Aims of the British Paediatric Surveillance Unit

To:

• Facilitate research into uncommon childhood infections and disorders for the advancement of knowledge and to effect practical improvement in prevention, treatment and service planning

• Allow paediatricians to participate in the 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 and respond rapidly to public health emergencies.

http://www.rcpch.ac.uk/bpsu
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By Dr Richard Reading
Chair, BPSU

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I am pleased to introduce this year’s British Paediatric Surveillance Unit (BPSU) annual report. I am sure that you will all be aware that this is now the thirtieth year of active surveillance through the BPSU. The BPSU has been involved in several academic activities to mark this milestone and celebrate the Unit’s ongoing impact. This has included a 30th anniversary conference in February in Birmingham, and a symposium at the college meeting in Liverpool. Both were well received. We have also published a 30 year anniversary report ([http://www.rcpch.ac.uk/bpsu/30yearreport](http://www.rcpch.ac.uk/bpsu/30yearreport)), covering the BPSU’s activities, studies and engagement with patients, family and the public over the course of the Unit’s existence. We hope that you have seen and read this! It takes the place of much of the material we usually include in the annual report and as such this year’s annual report has been ‘slimmed down’.

As ever, the BPSU has been active and forward looking this year. Surveillance of Rickets, Type 2 diabetes, and of young people with ADHD in transition to adult services all started this year. All of these conditions are of topical public health importance, and the resulting surveillance data is likely to have important implications for clinical policy and practice. We have commenced surveillance for congenital Zika virus syndrome, which has global public health importance. Although cases in the UK are likely to be rare, findings of surveillance in countries where transmission does not occur may have important implications. We have worked carefully with the public health authorities across the United Kingdom and Ireland and with our sister paediatric surveillance units in Australia, New Zealand and Canada in order to develop a protocol which will enable international comparison of the findings. Even so, we are proud to report that the BPSU is the first paediatric surveillance unit to commence surveillance in the world, a testament to the efficiency of our fast-track process for approval of studies with urgent public health implications, and to the hard work of the BPSU team.

Thanks as ever are due to all reporting paediatricians. The return rate for the monthly electronic reporting cards remains impressively high and we do all we can to facilitate the speedy and efficient processing of clinical questionnaires.

We look forward to another exciting and successful year for the BPSU!

Richard Reading. Chair BPSU, October 2016
Background

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

To address this problem in the UK and Ireland, the BPSU was set up in July 1986, enabling paediatricians to participate in the surveillance and further study of rare disorders affecting children.

Several agencies founded and continue collaborating to support the work of the BPSU: the Royal College of Paediatrics and Child Health (RCPCH), Public Health England, University College London - Institute of Child Health, GOSH Children's Charity and the Faculty of Paediatrics of the Royal College of Physicians of Ireland. The BPSU’s Scientific Committee meets every ten weeks to consider individual applications and the progress of studies.

Selection of studies for inclusion in the scheme

Details on the selection process and application process for the BPSU is now available online at http://www.rcpch.ac.uk/bpsu/apply.

Each application requires approval from the BPSU Scientific committee and require approval from the Research Ethics Committee (REC) and Confidentiality Advisory Group (CAG) of the Health Research Authority before commencement. Scottish Public Benefits and Privacy Panel approval is covered by existing BPSU approvals.

The reporting system

Surveillance is ‘active’ in that the BPSU office actively sends out cards to consultant paediatricians in the UK and Ireland asking for cases to be reported on the BPSU orange card (Figure 1). Each month, all clinicians participating in the surveillance scheme are sent an electronic orange card, listing the conditions currently under surveillance; follow-up reminders are sent to those who have not returned their card. A set of instructions for completing the card, including the case definition of the conditions listed on the card is also circulated. When a new study begins, the mailing also includes a specially produced protocol card and other information about the study.

Participants are also 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 us to measure compliance, which is continually monitored, to the reporting system.

Follow-up and confirmation of case reports

On receiving a case report the BPSU informs the relevant study team who send a short questionnaire to the reporting clinician to gather further information. As the questionnaire cannot be fully anonymised, the amount of patient identifiable data collected is strictly limited to preserve patient confidentiality. The study investigators report back to the BPSU, indicating when cases have been confirmed or are duplicate case reports (see Figure 2). Duplication of reporting is most likely to occur when the condition requires referral to another clinician, but this is encouraged, as it is better to receive duplicate reports than to miss a case.

To improve case ascertainment for specific studies where a child may see specialist clinicians, consultants working in a number of other specialties have been invited to participate in the scheme. Apart from helping to improve ascertainment such complementary data sources help to validate the surveillance system.
Six new studies have commenced in 2015, type 2 diabetes, Professor Julian Hamilton-Shield, University of Bristol; nutritional rickets, Dr Priscilla Jules, Royal Free London; acute rheumatic fever, Dr Mary Salama, Birmingham Children’s Hospital; Behcet’s syndrome, Dr Claire Pain, Alder Hey Children’s Hospital, Liverpool; visual impairment and blindness, Professor Jugnoo Rahi, UCL – Institute of Child Health; and female genital mutilation, Dr Deborah Hodes, University College London Hospitals.

Three studies had their period of surveillance extended: HIV, congenital rubella, and progressive intellectual and neurological deterioration (PIND).

During 2015-16, there were six publications relating to BPSU studies and 39 conference presentations (see Appendix, p.24).

Participation in the scheme during the year 2015

Reporting rates for returning the orange cards remain high - the overall card return compliance rate for the year 2015, calculated as a proportion of orange cards returned, was 94.3% (39,066/41,424) a rise of 0.2% from 2014. This is encouraging given difficulties the electronic card had with passing through certain Trust firewalls in the last quarter after the system was moved to UCL’s data safe haven server. Monthly response rates ranged from 91% in December to 97% in February with a median of 94.2%. Details of regional response rates are provided in Table 1 (p.5).

The BPSU has continues to develop its e-reporting system and has been working with several of the research teams on collecting data online. Feedback from reporting clinicians who have used these systems has been positive.

Table 2 summarises the outcome of the follow-up of cases and provides evidence for their level of accuracy of reporting by clinician. By the end of a study 80-95% of the questionnaires will have been returned. The time taken to follow-up varies between conditions and may be longer if microbiological/pathological details are required, or if a specialist committee has to convene to adjudicate on the case data.

Workload of those reporting in the scheme: 904 of 3,698 (24%) receiving a card in 2015 reported a case in 2015. 15% (573) reported a single case, 8% (288) reported between two and four cases and 1% (43) reported five or more cases. The greatest number of cases reported was by HIV specialists, one of whom reported 83 cases.

Public Patient Engagement

The BPSU is committed to wider public patient engagement in the development and dissemination of our work and that of the studies. To support clinicians when preparing their protocols several resource packs have been introduced. These are available at http://www.rcpch.ac.uk/bpsu/nni.

In February 2016, the BPSU in collaboration with Rare Disease UK hosted its third annual rare disease day tea party (http://www.rcpch.ac.uk/bpsu/rarediseaseday16) as part of the BPSU celebratory 30th year conference at the University of Birmingham (http://www.rcpch.ac.uk/bpsu/rcdf17). Similar events are planned for the future.

International activities

The BPSU continues to take an important role in the activities of the International Network of Paediatric Surveillance Units (INoPSU). The past year has seen the launch of a revamped INoPSU website - http://www.inopsu.com. Here you will find information on affiliated national paediatric surveillance units, studies currently being undertaken; published papers; study protocols; and questionnaires.

