmed congenital rubella are registered with the NCRSP. 70% of those born since the beginning of 1990 (22/33, see table 5) were first reported through the SU.

The incidence of congenital rubella is now very low and most affected infants are born to women who came to the UK as adults and were not covered by the schoolgirl immunisation programme. Ways of offering immunisation to recent immigrants should therefore be considered. In the last six years, six children were born to women who had acquired their own infection in early pregnancy outside the UK (imported cases).

It is essential that case ascertainment is as complete as possible. Please notify to the SU all children suspected of having congenital rubella, whether or not they have the associated typical defects. We are grateful for your effort and cooperation.

Ms Pat Tookey, Professor Catherine Peckham, Department of Epidemiology and Biostatistics, Institute of Child Health, 30 Guilford Street, London WC1N 1EH Tel: 0171 242 9789

Table 5 *Confirmed congenital rubella births reported to the NCRSP 1971-1995**

Year of birth	Primary source of notification		Total
	SU	Other	
1964-69	0	39	39
1970-79	1	453	454
1980-89	12	320	332
1990-95	23	10	33
1990	*8*	*4*	*12*
1991	*2*	*1*	*3**
1992	*5*	*2*	*7***
1993	*2*	*1*	*3*
1994	*5*	*2*	*7*
1995	*1*	*0*	*1*
Total	**36**	**822**	**858**

* The data for recent years are provisional

** Includes one set of triplets

Subacute sclerosing panencephalitis (SSPE)

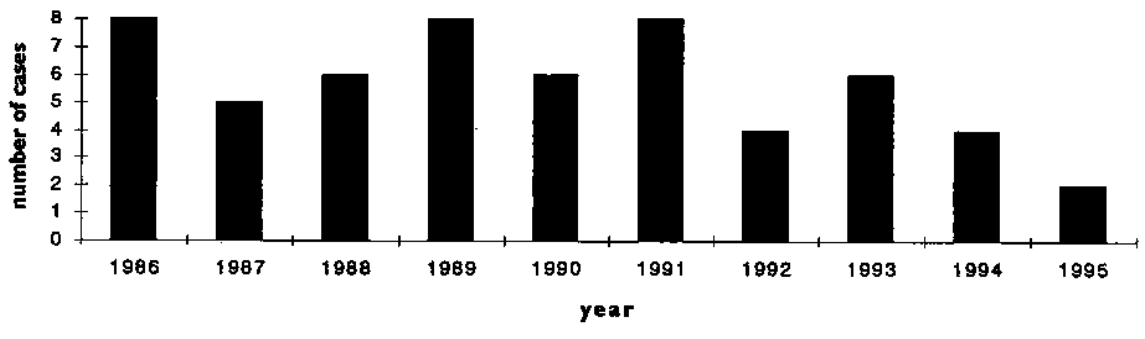
SSPE was placed back on the orange card in Autumn 1995 as no new cases had been reported since its removal a year earlier and it was necessary to know if this was a true reflection of incidence. Subsequently, two new cases were reported with onset in 1995.

The annual number of new cases identified with onset in the last ten years has been in single figures with 1995 being the lowest ever. An update of Dr Christine Miller's paper - 'The Epidemiology of Subacute Sclerosing Panencephalitis in England and Wales 1970-1989' - is currently under way, and, by kind permission of the Association of British Neurologists (ABN), a letter has gone out with their quarterly newsletter, asking members to notify the researchers of any cases of SSPE seen since 1990. This request was made to enable the identification of cases developing in adolescents and young adults who are referred directly to neurologists and thus possibly escaping the 'net' of SU reporting.

Thus, with the ABN coming alongside the SU in the reporting of cases, the paper should give a truly comprehensive picture of SSPE in England & Wales at the present time. The report will be completed by the end of 1996 and when available copies may be obtained upon request.

Dr E Miller, PHLS Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ tel: 200 6868

Figure 3 *Cases of SSPE in England and Wales by year of onset 1986–1995*



Congenital syphilis

Background

The SU survey of congenital syphilis began in July 1993. Its aim has been to undertake surveillance for congenital syphilis in the United Kingdom and the Republic of Ireland. Previously, the only surveillance of congenital syphilis was through the genitourinary medicine (GUM) clinics and it was unclear whether all affected children might be attending such facilities.

The importance to public health of this survey has increased since it began as suggestions have been made that antenatal serological screening for syphilis should cease[1]. It is thought that almost all women who receive antenatal care in the United Kingdom are screened for evidence of syphilis and other treponemal infections, such as yaws and pinta, which are serologically indistinguishable. Although national data suggest that infectious syphilis in women is uncommon in the United Kingdom, it still occurs. Totals of new cases in women between the ages of 15 and 59 attending GUM clinics in England during 1991, 1992, 1993 and 1994 were 110, 110, 108 and 110 respectively. Moreover, the current levels of infection may not remain low indefinitely. In the United States, a substantial epidemic of adult syphilis and failure to provide universal antenatal care (including serologic screening) has resulted in a substantial epidemic of congenital syphilis. More recently, there has been a resurgence of adult syphilis in the former USSR and adjoining parts of Eastern Europe.

Objective

To determine the minimum incidence of congenital syphilis in children, detect possible maternal and other risk factors, and look for trends while the study continues.

Case definition

A confirmed case is an infant, stillbirth or child under 16, in whom direct evidence of *Treponema pallidum* is found. **A presumptive case** is **either** an infant, stillbirth or child under 16, whose mother had untreated or inadequately treated syphilis at the time of delivery **or** an infant, stillbirth or child under 16, with a reactive specific treponemal test (TPHA or FTA-Abs **not** just VDRL or RPR) and evidence of infection. **A possible case** is an infant, stillbirth or child under 16, treated for syphilis, who does not fulfill confirmed or presumptive criteria.

Duration

The study commenced in July 1993 and ended in July 1996.

Results

Between July 1993 and May 1996, twenty-two reports were made - six in 1993, three in 1994, seven in 1995 and, so far, six in 1996. Three reports (one each in 1993, 1995 and 1996) were not confirmed as cases when further information became available. Three reports are awaiting further information (one in 1995, two in 1996). Of the sixteen confirmed cases, eight were "presumptive" and eight "possible". All except one came to medical attention via maternal screening. The exception was a Black-Caribbean child born in November 1995 (presumptive case) who came to medical attention because of hepatosplenomegaly. The mother was then found to be seropositive. The mothers of all the presumptive cases and six of the possible cases were treated or inadequately treated before or during pregnancy.

The low numbers may be explained in four ways: there may be few cases to diagnose and report, there may be a failure to make the diagnosis (especially in "possible" cases without symptoms), diagnosed cases may not be reported and diagnosed cases may not see paediatricians (it is known that some are referred to specialists in genitourinary medicine with their mothers).

The research team is investigating the low numbers coming through the SU scheme. In addition, the British Cooperative Clinical Group (BCCG), a group of GUM physicians in the UK, has begun a reporting scheme. This is analogous to the SU scheme, but reports are made quarterly, and the scheme is also looking for cases of treponemal infection (including syphilis) requiring treatment, in pregnant women. This will suggest how many infections are being detected by antenatal screening. Routine quarterly reporting to the six PHLS reference laboratories of all cases of treponemal infection began in late 1994. It is planned that laboratory reporting will form the basis of long term surveillance. The data from these surveys and laboratory reporting will form the basis of a policy analysis of the value of antenatal screening for syphilis.

Reference

1 Nicoll A, Moisley C. Antenatal screening for syphilis. BMJ 1994, 304: 1253-4

Dr A Nicoll, PHLS, Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ Tel: 0181 200 6868
Dr T Lissauer, Department of Child Health, St Mary's Hospital, London W2 1NY Tel: 0171 725 6402

First contact for further information: Ms Linda Ratcliffe, Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ Tel: 0181 200 6868 x 4561

Invasive Haemophilus influenzae infection

Background

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

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

Objectives

To identify cases of invasive *H.influenzae* disease occurring in:

1. children who have been vaccinated thereby enabling the:
   i) estimation of the efficacy of Hib conjugate vaccine in British and Irish children;
   ii) determination of the importance of disease due to non type b *Haemophilus influenzae*
   iii) documentation in cases of vaccination failure of host factors that might be relevant, the clinical presentation of the disease and the acute and convalescent concentrations of Hib antibody.
2. children who have not received Hib conjugate vaccine.

