Vol 31 No 1 April 2015

BPSU

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

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BPSU Bulletin

National rare disease register highlighted at BPSU tea party

March 5th saw BPSU host its 2nd rare disease day tea party in collaboration with Rare Disease UK and the RCPCH Youth Advisory Panel. Over 80 guests attended the invitation only event. The tea party brought together patients and carers, healthcare professionals, industry, researchers and policy makers to discuss rare disease.

Thaïs (age 4) and her brother Matthieu (age 6) from France hand in hand against their rare disease. They both have Hurler syndrome (Photo courtesy: EURORDIS photo competition)

Delegates joined us at the RCPCH to hear presentations from the Earl Howe congratulating the BPSU on 30 years of surveillance and announcing the implementation of the proposal to have a named care coordinator for patients with rare disease. Professor Tim Cox from University of Cambridge highlighted research into Tay-Sachs and Daniel Lewi, founder of the Tay-Sachs support group (CATS) spoke poignantly from the perspective of a father of a child living with the condition.

Presentations were also received from Dr Nick Sireau, a father of a child with Alkaptonuria and founder of the FINDACURE initiative. Professor Tim Barrett, with whom the BPSU are working on the Type 2 diabetes study, updated the audience on the Translational Research Collaboration (TRC) activity. Thines Ganeshamoorthy, of the RCPCH Youth Advisory Panel who has Brittle bone disease, gave an inspired talk on the issues of living with a rare disease and the difficulties faced in navigating the NHS processes. Finally, Professor John Newton, PHE Chief Knowledge Officer spoke on the development of the national congenital anomaly and rare disease register which is to launch this April. Following which, Elizabeth Starkey, the 2014 Sir Peter Tizard bursary winner received her award. Dr Starkey is now working with the BPSU to undertake surveillance of children with acute severe poisoning.

Guests, including clinicians, researchers, patients and pharma representatives then enjoyed tea and cakes, and the obligatory cucumber sandwiches whilst networking and visiting the stands from SPARKS, TRC and FINDACURE.

Health Education England also used the event to help launch their rare disease podcasts; one aimed at parents and patients and the other aimed at clinicians.

These, along with further details on the day, can be viewed at www.rcpch.ac.uk/bpsu/rarediseaseday

BPSU moves further into the E-world

The BPSU will be moving further into the E-world with the transfer of the remaining clinicians to the E-card over the next few months. Furthermore, after 25 years, the regular bulletin will also be changing format to that of an e-newsletter with a more extensive focus on the world of paediatric rare disease.

The Twitter feed by the RCPCH Youth Advisory Panel that launched BPSU rare disease day activities was well received. Such has been the interest of this and the tea party on Twitter that the BPSU has decided to launch its own Twitter feed to promote the work of the Unit and highlight research, policy and advocacy around Paediatric rare disease.

Stay tuned for more information!

Supported by Public Health England, Royal College of Paediatrics and Child Health, and UCL-Institute of Child Health

Public Health England
RCPCH Royal College of Paediatrics and Child Health
UCL INSTITUTE OF CHILD HEALTH

Studies to commence

Several studies are due to commence over the next few months and they are described, with contributions from their study leads, below.


Prof Mitch Blair

Nutritional rickets presenting to secondary care: Surveillance for this condition commenced on March 1st and will run for 13 months. The study is led by Dr Priscilla Julies of the Royal Free Hospital London and Professor Mitch Blair (inset), Imperial College in collaboration with the RCPCH research and policy division. This will be the first UK study on the incidence of rickets since 1945.

Rickets was a common Victorian disease and eradicated in the UK by the 1950's by food fortification, cod-liver oil supplementation and other environmental changes. In recent years it has re-emerged as a major public health concern world-wide, particularly in immigrant, non-Caucasian children. Risk factors for the disease include pigmented skin, lack of sun exposure in high latitude areas, pollution, cultural and religious practices preventing sun exposure, exclusive prolonged breastfeeding, and vitamin D deficient mothers. A Canadian Paediatric Surveillance Program study (2002-2004) identified 104 new cases of VDD presenting with significant morbidity including limb deformities (42%) and fractures (11%). The annual incidence was estimated at 2.9/100 000 children. An Australian Surveillance Paediatric Unit Study (January 2006 to July 2007) identified 398 children under 15 years, with VDD. The annual incidence was 4.9/100 000.