Funding

BPSU is currently funded through grants from Great Ormond Street Children’s Charity, University College London - Institute of Child Health, RCPCH, and Public Health England, along with contributions from researchers.
Table 1: Regional Response rate 2014 and 2015

<table>
<thead>
<tr>
<th>Region</th>
<th>% return</th>
<th>Rank 2015</th>
<th>Rank 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>East Anglia</td>
<td>97.8%</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Mersey</td>
<td>94.3%</td>
<td>12</td>
<td>17</td>
</tr>
<tr>
<td>NET</td>
<td>91.5%</td>
<td>19</td>
<td>15</td>
</tr>
<tr>
<td>North Scotland</td>
<td>99.0%</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>North Western</td>
<td>92.3%</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>Northern</td>
<td>95.9%</td>
<td>5</td>
<td>14</td>
</tr>
<tr>
<td>Northern Ireland</td>
<td>93.0%</td>
<td>17</td>
<td>19</td>
</tr>
<tr>
<td>NWT</td>
<td>94.1%</td>
<td>13</td>
<td>16</td>
</tr>
<tr>
<td>Oxford</td>
<td>94.3%</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>Republic of Ireland</td>
<td>90.9%</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>SET</td>
<td>93.8%</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td>South Scotland</td>
<td>94.9%</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>South Western</td>
<td>94.0%</td>
<td>14</td>
<td>11</td>
</tr>
<tr>
<td>SWT</td>
<td>96.2%</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Trent</td>
<td>94.8%</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Wales</td>
<td>95.5%</td>
<td>7</td>
<td>3</td>
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<tr>
<td>Wessex</td>
<td>94.8%</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>West Midlands</td>
<td>93.7%</td>
<td>16</td>
<td>10</td>
</tr>
<tr>
<td>West Scotland</td>
<td>94.7%</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Yorkshire</td>
<td>95.6%</td>
<td>6</td>
<td>7</td>
</tr>
</tbody>
</table>

Table 2: Outcome of follow-up of the cases reported in 2015 for conditions under surveillance at May 2016

<table>
<thead>
<tr>
<th>Condition under surveillance</th>
<th>Date when reporting began</th>
<th>Valid reports</th>
<th>%</th>
<th>Duplicates</th>
<th>Errors (D&amp;E)</th>
<th>%</th>
<th>Not yet known</th>
<th>%</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>Jun-86</td>
<td>8,602</td>
<td>75</td>
<td>859</td>
<td>779</td>
<td>14</td>
<td>1,242</td>
<td>11</td>
<td>11,482</td>
</tr>
<tr>
<td>CRU</td>
<td>Jun-91</td>
<td>92</td>
<td>47</td>
<td>39</td>
<td>65</td>
<td>53</td>
<td>0</td>
<td>0</td>
<td>196</td>
</tr>
<tr>
<td>PIND</td>
<td>May-97</td>
<td>2,190</td>
<td>55</td>
<td>515</td>
<td>1,285</td>
<td>45</td>
<td>1</td>
<td>0</td>
<td>3,991</td>
</tr>
<tr>
<td>KAW</td>
<td>Jan-13</td>
<td>481</td>
<td>55</td>
<td>99</td>
<td>111</td>
<td>24</td>
<td>190</td>
<td>22</td>
<td>881</td>
</tr>
<tr>
<td>HEP</td>
<td>Jan-14</td>
<td>69</td>
<td>61</td>
<td>8</td>
<td>32</td>
<td>35</td>
<td>4</td>
<td>4</td>
<td>113</td>
</tr>
<tr>
<td>GBS</td>
<td>Apr-14</td>
<td>716</td>
<td>63</td>
<td>116</td>
<td>56</td>
<td>20</td>
<td>109</td>
<td>18</td>
<td>856</td>
</tr>
<tr>
<td>EPM</td>
<td>Jul-14</td>
<td>378</td>
<td>70</td>
<td>23</td>
<td>69</td>
<td>17</td>
<td>68</td>
<td>13</td>
<td>538</td>
</tr>
<tr>
<td>EBT</td>
<td>Oct-14</td>
<td>116</td>
<td>67</td>
<td>28</td>
<td>6</td>
<td>18</td>
<td>25</td>
<td>14</td>
<td>173</td>
</tr>
<tr>
<td>RKT</td>
<td>Mar-15</td>
<td>58</td>
<td>41</td>
<td>5</td>
<td>53</td>
<td>41</td>
<td>27</td>
<td>19</td>
<td>143</td>
</tr>
<tr>
<td>T2D</td>
<td>Apr-15</td>
<td>83</td>
<td>73</td>
<td>7</td>
<td>8</td>
<td>13</td>
<td>16</td>
<td>14</td>
<td>114</td>
</tr>
<tr>
<td>BEH</td>
<td>May-15</td>
<td>22</td>
<td>31</td>
<td>10</td>
<td>9</td>
<td>27</td>
<td>30</td>
<td>42</td>
<td>71</td>
</tr>
<tr>
<td>ARF</td>
<td>May-15</td>
<td>14</td>
<td>40</td>
<td>4</td>
<td>6</td>
<td>29</td>
<td>11</td>
<td>31</td>
<td>35</td>
</tr>
<tr>
<td>VIB</td>
<td>Oct-15</td>
<td>38</td>
<td>40</td>
<td>0</td>
<td>34</td>
<td>35</td>
<td>24</td>
<td>25</td>
<td>96</td>
</tr>
<tr>
<td>FGM</td>
<td>Nov-15</td>
<td>2</td>
<td>20</td>
<td>1</td>
<td>6</td>
<td>70</td>
<td>1</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>ADHD</td>
<td>Nov-15</td>
<td>32</td>
<td>50</td>
<td>0</td>
<td>25</td>
<td>39</td>
<td>7</td>
<td>11</td>
<td>64</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>12,686</td>
<td>68</td>
<td>1,703</td>
<td>2,541</td>
<td>1,788</td>
<td>10</td>
<td>18,718</td>
<td></td>
</tr>
</tbody>
</table>

HIV: HIV infection and perinatal HIV exposure  
CRU: Congenital rubella  
PIND: Progressive intellectual and neurological deterioration  
KAW: Kawasaki disease  
HEP: Acute infectious hepatitis  
GBS: Group B streptococcal disease  
EPM: Enterovirus and parechovirus meningitis  
EBT: Neonatal exchange blood transfusion  
RKT: Nutritional rickets  
T2D: Type 2 diabetes  
BEH: Behçet’s syndrome  
ARF: Acute rheumatic fever  
VIB: Visual impairment and blindness  
FGM: Female genital mutilation  
ADHD: Attention deficit and hyperactivity disorder
Once again individual reports have concentrated on the summary of the condition and on the analysis. General methodology information is contained in the study protocols and can be found at http://www.rcpch.ac.uk/bpsu/currentstudies. Please take into consideration that the analysis presented here is provisional and has yet to be peer reviewed.

The investigators would like to acknowledge all those who are involved in their projects but are not mentioned. The BPSU would like to thank all those who have returned cards, reported cases and completed the questionnaires.

Behçet’s syndrome

Key points

- 90 prevalent and incident cases have been reported.
- The mean age at diagnosis is nine years.
- Children present with a wide range of symptoms, of which oral ulceration is the most common.
- Around 43% of children were managed with topical treatments, but 50% required systemic immunosuppression.

Summary

Behçet’s syndrome is a rare multi-system inflammatory condition characterised by recurrent oral ulceration, genital ulceration, eye and skin involvement. Complications such as blindness and neurological involvement or major blood vessel involvement can lead to marked disability, typically in young people. There is currently very little data on incidence and prevalence of Behçet’s syndrome in children and in particularly within the UK population.