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

Case definition

True vaccine failure is defined as the occurrence of invasive Hib disease after three doses of vaccine, or more than one week after two doses given in the first year of life, or more than two weeks after a single dose given to a child over twelve months of age. An *apparent vaccine failure* is defined as Hib disease that occurs after vaccination has been given but before protection could be reasonably expected to develop, for example, Hib disease occurring after one dose in the first year of life.

Study duration

The study began in September 1992 and is reviewed annually.

Analysis

By 31 December 1995, 215 reports had been made including 81 by paediatricians, 97 by microbiologists and 36 by public health physicians. Fifty nine cases represented true vaccine failure (TVF), 61 were apparent vaccine failures, 38 were not capsulate strains of *H. influenzae* and fourteen were non b capsulated strains, mostly type f. There were seven possible cases of vaccine failure (protective course of vaccination received, isolate of *H. Influenzae* obtained but not typed), and thirty-six reports did not meet the case definition criteria. The majority of reports have come from England (170) followed by the Republic of Ireland (30) Northern Ireland (6), Scotland (6) and Wales (3).

Fifty two of the 59 cases of TVF were vaccinated in the first year of life; 43 received three doses and nine received two doses. Seven were vaccinated when older than 12 months of age. Of those vaccinated in the first year of life 19 developed disease in the first year of life, 24 in the second year of life and nine in the third year of life. Surveillance has allowed the following point estimates of vaccine efficacy to be made: 99.1% (95%C.98.3-99.6%) first year of life, 97.3% (95.6-98.4%) second year and 94.7% (88.4-98.1%) for the third year of life.

The modes of presentation and associated medical and immunological conditions amongst the cases of TVF are detailed in the table (page 24). Overall, 29 (49%) were shown to have an associated condition.

Convalescent sera were available in 54 cases of TVF. Twenty one (39%) demonstrated a poor antibody response to disease (<1mg/ml). 92% of those who have since received a booster dose (11/12) achieved a protective antibody concentration.

In the first two months of the widened surveillance (November and December 1995), 16 additional cases of *H. influenzae* occurring in non vaccinated children were reported. Only one of these was of serotype b, a case of meningitis in a nine month old child.

Comment

This surveillance has confirmed high levels of protective efficacy of Hib conjugate vaccine to at least three years of age without a booster. In those who develop disease despite vaccination, medical and immunological factors have featured strongly. It has also become clear that such individuals cannot be assumed to be protected following natural infection and that their antibody levels should be measured. It has been reassuring, however, that the vast majority of such cases do then respond to a booster dose of vaccine. Finally, the study has highlighted that many reports of possible vaccine failure actually represent disease due to non vaccine preventable strains. Verification of the isolate is an important tool in maintaining confidence in a vaccination programme.

It is too premature to draw conclusions from widened surveillance system in place since November 1995. It is of interest that the only non vaccinated child with type b disease was of an age where a complete course of immunisation could have been provided. This enhanced surveillance should allow a complete picture to be gained of *Haemophilus influenzae* disease in children in the post vaccine era.

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

Table 6 *Presenting illness and associated conditions of true vaccine failures (TVF) September 1992 - December 1995*

Presenting Illness		Associated condition	
Meningitis	35	Prematurity	6
Epiglottis	13	Cromosomal abnormality	4
Bacteremia	5	(Down's syndrome	3)
Pneumonia	3	Dysmorphic	2
Septic arthritis	2	Malignancy	2
Orbital celluliti	1	Cyclical neutropenia	1
		Immunoglobulin deficiency	18

Dr P Heath, Professor R Moxon, Dr M Slack, Oxford Vaccine Group and National Haemophilus Reference Laboratory, John Radcliffe Hospital, Oxford OX3 9DU Tel: 01865 221068/220859
Dr M Ramsay, PHLS Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ Tel: 0181 200 6868
Dr J Fogarty, Dept of Public Health Medicine, Merlin Park Hospital, Galway, Republic of Ireland Tel: 00353 091 751131

Biliary atresia

Background

Biliary atresia is an uncommon disease of infancy, which is fatal if not treated. It is the commonest cause of liver disease in children of such severity as to require liver transplantation. The aetiology and incidence of the condition in the United Kingdom and the Republic of Ireland are unknown.

Objectives

The Surveillance Unit survey sought to answer the following questions. What is the national incidence of biliary atresia? Are there any recognisable aetiological features? What is the current pattern of referral and why is referral delayed? What is the outcome for affected children following modern management and how many will eventually need liver transplants.

Study duration

This study began in March 1993 and ended in February 1995.

Analysis

More than 80 cases have been confirmed and a number await confirmation. A number of duplicate reports were made, confirming that the scheme provides comprehensive coverage. Two cases have been identified by other means and not through the Surveillance Unit.

Paediatricians who are likely to have seen children with liver disease are being contacted, reminding them that the study has come to an end, and asking for information about any children with biliary atresia who may not have been reported.

The mean age at which children with biliary atresia undergo surgery has fallen to 59 days. In many cases,

however, there remains an unacceptable delay and in three cases children were referred too late for surgery to be appropriate. It is disappointing to note that, for a rare condition, surgery is still being carried out at a large number of centres. Eleven centres have operated on children with biliary atresia in the past two years, but only three of these centres saw more than two children a year.

Results

Ninety cases were confirmed giving an incidence of 1:18,000 live births in the British Isles. Children were referred to a paediatrician at a median age of 32 days (range 1-85), and to a surgical centre at a median age of 40 days (5-281).

Surgery was carried out on 87 children in 14 centres at a median age of 53 days (14-294). Forty six per cent of children were operated on later than 56 days of age. Only two centres operated on more than five children yearly, and only seven centres operated on more than one child yearly. Time between referral and surgery was significantly shorter in those centres operating on more than five children yearly.

Conclusion

1. As a result of late referral many children with biliary atresia are undergoing surgery too late to obtain maximum benefit.
2. Too many surgical centres are operating on children with biliary atresia resulting in dilution of surgical and medical expertise.

Dr J P McKiernan, Dr D Kelly
The Children's Hospital, Ladywood Middleway, Birmingham B16 8ET
Tel: 0121 454 4851
Dr A Baker
King's College Hospital, Denmark Hill, London SE5 8RX
Tel: 0171 274 6222

Medium chain acyl-CoA dehydrogenase deficiency

Background

Medium chain acyl-CoA dehydrogenase is an inborn error of fatty acid oxidation with a variable presentation. Some patients develop hypoketotic hypoglycaemia or an acute encephalopathy (similar to Reye's syndrome), whereas others may present with hypotonia, hepatic dysfunction, or they remain asymptomatic. The sudden and unexpected death of some cases may be attributed to sudden infant death syndrome. Studies of the frequency of the common mutation in heterozygotes suggest that medium chain acyl-CoA dehydrogenase (MCAD) deficiency is relatively common, with a birth prevalence of about one in 10,000. It seems, however, that the proportion diagnosed varies greatly, both internationally and from one region of the UK to another. In many places less than 50% of the predicted cases are diagnosed clinically. Neonatal screening for MCAD deficiency by tandem mass-spectrometry is a feasible proposition and has been performed on over 80,000 babies in the USA.[1]

Objectives

To identify all patients in the United Kingdom diagnosed during the period of the study. To provide data to inform decisions about whether to include MCAD in a neonatal screening programme. It is hoped that by increasing general awareness of the disorder the management of individual patients and their families will benefit.

Case definition

Through an accepted laboratory criterion. Data on genotype are also being collected which will allow sub group analysis.

Case duration

The study began in March 1994 and is due to end in March 1996.

Analysis

Eighty-six returns were made up to the end of December 1995, producing 47 newly-diagnosed patients in 44 families. Most of the discrepancy between the number of returns and the number of patients was due to multiple reporting, reflecting the tendency for such patients to be referred on to specialist centres either prior to or following diagnosis. A separate circulation to diagnostic laboratories has confirmed the validity of the returned data.

