Here is the latest edition of the Sepsis Bulletin. The bulletin covers the latest information on sepsis and comes out fortnightly. Next edition is due 29 March 2019. Older editions are available as pdfs on the Keeping Up To Date library guide (http://libguides.bodleian.ox.ac.uk/Keeping_up_to_date)

Please also pass the bulletin on to other interested people and encourage them to sign up. Anyone can be added to the mailing list.

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SEPSIS BULLETIN
15 March 2019

Neonatal, paediatric and maternal sepsis

Can Base Excess be Used for Prediction to Early Diagnosis of Neonatal Sepsis in Preterm Newborns?
Arayici S. et al.
Mediterr J Hematol Infect Dis. 2019 Mar 1;11(1):e2019014.
Neonatal sepsis remains an important and potentially life-threatening clinical syndrome and a major cause of neonatal mortality and morbidity. The aim of this study to investigate whether values of base excess before the onset of clinical signs and symptoms of sepsis indicate infection in the early diagnosis of neonatal sepsis. This is the first study to determine the relationship between the decreased value of the base excess and early stage of neonatal sepsis. If the value of base excess <-5 mmol/L without an underlying another reason, may need close follow up of infants for neonatal sepsis and it may help early diagnosis.

Group B Streptococcus (GBS) Colonization and Disease among Pregnant Women: A Historical Cohort Study.
Edwards J.M. et al
Infect Dis Obstet Gynecol. 2019 Feb 3;2019:5430493.

Adult sepsis

Astroglia in Sepsis Associated Encephalopathy
Shulyatnikova, T. and Verkhratsky, A.
Neurochemical research, 18 February 2019
Cellular pathophysiology of sepsis associated encephalopathy (SAE) remains poorly characterised. Brain pathology in SAE, which is manifested by impaired perception, consciousness and cognition, results from multifactorial events, including high levels of systemic cytokines, microbial components and endotoxins, which all damage the brain barriers, instigate neuroinflammation and cause homeostatic failure. Astrocytes, being the principal homeostatic cells of the central nervous system contribute to the brain defence against infection. Forming multifunctional anatomical barriers, astroglial cells maintain brain-systemic interfaces and restrict the damage to the nervous tissue. Astrocytes detect, produce and integrate inflammatory signals between immune cells and cells of brain parenchyma, thus regulating brain immune response. In SAE astrocytes are present in both reactive and astrogliopathic states; balance between these states define evolution of pathology and neurological

Maternal GBS colonization is associated with early-onset neonatal sepsis and extensive efforts are directed to preventing this complication. Less is known about maternal risks of GBS colonization. We seek to provide a modern estimate of the incidence and impact of maternal GBS colonization and invasive GBS disease. This modern-day large cohort of all births over a 12-year period demonstrates a GBS colonization rate of 21.6%. This data reflects a need to assess maternal and perinatal outcomes in addition to neonatal GBS sepsis rates to inform decisions regarding the utility of maternal vaccination.

Reduction of hospital-acquired infections in the neonatal intensive care unit: A long-term commitment.
Flidel-Rimon O. et al.
Am J Infect Control. 2019 Mar 5. pii: S0196-6553(19)30005-7.
We instituted quality improvement program. We compare the infection rate before (2011-2012) and after (2013-2015). Central line associated blood stream infection episodes decreased from 15.2 to 2.29 episodes per 1000 catheter days (P = .004). We found two major changes, 1. Hand hygiene increased mainly "before aseptic task", from 69.9% to 89.9% and 2. A significant decrease in the length of the catheter use from 5.4 ± 4.5 before to 4.4 ± 2.5 days after the intervention (P = .001).

Evaluation of the effect of antenatal betamethasone on neonatal respiratory morbidity in early-term elective cesarean.
Mirzamoradi M. et al.
J Matern Fetal Neonatal Med. 2019 Mar 5:1-6.
Compared with vaginal delivery, early-term cesarean section (CS) is associated with an increased risk of neonatal respiratory morbidity. Given the role of steroids in lung maturation in preterm labor, few studies have investigated their effects on early-term delivery. Therefore, this study aimed to investigate the effect of antenatal betamethasone on neonatal respiratory morbidity in early-term elective cesarean (37-38 weeks and 6 d). The findings of this study showed that intramuscular injection of 12 mg of betamethasone in two doses, with an interval of 24 h, after 37 weeks of gestation in women undergoing early-term CS did not have a significant effect on respiratory morbidities in neonates. However, it decreased the frequency of admission to NICU, especially admission due to respiratory distress; it could indicate that the respiratory morbidities were less severe in betamethasone group than in the control group.

outcomes. In humans pathophysiology of SAE is complicated by frequent presence of comorbidities, as well as age-related remodelling of the brain tissue with senescence of astroglia; these confounding factors further impact upon SAE progression and neurological deficits.