Recent National Commissioning has led to the development of three National Centres of Excellence for Behçet’s syndrome. However, the disease burden of Behçet’s in patients under 16 years of age in the UK, and how and by whom these patients are managed, is not well described.

This is the first year of this study of the incidence and prevalence of Behçet’s syndrome in children in the UK. The study is also assessing delay to diagnosis, presenting features and management. By answering these questions, the study will provide vital data that will be of value in defining specialist services to address the needs of children with Behçet’s syndrome.

A one year follow-up study will examine any changes in diagnosis and examine early disease progression and complications.

Surveillance period

May 2015 - June 2017 (inclusive). Follow-up period: Follow-up questionnaire at 12 months after initial diagnosis, ending in June 2018.

Methodology

Data capture uses standard BPSU methodology. Details of the study protocol are available at http://www.rcpch.ac.uk/bpsu/bht.

Analysis

To April 2016 there have been 90 notifications; 88 cases were reported through the BPSU orange card reporting scheme and two by dermatologists who responded to a monthly email to members of British Society of Paediatric Dermatologists. 16 reports have been excluded, of which eight were reported in error (five children were over 16 years of age and three did not meet the reporting criteria) and eight were duplicates. For the remaining 74 cases, there are 29 completed questionnaires (39% response rate) and 45 questionnaires are outstanding.

Of the 29 returned questionnaires; seven are incident cases and 21 are prevalent cases.

21 cases fulfil the criteria for definite Behçet’s syndrome based on International Criteria for Behçet’s disease ICBD scoring system, and a further eight are awaiting review by the expert panel to ascertain whether these are cases of probable Behçet’s or are not deemed to be due to Behçet’s but an alternative diagnosis.

Of the 28 questionnaires for which we have completed data 16 (57%) were female, 12 (43%) were male.

Age at onset was 8.75 years and at diagnosis 9.35 years which is less delay in diagnosis than has been reported by other studies.1,2,4

With regards ethnicity, 22 (79%) cases reported are white, which is slightly less than the percentage in the UK population.

Children presented with a wide array of clinical manifestations - 27/28 (96%) with oral ulceration, 19 (67%) with genital ulceration, 13 (46%) with skin involvement. Eye involvement was reported in 6 (21%), whilst neurological and vascular involvement were less common affecting 3
(11%) and 2 (7%) of children respectively. All children 29 (100%) were followed up in tertiary care by a number of different specialty clinicians and around 43% of children were managed with topical treatments, however 50% required systemic immunosuppression.

Whilst some patients were stable off treatment, over half of all patients required treatment to control their disease and 29% still had active disease despite treatment.

Discussion

Data collection is ongoing but initial figures confirm the rarity of Behçet’s syndrome in UK and Irish children. The majority of children reported are of white ethnicity. The distribution of Behçet’s syndrome is spread along the former Silk Route from the Far East to the Mediterranean with higher prevalence of disease in countries from these areas. Previous studies have identified different frequencies of disease manifestations in different ethnicities with country of residence and ethnic background both of impact on prevalence of the disease. Comparison of the frequency of disease manifestations with non-UK cohorts will be important in future analyses as there may be differences to the UK population.1

As expected from previous published cohorts, oral ulceration is the most common clinical feature, followed by genital ulceration and skin involvement.1,2,4 Eye, neurological and vascular involvement were all less frequent. This is important when considering the design of specialist services to deliver the needs of children with this disease.

Delay in diagnosis appeared less in the small number of cases analysed when compared to other published studies.1,2,4 Age of onset was defined as age of onset of first symptom attributable to Behçet’s syndrome e.g. first episode of oral ulceration. This will need further evaluation when more cases are analysed.

Due to the low number of reported cases, particularly of incident cases, surveillance will continue for a further year to ensure there is a sufficiently large dataset for analysis.

Public and patient engagement

Behçet’s Syndrome Society
Web: http://www.behcets.org.uk/

Funding

This study is funded by Alder Hey Children’s Charity, Behçet’s Syndrome Society Charity (from funds raised by the Worshipful Company of Horner’s), Professor Farida Fortune, Professor Robert Moots and Vasculitis UK.

References

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Queen’s Medical Centre, Nottingham:
Dr Ruth Murphy
University of Liverpool:
Professor Michael W. Beresford
Congenital rubella

Key points

- Since 2005, 12 congenital rubella births have been reported in the UK; none were reported between April 2015 and March 2016.
- Congenital rubella syndrome can occur when a woman contracts rubella during the first trimester of pregnancy. It can cause deafness, blindness and heart defects in the fetus, amongst other symptoms.
- Antenatal screening for rubella susceptibility was discontinued in England in April 2016.

Summary

Surveillance of congenital rubella (CR) has been in place since 1971, when the National Congenital Rubella Surveillance Programme (NCRSP) was set up to monitor the impact of rubella vaccine; there has been active surveillance throughout the UK and Ireland through the BPSU since 1990. Three CR births were reported in the 12 months between April 2014 and March 2015 (and all were included in the last BPSU Annual Report); none were reported in the 12 months April 2015 to March 2016.

Following policy reviews in 2003 and 2012,1 antenatal screening for rubella susceptibility was discontinued in England in April 2016. The other countries of the UK are reviewing their antenatal screening policy. The National Screening Programme supports on-going national surveillance of CR through the BPSU, in order to help maintain professional awareness of this rare but potentially devastating infection, and to provide a mechanism for the timely reporting of the circumstances of any cases which do occur. Congenitally infected infants can shed rubella virus for an extended period of time, and every infected infant must be diagnosed and managed appropriately to avoid the risk of contributing to further community transmission.

A review by the World Health Organization (WHO) in 2008 estimated that more than 110,000 infants were born with congenital rubella syndrome (CRS) each year in developing countries, and rates are highest in the WHO African and South-East Asian regions where vaccine coverage is lowest. In April 2015 the WHO Region of the Americas became the first in the world to be declared free of endemic transmission of rubella, and the WHO aims to eliminate measles, rubella and congenital rubella (elimination defined as <1 case of CRS per 100,000 births) from five of the seven WHO Regions by 2020. Although in the UK reported cases of CRS have been below this level for many years, rubella outbreaks and associated CR births have been reported in several European countries in the last decade, including Romania, Poland and Italy, and continued vigilance is necessary.

Surveillance period

January 1990 and is reviewed yearly.

Methodology

Data capture uses standard BPSU methodology; details of the study protocol are available at http://www.rcpch.ac.uk/bpsu/cr

Analysis

The only BPSU report received in the 12 months between April 2015 and March 2016 related to a teenager with congenital rubella who lived in England but was born elsewhere in Europe. In the previous 12 months three births were reported (infants born in 2014/2015, all included in the previous BPSU Annual Report). The surveillance case definition was revised in 2005 to include newly diagnosed children who were born abroad, in order not to miss any cases, and to contribute to European surveillance data.

Congenital rubella births in the UK or Ireland 1990-2016: 67 children and four stillborn infants with confirmed or compatible congenital rubella have been born and reported since active surveillance was established in 1990; 54 of these (76%) were first reported through the BPSU (Table 3).

