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In this newsletter we focus on recent new studies included in our surveillance, X-linked Hypophosphataemic Rickets and Neuropsychiatric Side Effects associated with Montelukast and provide updates on some of our ongoing studies.

There have been a number of important publications in the last 12 months and a summary of these will be presented in our next newsletter.

- The unexpected COVID-19 pandemic has highlighted the importance of comprehensive and representative surveillance to allow for rapid understanding of emerging clinical problems and to inform policy. APSU continues its important role in national surveillance and we will ensure that the process remains effective, efficient and manageable for our contributors.
- APSU is keenly aware of the additional challenges faced by clinicians throughout this year due to the pandemic and we greatly
- 8 appreciate the diligence with which so many of you have continued to participate and support our surveillance.

C#VID-19



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2020 has seen a worldwide research focus on COVID-19 / SARS-CoV-2. As surveillance of COVID-19 is

already well covered by public health units across Australia, and APSU recognises the increased burden on clinicians within the current work environment, we made the decision not to conduct a COVID-19 specific study. However, we included COVID-19 co-infection related questions in the Seasonal Surveillance of Severe Complications of Influenza case report form. This study ran from 1 May 2020 to 30 September 2020, although outstanding cases can still be reported. Case Report Forms can be accessed here: ONLINE FLU Case Report Form or printable PDF FLU Case Report Form

Our colleagues in the British Paediatric Surveillance Unit (BPSU) conducted a brief study exploring delayed presentation due to concern about the reduction in the number of children attending emergency departments (ED) and assessment units (AU) in the UK during the first wave of the COVID-19 pandemic. The BPSU asked its network of paediatric consultants if children were presenting later than expected to hospital. 241 paediatricians out of 752 working in ED/AU observed delayed presentations, particularly of diabetes, sepsis and malignancies. Read the published article here: Lynn RM, Avis JL, Lenton S, Amin-Chowdhury Z, Ladhani SN. Delayed access to care and late presentations in children during the COVID-19 pandemic: a snapshot survey of 4075 paediatricians in the UK and Ireland. Archives of Disease in Childhood. 2020 Jun 24.

A similar study is currently underway with the New Zealand and Welsh Paediatric Surveillance Units.

New Surveillance Studies

X-Linked Hypophosphataemic Rickets Prevalence Study

X-linked hypophosphataemia (XLH) is a disorder of renal phosphate wasting, defective bone mineralisation, and impaired growth plate ossification.

Chronic low serum phosphorus levels result in defective bone mineralisation manifesting as rickets or osteomalacia. It is most commonly treated with daily oral phosphate and Vitamin D, however the monoclonal antibody Burosumab is a recent additional treatment available for adults and children with XLH.

We are conducting a one off survey with the aim to determine current prevalence, clinical features, complications, access to genetic diagnosis and treatment to better understand the condition in Australian children.

To date we have received over 50 completed case report forms but will continue to accept notifications and completed case report forms over the next few months.

Please report any children up to age 18 years with XLH defined as:

Rickets during childhood: Radiological evidence of rickets, alkaline phosphatase (ALP) above the normal age and gender-matched limits of the local laboratory range and serum phosphate below the normal limits of the local laboratory range

AND

Pathogenic mutation in the PHEX gene

OR

FGF23 levels above the limits of the local laboratory range

OR

Family history that supports
X-linked inheritance

Montelukast and Neuropsychiatric Events



As a result of a request from the Therapeutic Goods Administration (TGA) the APSU has commenced a one year study to identify neuropsychiatric side effects associated with Montelukast. This study will inform the ongoing review of Montelukast safety.

Over the last 20 years a range of neuropsychiatric side effects have been reported following prescription of Montelukast for indications such as asthma and allergic rhinitis.

Please report: any child with new onset of neuropsychiatric symptoms following prescription of Montelukast at any dose.

Symptoms may include:

- agitation
- restlessness
- tremor
- dream abnormalities / nightmares
- anxiousness
- depression
- Irritability
- suicidal ideation or behaviour
- disorientation
- sleep disturbance
- somnambulism
- aggressive behaviour

Surveillance Study Updates

Acute Flaccid Paralysis (AFP)

In 2019, APSU surveillance for cases of children aged <15 years with AFP, together with cases identified through the Paediatric Active Enhanced Disease Surveillance (PAEDS) surveillance system and cases reported directly to the National Enterovirus Reference Laboratory (NERL), contributed to Australia's Polio-free certification status by the WHO Western Pacific Region.

A total of 83 children with suspected AFP were reported and 63 were confirmed with non-polio AFP. The confirmed AFP case rate was 1.34 cases per 100,000 children aged <15 years, meeting the WHO target of one case per 100,000. This case rate has been consistently achieved in Australia for the past 12 years.