In ten of the cases there was a family history. Three of the new cases were babies born into families where MCAD deficiency had been diagnosed in an older sib. Two others were investigated for MCAD deficiency because an older sib had died of Reye's syndrome. In two families an older sib, in one a twin, and in one a younger sib of newly-diagnosed cases of MCAD deficiency were also diagnosed to have the condition though as yet they had shown no clear symptoms. A further child, born into a family known to be at risk, was erroneously diagnosed as unaffected shortly after birth but then had a hypoglycaemia episode at one year of age.

Age at diagnosis in the 37 index cases ranged from two days (fortuitously in the course of another investigation) to 14 years. In four cases an episode occurred in the first week of life, in one case proving fatal. Overall, six patients died following the initial attack. Six surviving patients show some degree of neurological impairment. Despite the apparently good diagnostic performance in the UK, with 80% of symptomatic patients diagnosed after only one episode, there is clearly still substantial morbidity and mortality, with a death either definitely or probably attributable to MCAD deficiency in 13 of the 44 affected families.

The uneven geographical distribution of diagnosed cases noted in the first year persists, although as the number of cases reported increases it appears less marked. It is known that there are regional differences in gene frequency, but there is also evidence of regional differences in the proportion of symptomatic cases diagnosed.[2]

Further work

Data collection through the SU ended in March 1996. There will be a further circulation to selected diagnostic laboratories in order to consolidate the data and check diagnostic information. The results will then be summarised for publication and will also be used in the health technology assessment of neonatal metabolic screening currently being performed as part of the NHS R&D programme.

References:

1 Ziadeh R, Hoffman EF, Finegold DN, Hoop RC, Brackett JC, Strauss AW, Naylor EW. Medium chain acyl-CoA dehydrogenase deficiency in Pennsylvania: neonatal screening shows high incidence and unexpected mutation frequencies. *Paediatric Research* 1995; **37**: 675-678

2 Seddon HR, Green A, Gray RGF, Leonard JV, Pollitt RJ Regional variations in medium-chain acyl-CoA dehydrogenase deficiency. *Lancet* 1995; **345**: 135-6

Dr R J Pollitt, Neonatal Screening Laboratory, Children's Hospital, Sheffield, S10 2TH Tel: 0114 271 7302
Professor J V Leonard, The Medical Unit, Institute of Child Health, 30 Guilford Street, London WC1N 1EH Tel: 0171 242 9789

Adverse neonatal outcomes of delivery or labour in water

Background

A survey by the National Perinatal Epidemiological Unit (NPEU) established that about 4500 women gave birth in water during 1992 and 1993 in England and Wales. A further 8000 women were reported to have laboured, but not delivered, in a birthing pool.[1] A handful of reports of perinatal death or damage following, but not necessarily attributable to, labour and/or delivery in water, highlighted the need to determine the risk of adverse paediatric outcomes. Facilities for waterbirths are now widely available and adverse events are rare for the low risk women who use them. A national surveillance study was therefore set up in collaboration with the NPEU.

Objective

a) To estimate the incidence of adverse neonatal outcomes in babies delivered in water;
b) To identify babies who are admitted to special care baby units or who die, following labour in water, and to examine whether there is evidence that the use of water during labour is associated with adverse outcomes.

Case definition

Following delivery or labour in water
a) any perinatal death and
b) any admission to special care unit within 48 hours of birth, occurring between 1 October 1993 and 30 March 1996 (first six months reported retrospectively).

Study duration

Appeared on orange card from April 1994 to April 1996 (25 months).

Analysis

The incidence of adverse neonatal outcomes in babies delivered in water will be estimated (the total number of deliveries in water will be established from a separate NPEU survey). Appropriate comparison rates for low-risk pregnancies do not currently exist and will be determined from existing data sources. No incidence estimate will be made for adverse outcomes following labour only in water, but all cases will be scrutinised for clues about risk factors and mechanisms.

Over the study period 79 notifications were made through the SU. Of these, 60 satisfied the case definition, 11 were duplicate reports and six were errors; two notifications

are still being investigated. 16 additional cases were notified direct to the investigators. Notifying paediatricians were sent a form requesting antenatal and paediatric details. Just under 60% of notifications were of deliveries in water. Follow-up information on those who were admitted to special care is being sought.

Because it is necessary to collect denominator data, full results will not be available until the end of 1996. The investigators wish to express their thanks to the reporting paediatricians and their colleagues in midwifery for notifying cases and completing study questionnaires.

Funding

The study is funded by the Department of Health.

References

1 Aldernice F, Renfrew M, Marchant S, Ashurst H, Hughes P, Berridge G, Garcia J. Labour and birth in water in England and Wales. BMJ 1955; 310:837.

Ms Pat Tookey and Dr Ruth Gilbert, Institute of Child Health, 30 Guilford St, London WC1N 1EH Tel: 0171 242 9789.

Transient and permanent neonatal diabetes

Background

Transient neonatal diabetes is a very rare condition that affects babies born at term. Failure of beta cell maturation has been proposed as the underlying pathology.

Objective

The study was designed to establish the incidence of both transient and permanent forms of neonatal diabetes. It was also hoped that the study would define the clinical, physiological and genetic characteristics of these conditions.

Case definitions

Neonatal onset diabetes: all infants of 37 weeks gestation or older who develop persistent hyperglycaemia requiring insulin treatment within the first 6 weeks after birth.
Transient neonatal onset diabetes: those who still require insulin treatment at the age of 1 year (and, by inference, permanently thereafter).

Study duration

This study was commenced in July 1994 and ended in August 1995.

Analysis

Within the study period, two new cases of neonatal diabetes were notified giving an incidence rate of approximately one per 400,000 births. In addition a further two cases have been reported to the investigating team subsequent to the study as have eleven retrospective cases.

From these sources we have been able to examine both the aetiology and genetic background to these unusual conditions. Neither the transient nor the permanent forms of neonatal diabetes are due to the classical autoimmune disease associated with insulin dependent diabetes of childhood. The defect appears to lie in insulin secretory capacity at birth and possibly in utero as the birth weights of the majority of children lie below the 3rd percentile. Transient neonatal diabetes appears to predispose to, or be a marker for the development of maturity onset diabetes in later life.

There are pointers to a genetic basis for transient neonatal diabetes. Three patients have now been identified with paternal uniparental isodisomy of chromosome six while a further case carries an unbalanced duplication of 6q22-23. We postulate that transient neonatal diabetes is due to the over-expression of an imprinted gene(s) in the region of this duplication. This very rare condition may have important implications for understanding the relationship between intra-uterine growth retardation and later maturity onset diabetes.

The investigators are still keen to hear of any additional cases: each one may add critically to understanding the genetic basis of this disorder.

Funding

This study was financed through a small grant award from the British Diabetic Association.

Dr J Shield, Professor J D Baum, Institute of Child Health, St Michael's Hill, Bristol BS2 8BJ Tel: 0117 9215 411 (Bleep 2353, Dr Shield)

Pyridoxine dependency

Background

Pyridoxine dependency is a rare, but treatable, recessively inherited cause of seizures starting in early childhood. Since its description in 1954 less than 50 definite cases have been described in published literature, all in case reports or small hospital based series. No large scale or population based study has ever been reported. The incidence and prevalence are unknown. Up to one third of reported cases present atypically with, for example, an onset of convulsions after the neonatal period (up to two years) or a transient response to standard anticonvulsants. Other clinical complications occur such as abdominal symptoms, early visual agnosia, structural changes in the nervous system, or seizures provoked by intercurrent infections, but their frequency is unknown. The condition may be under-recognised. The outcome for psychomotor development is reputed to be poor even in cases treated early, but this is debatable as no formal study has been undertaken. The reported dose of pyridoxine required for individual patients varies between 10 and 1000mg daily, but it is not usually changed with age and the optimal dose is unknown. Individual case reports suggest a disorder of GABA metabolism may be at fault but neither the metabolic nor the genetic abnormality is identified.

