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MANAGEMENT OF SEPSIS

N Ninis. *St Mary's Hospital, London, UK*

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Sepsis is 'A life-threatening organ dysfunction caused by a dys-regulated host response to infection' This definition is perhaps the start of the problem.

The exact incidence of sepsis is unknown, an apparent increased incidence may just be due to better recording of cases. Cases of missed sepsis have recently been highlighted in the press, been the subject of the Health Services Ombudsman website 'Time to Act' and even resulted in criminal prosecution for doctors mismanaging sepsis. The Department of Health has made the recognition and early management of sepsis the target of a major national campaign.

Recognition of sepsis involves measuring basic clinical data and simple laboratory tests. It is not complex but it remains an area fraught with difficulty for clinicians.

There are a myriad of guidelines both long (NICE sepsis) and short (sepsis 6) which are not complex, so why is it still so hard?

Human factors result in both diagnostic errors and failure to adhere to protocols. This talk will focus on the cognitive biases which impede sepsis recognition and contribute to clinical errors. Improving sepsis recognition may take more than more protocols.

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SWINE 'FLU VACCINATION – THE GOOD NEWS AND THE BAD NEWS

AM Winstone, L Stellitano, C Verity. *PIND Research Group, Addenbrooke's Hospital, Cambridge, UK*

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Background Guillain-Barré syndrome (GBS) can be associated with 'swine 'flu' vaccination, so in 2009 surveillance for GBS and Fisher syndrome (FS) was established via the British Paediatric Surveillance Unit (BPSU) before UK immunisation against pandemic H1N1 influenza commenced. Then in 2010 there were reports from Scandinavia of an association between narcolepsy and Pandemrix (a monovalent pandemic strain 'flu vaccine containing the oil-in-water adjuvant AS03). To investigate this in the UK it was necessary to identify retrospectively children who had been diagnosed with narcolepsy from before the 2009 pandemic: the BPSU system was not suitable for this.

Results BPSU GBS study: 112 children with GBS (66 boys and 46 girls) and 3 boys with FS were identified between September 2009 and September 2011 inclusive. There was an infection in the 3 months preceding onset in 92/112 GBS and 3/3 FS cases. In England, 7 had received pandemic A/H1N1 seasonal influenza vaccine before GBS onset (3/7 within 6 months, including 1 within 3 months). The number of GBS cases who had been vaccinated was no greater than expected by chance.

Narcolepsy study: 16 sleep centres and paediatric neurology centres in England identified 75 cases aged 4–18 years with narcolepsy onset after January 1 st 2008. Eleven were vaccinated before onset; seven within 6 months. The odds ratio for vaccination at any time prior to onset in cases diagnosed by July 2011 was 14.4 (95% confidence intervals 4.3 to 48.5) and 16.2 (3.1 to 84.5) for vaccination within 6 months of

onset. The relative incidence in a self-controlled case series analysis with onset from October 2008 to December 2010 was 9.9 (2.1 to 47.9). The attributable risk was between 1 in 57 500 and 1 in 52 000 doses.

Conclusion The BPSU GBS study found no increased risk of GBS in those children living in England after pandemic A/H1N1 2009 influenza vaccine or 2010/2011 seasonal influenza vaccine. In contrast, the narcolepsy study indicated that there was a causal association between vaccination with AS03 adjuvanted pandemic A/H1N1 vaccine and narcolepsy, confirming reports from Finland and Sweden.

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RISK OF HOSPITALISATION WITH FEVER FOLLOWING MENB VACCINATION: SELF-CONTROLLED CASE SERIES ANALYSIS

¹H Murdoch, ²L Wallace, ²J Bishop, ^{3,4}C Robertson, ¹JC Cameron. ¹Immunisation Team, Health Protection Scotland, NHS National Services Scotland, Glasgow, UK; ²Consultancy Services, Information Services Division, NHS National Services Scotland, Glasgow, UK; ³Department of Mathematics and Statistics, University of Strathclyde, Glasgow, UK; ⁴International Prevention Research Institute, Lyon, France

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Aims To investigate a possible association between fever admissions and 4 component Meningococcal B (4CMenB).

