



Royal College of Paediatrics and Child Health

The British Paediatric Surveillance Unit (BPSU) is part of the Research Division of the Royal College of Paediatrics and Child Health

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Langerhans cell histiocytosis survey to commence this June

A new study of the epidemiology of Langerhans Cell Histiocytosis (LCH) is starting in June 2003, funded by the Histiocytosis Research Trust.

LCH, previously known as Histiocytosis X, is a serious and enigmatic cancer-like disorder which can affect many parts of the body especially the bones (single or multiple lesions), skin (rash), pituitary gland (diabetes insipidus, hormone deficiency) and also digestive tract, bone marrow, liver, spleen, lungs and brain.

The disease, more common in children than adults, is of unknown aetiology and uncertain prognosis. Around 15% of cases, usually infants, die. Those who survive are often left with long-term organ damage which has a significant impact on their health and quality of life. Patients may require surgery or chemotherapy or, in extreme cases, bone marrow transplant. However, in some cases the disease can regress spontaneously regardless of treatment.

There have been few epidemiological studies of LCH but it is estimated that about 100 or so children are diagnosed each year in the UK.

Please report any new or suspected case you have seen in the last month whatever the reason for referral and whether or not you are the main clinician responsible for the patient.

Case definition includes children of any age newly diagnosed with either (a) or (b) as follows:

- (a) Biopsy-proven LCH; lesional cells (LCH cells) must contain Birbeck granules on electron microscopy or be CD1a positive or S100 positive with characteristic H&E morphology. Central review of histopathology slides is available.
- (b) Lytic bone lesion or pituitary/hypothalamic abnormality with the characteristics of LCH but not biopsied
 - i) because clinical features suggest spontaneous resolution **or**
 - ii) because the risk of the biopsy procedure in view of the location of the lesion (e.g. cervical vertebra, pituitary mass) is considered too great

After reporting a case, details will be sought by questionnaire and follow-up information will be collected one year after diagnosis. The study is being run at the University of Newcastle in association with the BPSU and, in addition to describing the epidemiology of LCH in the UK and Republic of Ireland, it will assess the presenting features, referral patterns and outcome for the disease. Dr Nanduri one of the lead investigators stated that "*as well as increasing our knowledge of LCH, it is hoped that raising awareness of the disease will encourage early diagnosis and treatment and thus improve the long-term outcome for these children*".

The study protocol is included in this month's mailing along with an illustrated information leaflet. Further copies of both are available from the BPSU office or via our website at <http://bpsu.inopsu.com/current.htm#LCH>

If you need any advice regarding the eligibility of a particular case for inclusion in the study, please contact

Dr Vasanta Nanduri (Tel : 01923 217992 E-mail: vasanta.nanduri@whht.nhs.uk) or
Dr Kevin Windebank (Tel: 0191 202 303 E-mail: k.p.windebank@ncl.ac.uk).

Study News

Surveillance of severe hyperbilirubinaemia in the newborn commenced this May

In the past decade, severe neonatal jaundice and bilirubin encephalopathy have been reported with increasing frequency in North America and Europe. A Pilot Kernicterus Registry, established in the United States in 1992, has accumulated data on 90 affected infants in 10 years. In Denmark, six cases of kernicterus were reported in the five years from 1994 to 1998, no cases having been seen within the preceding 20 years. These findings are of major concern, since bilirubin encephalopathy secondary to severe Rhesus isoimmunisation was virtually abolished by the development of measures to prevent and treat Rhesus disease. There has been speculation that a more permissive approach to the management of neonatal jaundice, along with the increasing trend to earlier discharge of babies from maternity units, has been responsible for the apparent resurgence of bilirubin encephalopathy in North America and Europe. While we have received anecdotal reports of bilirubin encephalopathy from colleagues in Britain and Ireland, to our knowledge there have been no case reports or series' from Britain published in the past decade. Whether this means that the problem is less severe than in North America and Europe, or whether it represents under-reporting, is not clear.