Table 3: Confirmed and compatible congenital rubella births in the UK and Ireland 1990 to March 2016

<table>
<thead>
<tr>
<th>Year of birth</th>
<th>Primary Source of notification</th>
<th>BPSU</th>
<th>Other</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td>1990-94 * ^</td>
<td></td>
<td>22</td>
<td>10</td>
<td>32</td>
</tr>
<tr>
<td>1995-99</td>
<td></td>
<td>12</td>
<td>4</td>
<td>16</td>
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<td>2000-04 *</td>
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<td>1</td>
<td>11</td>
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<td>2005-09 *</td>
<td></td>
<td>4</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>2010-16</td>
<td></td>
<td>6</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>54</td>
<td>17</td>
<td>71</td>
</tr>
</tbody>
</table>

* includes a stillborn infant
* includes a set of triplets, one of whom was stillborn

Since 2005 there have been 12 confirmed reports, including one stillborn infant. None of the mothers were UK-born, and none had a previous pregnancy in the UK. Three women arrived in the UK in childhood, and at least one reported having had MMR vaccination as a teenager. Half of the women acquired their infection abroad in early pregnancy, but six came into contact with rubella in the UK.
Discussion

Very few cases of CR have been reported in the last decade and most reports concern infants with neonatal symptoms who also have serious rubella-associated defects identified at birth or soon afterwards. About half of the recent maternal infections were acquired in the UK. Pregnant women may enter the UK having acquired infection in early pregnancy elsewhere, and susceptible women resident in the UK who travel abroad during early pregnancy may also come into contact with rubella. Health professionals, particularly paediatricians and those working in primary care and antenatal care, or with refugees or other recent migrants, must continue to be aware of the potential serious implications of rash illness in early pregnancy, the guidelines for the management of rash illness in pregnancy, and also of the early signs of congenital rubella.

Funding

UCL Great Ormond Street Institute of Child Health and the NHS Infectious Diseases in Pregnancy Screening (IDPS) programme (PHE).

Public patient engagement

Sense.
Web: http://www.sense.org.uk

References


Researcher contacts

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Group B streptococcal disease in infants <90 Days of age

Key points

- 856 confirmed cases - UK and ROI incidence of 0.94 per 1,000 live births.
- An increase, since 2000-2001 surveillance, in both early and late onset disease, and decrease in case fatality.
- The most common serotypes for both early and late onset disease are III and Ia; a pentavalent conjugate vaccine (ST Ia, Ib, II, III, V) would cover around 95% of all UK and Irish disease-causing serotypes.

Summary

Group B Streptococcus (GBS) is the most common cause of serious bacterial infections (e.g. septicaemia, pneumonia) in the first week of life and of meningitis in the first three months of life.1–3 Approximately 10% of babies with GBS disease will die and neurodisability occurs in up to 50% of survivors of GBS meningitis.4 Our previous BPSU study (2000-2001) remains the only national UK and Ireland enhanced surveillance study.5

Antibiotics given intravenously to the mother during labour may prevent early onset (EO) GBS disease; national guidelines introduced in 2003 and updated in 2012 currently recommend this for women with certain risk factors.6 Late onset (LO) disease however is not currently preventable. A vaccine against GBS has been developed and is currently being tested in pregnant women. We therefore need to collect the best available evidence in order to assess the impact of current prevention guidelines as well as providing the baseline for a GBS vaccine program.

Surveillance period

April 2014 - April 2015 (inclusive).

Methodology

Details of the study protocol are available at http://www.rcpch.ac.uk/bpsu/gbs.

Data capture ascertainment was enhanced through microbiology laboratory notifications to the public health agencies of England, Wales, Scotland, Northern Ireland, and the Republic of Ireland. The notifications were then matched with notifications from paediatricians. Each laboratory was also contacted individually in order to confirm the completeness of the laboratory surveillance. Paediatricians or laboratories were then contacted if the case was not confirmed from both sources.

Isolates for the cases were collected by Public Health England, Health Protection Scotland, Public Health Agency Northern Ireland, Health Protection Surveillance Centre ROI, and Public Health Wales. Serotyping and whole genome sequencing was performed by Public Health England and Health Protection Ireland.

Analysis

There were 856 cases of invasive GBS in infants <3 months of age captured over the 13 month surveillance period. In 657 (76.8%) of the cases complete information from both clinicians and microbiology laboratories was available whilst in 142 (16.6%) the information was from microbiology laboratories alone. In 59 cases (6.9%) the information was only from paediatricians, with no laboratory confirmation.

Initial sources were paediatrician notifications to the BPSU, laboratory notifications, isolates sent to the

Figure 4: Initial sources of cases - Euler diagram 1
reference laboratories, and direct contact with the laboratories. The distribution of these is displayed in Euler Diagram 1 (Figure 4). The distribution of all of the sources the cases were notified from is displayed in Euler Diagram 2 (Figure 5).

The overall incidence of invasive GBS in young infants in 2014–2015 was 0.94 per 1,000 live births. The EO incidence is 0.57 per 1,000 live births (n=517, 95% CI; 0.52-0.62); the LO incidence is 0.37 per 1,000 live births (n=339, 95% CI; 0.33-0.41). Since the BPSU surveillance of 2000–2001 there has been an increase in the incidence of invasive GBS disease in all five British Isles countries, both in EO and LO disease. The burden of EO incidence has not declined despite the presence of national prevention guidelines. The incidence was similar across the five countries; the lowest incidence (total, EO and LO) was in the Republic of Ireland. Since the 2000–2001 surveillance there has been an increase in overall, EO, and LO incidence.

There were 53 deaths, 41 of these were within seven days of infection, and 21% of the deaths were in infants with meningitis. The case fatality rate is 6.2%. The overall case fatality rate fell significantly from 2000–2001 (9.7% to 6.2%, p=0.04) with a greater decrease in early onset case fatality (10.6% to 5.2%, p=0.01) than in late onset (8% to 7.7%, p=0.97). Half of the deaths were in babies born prematurely, of both the EO and LO deaths of babies born prematurely, 45% were in babies born at fewer than 27 weeks and weighing under 1500 g.

There were 155 meningitis cases. The meningitis incidence is 0.17 per 1,000 live births (95% CI; 0.10-0.20). Of those cases with available clinical information there were 57 cases of early onset meningitis (11%) and 98 cases of late onset meningitis (29%). Three of the 57 babies with early onset meningitis and eight of the 98 babies with late onset meningitis died. 86% of all cases of invasive GBS had a lumbar puncture performed, of the 14% who did not the procedure was either unsuccessful or the baby deemed too ill in 65%. We are only aware of one situation in which the family refused the procedure.

The median duration of EO antibiotic treatment was 10 days (IQR 7-10 days), and of LO antibiotic treatment 10 days (IQR 10-14 days). The median duration of antibiotic treatment for meningitis was 14 days (IQR 14-21 days).

Of those EO cases where clinical information was available (n=429) 35% had one or more of the Royal College of Obstetricians and Gynaecologists (RCOG) Green-top Guideline No. 36 (The Prevention of Early-onset Neonatal Group B Streptococcal Disease) – specified risk factors for EO disease (maternal swab positive for GBS at any time in pregnancy, suspected chorioamnionitis, maternal fever in labour, previous baby with GBS disease, GBS bacteriuria). Of the mothers with these recognized risk factors 44% received antibiotics during labour (intra-partum antibiotic prophylaxis (IAP)). The median time of the IAP administration was 2 hours before birth (IQR 1-4 hours). 12 different antibiotic combinations were used. For the 9% of mothers who had a swab positive for GBS during pregnancy there were a variety of reasons that these were done, the commonest being vaginal discharge. 45% of these women received antibiotics during labour.

22% (n=94) of early onset cases and 39% (n=107) of late onset cases were babies born prematurely. 20% (n=55) of late onset cases were neonatal unit patients who had not yet been discharged, 95% of these babies had been born prematurely.