Objectives

The study is to:

a) determine the prevalence of definite or possible pyridoxine dependent seizures in children under 16 years of age

b) prospectively study the incidence in children under five years of age.

c) define the clinical presentation, natural history, and clinical management of pyridoxine dependency.

Pyridoxine dependent seizures: recurrent seizures that respond to pyridoxine, or any child receiving pyridoxine for suspected pyridoxine dependency.

Definite cases are defined as neonates, infants or young children with recurrent (that is, two or more) seizures of any type, including infantile spasms, that cease within seven days of the administration of oral pyridoxine (usual dose: 30 mg/Kg/day, minimum 15 mg/kg/day, maximum 1000 mg/day) or within 30 minutes of intravenous pyridoxine (usual dose 100mg, minimum 50 mg), or within 30 minutes of intravenous pyridoxine (usual dose 100 mg), that recur when pyridoxine supplementation is withdrawn, and that cease again when pyridoxine is given as above.

Possible cases are defined as above, but without an attempt to withdraw pyridoxine.

Please include cases in whom there are other suspected or definite causes of seizures, to ensure complete reporting.

Study duration

September 1995 - October 1996

Current progress

Twenty-two cases have been reported: three are duplicates. Four more have been informally notified. Seven cases previously studied in the Northern Region have not been notified.

Questionnaires have been returned on fifteen (two duplicates).

Eight of the reported cases are "possible" or "definite." Formal trials of withdrawal have not been attempted, but in four the initial seizures responded to a single dose of pyridoxine and then recurred after a few hours or days, with a further response to a second dose of pyridoxine. Three are aged under one year and the other five between 18 months and 16 years: this predominance in infants could have several reasons. None of these patients were born since the beginning of the study. All presented with neonatal seizures, but diagnosis has been delayed by up to five months. In one preterm child, seizures began just before the expected date of delivery and in another neonate the initial response was incomplete but a further dose of pyridoxine led to clinical and electrical improvement. Some of the older children are showing varying degrees of developmental delay.

Two other children on whom questionnaires have not yet been returned presented with infantile spasms that responded to pyridoxine.

Four more cases have been reported who do not have classical pyridoxine dependency in that the response to pyridoxine was incomplete or seizures did not recur after pyridoxine withdrawal. In the interesting group pyridoxine appears to have some anticonvulsant effect. Further reports of similar cases would be of interest and would be gratefully received.

Dr Peter Baxter, Consultant Paediatric Neurologist, Northern General Hospital Sheffield S5 7AU

Cerebral oedema and death following diabetic ketoacidosis

Background

Cerebral oedema is a devastating complication of diabetic ketoacidosis (DKA) in children, and appears to be sporadic and unpredictable. The most recent figures available show that between ten and twenty children under 19 years of age die per year from DKA in Britain. 50% of these deaths may be attributable to cerebral oedema, although the incidence of cerebral oedema following DKA in Britain is not known, neither is the aetiology understood.

Even with optimum management by current standards, cases still occur. Retrospective studies suggest that cerebral oedema is more common in children with newly diagnosed diabetes, especially under five years of age. Possible contributory factors may be the severity of DKA, the rate and/or quantity of intravenous fluid administration, a fall in plasma sodium concentration and hypoxia from bicarbonate administration. Animal studies have suggested that insulin itself is required for cerebral oedema to occur. There have been no sizeable case-control studies to support any of these theories.

This study will compare the clinical course of cases of cerebral oedema with controls with DKA but without cerebral oedema, ascertained by a separate reporting mechanism which we are developing. This will be the first large prospecitve case-control study in this important area of research.

Objectives

1 To analyse all deaths attributable to DKA and all cases of cerebral oedema (whether fatal or not).

2 To establish an independent national procedure for the ascertainment of cases DKA in the childhood population.

3 To estimate the absolute risk of cerebral oedema among children with diabetic ketoacidosis.

4 To identify factors in the clinical presentation and subsequent clinical course of the child with DKA which may influence the development of cerebral oedema.

5 To study the outcome of cerebral oedema in Britain in terms of mortality and morbidity.

Case definition

1 Sudden or unexpected deterioration in conscious level in a child with ketoacidosis.

2 Any death during assessment or management of DKA.

Study duration

October 1995 - November 1996; extension subject to review.

Analysis

During the first five months of the study, 27 returns were made through the SU. The questionnaires have so far been returned, from which five cases of cerebral oedema have been confirmed. One report was of a death during DKA which was not due to cerebral oedema, one was a death due to another neurological condition in association with DKA, and three have been duplicate reports. Only one of the children with cerebral oedema had died. Thirteen of the reports were made during the first month and we have yet to confirm whether or not these are retrospective reports.

We have also tried to contact all the paediatricians in England, Scotland and Wales who may admit children with diabetic ketoacidosis to ask for their help in collecting possible control cases. If there are any paediatricians who have not yet been contacted, we should be very grateful if they could get in touch with us. We are asking for confidential monthly returns notifying cases of DKA anonymously.

We are most grateful to all those paediatricians who have notified cases and completed questionnaires.

Funding

The study has received financial support from the British Diabetic Association.

Dr J Edge, Dr M Hawkins, Dr D Dunger, Department of Paediatrics, John Radcliffe Hospital, Headington, Oxford OX3 9DU
Tel: 01865 221065 Fax: 01865 220479

Congenital cataract

Background

Despite considerable recent progress in the surgical and optical management of congenital and infantile cataract, a significant proportion of treated children continue to be registered blind (up to 30% in the United States of America). Congenital and infantile cataract can also cause mild or moderate visual impairment which may go unrecognised, particularly if it is unilateral. In children with multiple disabilities, it may be the most readily treatable eye disorder and the improved vision that results from treatment may contribute to the child's overall development.

Early detection and treatment of congenital and infantile cataract is probably the most important of a number of factors relevant to good visual outcome. In humans the 'critical period' during which interventions to prevent the development of irreversible amblyopia are likely to be most successful is from birth to 10 weeks of age. The best reported visual outcomes are in children who undergo surgery early within this period. Early surgical intervention requires detection and ophthalmic referral in the neonatal period. Children not identified by specific neonatal examination will present at different ages and to various health professionals, depending on the severity of visual loss and the presence or absence of other ocular or systemic disorders. The current patterns of presentation and detection in the United Kingdom, including the age at presentation, to whom the child first presented, and the reason for first presentation are not known.

Epidemiological data on congenital and infantile cataract are important to the development of effective recommendations about its early detection and ophthalmic management. The main sources of data on congenital and infantile cataract in the United Kingdom are registers of partial sight and blindness, surveys of children attending schools for the blind and clinical case series. All these sources are limited in terms of completeness, potential bias or detail and most studies based on them have been retrospective. Hospital data suggest ophthalmologists in the United Kingdom see about 150 new cases each year but the birth prevalence is not known.

Numerous causes of congenital and infantile cataract have been reported but it is not known if the underlying cause is associated with the patterns of detection or of ophthalmic referral. Surgical and optical treatment techniques for congenital and infantile cataract have advanced in recent years but there are no uniform treatment policies for either unilateral or bilateral cases. Different centres have reported the results of their management regimens. Many reports involve small numbers of patients and provide limited data.

Research questions

1. To estimate the birth prevalence of congenital and infantile cataract in the British Isles.
2. To determine the national and regional patterns of presentation and ophthalmic referral.
3. To assess aetiology in incident cases and to determine the proportion attributable to preventable causes.
4. To determine the factors associated with good visual outcome.

Case definition

Any child under 16 years of age who has suspected or confirmed cataract(s), which may be unilateral or bilateral and of any severity. This includes any child who has been treated for cataract(s) in the past four weeks.

Study duration

The study began in October 1995 and will continue until October 1996.

