



## 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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## Non – type 1 diabetes survey commenced this October

A one-year surveillance of non-type 1 diabetes commenced this October. This study is being undertaken in response to the growing body of evidence that the epidemic of obesity in UK children has resulted in a rising incidence of type 2 diabetes. Type 2 diabetes is associated with greatly increased morbidity and mortality in adults and the prognosis is likely to be worse in those developing the disease at an early age. It is important to establish the incidence of type 2 diabetes in UK children, to identify the proportion of cases attendant on obesity and to examine associated morbidity. As type 2 diabetes is an evolving clinical problem for paediatricians it can be difficult to distinguish from both classical type 1 and syndromic diabetes.

Run by the RCPCH research division in collaboration with Dr Julian Shields (Bristol Children's Hospital) and Dr Tim Barrett, (Birmingham Children's Hospital) the study aims to identify a) the incidence of all non-type 1 diabetes in children 0 - 16 years; b) the relative incidence of obesity-related type 2 diabetes, familial type 2 diabetes and other syndromic diabetes; c) the clinical features at presentation that distinguish type 2 diabetes from syndromic and type 1 diabetes in childhood; d) how type 2 diabetes being diagnosed and treated by paediatricians; e) the short-term morbidity associated with obesity-related diabetes.

The **case definition** is "Any new diagnosis of non-type 1 diabetes (suspected or confirmed) in a patient 0-16 years of age (i.e. up to but not including their **17<sup>th</sup> birthday**). NB These may not be new cases of diabetes, but newly recognised as atypical for type 1."

Reported cases will be followed up one year later to confirm the diagnosis of non-type 1.

The study has been funded by Diabetes UK and has approval from South West MREC. Further details are included in the study protocol card which was included in the October orange card mailing. If you would like further copies please contact the BPSU office. Details are also available on the BPSU website. **Correction:** one minor error was identified on the protocol card in relation to current NICE guidelines. Current NICE guidelines states that screening for coeliac disease (as opposed to antibodies) is recommended only every 3 years (not annually as stated), while screening for thyroid disease (again not antibodies) is done annually.

On speaking to the bulletin, Linda Haines RCPCH principal research officer stated, "with the current level of public and professional anxiety about a possible "epidemic" of obesity in children this is an important study. Not only will it provide the first national picture of the incidence of obesity-related type 2 diabetes but it will also act as a benchmark for future incidence studies which will help to inform and evaluate public health policy. The study also represents an important strand of the Colleges' overall strategy on childhood obesity. We are very grateful to those who have already reported cases and would like to encourage paediatricians to continue to report cases of suspected or confirmed non-type 1 diabetes. The contribution of all those who regularly return the BPSU orange cards will ensure that this becomes a very important project both for the RCPCH and for children's health and well being."

Free information on all forms of diabetes is available to the public from Diabetes UK, 10 Parkway, London NW1 7AA Tel: 020 7424 1000, [www.diabetes.org](http://www.diabetes.org).

For more information please contact Mrs Linda Haines, Principal Research Officer, RCPCH, 50 Hallam Street London W1W 6DE. Tel 020 7 3075673 or visit <http://bpsu.inopsu.com/current.htm#NTD>.

## Study News

**Amendment to MCADD Case Definition:** Surveillance of MCADD commenced in June 2004. We are very pleased to report that we have received 45 notifications to date. Of these, seven have resulted in the identification of newly diagnosed clinical cases of MCADD. In addition, we have received 18 reports of cases diagnosed through newborn screening and five duplicate notifications. Three notifications were received of previously diagnosed cases which fell outside our case definition. We are awaiting confirmation in a further 11 cases. All such notifications are and have been extremely useful for confirmatory and validation purposes. Notifications of duplicate cases and cases known to the study through other routes are very important in such a rare condition.

Ascertainment of cases through the BPSU allows:

- Assessment of test performance in a UK setting, notably false negative rate.
- Evaluation of clinical outcome to 2 years of age in those diagnosed through clinical presentation, family history or through screening.