Overall, of the babies who survived and whose discharge status is known, 91% were clinically well at discharge: 93% of the early onset babies and 88% of the late onset babies. In 2000–2001 7% of those with known discharge status were felt to have major, minor, or possible disability. In 2014–2015 this is similar at 9.4% (7.4% in EO and 12.4% in LO).
The commonest serotypes of the isolates causing invasive GBS were ST III and Ia. There was wider variation in the early onset serotypes with 51% being ST III and 19% ST Ia compared with 70% and 14% respectively in the late onset isolates. Of note, resistance to clindamycin and erythromycin was found in 17% and 24%, particularly in serotypes II and V.

Discussion
This surveillance study provides us with detailed information on the current burden of invasive GBS disease, the presence of risk factors, and the changes in disease incidence since the previous national surveillance 15 years ago. It provides comprehensive serotype and resistance information on GBS isolates. It will allow us to emphasise the on-going burden of this disease (and to estimate the costs associated with this disease) despite the presence of national guidelines on prevention, to reinforce and reinvigorate these risk-based guidelines to ensure better compliance and to feed into the current review on the place for swab-based screening. As neither of these approaches will impact on LO disease, which has increased most significantly over this period, it emphasises the potential role for prevention through maternal vaccination which might impact on both EO and LO disease. It identifies which serotypes should be included in such a vaccine to provide optimal coverage for UK and Irish babies.

Funding
Meningitis Now.
Web: https://www.meningitisnow.org/

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References

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Co-investigators
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Dr Catherine O’Sullivan
HIV infection & perinatal HIV exposure

Key points

- The number of children born each year in the UK and Ireland to women with diagnosed HIV infection has stabilised in recent years and is currently under 1,200; the mother to child transmission rate from diagnosed women is now under 0.5%.
- New diagnoses of children born in the UK and Ireland have fallen from 40-50 per year in the early 2000s to under 10 per year since 2012.
- The NSHPC continues to audit circumstances of all perinatal infections reported in the UK (from 2006); 124 children were reported by end 2015, with around two-thirds born to women undiagnosed at the time of delivery.

Summary

National surveillance of paediatric AIDS started in 1986 and was extended to include HIV infection and perinatal HIV exposure in 1989; it is based on comprehensive, anonymised, paediatric and obstetric reporting. Data from all sources are combined as the National Study of HIV in Pregnancy and Childhood (NSHPC) at the UCL - Institute of Child Health.1 The NSHPC monitors changing patterns of HIV infection and diagnosis in pregnant women and children and tracks changes in pregnancy management and mother-to-child transmission (MTCT) rates.

Amongst almost 2,600 children diagnosed with HIV infection in the UK and Ireland, the majority acquired infection through MTCT, and around two-thirds were born abroad, mostly in sub-Saharan Africa.

The number of births in the UK and Ireland to diagnosed women increased markedly from about 100 in 1997 to over 1,400 annually between 2007 and 2010. There has been some decline since then, with fewer than 1,200 births reported each year since 2013. Antenatal HIV screening, introduced as a universal offer from 2000, is taken up by over 95% of pregnant women in the UK, so very few HIV-positive women now remain undiagnosed at the time of delivery (https://www.gov.uk/government/organisations/public-health-england). By 2009 40% of pregnancies were a second or subsequent pregnancy since the woman's HIV diagnosis.2 MTCT rates among diagnosed women reduced from 2.1% in 2000-2001 to under 0.5% since 2010-2011; this compares with an estimated 20-30% from undiagnosed women.3 Fewer than 10 infants now acquire infection each year in the UK and Ireland, and most of these have mothers who were not aware of their HIV at the time of delivery. The circumstances of recent UK-born cases were explored in the NSHPC audit of perinatal HIV infection.

Methodology

Data capture uses standard BPSU methodology; details of the study protocol are available at www.rcpch.ac.uk/bpsu/hiv.

Surveillance period

Surveillance started in June 1986 and is reviewed annually. Follow-up period: Infection status of perinatally-exposed infants is usually reported during the child’s first year of life. Long-term follow-up information on children with confirmed HIV infection is collected through the Collaborative HIV Paediatric Study (CHIPS), a collaboration between the NSHPC, the MRC Clinical Trials Unit, and clinicians (http://www.chipscohort.ac.uk).

Analysis

There had been 11,157 BPSU reports by the end of 2015. Of these 8,548 were confirmed cases of HIV infection or exposed infants at risk of vertical transmission; 1,020 reports have not yet had status confirmed. The remaining 1,589 reports were duplicates or errors. A further 12,563 confirmed cases and exposed infants have been reported through other sources (see study protocol). The remainder of this report includes verified data from all reporting sources.

By the end of December 2015, 21,112 HIV-infected or exposed children had been reported to the NSHPC, 19,110 (91%) of these since 2000 (see Table 4). In England, the proportion of reports made from the London regions has decreased from over 70% prior to 2000 to around half since then.

Children born to HIV-positive women: Most paediatric reports (20,683/21,112, 98%) were of
children born to HIV-positive women (Table 5). Of these children, 2,167 (10%) were known to be infected, and 15,808 (76%) uninfected by the end of 2015; infection status for the remaining 2,708 (13%) had not yet been reported, but the majority were recent reports and very few are likely to be infected children.

Since 2013 the annual number of births to diagnosed women in the UK and Ireland stabilised at under 1,200 (reports for recent years are still incomplete) (Table 5). The NSHPC reported an overall transmission rate of just under 0.5% for births to diagnosed women 2010-2011 (9/1,975, 0.46%, 95% CI: 0.2-0.9%), declining from 2.1% in 2000-2001. The primary reasons are the increased proportion of women on combined antiretroviral therapy (cART) in early pregnancy and decreased frequency of late initiation or non-receipt of antenatal cART. A substantial proportion of pregnancies reported are second or subsequent pregnancies since maternal HIV diagnosis. 2

Infected children: Since surveillance started in 1986, 2,596 children with HIV infection have been reported; this includes 267 probably infected in the course of treatment for haemophilia, all born before 1985 and reported before 1995, leaving 2,329 mostly perinatally infected children. Overall 55% of children reported with HIV infection were born abroad, the majority in sub-Saharan Africa (89%); this proportion increased from about one-third of those diagnosed before 2000 to about two-thirds of those diagnosed since. Among 2,329 mostly perinatally infected children, 282 (12%) are known to have died, 126 (5%) to have gone abroad and 519 (22%) to have transferred to adult services; a further 385 (17%) are lost to follow up. To date there have been nearly 100 pregnancies in 63 perinatally infected women reported to the NSHPC as children.

New diagnoses for UK and Irish born children fell from 40-50 per year (2000-2006), to 20-30 (2007-2011), then further to below 10 (2012 onwards). There has been a decline in the age at diagnosis over time. Among children born in the UK and Ireland between 2000-2004, the median age at diagnosis was 1 year (IQR: 0.3-3) compared with 3 months (IQR: 0-0.8) for those born since 2010. Children born abroad were diagnosed at a later age but their median age has declined from 6 years (IQR: 2.8-8.2) for those born 2000-2004 to 2.5 years (IQR: 0.3-3.1) for those born since 2010.