Neurodevelopmental outcome at 2 years of age in preterm infants with late-onset sepsis
Zonnenberg, I A et al.
European journal of pediatrics, 18 February 2019
Late-onset sepsis is associated with impaired neurodevelopmental outcome in preterm infants. Preterm infants encountering late-onset sepsis by coagulase-negative staphylococci show a better cognitive outcome in comparison to other causal infectious agents in this cohort. No differences were found in neurodevelopment at 2 years of age in preterm infants with suspected lateonset sepsis, between proven and no proven infection groups. Confirmation is needed in larger cohorts with a substantial control group.

Mitochondrial quality control mechanisms as potential therapeutic targets in sepsis-induced multiple organ failure
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Journal of molecular medicine (Berlin, Germany), 21 February 2019
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Intercenter variability and factors associated with survival without bronchopulmonary dysplasia in extremely preterm newborns.
García-Muñoz Rodrigo F. et al.
J Matern Fetal Neonatal Med. 2019 Mar 5:1-8.
Variability in clinical practice may influence morbidity and mortality in extremely preterm infants. We aimed to know if there are differences in survival and survival without bronchopulmonary dysplasia (BPD) in extremely preterm infants in Spanish tertiary hospitals and the potential associated factors. Among the studied hospitals, we found great variability in clinical practice and in the rates of survival and survival without BPD. A more conservative approach to the use of oxygen and respiratory support seems to be related to an increase in survival without BPD. Complications such as PDA, sepsis, and/or NEC decrease survival without BPD. Other variables not included in the present study could be relevant and deserve further study.

Evaluation of myocardial function in neonatal sepsis using tissue Doppler imaging.
Fahmey S.S. et al.
J Matern Fetal Neonatal Med. 2019 Mar 5:1-5.
Neonatal sepsis is an important cause of neonatal morbidity and mortality especially in developing countries. Cardiac dysfunction is a major complication of severe sepsis and occurs as a part of multiple organ failure. Neonates with sepsis have evidence of left ventricular diastolic dysfunction and elevated pulmonary systolic pressure. Reduced left ventricular fractional shortening is associated with poor prognosis.

Impact of preterm birth and low birth weight on medical conditions, medication use and mortality among neonates: a prospective observational cohort study.
Undela K. et al
World J Pediatr. 2019 Mar 4.
There is a paucity of studies conducted in India on neonatal outcomes of preterm birth and low birth weight. Hence, we aimed to assess the impact of preterm birth and low birth weight on medical conditions, medication use and mortality among neonates. Medical conditions, medications prescribed and mortality rate were significantly higher among preterm and underweight neonates admitted to NICU.

Effect of a surveillance system for decreasing neonatal nosocomial infections.
Estañ-Capell J. et al

mitochondrial quality control on the progression of sepsis.

Admission characteristics predictive of in-hospital death from hospital-acquired sepsis: A comparison to community-acquired sepsis
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Hypogelsolinemia in Patients Diagnosed with Acute Myeloid Leukemia at Initial Stage of Sepsis
Wątek, M. et al
Medical science monitor : international medical journal of experimental and clinical research, 23 February 2019, Vol.25, pp.1452-1458
Gelsolin (GSN) is an actin-binding and PIP_2/Ca^{2+}-regulated protein found in the cytoplasm and blood plasma. Hypogelsolinemia occurs in a wide range of traumatic injuries and inflammatory reactions. We hypothesize that blood GSN levels will be altered in patients diagnosed with acute myeloid leukemia (AML)

Early Hum Dev. 2019 Feb 27;131:36-40.
Nosocomial infection in very low birthweight (VLBW) infants is a common complication with high morbimortality. New strategies to reduce its occurrence have recently led to the development of neonatal surveillance programs. Surveillance systems are useful to reduce nosocomial infection in VLBW infants. Reduction in antibiotic and CVC use requires longer intervention time. Promotion of breastfeeding seems to be a very effective associated strategy.

Determinants of Initial Antibiotic Duration in Very Low Birth Weight Neonates.
Charron A.C.et al
Infect Dis Ther. 2019 Mar 1.
Very low birth weight (VLBW) neonates (< 1500 g) are commonly exposed to prolonged antibiotic courses related to concerns for presumed early onset sepsis often with unclear indications. While antibiotics can be life-saving medications, prolonged antibiotic exposure (> 5 days) increases an infant's risk for necrotizing enterocolitis, late onset sepsis, colonization or infection with resistant organisms, and death. The aim of this study is to describe clinical and laboratory factors that influence the length of initial antibiotic courses in VLBW neonates. In the VLBW population, the clinical status of the neonate, as represented by maximum ventilator support in this study, was the most important factor in determining the duration of initial antibiotic treatment. Laboratory values and perinatal risk factors did not significantly influence prescribing patterns.