Dr J Rahi, c/o Dept of Epidemiology & Biostatistics, Institute of Child Health, 30 Guilford Street, London WC1N 1EH
Tel: 0171 242 9789 Fax: 0171 813 8233

6 New studies for 1996

Neonatal meningitis

Ten years ago the Karim Centre for Meningitis Research carried out a survey to determine, over a two year period, the incidence of meningitis in children aged under one year. At the time no country-wide survey had ever been completed. The incidence of neonatal meningitis was 0.32 per 1000 live births and the principal infecting bacteria were group B â haemolytic streptococci, *Escherichia coli* and *Listeria monocytogenes*. Data from the study showed that 50% of neonates had been treated with a regimen based upon chloramphenicol and 50% upon aminoglycosides. The diagnosis was usually based on a positive culture from the cerebrospinal fluid (CSF), cell counts in the CSF and the clinical picture. Over 30% of the babies who survived had an identifiable neurodevelopmental problem at five years of age.

Over the intervening years paediatric practice in diagnosis and treatment of neonatal meningitis has changed. Lumbar punctures are now often omitted from routine infection screens and may also be omitted when the baby has serious signs indicative of meningitis. The first line treatment with a combination of a penicillin and chloramphenicol or an aminoglycoside has been replaced by a combination of ampicillin and a third generation cephalosporin and it is suggested there is also increasing use of steroids and immunoglobulins in this age group.

A two year prospective study is to be conducted through the SU by the Karim Centre for Meningitis Research in order to determine the incidence, mortality, morbidity, diagnostic procedures, principal infecting organisms and treatment of meningitis in the newborn period. This is to revise our knowledge of the disease, its diagnosis and treatment, which we first surveyed ten years ago. The population of children identified by the study will subsequently be examined at five and nine years of age to determine long term morbidity after modern treatment.

Paediatricians and microbiologists will be asked to provide clinical and laboratory details on notified cases and we will ask for a sample of CSF to be supplied if this is available. Our case definition is:

> Meningitis in newborn babies, including those born preterm, of 28 days of age or less, as diagnosed by local procedures. Those cases where diagnosis was by clinical signs and not proven by CSF analysis and culture, but were treated as neonatal meningitis by the paediatrician should be included. Cases of viral meningitis should be included. Babies where meningitis was diagnosed at autopsy should be included. Cases with neural tube defects should be excluded.

The investigators would be pleased if you could report all babies meeting these criteria. Confidentiality will of course be preserved at all times.

Mrs Sue Halket or Dr Daphne Holt, Karim Centre for Meningitis Research, Queen Charlotte's & Chelsea Hospital, London W6 0XG Tel: 0181 740 3924. Fax: 0181 741 1838. email: dholt@mpcc3.rpms.ac.uk.

Enquiries of a clinical nature may be addressed to Professor David Harvey, Tel: 0181 740 3270

7 Past studies revisited

Juvenile dermatomyositis

Background

Juvenile dermatomyositis is a rare rheumatic disease in childhood, which because of its chronic course, is an important cause of disability. Little is known about the incidence in the United Kingdom, but estimates from the United States suggest an annual incidence of 1-3.2 cases per million children.

There have been reports of clustering of cases in the United States. Some clusters were in the spring, others in the autumn.

Clinical experience suggests that presentation varies between children. The mode of presentation and initial treatment may influence the ultimate prognosis.

Objectives

The aims of the SU surveillance were to attempt to estimate the incidence of juvenile dermatomyositis, to look at clusters in time and place, evaluate the presenting features and the delay between diagnosis and to document initial drug treatment. Those reporting cases were sent a questionnaire to complete which sought demographic details, the mode of presentation and the treatment of cases.

Case definition

Any child under 16 years of age with clinical evidence of symmetrical proximal muscle weakness and evidence of skin and soft tissue changes, together with supporting evidence from elevated creatinine kinase and other investigations including electromyography, muscle ultrasound, muscle biopsy and magnetic resonance imaging.

Analysis

In our study, 121 notifications were received over a 24 month period from 1 January 1992 - 31 December 1993. Fifty one of the cases satisfied the diagnostic criteria of Bohan and Peter[1], while 49 satisfied the case definition of the study. Three of the children had no rash, and estimates of the incidence of juvenile dermatomyositis were based on the remaining 48 cases. The overall incidence rate for the four countries of the British Isles (England, Scotland, Northern Ireland, Wales and the Republic of Ireland), was 1.9 per million children (95% CI 1.4-2.6). Forty of the 48 confirmed cases were female and the median age of onset for the whole group was 6.8 years (range 1.3-15.2 years). The median age of onset was higher for girls (7.8 years), than boys (5.5 years). Interestingly, there were two peaks of onset for girls at ages 6 and 11 whereas all the boys were aged ten years or under.

Forty-two of the 48 cases (88%), were Caucasian. The remaining six children comprised two black Caribbean, two Pakistani, one Chinese and one of mixed race.

The median delay in diagnosis was four months (range 0.3-31 months), with the delay being slightly longer in boys than in girls. When all cases were considered together there were peaks of onset in the summer (May to June) and winter (December-January) months. During 1992 there was only a summer peak.

The most common presenting feature was proximal muscle weakness, followed by skin rash. None of the children had localised or generalised calcinosis at presentation.

Initial drug therapy

Five children received no initial drug therapy. All the remaining 46 children received steroids using a daily dose regime and six children received additional immuno suppressants.

Conclusion

The first attempt to estimate the incidence of juvenile dermatomyositis in the UK and Ireland provided a figure of 1.9 per million children under 16. This is similar to estimates from the USA (2.5 per million children under 15 years). Due to possible under-reporting as a result of cases presenting to other specialists not included in the SU scheme, these figures may well have been an underestimate. It is interesting to note that there was some seasonal clustering of cases but no geographical clustering either between or within countries. The male:female ratio (5.1), was higher than that found in other series. For example, in a pooled series by Cassidy and Petty and an overall male:female ratio was 1.7:1.[2]

Summary

This study has therefore provided important information about the incidence of juvenile dermatomyositis in the UK and Ireland and further follow up studies on this cohort may reveal further information about clinical and therapeutic predictors of prognosis.

References

1 Bohan A, Peter JB. Polymyositis and Dermatomyositis. New Engl J Med 1975; 297:344-7

2 Cassidy JT, Petty RE (Eds). Juvenile Dermatomyositis in Textbook of Paediatric Rheumatology, 2nd ed Edinburgh, Churchill Livingstone, 1990:331-75

3 Symmons DPM, Sills JA, Davis SM, The Incidence of Juvenile Dermatomyosiitis, Results From a Nationwide Study, British Journal of Rheumatology,1995; 34 :732-736

8 International developments

One of the successes of the Surveillance Unit has been in its ability to transplant the unit's methodology internationally. Several countries have developed 'active' systems of paediatric surveillance to monitor rare disorders, along similar lines to the system used by the British Surveillance Unit.

In order to forge closer links with other national surveillance units there have been regular exchanges of correspondence and data. Closer liaison between researchers has already been seen, in particular with vitamin K deficiency bleeding, *Haemophilus influenzae* type b and transient and neonatal diabetes.

In early 1995 a meeting between the European units, Britain, Germany, Netherlands, and Switzerland was held in Leiden. At that meeting it was agreed that pan-European surveillance of particular disorders should be encouraged. To this end an application to EC BIOMED is being considered, which if successful will allow simultaneous surveillance using similar research protocols to produce a larger pool of data for analysis.

German Paediatric Surveillance Unit

The German surveillance scheme was set up in July 1992. After a few development problems the system is now running well. The German unit covers a child population of approximately eight million children (800,00 birth rate) Cards are circulated to 480 clinicians, the response rate has improved dramatically and now stands at 94.5% with a questionnaire follow-up rate of around 90%.

Conditions presently under surveillance include: Tick borne encephalitis, pertussis complications, insulin dependent diabetes under 5, acute liver failure, vitamin K deficiency bleeding, autoimmune hepatitis, fatal and near fatal asthma, fatal and near fatal poisoning in children under 5. Several studies have been completed: Kawasaki disease, Reye's syndrome, Ondine's curse (primary failure of respiratory regulation), acute renal failure, systemic meningococcal disease, systemic *Haemophilus influenzae* infections and neonatal thrombosis.