Discussion

The epidemiology of HIV in pregnancy in the UK has changed considerably since surveillance started. Today, only 15% of reported pregnancies are in women unaware of their HIV infection status at the start of their pregnancies, with a high

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>England total</td>
<td>1,571</td>
<td>16,450</td>
<td>18,021</td>
</tr>
<tr>
<td>London</td>
<td>1,119 (71%)</td>
<td>8,086 (50%)</td>
<td>9,204</td>
</tr>
<tr>
<td>North</td>
<td>181 (11%)</td>
<td>2,606 (16%)</td>
<td>2,787</td>
</tr>
<tr>
<td>Midlands &amp; East</td>
<td>128 (8%)</td>
<td>3,642 (22%)</td>
<td>3,770</td>
</tr>
<tr>
<td>South</td>
<td>144 (9%)</td>
<td>2,116 (13%)</td>
<td>2,260</td>
</tr>
<tr>
<td>Wales</td>
<td>26</td>
<td>269</td>
<td>295</td>
</tr>
<tr>
<td>Northern Ireland</td>
<td>4</td>
<td>118</td>
<td>122</td>
</tr>
<tr>
<td>Scotland</td>
<td>231</td>
<td>601</td>
<td>832</td>
</tr>
<tr>
<td>Ireland</td>
<td>170</td>
<td>1,672</td>
<td>1,842</td>
</tr>
<tr>
<td>Total</td>
<td>2,002</td>
<td>19,110</td>
<td>21,112</td>
</tr>
</tbody>
</table>

Table 4: HIV infection and infants born to HIV-positive women (all reporting sources) Region and time period of report (notified by 31 December 2015)

<table>
<thead>
<tr>
<th>Year of Birth</th>
<th>Infected</th>
<th>Indeterminate</th>
<th>Not infected</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1984-1999</td>
<td>111</td>
<td>141</td>
<td>898</td>
<td>1,150</td>
</tr>
<tr>
<td>2000-2005</td>
<td>62</td>
<td>308</td>
<td>4,629</td>
<td>4,999</td>
</tr>
<tr>
<td>2006-2008</td>
<td>26</td>
<td>166</td>
<td>3,691</td>
<td>4,083</td>
</tr>
<tr>
<td>2009-2011</td>
<td>16</td>
<td>304</td>
<td>3,776</td>
<td>4,096</td>
</tr>
<tr>
<td>2012-2015*</td>
<td>9</td>
<td>1,712</td>
<td>1,712</td>
<td>3,443</td>
</tr>
<tr>
<td>Total</td>
<td>224</td>
<td>2,631</td>
<td>14,500</td>
<td>18,360</td>
</tr>
</tbody>
</table>

*reports for recent years are subject to reporting delay
proportion conceiving on cART. In the context of the policy of treating all people living with HIV early, this proportion is likely to increase in the future. The number of births to HIV-positive women in the UK and Ireland has declined from a peak of 1,400 per year around 10 years ago, and has been relatively stable at around 1,100-1,200 a year since 2013; this decline partly reflects a stabilization in relatively stable at around 1,100-1,200 a year since 2013; this decline partly reflects a stabilization in the number of sequential pregnancies to women having subsequent pregnancies after their initial HIV diagnosis. MTCT rates from diagnosed women have declined from about 2% in 2000 to under 0.5% since 2010-11 with extremely low rates among women who received optimal treatment according to the British HIV Association guidelines (http://www.bhiva.org.uk). These trends mean that there are now large numbers of HIV-exposed uninfected children born each year who were exposed to antiretroviral drugs for their entire gestation.

Despite high uptake of antenatal testing and interventions to prevent MTCT, some infants are still acquiring HIV infection perinatally or through breastfeeding. The NSHPC audit of perinatal HIV infection covering children born from 2006, confirmed that at least 60% of these (77/124) were born to the minority of women with HIV infection who remain undiagnosed at delivery, with a few likely infected following maternal seroconversion since delivery. The audit has provided supplementary information to understand better the circumstances around transmissions that occur despite low background MTCT rates. Findings have shown that the majority of these mothers had at least one additional complicating issue such as immigration status or housing problems. Other issues reported included difficulties with adherence, declining screening in pregnancy and seroconversion during or after pregnancy.

Almost two-thirds of infected children diagnosed since 2000 in the UK or Ireland were born abroad, mostly in sub-Saharan Africa. Median age at diagnosis continues to decline as children are picked up earlier through maternal screening and an increasing proportion are being diagnosed prior to arrival in the UK; however median age of newly diagnosed children is likely to remain higher than for those born in the UK.

It is essential to continue to monitor the health and well-being of perinatally infected young people into adult life. Following on from the NSHPC and CHIPS surveillance studies, a prospective cohort study started recruitment at the end of 2012, and by 2015 had recruited over 300 young people living with HIV, and about 100 controls. AALPHI (Adolescents and Adults Living with Perinatal HIV) aims to explore the impact of life-long HIV and long-term antiretroviral therapy on neurocognitive, cardiac and metabolic function, growth, and sexual and reproductive health (more details at http://www.ctu.mrc.uk). The pregnancies now being reported in women themselves infected vertically highlight how the HIV epidemic in the UK is maturing.

Acknowledgements

During 2015 the NSHPC team at UCL-ICH included Rebecca Sconza, Helen Peters, Kate Francis, Anna Horn, Grazziela Favaro and Icina Shakes. We were also supported by Catherine Peckham and our steering group (https://www.ucl.ac.uk/nshpc/people/steering-group). Past and current PhD students (Claire Townsend, Shema Tariq, Clare French and Laura Byrne) have also made substantial contributions to recent analyses and publications.

Funding

This study is funded mainly from Public Health England’s Centre for Infectious Disease Surveillance and Control, and NHS Infectious Diseases in Pregnancy Screening (IDPS) programme (part of PHE); additional support has come from the collaborating institutions.

Public patient engagement

Positively UK.
Web: http://www.positivelyuk.org

Body and Soul.
Web: http://www.bodyandsolecharity.org

References


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Co-investigators

UCL Great Ormond Street Institute of Child Health:
Dr Pat Tookey; Professor Mario Cortina-Borja
Key points

- The study aims to ascertain the current incidence and complication rates associated with exchange blood transfusion (EBT) in newborns under 28 days of age.
- 112 babies underwent 142 EBTs (range 1-5 per baby).
- The commonest indication for EBT was hyperbilirubinaemia secondary to Rhesus haemolytic disease of the newborn.
- First BPSU study to involve the National Blood Transfusion Service.

Summary

Many babies develop a mild or moderate level of jaundice (a yellow colouring of the skin and eyes) in the newborn period. Often this can be treated with light therapy (phototherapy) and is harmless. Some babies, however, develop particularly high levels of bilirubin (the substance which causes jaundice) in the newborn period. An important cause is a blood group difference between the mother’s and the baby’s blood that leads to the development of antibodies. These antibodies cause the baby’s red cells to break down, leading to low haemoglobin (anaemia) and high levels of bilirubin (a yellowish pigment found in bile and made by the liver). Very high bilirubin levels can cause brain damage resulting in cerebral palsy and / or deafness. Neonatal Exchange Blood Transfusion (EBT) is a treatment that removes the bilirubin and maternal antibodies from the baby’s bloodstream and can prevent brain damage.

The study aims to ascertain the current incidence and complication rates (including death) of EBT, as well as the practical difficulties of performing an EBT. There is very little known about our understanding of the effect of current EBT procedures on the baby’s clotting and platelet count, and therefore uncertainty about when the baby should have additional blood component support. The data collected will enable better recommendations, and will be invaluable to guide future clinical practice and the development of new neonatal exchange red cell components. The information will also be useful for counselling parents about the procedure.

Surveillance period

October 2014 - October 2015 (inclusive).

Methodology

Data capture uses standard BPSU methodology; details of the study protocol are available at http://www.rcpch.ac.uk/bpsu/ebt.

Analysis

During the surveillance period 160 notifications were received, 5 were errors and 25 duplicates. Data for 18 children remains outstanding.