Following the publication of 'Sudden Unexpected Death in Infancy: The report of a working group convened by The Royal College of Pathologists and The Royal College of Paediatrics and Child Health', some minor changes have been made to the case definition of MCADD. We hope that these changes have simplified the case definition and will also enable us to ensure that, in addition, we are notified of cases identified at post-mortem.

### Amended case definition:

The diagnosis of MCADD may be made following clinical presentation, investigation of a sudden unexpected death, diagnosis in an affected family member or through newborn screening. A child will be considered to have a diagnosis of MCADD if one or more of the following criteria are met:

- Elevated octanoyl carnitine in blood test using tandem mass spectrometry (or in other body fluids if a post-mortem diagnosis)
- Characteristic urine profile of organic acids with hexanoyl, suberyl and phenylpropionyl glycine
- Molecular genetic studies confirming presence of a mutation characteristic of MCADD
- Enzyme studies based on skin fibroblasts showing reduced activity of medium chain fat oxidation

### Reporting instructions:

Paediatricians are asked to notify any newly confirmed or suspected cases using this amended case definition on the orange card in the normal way as from December 2004. An amended protocol card is enclosed in this mailing so please discard your existing MCADD protocol card. As before, the co-ordinating centre will then send a case notification questionnaire to the notifying paediatrician. If necessary, this may be followed-up at 4 months with a brief questionnaire to confirm diagnosis. Follow-up questionnaires will be sent at one and two years after initial notification to establish clinical outcome following diagnosis.

We remain extremely grateful to all the clinicians who have reported children with suspected MCADD to this study and will continue to provide updates through the BPSU bulletin as the study progresses.

If you need any further information or advice please contact: Professor Carol Dezateux (Tel: 020 7905 2362, Email [c.dezateux@ich.ucl.ac.uk](mailto:c.dezateux@ich.ucl.ac.uk)) Juliet Oerton (Tel: 020 7905 2241, Email [mcadd@ich.ucl.ac.uk](mailto:mcadd@ich.ucl.ac.uk))

Dr Stephen Teo reports on the progress of the **Childhood tuberculosis (TB)** study: *"This study commenced in December 2003. We have had 440 reports; analyses of the first 282 of these are reported. Most cases have been in England. While currently areas outside London seem to account for more than Greater London, (Table 1), this may change as further data are gathered. There have been cases across all age groups with no particular trend at this stage (Table 2). So far there have been 217 cases of pulmonary TB, i.e. with parenchymal CXR changes, hilar lymphadenopathy and/or pleural disease.*

**Table 1** TB Cases by region and gender as of Dec 2004

	Female	Male	Total
England not London	74	71	145
London	55	52	107
Northern Ireland	1	3	4
Republic of Ireland	2	2	4
Scotland	8	6	14
Wales	4	4	8
<b>Total</b>	<b>144</b>	<b>138</b>	<b>282</b>

**Table 2** TB cases by age and gender as of Dec 04

Age (years)		< 3	4 – 7	8 – 11	12 -15	Total
No of cases	Male	40	26	24	54	<b>144</b>
	Female	48	34	26	30	<b>138</b>
<b>Total</b>		<b>88</b>	<b>60</b>	<b>50</b>	<b>84</b>	<b>282</b>

*The surveillance period ends in December 2004. We thank those who have taken the time to return the questionnaires. For those who have yet to return a questionnaire could we encourage you to do so.* Dr. Delane Shingadia. Tel: 0207 882 2616, Email [d.v.shingadia@qmul.ac.uk](mailto:d.v.shingadia@qmul.ac.uk), Dr. Stephen Teo, Tel: 0207 882 2619, Email [s.teo@qmul.ac.uk](mailto:s.teo@qmul.ac.uk)

## Study News, contd.

A survey of **Langerhans Cell Histiocytosis (LCH)** began in June 2003. LCH can affect many different parts of the body, most commonly the skin or bones. Little or no treatment may be required if only one system is affected and usually the disease regresses with time although this may take years. LCH can also be multi-system and is most serious in children under the age of two who have lung, liver, bone marrow or spleen involvement. In these cases children are treated on an international protocol (via the UK Children's Cancer Study Group (UKCCSG)). The survey has identified 48 cases to date including 29 males and 19 females. There are 34 cases with single system disease and 11 with multi-system disease (three are not yet known or have not been confirmed); two children have died.