The objectives of this 13 month BPSU study are:

1. To establish the incidence of severe neonatal hyperbilirubinaemia in the United Kingdom, Channel Islands and Republic of Ireland.
2. To identify clinical or demographic variables, such as early postnatal discharge, mode of feeding or specific diseases, associated with severe neonatal hyperbilirubinamia.
3. To determine short to medium term complications of severe neonatal hyperbilirubinaemia, such as death, encephalopathy, hearing and developmental impairment.

Please report cases of Unconjugated hyperbilirubinaemia (serum bilirubin >510 micromol/L) in the first month of life.

Dr Manning said: *"We believe that this study poses a question to which either answer is important. If severe neonatal jaundice and associated encephalopathy are on the increase, the public health implications are profound. Paediatricians, midwives and general practitioners would need to reconsider the management of neonatal jaundice. If, on the other hand, the problems are less frequent and severe than in North America, this might be due to transatlantic differences in practice, and might suggest that our system of close primary care surveillance of recently discharged neonates provides important protection against development of severe jaundice. Thus the study is an important example of international child health surveillance, to which the BPSU is committed"*.

Contact: Dr Donal Manning, Consultant Paediatrician, Wirral Hospital, Arrowe Park, Wirral, Merseyside CH49 5PE.
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Study update

The study on **severe complications of varicella (chickenpox) in hospitalised children** aims to estimate the incidence, clinical features, financial costs and annual mortality of severe complications of varicella in hospitalised children, for which there are currently few data in the UK and the Republic of Ireland. The study was first included on the orange card in November 2002 and will be retained for 13 months. In the first five months of surveillance (November 2002 to March 2003), there have been 91 case notifications sent to the Scottish Centre for Infection and Environmental Health through the BPSU. Follow-up questionnaires are sent out for all notifications, requesting further information on the patients, clinical features, underlying medical conditions, clinical outcome and length of hospital stay. Interim analysis has commenced for the first six-month period. To date, no problems have been encountered with surveillance. Several paediatricians have commented that the case definition may be too restrictive, reducing reporting rates on what they still consider to be severe cases of disease. It is acknowledged that there is a larger group of children in hospital with varicella, either for specific treatment, or with a co-incident condition. These patients are an important group, but would be too numerous if all included in the study. The case definition has therefore been designed to identify the most severe cases of complicated hospitalised varicella only. Comments from paediatricians on surveillance and possible problems arising are always welcome.

Contact: Dr JC Bramley, Mrs G Allan, Scottish Centre for Infection and Environmental Health, Clifton House, Clifton Place, Glasgow G3 7LN. Tel: 0141 300 1191. Fax: 0141 300 1170. E-mail: claire.bramley@scieh.csa.scot.nhs.uk.

Study end

This June see the final reporting month of the **suspected fatal adverse drug reaction** study. As reported in previous BPSU Quarterly Bulletins the number of cases reported has been less than expected (Table 2, p. 4). This may reflect the genuine level of cases. However it is not too late to report cases seen in the past year, either to the BPSU office or direct to the investigator. Dr K Cheng E-mail: katharine.cheng@mca.gsi.gov.uk

Over the years, the BPSU has developed an excellent working relationship with Contact a Family (CaF). They have helped us to promote and publicise our studies and we in-turn have been happy to attend their conference to explain the work of the BPSU and publicise their activities at our seminars and through our newsletter. In the article below CaF outline what they can offer patients and clinicians alike. There are over half a million disabled children and young people in the UK. Discovering that a child has a disability or a health problem is always very difficult and, for the parents, the feeling of isolation can often be acute. If a child is diagnosed with a very rare condition, these feelings can be magnified. It is likely that parents, friends and family will not have heard of the disorder and there may be little information about the disorder available. For the past 21 years Contact a Family has been working to support and inform families with disabled children, whatever the child's diagnosis.