Methods 4CMenB is given at 8 and 16 weeks in the first year of life. Children included in this study were aged under 1 year in Scotland pre- and post-introduction of 4CMenB vaccine (pre—September 2014 to August 2015 and post—September 2015 to June 2016). The main outcome measure was hospitalisation for fever attributable to 4CMenB vaccine. Analysis was by self-controlled case series using linked routinely collected healthcare data, where the risk period was the 3 days immediately following receipt of a vaccine dose.

Results The post-introduction model showed an increased risk in the 3 days after dose 1 (relative incidence (RI), 10.78; 95% CI: 8.31 to 14.00) and dose 3 (RI, 9.80; 95% CI: 7.10 to 13.62), with a smaller increased risk after dose 2 (RI, 2.20; 95% CI: 1.27 to 3.82). The magnitude of these effects was greater than in the pre-introduction model. The attributable fractions were 90.7%, 54.8% and 89.7%, equating to 162, 14 and 84 vaccine attributable cases per 1 00 000 doses, respectively. This is equivalent to 102 extra hospitalisations in Scotland annually, based on a birth cohort of 55 100 and extrapolated to 1430 across the UK based on a birth cohort of 7 77 165.

Conclusion There is an increased risk of hospital admission with fever within 3 days of the routine childhood immunisations at 8 and 16 weeks following introduction of 4CMenB vaccine. The results indicate that further understanding of the current use of prophylactic paracetamol is needed. Communication to parents and health professionals has been re-examined, and guidance on the use of prophylactic paracetamol reinforced.

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NEONATAL MENINGITIS – FROM SURVEILLANCE TO EVIDENCE BASED MANAGEMENT ALGORITHM AND GUIDELINES

IO Okike. *Derby Children's Hospital, Derby, UK*

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Bacterial meningitis is a medical emergency. Prompt recognition and management is required for best outcome. Using several surveillance systems (including the BPSU, national laboratory systems, neonatal infection network and meningitis charities), we showed that the incidence has not declined amongst UK young infants in contrast to other age groups. These young infants also had a rate 70 times those of adults. We identified that nearly half of the infants did not present with fever and that there is no progression of features in the first 24 hours in contrast to what is known about children with meningococcal disease.

Additionally, there was a wide variation in management of infants including empiric antibiotics and the role of listeria has been over-estimated over time leading to wide use of a penicillin based antibiotics including infants over 1 month of age. There was also variation in follow up practice.

The findings of the our studies in addition to literature review forms the basis of our bacterial meningitis management algorithm and etool aimed at trainee doctors to communicate lessons from our research, highlight gaps in recognition and management and promote best practice.

We used anonymised case studies to create modules about recognition of clinical features, decision making, investigations, management and follow-up. We addressed key issues around timely lumbar puncture, appropriate empiric antibiotics and requirement for on-going monitoring.

The etool has been endorsed by the RCPCH and passing a test at the end of it will allow the user to collect CPD points. A pilot roll out received positive feedback with 90% rating it as useful or very useful and 97% saying that they would recommend the etool to a colleague.

We believe that this educational package will contribute to improved outcomes for these vulnerable infants. Parents of survivors show appreciation for our dissemination of the findings to improve the management of future cases. We have demonstrated the huge potential benefit of collaboration between all the surveillance systems especially when dealing with rare diseases. Our study is the pioneer BPSU study to produce a management etool.