As well as surveillance through the BPSU, the study group, which is based at the University of Newcastle, is also ascertaining cases through a complementary mailing system to other clinicians who may come across children with this disease - endocrinologists, dermatologists, radiologists, pathologists and orthopaedic surgeons. In addition, cases are being cross-referenced with those registered with the UKCCSG. Mailing of one-year follow up questionnaires began in the summer and so far nine have been returned.

A presentation of the study was given by Dr Vasanta Nanduri at the Histiocyte Society Meeting in Stockholm in September. The survey has also raised awareness of the number of adults with LCH, in which diagnosis and treatment is less well defined. This has resulted in interested clinicians meeting to discuss ways in which adult services may be coordinated in the future.

Please continue to notify us of new cases. If you have any problems completing the questionnaire or queries regarding diagnosis, please contact Dr Vasanta Nanduri, Watford General Hospital, Tel 01923 217992, Email [vasanta.nanduri@whht.nhs.uk](mailto:vasanta.nanduri@whht.nhs.uk) or Dr Kevin Windebank, Chairman of the UKCCSG Histiocytosis Working Group, Royal Victoria Infirmary, Newcastle upon Tyne Tel 0191 202 3026, Email [k.p.windebank@ncl.ac.uk](mailto:k.p.windebank@ncl.ac.uk). The study is sponsored by the Histiocytosis Research Trust

<http://www.hrtrust.org>.

## BPSU Secures Financial Support

The BPSU can confirm that the Department of Health (DH) have, as part of their R&D programme, awarded the BPSU a grant of £856,000 over the next five years. This is an extension and expansion of the grant first awarded to the BPSU in 1997.

Professor Mike Preece, chair of the BPSU Executive stated, *"that this grant recognises the many achievements of the BPSU in supporting child health epidemiological research in the British Isles. Can I say that these achievements would not have been possible without the enthusiastic participation of individual reporting clinicians and on behalf of the BPSU Executive and study researchers could I extend our thanks and appreciation"*

It is anticipated that the funding will cover the main day to day running costs of the unit, allow its development to meet increasing demands and also ensure that any contributions required from those wishing to undertake a study can be kept to a minimum.

## Yearly Review

Once again we have reached the time of year when it is traditional to look back over the year's activities. During 2004 the BPSU Executive Committee met 6 times to discuss surveillance proposals and applications.

Ten studies are currently being undertaken, four of which commenced this year, neonatal herpes simplex virus, medium chain Acyl CoA dehydrogenase deficiency, the Sir Peter Tizard bursary survey on childhood thyroptoxicois and non-type 1 diabetes in children. A survey on early onset eating disorders in children aged 5 – 13 years has been approved and will commence in the New Year. Surveillance on two studies, invasive fungal infections in VLBW infants and congenital toxoplasmosis, ended this year.

This year six Phase one applications and five full applications were considered by the committee. If you are interested in submitting a study application full guidelines for applying can now be download from the BPSU website at <http://bpsu.inopsu.com/methodol.htm> alternatively contact the BPSU scientific coordinator. To encourage those wishing to gain experience in epidemiology the BPSU, with support from the RCPCH, once again offered a research bursary named in honour of Sir Peter Tizard, to the value of £15,000. The response was excellent with 15 applications considered, a study on malaria in children was chosen, investigator Dr Shamez Ladhani from the St Mary's Hospital, London. We will be advertising for the next bursary in the Spring of 2005. Orange card response for 2003 was excellent at 92.7% though the first nine months of 2004 has shown a worrying fall to around 90%. There have been 1584 cases reported for the 12 months to October of which 960 have been confirmed

In-house the Unit was successful in securing DH funding for a further five years, a major achievement. The distribution of the annual report greater than ever and we have developed information leaflets for clinicians and the public and these are now available via the website and will be circulated in a forthcoming mailing. The BPSU web site itself continues to expand and improve and will be re-vamped once again in the coming year. Finally we say a fond farewell to Dr Gabrielle Laing after serving on the BPSU Executive these past five years, Gabrielle's contribution has been invaluable. Through the RCPCH newsletter we are currently seeking a replacement, so if you are interested in joining the Executive please contact us.