Families tell us that the greatest need is for information. This includes information about entitlements to support and provision for special educational needs. And, perhaps more importantly for those with a child only recently diagnosed with a rare condition, there is a desperate need for accessible medical information and some contact with other families in a similar situation. This enables families to share experiences and benefit from the mutual support this contact can bring.



What Contact a Family can do for you

Contact a Family is committed to working with clinicians to provide high quality information about disorders. The medical information which we provide for families is taken from the *Contact a Family Directory of Specific Conditions, Rare Disorders and UK Family Support Groups*. Each entry is written or checked and approved by a leading medical expert in the field. The aim is to provide information which is accessible to non-medical professionals and which will promote useful questions and discussion between patient, families and doctors.

Our website also has lots of useful information and contains an on-line version of the directory of rare conditions and syndromes affecting children. Entries have a printer friendly version which enables families and professionals to distribute information as needed.

Backing up the work of the whole organisation is a prestigious panel of medical advisors. Full details of membership can be found on the Contact a Family web site <http://www.cafamily.org.uk/backinfo.html>.

What Contact a Family can do for your patients

The Freephone Helpline offers a wide range of services to both families and professionals working with them. Our team of experienced advisers can:

- put callers in touch with support groups or link them directly on a one-to-one basis with another family.
- give information about other specialist voluntary organisations which may be able to help.
- give medical information on all conditions affecting children and young people.
- advise on services like respite and rights to benefits and other help which may be available.
- send any one of our range of free factsheets on subjects such as living without a diagnosis, grandparents, fathers, siblings and a free practical guide to all aspects of education for disabled children and leaflets on the benefits system.
- talk to you via an interpreter in over 100 languages if you prefer to use a language other than English.

Please feel free to refer families to us directly or contact us for further information:

Freephone Helpline: 0808 808 3555 (10am-4pm, Monday to Friday) Minicom: 0808 808 3556

www.cafamily.org.uk helpline@cafamily.org.uk 209-211 City Road, London, EC1V 1JN

Study Extension

The BPSU study on **Progressive intellectual and neurological deterioration - PIND** (principal investigator Dr C Verity) will continue for a further year to April 2004. The study is producing unique national population-based data on the cases of PIND. The majority of the children with PIND have a confirmed or likely underlying diagnosis that is not vCJD. To the middle of March, 1504 children have been reported. The Expert panel of six paediatric neurologists have so far discussed 1073 cases. In the 625 children with a confirmed diagnosis there were 104 different neurodegenerative conditions. The five most commonly occurring diagnoses are the neuronal ceroid-lipofuscinoses (70 cases), the mucopolysaccharides (69 cases), the gangliosidoses (65 cases), the mitochondrial encephalomyelopathies (63 cases), and peroxisomal disorders (45 cases). Six cases of vCJD (four definitive and two probable) have been notified – the youngest was a girl aged 12 years at onset. The other five were three girls (two aged 14 years and one aged 13 years at age of onset) and two boys aged 15 years at onset. All have now died and neuropathology has confirmed vCJD in 4 cases; a post mortem was not carried out on the remaining two cases. Two of the children have been reported within the past 2 years, therefore the possibility remains that further cases will present over the next few years.

Publications and Presentations

A paper outlining data from the BPSU congenital brachial palsy study has just been published, **Congenital brachial palsy: incidence, causes, and outcome in the United Kingdom and Republic of Ireland**. Evans-Jones G, Kay S P J, Weindling A M, Cranny G, Ward A, Bradshaw A, Hernon C *Arch. Dis. Child. Fetal Neonatal Ed.* 2003;**88**:F185 It is also available as a pdf file from the BPSU website at <http://bpsu.inopsu.com/Complete.htm#CBP>.