The APSU would like to thank all Contributors who reported AFP cases in 2019 and/or so far in 2020, especially those located outside of major cities and/or PAEDS hospitals, including John Hunter Children's Hospital, Alice Springs Hospital, Canberra Hospital, Gold Coast University Hospital, Royal Hobart Hospital, Bundaberg Hospital, Rockhampton Hospital, Northern Hospital (Epping) and Orange Health Service.

Your efforts towards achieving Australia's goal of remaining Polio-free are very much appreciated!









The Polio Expert Panel encourages all paediatricians to continue reporting all cases of AFP to the APSU.

High quality acute flaccid paralysis (AFP) surveillance is essential to maintain polio-free status.

The APSU protocol, online and PDF case report forms can be found here:

APSU AFP Protocol, ONLINE or PDF Case Report Form

Two stool samples for testing to exclude polio virus should be collected within 14 days of the onset of paralysis and sent to the National Polio Reference Laboratory.

More details at: www.vidrl.org.au/laboratories/poliovirus-reference/specimen-referral

Severe Indoor Trampoline Park Injury

Data collection commenced in November 2018 and to date we have received over 25 notifications of injuries sustained in indoor trampoline parks. The majority of injuries have been upper limb fractures but have included head and neck injury. Nearly 80 per cent have required surgical intervention.

The study was suspended for several months as indoor parks were closed throughout the country as a result of the pandemic. As the parks are re-opening, the study will be extended into mid 2021.

Please report any outstanding cases where injury has occurred during the study period—even if there has been a delay between the injury and notification to APSU.

Work continues on the standards for indoor trampoline park safety through Standards Australia and results of this study will be important to inform this process.

The case report form is available on the APSU website or follow this link: www.apsu.org.au/studies/current/



Surveillance Study Updates

Congenital Cytomegalovirus (cCMV)

Did you know that the APSU study of congenital cytomegalovirus (cCMV) infection in newborn babies and young infants aged up to 12 months is now the **longest continuously running prospective cCMV surveillance study in the world**, having commenced in 1999?

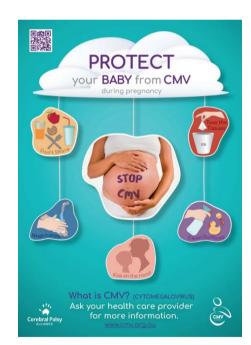
Congenital CMV infection is transmitted from infected mothers to their unborn children during pregnancy. It is often asymptomatic but can result in a spectrum of clinical abnormalities in infected children, notably hearing or visual loss, cerebral palsy and developmental delay and in rare cases, can result in death. While there is no vaccine against CMV, there are antiviral treatments for symptomatic cCMV infection, which are thought to improve outcomes in infected children.

Awareness of cCMV infection in Australia remains worryingly low, despite being the most common infectious cause of disabilities in newborn babies. Data from the APSU cCMV study have shown that the incidence of cCMV has not changed appreciably over the last 21 years. The ongoing APSU study is therefore a crucial mechanism for increasing awareness in expectant mothers and health care professionals and for improving diagnosis.

Thank you to all the APSU Contributors who have reported cCMV cases over the last 21 years

Data from the APSU cCMV study have contributed to:

- A NSW Ministry of Health agreement to enhance congenital CMV awareness through provision of information via public health units on congenital CMV.
- Development of information sheets for the general public, partly or wholly based on documents drafted by investigators from the APSU study group.
- A short online video funded and prepared by the Cerebral Palsy Alliance (led by Dr Hayley Smithers-Sheedy of CPA and Ms Kate Daly of the Congenital CMV Association of Australia) to raise awareness of congenital CMV infection and its role in the aetiology of cerebral palsy.
- Negotiations, led by Dr Lisa Hui and Dr Antonia Shand, with the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG), on including specific information for Obstetricians on congenital CMV prevention in RANZCOG-endorsed guidelines.



• Education of primary care, infectious diseases and pathology physicians about congenital CMV through webinars.

The APSU CMV case report form is currently being revised and will soon be available ONLINE.

Keep an eye on your monthly email report card for updates.

- Development of International Consensus Guidelines now used in public health and government negotiations for congenital CMV screening.
- Multiple presentations by the investigators including invited talks at the Annual Meetings of the Australian Institute of Medical Scientists/AACB, Australasian and European Societies of Infectious Diseases short course on Infectious Diseases in Pregnant women, foetuses and newborns, Australian and New Zealand Placental Research Association.

Fetal Alcohol Spectrum Disorder (FASD)

Since this study's inception in 2015, the APSU has received 904 notifications of FASD diagnosed in a child less than 15 years of age from clinicians from all over Australia. These clinicians have completed 841 case report forms, representing a response rate of 93%. After verification of case details and removal of duplicate cases, we currently have 666 confirmed cases of FASD in children less than 15 years of age.