Contact: **Professor E Schmidt, Dr R Von Kries**
Universitats-Kinderklinik, Moorenstrasse 5, 4000 Dusseldorf 1, Germany

Netherlands Paediatric Surveillance Unit

The Dutch unit started work in October 1992. Covering a population of three million children (185,000 births per year) about 340 paediatricians in general hospitals receive the monthly report card. In the eight university hospitals a specific contact person has been nominated for each disorder, with responsibility for the reporting of all cases in that hospital. The mailing card response rate now averages 94% with a questionnaire follow-up rate in excess of 90%.

Five disorders were included initially: coeliac disease, vitamin K deficiency bleeding, acute flaccid paralysis, sickle cell disease and thalassaemia major. Other studies since undertaken include diabetes mellitus, neural tube defects and haemolytic disease of the newborn (non ABO non RhD).

The overall response rate in the first three months was 81%; by the end of 1993 it had risen to 90%, and systematic failure to respond is rare. Specific research groups are confirming the notifications that have been received, adding information acquired through postal questionnaires and interviews.

Contact: **Dr P Vanloove-Vanhorick, Dr R Hirasing**
NIPG-TNO Postbus 124, 2300 AC Leiden, Netherlands

Swiss Paediatric Surveillance Unit (SPSU)

The SPSU commenced surveillance in February 1995. The unit has the support of the Swiss Paediatric Association and the Federal Office of Public Health. There are currently 39 paediatric clinics participating each with one or two clinicians responsible for the reports of the whole clinic. In the first 18 months five surveys have been undertaken: acute flaccid paralysis, congenital rubella, toxoplasmosis, and periventricular leucomalacia. Response rates are already high at 98% with a questionnaire follow-up rate of approximately 100%.

Contact: **Dr H P Zimmerman**
Swiss Paediatric Surveillance Unit, Hess-Strasse 27e 3097 Bern-Leibefeld, Switzerland

Australian Paediatric Surveillance Unit (APSU)

The APSU began active monthly surveillance in May 1993 and is a unit of the Australian College of Paediatrics. About 930 paediatricians and clinicians who deal specifically with children receive monthly report cards. Studies that have or are being surveyed include drowning/near drowning, extrahepatic biliary atresia, haemorrhagic disease of the newborn (vitamin K deficiency bleeding), HIV/AIDS, congenital rubella, Kawasaki disease, Rett syndrome, childhood dementia, acute flaccid paraysis, haemolytic uraemic syndrome and congenital and neonatal varicella. Many researchers are liaising with researchers who have undertaken similar surveys through the Surveillance Unit.

Currently negotiations with New Zealand clinicians is underway and it is hoped that a similar system can be developed either independently or jointly with the Australian system.

The APSU has now produced its first annual report, copies are available from the APSU. Further information can also be obtained by writing to the British Surveillance Unit.

Contact: **Dr Elizabeth Elliott,**
PO Box 3315 Parramatta, NSW 2124 Australia

Malaysian Paediatric Surveillance Unit (MPSU)

The MPSU was set up in December 1993 and surveillance began in September 1994 under the auspices of the Malaysian Paediatric Association. All 14 regions of Malaysia are included, covering a total population of 19 million, 7 million of whom are children. There are about 400,000 births each year. The unit adopts the same methodology as in Britain. Reporting cards are circulated to 297 paediatricians and surgeons. The response rate is 70%. Only 6% of respondents have never returned a card. Three conditions are currently under surveillance: paediatric HIV and AIDS, death from asthma, and neonatal meningitis.

Contact: **Dr Jacqueline Ho**
MPSU Coordinator, Paediatric Clinic, Hospital Ipoh, 30990 Ipoh, Malaysia

Canadian Paediatric Surveillance Programme

The Canadian Paediatric Surveillance Programme (CPSE) has been developed following discussions between the Canadian Paediatric Society and the Laboratory Centre for Disease Control and with advice from the BPASU. Surveillance, based on the BPASU methodology, commenced in January 1996. Currently three surveys are being undertaken: acute flaccid paralysis (AFP), congenital rubella and Group B streptococal infection (GBS). Considering the territory to be covered the response rate is already impressive, with 80% of the 2,000 respondents returning the card in the first reporting month. So far there have been 15 reports of AFP, 8 of congenital rubella and 218 of GBS. These surveys are currently being led by the CPSP, but it is hoped that clinicians will soon be vying to have their studies included in the system.

Contact: **Dr Paul Sockett**
Canadian Paediatric Society, Bureau of Infectious Disease, Laboratory Centre for Disease Control, 0603E1 Ottawa, Ontario KIA OL2, Canada
Dr Victor Marchessault
Ex Vice-President, Canadian Paediatric Society, 401 Smyth, Ottowa, Ontario, K1H 8L1 Canada

9 Surveillance Unit scientific seminar

To herald the unit's tenth year of surveillance a one day scientific seminar was held in June 1995 at the PHLS Central Public Health Laboratory in Colindale, North London. The aim of the seminar was to review the Surveillance Unit's contribution to national surveillance, understanding and control of rare conditions in childhood, and to identify future applications of the Surveillance Unit mechanism. Over a hundred paediatricians, researchers, and epidemiologists attended the meeting, along with representatives from our sister paediatric surveillance units in the Netherlands, Germany, and Malaysia, and from the British Neurology Surveillance Unit.

The morning session concentrated on studies that had provided particularly valuable lessons for the operation of the unit. Dr Elizabeth Miller (PHLS) highlighted the importance of a clinical reporting scheme for surveillance of rare vaccine preventable and vaccine associated conditions, using congenital rubella, SSPE, and meningoencephalitis after MMR vaccine as examples. For such disorders, ascertainment needs to be as complete as possible, for which Surveillance Unit reporting must be complemented by other reporting systems. The importance of this point was highlighted in the study of meningoencephalitis after MMR, in which relatively few cases were picked up by the Surveillance Unit. Many of the final total were identified by microbiologists. Dr Miller raised concern about the removal of SSPE from the orange card. It had been hoped that cases would be reported through other routes but these may not be sufficiently reliable, so the SU has agreed to reinstate SSPE.

Dr Paul Heath of the Oxford Haemophilus Reference Laboratory presented data from the Hib vaccine efficacy study. He indicated that 36% of suspected vaccine failure cases reported to date had not been ascertained through the Surveillance Unit but through microbiologists and public health physicians. He emphasised the value of telephone reporting in ensuring that specimens were collected for rapid confirmation of cases. It was stated, however, that some telephone reports had not been followed by an orange card report, which caused problems for the Surveillance Unit's administrative and self monitoring system.

Methodological aspects of two relatively common disorders, congenital dislocation of the hip and diabetes in under 5s, ascertained through the Surveillance Unit were presented by Dr Carol Dezateux and Dr Julian Shield. Both studies highlighted the value of using more than one data source to maximise case ascertainment. Other problems included matching data between sources, respondents remembering whether cases had been reported, and the substantial workload of such studies. Concerns were also expressed that the demise of regional health authorities might lead to increasing problems with using Hospital In-patient Episode Statistics for validation of the completeness of ascertainment.

In the afternoon session, Dr Ruth Gilbert gave an overview of lessons learnt by the Unit, which included a description of complementary data sources. Dr Tony Ades (ICH, London) spoke about capture-recapture methods as a means of estimating the 'true' size of a population. Professor Brent Taylor (Royal Free Hospital) then took us into the 'electronic future' using the Child Health Information System as an example. A presentation on ethics and confidentiality opened a detailed discussion over the ethics of collecting and holding data for epidemiological studies. Approval is more difficult to obtain for research than audit and surveillance appears to be a 'grey area'. All agreed on the need for a national ethics committee to approve national studies. Finally, Dr John Tripp (Royal Devon and Exeter Hospital) discussed links with other European surveillance systems. Using vitamin K deficiency bleeding as an example, the problem of agreeing case definitions, and study protocol, and allowing for differences in the populations and differences in management were discussed.

A summary of the proceedings of the meeting will be published. Abstracts of the meeting are available from the Surveillance Unit office.

Appendix A Completed studies prior to 1995

By the end of 1995 the Surveillance Unit had completed 26 studies. Information about these studies has been included in previous annual reports of the surveillance unit, which are available from the Surveillance Unit office. The studies and their principal investigators are listed below. For addresses see the list at the end of this report.