Epidemiology of Readmissions After Sepsis Hospitalization in Children.
Prout A.J. et al
Hosp Pediatr. 2019 Mar 1. pii: hpeds.2018-0175.
The decline in hospital mortality in children hospitalized with sepsis has increased the number of survivors. These survivors are at risk for adverse long-term outcomes, including readmission and recurrent or unresolved infections. We described the epidemiology of 90-day readmissions after sepsis hospitalization in children. We tested the hypothesis that a sepsis hospitalization increases odds of 90-day readmissions. Readmissions occur after 1 in 5 pediatric sepsis hospitalizations and increase health care costs. Sepsis hospitalization increased odds of readmission and commonly involved recurrent infection or sepsis. Clinicians caring for these patients should consider surveillance for recurrent or unresolved infection, and researchers should explore underlying mechanisms and potential interventions to reduce readmissions.

that develop sepsis, and assessment of GSN concentration will be a useful marker to determine their clinical outcome. The results presented here suggest the possible utility of GSN evaluation for diagnostic purposes. Overall, these data support the that reversing plasma GSN deficiency might be a possible new strategy in sepsis treatment.

A worldwide perspective of sepsis epidemiology and survival according to age: Observational data from the ICON audit
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Evaluating Newborns at Risk for Early-Onset Sepsis.
Good P.I. et al
Pediatr Clin North Am. 2019 Apr;66(2):321-331.
Early-onset sepsis (EOS) is an important cause of neonatal morbidity. Despite extensive study, identifying at-risk newborns remains challenging, especially if they are initially well appearing. Existing official EOS recommendations suggest a conservative approach that likely results in overtreatment of a low-risk population. Recent studies indicate that more precise risk assessment and alternative management strategies could decrease the number of infants exposed to blood draws and antibiotics during evaluations for EOS. This article reviews existing guidelines and provides an overview of the Bayesian sepsis calculator and serial observation as an alternative to laboratory studies and empirical antibiotics.

Temporal trends in neonatal mortality and morbidity following spontaneous and clinician-initiated preterm birth in Washington State, USA: a population-based study.
Richter L.L. et al
BMJ Open. 2019 Feb 1;9(1):e023004.
After a decade of increase, the preterm birth (PTB) rate has declined in the USA since 2006, with the largest decline at late preterm (34-36 weeks). We described concomitant changes in gestational age-specific rates of neonatal mortality and morbidity following spontaneous and clinician-initiated PTB among singleton infants. Timing of obstetric interventions is associated with infant health outcomes at preterm. The temporal decline in late PTB among singleton infants was associated with increased mortality among late preterm infants born following clinician-initiated delivery and increased combined mortality or severe morbidity among all late preterm infants, mainly due to increased rate of sepsis.

The value of delta neutrophil index in neonatal sepsis diagnosis, follow-up and mortality prediction.
Celik I.H. et al.
Early Hum Dev. 2019 Feb 13;131:6-9.
The complete blood cell count (CBC) and peripheral blood smear were the most commonly ordered tests for the diagnosis of neonatal sepsis. Delta neutrophil index (DNI) shows leucocyte differentiation and calculated while CBC is performed. DNI was found to be useful in the diagnose, follow-up and mortality prediction of neonatal sepsis without extra blood to CBC.

central nervous system contribute to the brain defence against infection. Forming multifunctional anatomical barriers, astroglial cells maintain brain-systemic interfaces and restrict the damage to the nervous tissue. Astrocytes detect, produce and integrate inflammatory signals between immune cells and cells of brain parenchyma, thus regulating brain immune response. In SAE astrocytes are present in both reactive and astrogliopathic states; balance between these states define evolution of pathology and neurological outcomes. In humans pathophysiology of SAE is complicated by frequent presence of comorbidities, as well as age-related remodelling of the brain tissue with senescence of astroglia; these confounding factors further impact upon SAE progression and neurological deficits.