We wish to thank all the clinicians and their administrative teams for their continued support. Our team is currently working on publishing the data from the five-year period of 2015 to 2019 – watch this space!

FASD Hub Australia Find information on Fetal Abortion Spectrum Closteric FASD in Australia Periodesionals, service providers, researches parents and cases. Wetch video FASD in Australia D

Visit the official FASD HUB Australia website for up to date Information around services, training and support, as well as the latest research findings and publications

www.fasdhub.org.au

Fetal Alcohol Spectrum Disorder Australian Register (FASDAR)

Currently, de-identified cases reported to the APSU FASD study constitute the FASDAR. New funding has recently secured from the Australian Government Department of Health which has enabled Dr Melissa Cheung to be employed as the FASDAR Manager on the FASD and FASDAR projects. Having obtained relevant approvals from the Sydney Children's Hospital Network Human Research Ethics Committee and Research Governance Office, as well as the Australian Institute of Aboriginal and Torres Strait Islander Studies Human Research Ethics Committee, the Register is moving towards inviting patients and families to be included in the register.

Surveillance Study Updates: Completed Studies

Sudden Unexpected Death in Infancy (SUDI)

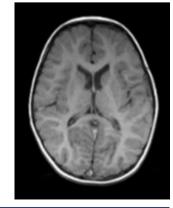
During September 2019, 234 paediatricians in NSW completed the survey on "Paediatrician experience with SUDI". The study examined paediatrician knowledge of and experience with using the NSW Health Policy Directive for Management of Unexpected Death, which has recently been updated. We were very grateful for the high level of participation and thoughtful comments provided. A summary draft report has been presented to the NSW Coroner's office and a manuscript has been submitted for publication. We believe this study will be important in developing a model of care to both support families and ensure accurate history is obtained to facilitate determination of cause of death and understanding of risk factors.

Stroke in children < 2 years old

Thankyou to all clinicians who notified children under 2 years of age with stroke, during the 2 year study period to 2019. Results from the study were to be presented at the 2020 PSANZ meeting in Sydney, which was unfortunately cancelled due to COVID restrictions.

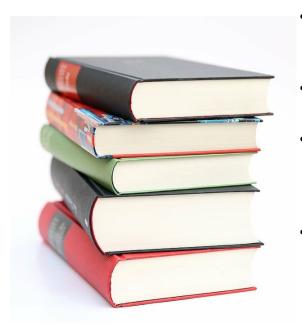
A total of 50 children were reported in whom arterial stroke was the most common type (54%). Nearly three quarters of infants presented in the first ten days of life with non-neurological presentations such as lethargy, respiratory symptoms and poor feeding and almost all were confirmed by MRI. The non specific nature of presentation means that it is likely that cases could be easily missed.

A follow up is now in progress and we appreciate the contribution made by clinicians who are also providing data to this study. We hope that this study will emphasise the need for a stroke register, similar to that in adults.



Key Publications, Presentations and Media in 2019/2020

- Erin Donnelley, Suzy Teutsch, Yvonne Zurynski, Carlos Nunez, David Lester-Smith, Marino Festa, Robert Booy, Elizabeth Elliott, Philip N Britton, and Contributors to the Australian Paediatric Surveillance Unit Seasonal population surveillance for severe neurological complications of influenza in Australian children 2008-2018. Abstract CIRCAN Virtual Symposium and RACP Trainee Research Awards. September 2020
- Teutsch SM, Nunez, CA, Morris A, McGregor S, King J, Brotherton JML, Novakovic D, Booy R, Jones, CA, Rawlinson W, Thorley BR, Elliott EJ. **Australian Paediatric Surveillance Unit Annual Report, 2019.** Commun Dis Intell (2018). 2020;44 https://doi.org/10.33321/cdi.2020.44.60. Epub 17/8/2020
- Nunez C, Morris A, Teutsch S, McGregor S, Brotherton J, Novakovic D, Rawlinson W, Jones C, Thorley B and Elliott E. Australian Paediatric Surveillance Unit Annual Report, 2018. Commun Dis Intell. https://doi.org/10.33321/cdi.2019.43.53 Published online: 18/11/2019
- Zurynski Y, Grover CJ, Jalaludin B, Elliott EJ. Vitamin K deficiency bleeding in Australian infants 1993–2017:
 an Australian Paediatric Surveillance Unit study. Archives of disease in childhood. 2019 Sep 13:archdischild-2018.
- Knight S, Elders S, Rodda J, Harvey A, Lubitz L, Rowe K, Reveley C, Hennel S, Towns S, Kozlowska K, Payne DN.
 Epidemiology of paediatric chronic fatigue syndrome in Australia. Archives of disease in childhood. 2019
 Feb 23:archdischild-2018.
- Giudice-Nairn P, Downs J, Wong K, Wilson D, Ta D, Gattas M, Amor D, Thompson E, Kirrali-Borri C, Ellaway C,
 Leonard H. The incidence, prevalence and clinical features of MECP2 duplication syndrome in Australian children. Journal of paediatrics and child health. 2019 Feb 12.
- Teutsch S, Zurynski Y, Nunez C, Lester-Smith D, Festa M, Booy R, Elliott E, and Contributors to the Australian Paediatric Surveillance Unit. Seasonal surveillance for severe complications of Influenza in Australian children. The Westmead Association Inc Hospital Week 2019 Research Symposium [Abstract & Poster]
- World Phonosurgery Congress Sep 5 6, 2019 Buenos Aires Argentina. Recurrent Respiratory
 Papillomatosis and the HPV vaccine (A/Prof Daniel Novakovic)
- ASEAN ORL-HNS Congress Aug 23, 2019 Singapore Invited Plenary Speaker Recurrent Respiratory
 Papillomatosis and the impact of the HPV vaccine (A/Prof Daniel Novakovic)
- AIPN conference Nov 2019: **Button batteries, the perfect product safety storm** (Dr Ruth Barker)