The lead investigator Dr Julies stated that – "*though the incidence of rickets is thought to be on the rise there has been no definitive study in the UK since 1945. With the help of BPSU reporting clinicians we hope to identify a new baseline for the condition within the country. We would like to identify the number of children who are diagnosed with rickets in the United Kingdom and Republic of Ireland each year and collect information about rickets, how it presents in children and is treated*".

Clinicians are asked to report any cases of children 0-16 years in the past month presenting with either clinical or radiological rickets as defined by the case definition . The study is funded by the Vitamin D Mission Fund through the Royal National Orthopaedic Hospital Research Board. The study has been approved by NRES Committee London - West London & GTAC (REC reference: 14/LO/2221; IRAS ID: 144785) and has been granted Section 251 HRA-CAG permission (CAG reference: 14/CAG/1042).

The study protocol information and a lay public information guide which can be distributed in your ward/clinics is available from www.rcpch.ac.uk/bpsu/RKT

For any queries regarding the study, please contact: Dr Priscilla Julies; Royal Free Hospital; Email: p.julies@nhs.net


Prof J Hamilton-Shield

Type 2 diabetes: This study is due to commence in April 2013 for 13 months with a one year follow-up. The study is led by Professor Julian Hamilton-Shield (inset) of Bristol University Hospitals.

Until recently, Type 2 diabetes was only seen in mature adults. However we are now seeing similar cases in children. Although rare, we believe the number of new cases is increasing. A BPSU study in 2004, funded by Diabetes UK, identified 78 new (incidence) cases in a year. In the 2004 survey, childhood obesity appeared to be a major association. Since 2004, levels of childhood obesity have continued to increase and we suspect that cases of Type 2 diabetes will also be increasing in parallel.

Professor Hamilton-Shield stated that – "*This 2nd BPSU study will ascertain whether the incidence of Type 2 diabetes has increased since the first survey ten years ago, and will re-assess diagnosis and management of this condition in the UK. Our previous survey demonstrated significant concerns regarding associated illness, screening, care delivery, treatment options and robust outcomes such as weight loss at one year and blood sugar control (glycated haemoglobin) attained. It is hoped that a second survey would see improvements in care from the time of the previous survey*"

Clinicians and specialist diabetes nurses will be asked to report "any new diagnosis of Type 2 diabetes in children under the age of 17 years". The study is funded via an NIHR grant through the Rare Disease Translational Research Consortium project. The study has been approved by South West MREC (REC reference: 1 14/SW/1143) and has been granted Section 251 HRA-CAG permission (CAG reference: 15/CAG/0102)

The study protocol information and a lay public information guide which can be distributed in your ward/clinics is available from www.rcpch.ac.uk/bpsu/T2D

For any queries the study, please contact: Professor J Hamilton-Shield; and Dr A A Majbar. University Hospital Bristol. Email: a.a.majbar@bristol.ac.uk

Studies to commence

Acute Rheumatic Fever (ARF): This study is due to commence in the Spring for 13 months in the first instance. The study is led by Dr Mary Salama from Birmingham children's hospital. This study is being funded through the Sir Peter Tizard Bursary programme for which Mary was the winning applicant.