There were 112 babies who underwent 142 EBTs; 79% (88) infants had just one EBT, 16% (16) had two and 5% (6) had three or more. The median gestational age at which the procedure was carried out was 36 weeks (range 28-41weeks). Median birth weight was 2,639g (range 617-4440g)

The primary indication for EBT was hyperbilirubinaemia (n=97 babies), anaemia (n=18) and hydrops (n=3). In some babies more than one indication was given (Figure 7)

The main underlying cause of hyperbilirubinaemia was Rhesus Haemolytic Disease of the Newborn (HDN) in 45 (40%), ABO incompatibility in 34 (30%). See Figure 8 overleaf.

EBT were performed in tertiary level Newborn Intensive Care Units (NICU) in 67% of babies, in level two Special Care Baby Units (SCBUs) in 28%, in Paediatric Intensive Care (PICU) or High Dependency Units (HDU) in 4%, and on the paediatric ward in 1%. Intravenous immunoglobulin was also frequently given (48%) and there were high rates of platelet transfusion post-EBT.

Mortality: Four deaths were reported (3.6%), three in severely ill infants (hemophagocytic lymphohistiocytosis, congenital leukaemia, congenital cytomegalovirus infection) and one from splenic rupture during the procedure.
**Overall morbidity:** 18 (16%) babies experienced comorbidities / complications: 11 were described as having neurological impairment, and the others had hypotension, haemorrhage, arrhythmia, and renal vein thrombosis. No cases of necrotising enterocolitis were reported.

**Discussion**
There were 112 babies who underwent EBT, of whom 21% had more than one transfusion. The commonest indication for EBT was hyperbilirubinaemia secondary to HDN, which is consistent with previous reports. One death occurred during the procedure (1%), however 16% of infants experienced comorbidities or complications.

**Funding**
This study has been funded by NHS Blood and Transplant Trustees Fund and NICU Endowment Fund, St. Mary’s Hospital, Manchester.

**Acknowledgements**
We wish to acknowledge Samantha Knight and Karen Sutcliffe of the NHSBT Audit department who have been instrumental in coordinating the sending out of questionnaires, reminders, letters of thanks, inputting and collating data. Samantha Knight was also instrumental in the audit undertaken by her department in NHSBT on the fate of issued exchange transfusion units.

**References**

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**Co-investigators**
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University College Hospital: Dr Janet Rennie
Great Ormond Street Hospital: Dr Simon Hannam
Cork University Hospital: Professor Tony Ryan
Nutritional Rickets presenting to secondary care

Key points

- 180 cases were notified, and 106 clinical questionnaires were completed. So far 60 cases meet the case definition.
- The total number of included cases was lower than expected, therefore approval to extend the study for an additional year to ascertain whether the study shows a true reflection of the number of cases was granted.
- Although a completely treatable condition, rickets continues to affect children in the UK and sadly one death has occurred as a result.

Summary

Rickets is a disease of growing children. It results in the softening of their bones, so that they bend (bow-legs or knock-knees, widening of the wrists and ankles) and in very severe cases, can break. Rickets also causes pain in the bones so children may be reluctant to walk. In the long term, if not treated, it can cause poor growth so that children are smaller than usual when they grow up. It is a completely preventable disease, and is also easily treated.

The commonest cause of rickets is a lack of vitamin D. The main source of vitamin D is the sun and whilst there is some vitamin D in certain foods, we cannot get enough vitamin D just from eating a balanced diet. Recently the number of cases of rickets appears to have been increasing. Possible reasons include: lack of good quality sunlight in the UK or, not exposing ourselves to sunlight. Children with darker skin e.g. African, Caribbean, Asian and Middle Eastern, those who are growing rapidly (premature babies, infants, adolescents) and overweight children are also more at risk.

We do not know for sure how great a problem rickets is in the UK. To inform policy and guidance on prevention and treatment, we aim 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 how it presents in children and how it is treated.

Surveillance period

March 2015 - March 2017 (inclusive).

Methodology

Data capture uses standard BPSU methodology; details of the study protocol are available at http://www.rcpch.ac.uk/bpsu/rkt.

Analysis

These are interim findings and the final results of the study are due to be published at the end of the second year of surveillance in 2017.

Over 13 months (from March 2015 to March 2016) a total of 60 cases met the case definition. There was no difference in the presentation of rickets by sex (males 52%, females 48%). The age-groups most likely to present were children aged 1-2 years, followed by children aged 2-5 years. Of notified cases, 25% were of Pakistani origin and 23% were of African origin. As expected there was seasonal variation with majority of cases diagnosed in the Spring (Figure 10). At the time of diagnosis only 14% of children were on vitamin D supplements. Following diagnosis, of the services available the majority of clinicians requested primary care services to administer treatment (41%).

Figure 9: Map of confirmed cases

![Figure 9: Map of confirmed cases](image-url)
Follow up appointments had been arranged for all cases. One child died of dilated cardiomyopathy that was caused by vitamin d deficiency. There was a good positive correlation between biochemical and radiographic data, for identifying rickets.

Discussion

The data presented is an interim analysis so we are not yet able to calculate the incidence. As the number of cases reported is less than expected, the surveillance period has been extended to March 2017 to allow a more precise estimation of incidence. However, it is clear that rickets continues to affect children in the UK and sadly one death has occurred as a result. It is important to identify mothers with vitamin d deficiency, as supplementing their children may help in preventing rickets in their offspring. As there was good correlation, we strongly recommend performing both x-rays and biochemistry to enable accurate case ascertainment.

Funding

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References


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RCPCH: Karina Pall
BPSU: Richard Lynn
Progressive intellectual and neurological deterioration in children (including Creutzfeldt - Jakob disease)

Key points

- Continuing surveillance of UK children with progressive intellectual and neurological deterioration (PIND) is important to ensure that new cases of variant Creutzfeldt-Jakob disease (vCJD) are not being missed among the numerous rare neurodegenerative disorders of childhood.
- The study provides unique information about the epidemiology of neurodegenerative diseases in UK children. From May 1997 until May 2016, 4,029 children have been notified; 1,728 children have a known diagnosis other than vCJD, with over 190 different neurodegenerative disorders in this diagnosed group.
- Six cases of vCJD have been reported to the study since December 1998; four have been classified as “definite” and two “probable”; all have now died.
- The National Creutzfeldt-Jakob Disease Surveillance Unit in Edinburgh reports that there have been 178 deaths from definite or probable vCJD in patients of all ages. Until 2016 all these cases were methionine homozygous at codon 129 of the prion protein gene (PRNP). It is significant that the first confirmed methionine / valine heterozygous vCJD adult case has recently been identified (2016).

Summary

Active prospective surveillance of UK children with progressive intellectual and neurological deterioration (PIND) commenced in May 1997.1 Funded by the Department of Health (England) [121/5443], it is being carried out via the BPSU in conjunction with the National Creutzfeldt-Jakob Disease Surveillance Unit in Edinburgh (NCJDSU) and Public Health England. The study strategy is to look at the broad group of rare neurodegenerative disorders affecting children, carefully examine the clinical details and determine whether there are cases of vCJD amongst these PIND cases. This unique dataset provides the opportunity to detect vCJD cases and highlight the variety of PIND conditions in the UK.2

Methodology

Data capture uses standard BPSU methodology; details of the study protocol are available at http://www.rcpch.ac.uk/bpsu/pind

Surveillance period

May 1997 – April 2017 (inclusive) and is reviewed annually.