18 KAWASAKI DISEASE – USE OF SURVEILLANCE DATA TO IMPROVE MANAGEMENT AND AWARENESS

^{1,2}RMR Tulloh, ¹AM George, ¹R Hughes, ²R McCormack. ¹Bristol Royal Hospital for Children and University of Bristol, Bristol UK; ²Societi Foundation, UK

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Background Kawasaki disease (KD) is the commonest acquired heart disease in the Western world. A British Paediatric Surveillance Unit (BPSU) study was to ascertain national incidence and demographics of KD compared to the last survey 20 years ago. In May 2016, an NHS England patient safety alert (PSA) was announced. Patients with coronary artery aneurysms (CAA+) were to be alerted to the PSA, recalled and to receive a patient specific protocol. In parallel, we wished to determine if admissions with KD increased recently.

Methods Those with KD were captured by the survey in the UK and Ireland between 02.2013 and 02.2015. BPSU 'orange card' methodology led to anonymous registration by paediatricians who completed a study questionnaire. Ethical and national information governance board approval avoided the need for consent. We also conducted a Freedom of

information (FOI) request in order to gain more knowledge about the current situation in the UK.

Results 553 children with KD satisfied inclusion criteria, boys: girls was 1.4:1, age range 2 months to 15.5 years. Most had complete disease but 119 had incomplete and 42 atypical disease. In those under 1 year of age, 51% were CAA+. Overall, 355 (68%) were Caucasian, but black African and ethnic Asian were over-represented. Peak incidence was January-March. There was an inverse relationship with population density, being most common in rural areas. Median time to treatment for the 24% of children with CAA + was 10.2 days compared to 6.8 days for those without. The FOI showed that incidence has been rising fast, increasing four-fold over the last 10 years. There has been little response to the PSA, with only 11 Trusts intending to inform patients. Many hospital trusts have no guidelines at all.

Conclusions We have made little improvement in managing KD. A marked increase in admissions in the UK coded as KD over the 10 years from 2006–2015 is associated with poor levels of awareness with late diagnosis beyond the recommended 5 days, with frequent CAA and long-term consequences. The survey and FOI will now inform new nationally agreed guidelines and an awareness and educational programme across the UK.

19 LISTERIOSIS IN NEONATES AND INFANTS IN SWITZERLAND AND CANADA

¹S Huang, ²B Abu Raya, ¹M Jost, ³R Bortolussi, ²J Bettinger, ⁴J Grabowski, ⁵T Lacaze, ⁶J Robinson, ⁷K Posfay-Barbe, ¹M Mäusezahl, ²TR Kollmann. ¹Federal Office of Public Health, Department of communicable diseases, Bern, Switzerland; ²Vaccine Evaluation Centre, BC Children's Hospital, Department of Paediatrics, Division of Infectious Diseases, University of British Columbia, Vancouver, Canada; ³Dalhousie University, IWK Health Centre, Halifax, Canada; ⁴Department of Paediatrics, University of Manitoba, Manitoba, Canada; ⁵Division of Neonatology, University of Ottawa, Ottawa, Canada; ⁶University of Alberta, Edmonton, Canada; ⁷University Hospitals of Geneva, Paediatric Infectious Diseases, Geneva, Switzerland

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Aims Neonates and infants with listeriosis are at high risk of serious disease outcomes, yet in many countries, little information is reported in routine surveillance. This study aims to begin closing this gap.

Methods Clinicians participating in the Swiss Paediatric Surveillance Unit (SPSU) or the Canadian Paediatric Surveillance Program (CPSP) recorded cases of listeriosis in neonates and infants up to the age of 6 months with information on demographic indicators, manifestation, treatment, clinical course, outcome, exposure and maternal and perinatal risk factors collected.

Results In Switzerland four cases occurred over the first 8 months of the study (April to November 2017). Half of the infants had early-onset disease (EOD, defined as onset of symptoms < 7 days of life (DOL)) and the other half had late-onset disease (LOD, defined as onset of symptoms > 7 DOL). EOD is considered to be mother-to-child transmitted, while the pathogenesis of LOD is unclear. All cases manifested with sepsis and meningitis, and one EOD case presented with skin and mucosal lesions as well. All infants made a full recovery with antibiotic treatment with no long-term sequelae noted. Notably, three of the four cases occurred in one hospital during the same week. However, it could not be established