1. **X-linked anhydrotic ectodermal dysplasia**
   (June 1986 – August 1986)
   Dr A Clarke
2. **Lowe syndrome**
   (June 1986 – February 1988)
   Dr C McKeown
3. **Insulin dependent diabetes in under 15s**
   (January 1988 – December 1988)
   Professor J D Baum
4. **Drowning and near drowning**
   (January 1988 – December 1989)
   Professor J Sibert
5. **Higher order births**
   (January 1989 – December 1989)
   Professor M Levene
6. **Haemorrhagic disease of the newborn**
   (March 1988 – February 1990)
   Dr A W McNinch, Dr H Tripp
7. **Haemorrhagic shock encephalopathy syndrome**
   (June 1986 – December 1988)
   Dr S Hall
8. **Haemolytic uraemic syndrome**
   (June 1986 – December 1989)
   Dr S Hall
9. **Kawasaki disease**
   (June 1986 – December 1992)
   Dr S Hall
10. **Congenital toxoplasmosis**
    (June 1989 – May 1990)
    Dr S Hall
11. **Acute rheumatic fever**
    (January 1990 – December 1990)
    Dr C Boyd-Scobie, Dr S Hall
12. **Rett syndrome**
    (April 1990 – June 1990)
    Dr A Kerr
13. **Measles, mumps, rubella/meningococcal meningitis**
    (January 1990 – December 1991)
    Dr N Begg
14. **Neonatal herpes**
    (June 1986 – Dec 1991)
    Ms P A Tookey, Professor C S Peckham, Dr R Dinwiddie
15. **Chemistry set poisoning**
    (January 1991 – April 1992)
    Dr E Mucklow
16. **Galactosaemia**
    (January 1988 – September 1991)
    Mrs A Green, Dr J Holton, Dr M Honeyman, Professor J Leonard
17. **Long term parenteral nutrition**
    (February 1992 – April 1992)
    Professor D Candy, Professor E Ross, Dr S Devane
18. **Insulin dependent diabetes**
    (January 1992 – December 1992)
    Professor J D Baum, Ms E Wadsworth
19. **Androgen insensitivity syndrome**
    (September 1991 – August 1993)
    Professor I A Hughes
20. **Juvenile dermatomyositis**
    (June 1992 – December 1993)
    Dr D Symmons, Dr A Sills
21. **Congenital dislocation of the hip**
    (April 1993 – July 1993)
    Dr C Dezateux, Ms S Godward
22. **Acute flaccid paralysis**
    (July 1991 - June 1994)
    Dr N Begg
23. **Haemophagocytic lymphohistiocytosis**
    (September 1991 - August 1994)
    Professor S Strobel, Dr J Pritchard, Dr M Leyton
24. **Non-accidental poisoning/Munchausen Syndrome by proxy**
    (September 1992 - August 1994)
    Professor J Sibert, Professor S R Meadow
25. **Neonatal necrotising enterocolitis**
    (October 1993 - October 1994)
    Dr A Lucas
26. **Vitamin K deficiency bleeding**
    (January 1993 - December 1994)
    Dr A McNinch, Dr J Tripp

Appendix B Recent publications

Published papers

Wagner R, Morgan G, Strobel S. A prospective study of CD45 isoform expression in haemophagocytic lymphohistiocytosis; an abnormal inherited immunophenotype in one family. *Clin Exp Immunol* 1995; 99: 216-20.

Dunn DT, Nicoll A, Holland FJ, Davison CF. How much paediatric HIV infection could be prevented by antenatal HIV testing? *J Med Screen* 1995; 2: 35–40.

Gibb DM, Fauknell W, Nokes I, Appleby S, Holland FJ, Berry T, et al. Coverage of routine neonatal metabolic screening in children born to women known to be infected with HIV-1. *Communicable Disease Report* 1995; 5: R123–4.

Symmons PM, Sills JA, Davis, SM. The incidence of Juvenile dermatomyositis: results from a nationwide study. Brit. Journ. Rheum. 1995; 34: 732-736

Hardie JRM, Newton LH, Bruce JC, Glasgow JFT, Mowat AP, Stephenson JBP, Hall SM. The changing clinical pattern of Reye's syndrome 1982-90. Arch. Dis. Child. 1996; 74 400-405

McClure RJ, Davis, PM, Meadow SR, Sibert JR. The epidemiology of Munchaussen Syndrome by Proxy, Non-accidental poisoning, and Non-accidental suffocation. Arch. Dis Child 1996; 75: 57-61

Tookey PA, Peckham CS. Neonatal herpes simplex virus infection in the British Isles. Paediatric and Perinatal Epidemiology 1996 (in press)

MacDonagh SE, Masters JM, Helps BA, Tookey PA, Ades AE, Gibb DM. Antenatal HIV testing in London: policy, uptake and detection Brit. Med. Journ. 1996 (in press)

Temple IK, Gardiner R, Kibirige MS et al. Further evidence for an imprinted gene for neonatal diabetes located to chromosome 6q 22-2. Human molecular genetics (In press).

Dexateux C, Godward S. A national survey of screening for congenital dislocation of the hip. Arch Dis Child 1996; 74: 445-448

Abstracts and conferences proceedings

European Society for Paediatric Research Annual Meeting 1995

Tookey P. Surveillance of congenital rubella in England, Scotland, and Wales.

Wadsworth EJK, Shield JPH, Hirasing RA, Herzig P, Rosenbauer J, et al. Diabetes incidence and ascertainment in children under 5 years for the UK, the Netherlands, and Germany.

Conyn-van-Spaendonck MAE, Heath P, Slack M, von Kries R. Paediatric Surveillance as a tool for the evaluation of National Immunisation Programmes, particularly of immunisation against invasive infections by *Haemophilus influenzae* type b.

Cornelissen M, McNinch A, Tripp J, Shrubiger G, Loughnan, von Kries R. Prospective studies on vitamin K deficiency bleeding in various countries.

Abstracts published in *Paediatric Research* 1995: 38: 423–33.

European Society for Paediatric Research Annual Meeting 1995

Surveillance of paediatric HIV in the UK: multiple source ascertainment. European Society for Paediatric Infectious disease, Elsinore, Denmark 1996. Tookey PA, Nicoll A, Ades AE, Goldberg D, Duong T, Mortimer J,Berry T, Peckham CS.

European Surveillance of rare infectious disease. European Society for Paediatric Infectious disease, Elsinore, Denmark 1996. Lynn RM, Hirasing R, von Kries R, Zimmerman, HP.

Obstetric and Paediatric surveillance in the United Kingdom. International HIV/AIDS conference, Vancouver, Canada 1996. Ades AE, Tookey P, Duong T, Berry T, Goldberg D, Nicoll A.

Evaluation of the antenatal HIV testing in London, UK (poster). International HIV/AIDS conference, Vancouver, Canada 1996. Gibb DM, MacDonagh SE, Masters J, Helps BA, Gupta R, Tuck P, Tookey PA, Peckham C, Ades AE.

National surveillance of adverse neonatal outcomes following labour or delivery in water. Waterbirth conference, Southampton 1996. Gilbert R, Tookey PA.

Ultrasound imaging of the neonatal hip: increase use of unevaluated technology. International Society of Technology. Assessment in healthcare. San Francisco. June 1996.

French Academy of Paediatrics Meeting 1996

Rudd P. Kawasaki Disease in the UK.

Appendix C Recent presentations

BPA Annual Scientific Meeting 1995

Invasive *Haemophilus influenzae* infection following Hib immunisation. Heath P, Booy R, Slack M, Begg N, Griffiths H, Anderson E, Bird G, Chapel H, Moxon R.

Paternal uniparental isodisomy of chromosome 6 is a cause of transient neonatal diabetes. Temple IK, Shield JPH, James RS, Crolla JA, Sitch FL, Betts P, Howell W, Baum JD, Jacobs PA.

Epidemiology of Munchausen syndrome by proxy, non-accidental poisoning and suffocation. McClure RJ, Davis P, Sibert JR, Meadow SR.