The RCPCH scientific meeting held recently in York saw four BPSU initiated papers. These were:

- 1) The BPSU study of biliary atresia: outcome after eight years: McKiernan PJ, et al .
- 2) Internal abdominal injury due to child abuse – findings of the first year of a BPSU study. Barnes M et al
- 3) Incidence of childhood stroke in the UK: Data from the British Paediatric Surveillance Unit and the Strategic Health Authority. O'Callaghan FJK et al
- 4) Why is mother-to-child transmission of HIV infection still occurring in the UK and Ireland? Reported Births 1998-2002. Tookey PA et al
- 5) Changes in vertically acquired paediatric HIV in the UK and Ireland over calendar time: The Collaborative HIV Paediatric Surveillance (CHIPS) study and national study of HIV in pregnancy and childhood (NSHPC). Doerholt K, et al.

A paper on the BPSU HUS study has been accepted for the prestigious world VTEC conference to be held in Edinburgh this month **Surveillance of Haemolytic Uraemic Syndrome in the UK and Ireland (1997-2001) Using the BPSU methodology**. Adak GK, Lynn RM et al.

Immunologic memory in Haemophilus influenzae type b conjugate vaccine failure. McVernon J, Johnson P D R, Pollard A J, Slack M P E, Moxon E R. *Arch. Dis. Child.* 2003; **88**: 379-383

The above abstracts and papers are available from the BPSU office.

Monthly Analysis

TABLE 1 - % RESPONSE RATE
July- Dec 2002

Region	% ret'd	Rank (May-Oct 2002)
North	90.6	14 (15)
Yorks	92.8	7 (7)
Trent	90.7	13 (11)
EAngl	94.2	3 (6)
NWT	85.9	19 (18)
NET	81.9	20 (20)
SET	87.8	17 (17)
SWT	86.4	18 (19)
Wessex	91.4	11 (14)
Oxford	92.6	8 (5)
SWest	93.5	5 (13)
WMids	90.2	16 (16)
Mersey	91.3	12 (10)
NWest	93.3	6 (3)
Welsh	94.7	2 (4)
NScot	98.1	1 (1)
SScot	91.7	10 (9)
WScot	90.3	15 (12)
NIre	92.4	9 (8)
RIre	93.9	4 (2)
Total	90.3	

TABLE 2 - ALL CASES REPORTED AND FOLLOW-UPS TO 12/05/2003

Condition	Started	I				NYK	Ttl	as % of total		
		VALID	INVALID		III			I	II	III
HIV/AIDS	1986	2117	346	461	159	3083	69	26	5	
CR	1990	66	24	44	6	140	47	49	4	
PIND	1997	891	161	365	85	1502	59	35	6	
VKDB	2001	4	3	11	24	42	10	35	57	
Thrombosis	2001	154	27	64	55	300	51	30	18	
CMV	2001	130	26	40	83	279	47	24	30	
IAI	2001	18	17	20	17	72	25	51	24	
SFADR	2002	3	0	4	1	8	50	37	13	
Con Toxo	2002	0	1	12	6	19	0	68	32	
Varicella	2002	0	0	0	1	45	0	2	98	
Total		3385	615	1020	480	5490	62	29	9	

I	= confirmed/already known	Ila	= duplicate
Iib	= reporting error or revised diagnosis	III	= status not yet reported to BPSU by investigator
AIDS/HIV	- Acquired Immunodeficiency Syndrome / Human Immunodeficiency Virus	CMV	- Congenital Cytomegalovirus
CR	- Congenital Rubella	IAI	- Internal abdominal injuries due to child abuse -in children under 14 yrs
PIND	- Progressive Intellectual Neurological Degeneration	SFADR	- Suspected fatal adverse drug reactions
VKDB	-Vitamin k deficiency bleeding	Con Toxo	- Congenital Toxoplasmosis
		Varicella	- Severe complications of Varicella (chicken pox)

ALL DATA IS PROVISIONAL AND IS CONTINUALLY BEING UPDATED