- October 30th 2019 Standards Australia: Presentation to industry group about need for horizontal standard (Dr Ruth Barker—Button Batteries)
- Choice: **Button battery safety failures** (article updated 14 March 2019)
- Choice collaboration: Sept 2019 Oral presentation at ministerial breakfast about button batteries followed by meetings with ministers and media opportunity (Dr Ruth Barker)
- 2019: Invited panel presentation at ACCC national Congress,
 March: General Safety Provision (Dr Ruth Barker)

APSU would like to acknowledge and send a sincere thank you for your long term contribution to APSU Surveillance studies. Dr Stuart G Anderson, Dr Vivian V Bayl, Prof Donald J S Cameron, Dr Andrew J Gardiner, Dr Ian E Humphrey, Dr Judith A Jaensch, Dr Edwin J Lowther, Dr Richard G Power, Dr Helen F Wilkinson, Dr Peter John Cooper, Dr John G Harvey, Dr Robert McCarthy, A/Prof Elizabeth M Thompson, Dr Margaret M Phelan, Dr Stuart Gadd, Dr Sona Kalyanpur-Rao, Dr Richard Cherry, Prof David Forbes AM, Dr Ian Shellshear, Dr Larry Roddick, Prof Mark Everard, Dr Donald Anderson, Dr Paul Tait, Dr Vicki Burneikis

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APSU staff updates

2019 and 2020 have seen two new staff members join the APSU. Dr Anne Morris has previously worked with the APSU as an investigator on AFP, Fetal Alcohol Syndrome, Pertussis in Infancy, Conversion Disorder and Early Onset Eating Disorder (EOED) study in 2008 and EOED 2 in 2018. She was also an investigator on the Canadian EOED study in 2002. Anne has returned to support the APSU research activities in addition to her clinical duties at The Children's Hospital Westmead.

In 2019 Melissa Cheung was appointed as the FASD and FASDAR Research Fellow. Melissa has a background in Pharmacy, and has recently successfully completed her PhD (Drawing Asthma: An Exploration of Patients' Illness Perceptions, Healthcare Professionals' Perspectives and University Educators' Feedback) in 2019.

Congratulations are also in order for Carlos Nunez who successfully completed his PhD (The Fat but Fit Hypothesis and Cancer Risk) in 2019.

APSU Scientific Review Panel (SRP)

Thanks are extended to our ongoing SRP members: Dr David Burgner, Dr Mavis Duncanson (NZ), Dr Fiona Mackie, Dr David Lester-Smith and Prof Elizabeth Elliott. We also welcomed new members Dr Jane Bell (retired), Dr Ravisha Srinivasjois, Dr Tasneem Karim and Dr Anne Morris.



We're working hard to bring you a better experience on our website: www.apsu.org.au

Is there something we can do better?

Do you have any suggestions?

Is there a resource you would like to see included?

Please contact us with your thoughts and suggestions at:

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APSU Contributors are now able to complete most case report forms ONLINE through our data capture management system (REDCap). Simply click on the link provided in the monthly report card email to complete the form. Links to the current APSU protocols and case report forms can be found in the monthly email report card and are also available on the APSU website. If you have any difficulties accessing the links or would like more information about completing the forms online, please contact us.

Still returning the yellow card by post? If you are one of the remaining 100 clinicians out of 1500 still receiving the yellow report card we would like to make responding easier for you.

Not currently an APSU Contributor? We would very much like you to become a member of the APSU and to contribute data to support our unique national surveillance effort.

Changed your contact details? Please let us know your new details.

To start responding via email, to join the APSU or to notify us of your changed contact details please contact us at: SCHN-APSU@health.nsw.gov.au