Screening for congenitally dislocated hips reappraised. Dezateux C.

Incidence of juvenile dermatomyositis: results of BPASU survey. Symmons DPM, Sills JA, Davis SM.

Some reflections on vitamin K prophylaxis. McNinch A.

BPA Annual Scientific Meeting 1996

Surgery for congenital dislocation of the hip in children aged 5 and under in the UK. Godward S, Dezateux C.

Neonatal diabetes: clinical characteristics, aetiopathogenisis and long term implications. Shield JPH, Temple IK, Wadsworth EJK, James RS, Howell WM, Baum JD.

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

Antenatal HIV testing in London: Policy, uptake and prevalence. MacDonagh SE, Masters J, Helps BA, Tookey PA, Ades AE, Gibb DM.

Appendix D Support groups for rare childhood disorders

Congenital Dislocation of the Hip
STEPS, 15 Statham Close, Lymm, Cheshire, WA12 9NN.

Congenital Rubella
National Rubella Council, 33-39 Pancras Road, London NW1 2QB.

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

Dermatomyositis & Polymyositis
Dermatomyositis & Polymyositis Support Group, 146 Newtown Road, Woolston, Southampton, Hampshire, S02 9HR.

Encephalitis Effects
Encephalitis Support Group, 59 Corporation Road, Darlington, Co. Durham, DL3 6AD.

Galactosaemia
Galactosaemia Support Group, Mrs S Bevington 18 Nuthurst, off Reddicap Heath Rd, Sutton Coldfield, W Midlands B75.

Guillain-Barre Syndrome
Guillain-Barre Syndrome Support Group,'Foxley', Holdingham, Sleaford, Lincolnshire, NG34 8NR.

Kawasaki Disease
Mrs S Davidson, 13 Norwood Grove, Potters Green, Coventry, CV2 22FR.

Liver Disease
Children's Liver Disease Foundation, 40-42 Stoke Road, Guildford, Surrey GU1 4HS.

Lowe Syndrome
Lowe Syndrome Association, 29 Gleneagles Drive, Penworthan, Preston, Lancashire, PR1 0JT.

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

Neonatal Herpes
Herpes Association, 41 North Road, London N7 9DP.

Poliomyelitis
Mr L Jackson, British Polio Fellowship, Bell Close, West End Road, Ruislip, Middlesex HA4 6LP.

Rett Syndrome
The Rett Syndrome Support Group, Mrs Y Milne, Heartpool, Golden Valley, Castlemorton, Malvern, Worcestershire WR13 6AA.

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

For information on a variety of
rare childhood disorders
a directory of support groups and their
addresses has been produced by:
'Contact a Family'
170 Tottenham Court Road,
London W1P OHA.

Appendix E Contact Addresses

Ms R Abbott, Infant and Child Nutrition Group, MRC Dunn Nutrition Unit, Downham's Lane, Cambridge CB4 1XJ

Dr A E Ades, Department of Epidemiology, Institute of Child Health, London WC1N 1EH

Dr A Baker, King's College Hospital, Denmark Hill, London SE5 8RX

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

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

Dr P Baxter, Consultant Paediatric Neurologist, Northern General Hospital, Sheffield S5 7AU

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

Dr R Booy, St Mary's Hospital, Praed Street, London WC1

British Neurological Surveillance Unit, Chalfont Centre for Epilepsy, Chalfont St. Peter, Bucks SL9 0RJ

British Orthopaedic Association, Lincoln's Inn Field, London SE1 9RT

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

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

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

College of Paediatrics and Child Health, 5 St Andrews Place, Regent's Park, London NW1 4LB

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

Dr C Davison, Department of Epidemiology and Biostatistics, Institute of Child Health, 30 Guilford Street, London WC1N 1EH

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

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

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

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

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

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

Dr E Elliot, Australian Paediatric Surveillance Unit, PO Box 34, Camperdown, NSW 2050 Australia

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

Dr C P Farrington, Statistics Unit, PHLS Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ

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

Dr R Gilbert, Department of Epidemiology & Biostatistics, Institute of Child Health, Guilford Street, London WC1N 1EH

Dr D Goldberg, Scottish Centre for Infectious & Environmental Health Ruchill Hospital, Glasgow G20 9NB

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

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

Dr M Guy, Consultant in Public Health Medicine, Brent and Harrow Health Authority, Crace House, Harrovian Business Village, Bessborough Road, Harrow HA1 3EX

Dr S Hall, c/o PHLS Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ

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

Dr P Heath, National Haemophilus Reference Laboratory, John Radcliffe Hospital, Oxford OX3 9DU

Dr P Heney, c/o St James's University Hospital, Leeds LS9 7TF

Dr J Ho, MPSU Coordinator, Paediatric Clinic, Hospital Ipoh, 30990 Ipoh, Malaysia

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

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

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

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

Ms G Jones, Dept of Paediatric Epidemiology and Biostatistics, Institute of Child Health, 30 Guilford Street, London WC1N 1EH

Dr D Kelly, The Children's Hospital, Ladywood Middleway, Birmingham B16 8ET

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

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

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

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

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

Dr I A F Lister Cheese, Department of Health, Wellington House, 133-155 Waterloo Road, London SE1 8EU

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

Dr S Logan, Community Paediatric Teaching Unit, Institute of Child Health, 30 Guilford Street, London WC1N 1EH

Dr A Lucas, Infant and Child Nutrition Group, MRC Dunn Nutrition Unit, Downham's Lane, Cambridge CB4 1XJ

Mr R Lynn, Scientific Coordinator, Surveillance Unit, College of Paediatrics and Child Health, 5 St Andrews Place, Regent's Park, London NW1 4LB

Dr R McClure, Academic Unit of Paediatrics and Child Health, St. James's University Hospital, Leeds LS9 7TF

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

Dr J P McKiernan, The Children's Hospital, Ladywood Middleway, Birmingham B16 8ET

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

Professor S R Meadow, Department of Paediatrics and Child Health, St James's University Hospital, Leeds LS9 7TF

Medical Research Fund, Children Nationwide, Nicholas House, London SE1 0LN

Dr C Miller, c/o PHLS Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ

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

Ms L Morgan, Hip Trial Coordinator, Perinatal Trials Service, John Radcliffe Hospital, Oxford OX3 9DU

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, St Mary's Hospital, Newport, Isle of Wight PO30 5TG

Ms L Newton, PHLS Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ

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

Office of National Statistics, St Catherine's House, Kingsway, London WC2 6JP

Professor C S Peckham, Department of Paediatric Epidemiology and Biostatistics, Institute of Child Health, 30 Guilford Street, London WC1 1EH

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

Dr J Rahi, c/o Dept of 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 J Pollock, College of Paediatrics and Child Health, 5 St Andrews Place, Regent's Park, London NW1 4LB

Dr D Reid (Director), Scottish Centre for Infection & Environmental Health, Ruchill Hospital, Glasgow G20 9NB

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

Professor E M Ross, King's College, South Western Hospital, Pulross Road, London SW9 9NU

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

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

Dr P T Rudd, Children's Centre, Royal United Hospital, Bath BA1 3NG

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

Professor J R Sibert, Department of Community Child Health, Lansdowne Hospital, Sanatorium Road, Cardiff CF1 8UL

Dr J Shield, Institute of Child Health, Royal Hospital for Sick Children. St Michael's Hill, Bristol BS2 8BJ

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

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

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

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

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

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

Dr P Vanloove-Vanhorick, NIPG-TNO Postbus 124, 2300 AC Leiden, Netherlands

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

Dr R Von Kries, Universitats-Kinderklinik, Moorenstrasse 5, 4000 Dusseldorf 1, Germany

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

Dr P A Waight c/o PHLS Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ

Wellcome Trust, 183-193 Euston Road, London NW1 2BE

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

Dr H P Zimmerman, Swiss Paediatric Surveillance Unit, Hess-Strasse 27e 3097 Bern-Leiberfeld, Switzerland

Surveillance Unit of the College of Paediatrics and Child Health
5 St Andrews Place, Regent's Park, London NW1 4LB
Tel: 0171 935 1866 Fax: 0171 224 2038