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Changing trend of microbiologic profile and antibiotic susceptibility of the microorganisms isolated in the neonatal nosocomial sepsis: a 14 years analysis.
Mutlu M. et al
J Matern Fetal Neonatal Med. 2019 Mar 4:1-8.
Neonatal sepsis, especially nosocomial sepsis (NS) is one of the main causes of mortality and morbidity in neonates. Our aim was to investigate microorganisms responsible for NS and antimicrobial susceptibility patterns and to compare them in a different period. Our result showed that multiresistant microorganisms, especially oxacillin-resistant staphylococci and gram-negative bacilli resistant to cephalosporin have an increasing rate. Every unit should evaluate the causative agents and antimicrobial susceptibilities in order to select an appropriate regime for nosocomial sepsis. Periodic surveillance of organisms and their antibiotic resistance patterns in every unit might help physicians for proper selection of antibiotics for treatment of neonatal NS.

A meta-analysis of interleukin-6 as a valid and accurate index in diagnosing early neonatal sepsis.
Sun B1, Liang LF1, Li J1, Yang D1, Zhao XB2, Zhang KG1.
Int Wound J. 2019 Feb 7.
We aimed to systematically assess the overall value of interleukin 6 (IL-6) in diagnosing neonates with sepsis. In this study, we performed a systematic review and meta-analysis to assess the diagnostic accuracy studies of IL-6 in diagnosing neonatal sepsis. Our results suggested that IL-6 is a valid and accurate index in diagnosing early neonatal sepsis, but it still needs to be combined with other laboratory tests and specific clinical manifestations.

Systematic Review of the Effectiveness of the Neonatal Early-Onset Sepsis Calculator.
Helmbrecht A.R. et al.
J Perinat Neonatal Nurs. 2019 Jan/Mar;33(1):82-88.
Neonatal early-onset sepsis is a serious health concern for term and late preterm infants. Screening for early-onset sepsis is often challenging due to variation in practice, nonspecific laboratory markers, and clinical findings that mimic immaturity. This systematic review evaluates the evidence for the effectiveness of the Neonatal Early-Onset Sepsis Calculator (EOScalc) as a screening tool to appropriately identify neonatal early-onset sepsis and the ability to decrease unnecessary antibiotic use in late preterm and term infants. Findings included in this review suggest that utilization of the EOScalc can reduce empiric antibiotic therapy, unnecessary laboratory testing, and separation of infants and mothers without increasing infant mortality.

through a series of processes including mitochondrial biogenesis, mitochondrial dynamics, mitophagy, and transport processes. Several studies have indicated that multiple organ failure is ameliorated by restoring mitochondrial quality control mechanisms and is further amplified by defective quality control mechanisms. This review will focus on advances concerning potential mechanisms in regulating mitochondrial quality control and impacts of mitochondrial quality control on the progression of sepsis.

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Hypogelsolinemia in Patients Diagnosed with Acute Myeloid Leukemia at Initial Stage of Sepsis
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Systematic review and consensus definitions for the Standardised Endpoints in Perioperative Medicine (StEP) initiative: infection and sepsis.
Barnes J. et al.
Br J Anaesth. 2019 Apr;122(4):500-508.
Perioperative infection and sepsis are of fundamental concern to perioperative clinicians. However, standardised endpoints are either poorly defined or not routinely implemented. The Standardised Endpoints in Perioperative Medicine (StEP) initiative was established to derive a set of standardised endpoints for use in perioperative clinical trials. We defined a consensus list of standardised endpoints related to infection and sepsis for perioperative trials using an established and rigorous approach. Each endpoint was evaluated with respect to validity, reliability, feasibility, and patient centredness. One or more of these should be considered for inclusion in future perioperative clinical trials assessing infection, sepsis, or both, thereby permitting synthesis and comparison of future results.

A Framework to Tackle Risk Identification and Presentation Challenges in Sepsis.
Capan M. et al.
Am J Hosp Med. 2018 Jan-Mar;2(1). pii: 2018.002.
Sepsis trajectories, including onset and recovery, can be difficult to assess, but electronic health records (EHRs) can accurately capture sepsis as a dynamic episode. Our study addresses identification of infection, organ dysfunction, and sepsis as dynamic episodes utilizing EHR data and provides a systematic approach to detect risk factors related to sepsis onset and in-hospital mortality.

Assessment of Nursing Response to a Real-Time Alerting Tool for Sepsis: A Provider Survey.
Miller K. et al.
Am J Hosp Med. 2017 Jul-Sep;1(3). pii: 2017.021
An information technology solution to provide a real-time alert to the nursing staff is necessary to assist in identifying patients who may have sepsis and avoid the devastating effects of its late recognition. The objective of this study is to evaluate the perception and adoption of sepsis clinical decision support. Performance and preference of providers were evaluated to identify strengths and weaknesses of the sepsis alert. Effective presentation of the alert, including how and what is displayed, may offer better cognitive support in identifying and treating septic patients.

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