Mary describes the condition and the study aims - *"Acute rheumatic fever is an illness, occurs as a result of the body reacting to an infection with a bacterium called group A streptococcus usually in the form of a sore throat. It can cause swelling or inflammation in certain parts of the body. This can include joint swelling and pain, a skin rash, abnormal movements and in some cases swelling of layers within the heart that can in extreme cases make you breathless. In the long term it can also lead to damage of certain parts of the heart, which can need medication or surgery and in a few severe cases heart failure or early death. This damage is made more likely with exposure to group A streptococcus so identified patients are started on preventative antibiotics."*

"Though now very rare in developed countries such as the UK; it had been less rare in the past and was studied by the BPSU in 1990 been more common so it is now difficult to see whether the pattern of the illness is changing. We want to see the pattern of illness it produces, its course and management."

Consultant paediatric cardiologists will be asked, along with paediatricians, to report all new diagnoses of ARF made during the past month in children aged up to and including 16 years of age. We would encourage clinicians to report any case they had the clinical suspicion to investigate and treat as ARF.

The study has been approved by NRES West Midlands (REC reference 13/WM/0412) and has been granted Section 251 HRA-CAG permission (CAG reference: 15/CAG/0111:)

The study protocol information and a lay public information guide which can be distributed in your ward/clinics is available form is available www.rcpch.ac.uk/bpsu/SCARF

For any queries the study, please contact: Dr Mary Salama, Birmingham Children's Hospital. Email: scarf@bch.nhs.uk

Dr Clare Pain

Behçet syndrome: This study is also due to commence in the Spring for 13 months with a one year follow-up. Dr Claire Pain (inset), a Paediatric Rheumatologist at Alder Hey Children's NHS Foundation Trust in collaboration with the Behçet's Syndrome Society.

Behçet's syndrome is a rare multi-system inflammatory condition characterised by recurrent oral ulceration, genital ulceration, eye and skin involvement. The prevalence of Behçet's syndrome in the UK is actually unknown but estimates put it at 0.64 per 100,000 of the population. Studies have shown that 4-26% of Behçet's syndrome occurs in those under 16 years of age. Recent National Commissioning has led to the development of three National Centre's of Excellence for Behçet's syndrome.

Because of the perceived rareness of the condition the investigators plan, 13-month period, to investigate both incidence and prevalence of paediatric Behçet's syndrome and will examine the current UK experience. By answering these questions, the study will provide vital data that will be of value in defining the need for additional supra-regional referral services and in designing future clinical trials. We aim to perform a one year follow-up study which would identify early disease progression and complications of Behçet's syndrome in children.

Paediatricians and Dermatologists will be asked to report any children under the age of 16 years seen in the last month with possible Behcet's syndrome (including new and follow-up cases).

The study is funded by Behcet's syndrome society (from funds raised by the Worshipful Company of Horner's) and Alder Hey Children's charity. The study has been approved by NRES North East (REC reference: 15/NW/0035) and has been granted Section 251 HRA-CAG permission (CAG reference: 15/CAG/0103).

Full details of the case definition , research protocol and lay public information guide which can be distributed in your ward/clinics are available at www.rcpch.ac.uk/bpsu/BHT

Support group: Bechet's syndrome society: http://behcets.org.uk/

For any queries the study, please contact: Dr Clare Pain, Alder Hey Children's Hospital. Email: clare.pain@alderhey.nhs.uk

Studies updates

Group b strep investigators update: In April 2014, the BPSU launched a new surveillance study to capture the incidence of invasive group B streptococcal disease in infants less than 90 days of age in the UK and Ireland. The study is led by Professor Paul Heath at St George's, University of London in collaboration with Public Health England.

Group B Streptococcus (GBS) is the most common cause of serious bacterial infections in the first week of life and of meningitis in the first three months of life. Approximately 10% of babies with GBS disease will die and neurodisability occurs in up to 50% of survivors of GBS meningitis.

Clinicians and microbiologists have been asked to report cases they have seen from 1st April 2014 onwards, and to continue to do so. Clinicians are asked to complete the BPSU questionnaire (following their orange card notification) while microbiologists and laboratory staff are asked to notify invasive GBS cases, and submit the isolates, to their national reference laboratory (e.g. PHE).