The International forum supplied the Unit with its main highlight of the year, with our involvement in the third INoPSU conference, held in Lisbon, Portugal. Representatives attended the business meeting from 11 countries, whilst many Portuguese clinicians and European organisations working in the field of rare disease surveillance attended the open sessions. The BPSU supported the development of the Trinidad and Tobago Surveillance Unit, whilst the Canadian Unit has helped develop a unit in Argentina. INoPSU as an organisation held a symposium as part of the International Paediatric Association conference in Cancun Mexico, which was well received. Time will tell whether or not more North and South American countries will join INoPSU but from initial interactions, prospects look promising. The BPSU continues to act as the central liaison for the Units and will host the 4<sup>th</sup> INoPSU conference in the Spring of 2006.

## Monthly Analysis

As you will see from **Table 3** the response rate for the six months to August is averaging 88.6%. The response rate is much lower than expected, in part being influenced by the continuing poor response rates in the London region. The validity of the BPSU as a surveillance system depends wholly on your support and involvement, so please keep those cards and questionnaires coming in. So as you can see the work and reputation of the BPSU goes from strength to strength and this is wholly attributable to the contribution given by members of the RCPCH. On behalf of the investigators and the BPSU we thank you all and wish you all a happy New Year.

**TABLE 3 - % RESPONSE RATE**

March - August 2004

Region	% retd	Rank (Jan-June 2003)
North	89.1	13 (10)
Yorks	92.6	2 (3)
Trent	88.6	14 (15)
EAngl	89.7	12(13)
NWT	84.5	19 (19)
NET	78.2	20 (20)
SET	87.9	15 (16)
SWT	87.9	16 (11)
Wessex	90.8	5 (8)
Oxford	90.6	6 (14)
SWest	90.0	10 (12)
WMids	89.8	11 (9)
Mersey	92.1	4 (4)
NWest	90.4	8 (6)
Welsh	95.6	1 (1)
NScot	90.2	9 (2)
SScot	86.1	18 (18)
WScot	90.5	7 (7)
NIre	92.3	3 (5)
RIre	87.4	17 (17)
<b>Total</b>	<b>88.6</b>	

**TABLE 4 - ALL CASES REPORTED AND FOLLOW-UPS TO 01/12/2004**

Condition	Started	I VALID		II INVALID		NYK	Ttl	as % of total		
		I	Ia	Ib	III			I	II	III
HIV/AIDS	1986	3115	452	511	243	4321	72	22	6	
CR	1990	70	25	50	2	147	48	51	1	
PIND	1997	1108	204	478	29	1819	61	37	2	
Se. Hyperbil	2003	64	9	28	26	127	50	29	21	
LCH	2003	39	18	26	22	105	37	42	21	
TB	2003	279	42	53	71	445	63	21	16	
NNH	2004	17	6	13	16	52	33	37	31	
MCADD	2004	22	4	4	16	46	48	17	35	
Thyrotoxicosis	2004	6	0	6	29	41	15	15	70	
Non type 1 diabetes	2004	0	0	0	24	24	0	0	0	
<b>Total</b>		<b>4720</b>	<b>760</b>	<b>1169</b>	<b>478</b>	<b>7127</b>	<b>66</b>	<b>27</b>	<b>7</b>	

I = confirmed/already known

Ib = reporting error or revised diagnosis

Ia = duplicate

III = status not yet reported to BPSU by investigator

AIDS/HIV - Acquired Immunodeficiency Syndrome / Human Immunodeficiency Virus

CR - Congenital Rubella

PIND - Progressive Intellectual Neurological Degeneration

Se. Hyperbil - Severe hyperbilirubinaemia in the newborn

LCH - Langerhans cell histiocytosis

TB - Tuberculosis in Childhood

NNH - Neonatal Herpes Simplex Virus infection

MCADD - Medium chain Acyl CoA dehydrogenase deficiency

**ALL DATA IS PROVISIONAL & CONTINUALLY BEING UPDATED**