Analysis

By May 2016, 4,029 children had been notified; 199 are still “under investigation” by their paediatricians; 1,830 did not meet the PIND definition, were duplicate or error notifications and 67 cases remain outstanding. The remaining cases were classified as follows:

Definite and probable cases of vCJD: Six cases of vCJD (four definite and two probable) have been notified - the youngest was a girl aged 12 years at onset. There were three other girls (two aged 14 years and one aged 13 years at age of onset) and two boys aged 15 years at onset. The last child who developed symptoms did so in 2000. All have now died and neuropathology has confirmed vCJD in four cases; a post-mortem was not carried out on the remaining two cases.

Children with PIND who have definite diagnoses other than vCJD: More than 190 distinct disorders were diagnosed in these 1,728 children. In the diagnosed cases the five commonest groups are outlined in Figure 12 overleaf.

Figure 11: Florid plaque vCJD x 400 haematoxylin eosin strain is characterised by amyloid plaques that sit in the regions of greatest spongiform change
Children with PIND and no underlying diagnosis (idiopathic group): The Expert Group meet regularly to discuss this group of children, currently 199. If a “new” variant of vCJD should arise or if the paediatric presentation differed from the adult presentation, this group could include such a phenotype. However, there is currently no evidence of a “new” unrecognised disorder in this group.

Discussion

During 19 years of surveillance, six children presenting with vCJD under 16 years of age have been notified to the study, including four with definite vCJD and two with probable vCJD. There remains concern that more childhood cases may appear, perhaps related to an underlying genotype, and children within the ‘idiopathic’ PIND group are under regular review. Children are still at risk of vCJD infection by blood, plasma products, surgical and dental instruments and theoretically via vertical transmission.

Continued surveillance is essential as there are still many unanswered questions about this relatively new disorder – in particular, the number of children who may be incubating vCJD, the length of the incubation period and the exact nature of transmission (particularly as the first confirmed adult case of heterozygous vCJD has recently been described). Meanwhile the study continues to yield unique information about the epidemiology of childhood neurodegenerative disorders in the UK. The PIND team continue to present these data at scientific meetings and to publish papers in the relevant journals.

References


Funding

Department of Health England.

Public patient engagement

Creutzfeldt-Jakob disease support network. Web: http://www.cjdsupport.net

Batten disease family association. Web: http://www.bdfa-uk.org.uk

Society for mucopolysaccharide diseases. Web: http://www.mpsociety.co.uk

ALDLife (Adrenoleukodystrophy). Web: http://www.aldlife.org


Researcher contacts

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Figure 12: Five most commonly reported PIND diagnostic groups
Surgical ligation of the patent ductus arteriosus in premature babies

Key points
- The incidence of PDA ligation was 146 per 10,000 live births in those less than 32 completed weeks of gestation.
- The commonest reason for PDA ligation was inability to wean respiratory support.
- Ligation related complications occurred in 20% but no deaths were attributable to ligation.
- Data has been presented to the World Congress of Perinatal Medicine in Madrid in November 2015 and to the Royal College of Paediatrics in April 2016.

Summary
The ductus arteriosus is a normal connection between the pulmonary artery and the aorta in the fetus but usually closes after birth. In premature babies the ductus arteriosus can remain open and is then called a patent ductus arteriosus (PDA). The abnormal flow of blood through the PDA has been associated with chronic lung disease, necrotising enterocolitis and retinopathy of prematurity. It can also cause symptoms of cardiac failure and poor growth. It is not always clear when a PDA becomes haemodynamically or clinically significant and therefore requires treatment. Medical treatment to close a patent ductus arteriosus is with non-steroidal anti-inflammatory drugs. If medical treatment is contraindicated or not successful, a small minority of premature babies are referred for surgical ligation of their PDA. Previous studies have been small and of a retrospective nature.

This study aims to describe the frequency of PDA ligation, and the clinical characteristics of babies who undergo ligation to manage this condition. The study will provide information to paediatricians to help to guide medical decision-making on which babies should be referred for ligation of a PDA and provide data regarding surgical and non-surgical morbidities to aid paediatricians in counselling parents of such babies.

Surveillance period
September 2012 - September 2013 (inclusive).

Methodology
Data capture uses standard BPSU methodology; details of the study protocol are available at http://www.rcpch.ac.uk/bpsu/pda.

Analysis
During the surveillance period a total of 731 cases were reported, of which 393 were confirmed, 201 errors 70 duplicates 67 not data collected.

Incidence: 35/100,000 live births in England; 146 per 10,000 live births in those less than 32 completed weeks gestation; 1 per 10,000 live births between 32 and 36 weeks gestation

Procedure: Echocardiography was performed (on all suspected cases) in 213/267 (80%) of the referring centres. Of the 248 completed replies NSAIDS were routinely offered prior to duct ligation in 172 (69%). Respiratory support in terms of ventilation was required in 217 of 263 (83%) for which replies were received. 105 ligations were undertaken as day cases. 240 were reported as open ligations, seven were reported as catheter occlusions

Post-operative complications: These were reported in 245 cases, five (2%) hand wound infections, 22 (9%) pneumothoraces and two chylothoraces (<1%). The most common ‘other’ complication was hypotension / hypoperfusion which was reported in nine (4%) cases. 17 deaths were reported – none directly related to the PDA closure. 156 were reported as having chronic lung disease, 12 had radiologically confirmed necrotising enterocolitis

Table 6: Patient characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median (range)</th>
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<tr>
<td>Male : Female</td>
<td>60 : 40</td>
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<tr>
<td>Birth gestation</td>
<td>25 weeks (22+5 - 34+4 weeks)</td>
</tr>
<tr>
<td>Birthweight</td>
<td>740g (421 - 3460g)</td>
</tr>
<tr>
<td>Age at ligation*</td>
<td>33 days (7 - 576 days)</td>
</tr>
<tr>
<td>Weight at Ligation*</td>
<td>1020g (500 - 4000g)</td>
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and two had an intraventricular haemorrhage with infarction.

Discussion

The median birth gestation of babies who received a PDA ligation was 25 weeks and the median birth weight was 740g. Chronic Lung Disease was the most common co-morbidity. There was variation in the type of procedure; around half were performed as day case procedures and the majority were open surgical ligations with very few undertaken as catheter occlusions.

The procedure was associated with complications in 38 of 267 (14%) cases; there were most frequently pneumothoraces, although clinically significant hypotension / hypoperfusion was also relatively common. There were 17 deaths but none were directly related to the ligation procedure.

Problems during the year: We have presented a poster at the RCPCH Annual Conference 2015 detailing our difficulties in getting a complete dataset. As outlined above, we therefore opted for analysis of those patients with a minimum dataset.

Funding

Sir Peter Tizard Research Bursary.

Public patient engagement

Bliss.

Web: http://www.bliss.org.uk

References


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University Hospitals of Leicester: Dr Arthi Lakshmanan
APPENDIX - Publications 2015 -2016

Acute pancreatitis

Congenital syphilis

HIV infection & perinatal HIV exposure


Intussusception

Progressive intellectual and neurological deterioration
### Membership of Scientific Committee 2015

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
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<tbody>
<tr>
<td>Dr Richard Reading</td>
<td>Chair</td>
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<td>Medical Advisor (non-infectious disease), UCL - Institute of Child Health</td>
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<tr>
<td>Dr Simon Lenton</td>
<td>Consultant Paediatrician</td>
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<td>Dr Simon Nadel</td>
<td>Consultant in Intensive Care</td>
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<tr>
<td>Dr Kevin Pollock</td>
<td>Senior Epidemiologist, Health Protection Scotland</td>
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<tr>
<td>Professor Alastair Sutcliffe</td>
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<tr>
<td>Dr Dominik Zenner</td>
<td>Public Health England</td>
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* Stepped down in 2016*