In the first six months of the study (April 2014 – September 2014) 380 notifications were made. Detailed completed questionnaires of eligible confirmed cases have been submitted for 180. 106 (59%) of the cases are early onset disease and 74 (41%) are late onset. 38 cases of meningitis (lumbar punctures were performed in 82% of cases) and 14 deaths have been described.

As the study is on-going, the microbiological information is not yet consolidated but for those isolates which are available the commonest serotypes are III and Ia. In early onset disease these serotypes make up 48% (III) and 20% (Ia) of isolates respectively and in late onset disease 48% (III) and 11% (Ia).

We would like to take this opportunity to thank those people (in paediatric, neonatal and microbiology departments) who have contributed information to date, and encourage all to continue to do so. If you require any further information about the study or have any queries please don't hesitate to contact us.

For further information please contact: Dr Catherine O'Sullivan, Paediatric Infectious Diseases Research Group, St George's, University of London, Cranmer Terrace, London SW17 0RE or visit www.rcpch.ac.uk/bpsu/gbs. Email: cosulliv@sgul.ac.uk

Progressive Intellectual and Neurological Deterioration (PIND): Continuation of this study was approved by the BPSU scientific committee for a further year. In justification the investigators stated that "the PIND study remains the only way to search for vCJD cases in children and young people with progressive neurological disease under the age of 16 years. If the PIND study finds no cases in this age group it provides supportive evidence that public health measures are effective, which has implications for public health policy in the UK and abroad. The PIND study yields unique data on the epidemiology of progressive neurological disease in children and the variation in the incidence of these disorders in different ethnic groups. These findings contribute to the appropriate planning of diagnosis, clinical management and the provision of services. Whilst surveillance for vCJD is continued in the UK in older patients it makes sense to continue with surveillance of children and young people via the PIND study".

BPSU Surveillance of Congenital Hypothyroidism (CHT) – three year follow-up to begin soon!

UK Collaborative Study of Congenital Hypothyroidism (UKCS CHT)

The BPSU Scientific Committee has recently approved a final, third year of follow-up for children reported to the BPSU surveillance study of congenital hypothyroidism. A final questionnaire will be sent to clinicians who are caring for a child for whom the diagnosis is still unconfirmed or a trial off therapy may be considered.

A very short questionnaire will be sent to clinicians when the child they reported to the study is between 3 and 4 years of age. It will ask about the outcome of any trial off therapy or further investigations in the last year. This information will help us understand better how many children with positive screening tests have transient rather than permanent hypothyroidism. It will provide a standard of clinical outcome data that has rarely been achieved in observational studies of congenital hypothyroidism and will inform screening policy in the UK.

Questionnaires will be sent out electronically between April 2015 and July 2015 but can also be sent by post if preferred. Any clinician who wishes to know more about the study should contact j.oerton@ucl.ac.uk or rachel.knowles@ucl.ac.uk

In general

Staff news: Congratulations go to the BPSU scientific coordinator, Richard Lynn (inset), who celebrates 25 years working at the RCPCH. Richard started as the British Paediatric Association research officer and BPSU administrator and after five years he took over the running of the BPSU full time. Over the years Richard has been instrumental in all the major strategic developments of the Unit from identifying funding to raise the Units' public and academic profile, to developing the e-reporting system. Richard has also been part of many research projects in particular the Reye syndrome study, that led to the warnings on aspirins being extended to teenagers; haemolytic uraemic syndrome and early onset eating disorders. The latter led him to co-found the BPSU's sister unit the Child and Adolescent Psychiatry Surveillance System. Outside of the BPSU Richard has contributed to the development of the UK Rare Disease Strategy; sits on Rare Disease UK management board; is a committee member of the International Network of Paediatric Surveillance Units; and is a mentor for the Sickle Cell & Young Stroke Survivors patient support group. Thankfully, despite his long service with the BPSU, Richard is still young, enthusiastic and full of ideas to help develop and expand the remit of the BPSU over the coming years.

R Lynn, Scientific Coordinator

Tay-sachs: The Cure & Action for Tay-Sachs (CATS) Foundation, are holding a meeting to discuss the planned clinical trial for Tay-Sachs and Sandhoff disease. There will be an overview of the history of gene therapy, case studies of patient organisation involvement in gene therapy trials for other diseases, along with a parents view and expectation of their child being involved in a clinical trial. The format of the meeting will allow for discussions around these subjects and we hope that a lot can be learnt from these openly discussed sessions.

Please check out the link below for more information and to register you attendance.

https://www.eventbrite.co.uk/e/gene-therapy-for-gm2-gangliosidosis-scientific-meeting-registration-16199065842

CATS have also announced that in collaboration with its Spanish charity partner Acción y Cura para Tay-Sachs (ACTAYS) has been awarded a €7,000 grant to develop a European patient registry for Tay-Sachs and Sandhoff disease and are joint member of the European Tay-Sachs Charity Consortium (ETSCC).

Reports and Analysis

Analysis: For the period June to November 2014 orange card return rates stand at 92.6% (Table 1). There have been some significant shifts in response rates over the last year with Republic of Ireland's response rate falling from their high response rates in 2013 of 94.7% to 85.5% for 2014. On the other end of the scale, East Anglia's responses have improved significantly since 2013, jumping to 98.2% in 2014 and is regionally the best returner of orange reporting cards. Well done!

However, it is important to maintain the questionnaire response rate. This currently stands at 86%, but some studies have, of late struggled to get over 80% and we need to raise this to over 90%.

We are now running online data collection with the nutritional rickets study. If you have reported a case to the BPSU, please do expect an email from the rickets team with a link to their online questionnaire.

Table 1 - % Regional Response Rates June-November 2014

Region	Return %	Rank
Eangl	98.20%	1
Mersey	90.90%	18
NET	91.40%	15
NScot	97.40%	2
Nwest	91.30%	16
Northern	91.50%	14
Nire	88.90%	19
NWT	91.10%	17
Oxfrd	92.60%	11
Rire	85.50%	20
SET	93.00%	8
SScot	93.20%	7
Swest	94.90%	4
SWT	92.40%	12
Trent	92.80%	10
Wales	96.60%	3
Wessex	93.50%	6
WMids	92.20%	13
WScot	93.60%	5
Yorks	93.00%	9
Average	**92.60%**	

Table 2: All cases reported and follow ups to 18.03.2015

		VALID			INVALID		C&R	D&E	X
Condition	Start	C/R	D	E	X	TOTAL	(as % of total)		
HIV	1986	8,121	840	768	1,241	10,970	74	15	11
CR	1990	90	38	65	0	193	47	53	0
PIND	1997	2,147	471	1,088	127	3,833	56	41	3
SYP	2010	52	35	27	15	129	40	48	12
HUS	2011	191	173	103	129	596	32	46	22
KAW	2013	381	67	98	323	869	44	19	37
APAN	2013	105	33	41	42	221	48	33	19
HEP	2014	61	2	19	27	109	56	19	25
GBS	2014	212	23	27	348	610	35	8	57
EPM	2014	174	8	23	161	366	48	8	44
EBT	2014	11	5	1	47	64	17	9	73
Total		**11,545**	**1,695**	**2,260**	**2,460**	**17,960**	**64**	**22**	**14**

HIV	Human immunodeficiency virus in childhood
CR	Congenital rubella
PIND	Progressive intellectual & neurological deterioration
SYP	Congenital syphilis
HUS	Haemolytic uraemic syndrome
KAW	Kawasaki Disease
APAN	Acute pancreatitis
HEP	Acute Symptomatic Hepatitis
GBS	Group B streptococcal disease
EPM	Enterovirus and parechovirus meningitis
EBT	Exchange blood transfusion

C/R = confirmed/already known

D = duplicate

E = reporting error or revised diagnosis

X = status not yet reported to BPSU by investigator

ALL DATA IS PROVISIONAL & CONTINUALLY BEING UPDATED