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 26 April 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)

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SEPSIS BULLETIN
12 April 2019

Neonatal, paediatric and maternal sepsis

Complication Rates for Pediatric Hepatectomy and Nephrectomy: A Comparison of NSQIP-P, PHIS, and KID.
Corkum KS et al
J Surg Res. 2019 Apr 4;240:182-190.
Three large national data sets are commonly used to assess operative outcomes in pediatric surgery; National Surgical Quality Improvement Program Pediatric (NSQIP-P), Pediatric Health Information System (PHIS), and Kids' Inpatient Data set (KID). Hepatectomy and nephrectomy are rare pediatric surgical procedures, which may benefit from large administrative data sets for the assessment of short-term complications. Administrative data sets provide large sample sizes for the study of low-volume procedures in children, but there are significant variations in the reported rates of perioperative outcomes between NSQIP-P, PHIS, and KID. Therefore, surgical outcomes should be interpreted within the context of the strengths and limitations of each data set.

Adult sepsis (cont.)

Sepsis-induced heparin resistance during extracorporeal membrane oxygenation
Hage, Ali et al
Canadian Medical Association. Journal; Mar 2019; vol. 191 (no. 10); p. E283
Hage and Louzada discuss patients with sepsis inducing heparin resistance during extracorporeal membrane oxygenation. The differential diagnosis for heparin resistance is large, and includes acquired antithrombin deficiency and non-antithrombin-mediated sequestration of heparin, when thrombocytopenia occurs in patients with sepsis who are on ECMO, heparin-induced thrombocytopenia and disseminated intravascular coagulation must be ruled out before sepsis can be presumed to be the cause.

Epidemiology of disseminated intravascular coagulation in sepsis and validation of scoring systems
Saito, S. et al
Journal of Critical Care; Apr 2019; vol. 50 ; p. 23
We investigated the epidemiology and outcome of disseminated intravascular coagulation (DIC) in patients with sepsis. Patients with sepsis and DIC have

Clinical impact of vancomycin heteroresistance in staphylococcal strains involved in neonatal sepsis: Discussion of a case report.
Butin M. et al
Arch Pediatr. 2019 Apr 3. pii: S0929-693X(19)30058-2.
Heteroresistance to vancomycin (HRV) represents a decreased susceptibility to vancomycin and is frequently observed in multidrug-resistant coagulase-negative staphylococci. The clinical significance of such heteroresistance is controversial, but several failures of vancomycin therapy have been related to HRV, especially in the neonatal population. Here we report the case of a preterm neonate, born at 26 weeks of gestation, who developed sepsis due to a multidrug-resistant HRV Staphylococcuscapitis isolate. Bacteremia persisted despite adequate vancomycin serum concentration and catheter removal. The patient finally recovered after replacing vancomycin by linezolid. Through this case report, we would like to alert clinicians of the potential clinical impact of HRV and to discuss the lack of therapeutic alternatives in neonates.

Risk Factors for Late-Onset Sepsis in Preterm Infants: A Multicenter Case-Control Study.
El Manouni El Hassani S. et al
Neonatology. 2019 Apr 4;116(1):42-51.
Late-onset sepsis (LOS) in preterm infants is a leading cause of mortality and morbidity. Timely recognition and initiation of antibiotics are important factors for improved outcomes. Identification of risk factors could allow selection of infants at an increased risk for LOS.The length of parenteral feeding was associated with LOS, whereas breastmilk administration was protective against CoNS-LOS. A rapid advancement of enteral feeding, preferably with breastmilk, may proportionally reduce the number of parenteral feeding days and consequently the risk for LOS.

Children with dyskinetic cerebral palsy are severely affected as compared to bilateral spastic cerebral palsy.
Préel M. et al
Uldall Acta Paediatr. 2019 Apr 1.
We aimed at describing clinical findings in children with dyskinetic as compared to bilateral spastic cerebral palsy (CP). Cases of dyskinetic CP had overlapping clinical features with cases of bilateral spastic CP, but differed significantly in several perinatal risk factors. The children with dyskinetic CP had experienced more peri- or neonatal adverse events, and neurodevelopmental impairment was severe.

Optimizing antibiotic use for early onset sepsis: A tertiary nicu experience.
Arora V. et al

high mortality. However, the DIC are not independently associated with in-hospital mortality.

Hemodynamic response to β-blockers in severe sepsis and septic shock: A review of current literature
van Loon, Lex M et al
Journal of Critical Care; Apr 2019; vol. 50 ; p. 138
The administration of β-blockers in patients with sepsis is a trending topic in intensive care medicine since the landmark study by Morelli and colleagues, showing a striking decrease in 28-day mortality compared to standard care. While the available evidence suggests that the use of β-blockers in septic shock is safe, the effects on hemodynamics are controversial. In this paper, we review the effect of β-blockade in septic shock on hemodynamics from animal models to critically ill patients.

Crystalloids vs. colloids for fluid resuscitation in the Intensive Care Unit: A systematic review and meta-analysis
Martin, Greg S; Bassett, Paul
Journal of Critical Care; Apr 2019; vol. 50 ; p. 144
Guidelines recommend crystalloids for fluid resuscitation in sepsis/shock and switching to albumin in cases where crystalloids are insufficient. We evaluated hemodynamic response to crystalloids/colloids in critically ill adults. Crystalloids were less efficient than colloids at stabilizing resuscitation endpoints; guidance on when to switch is urgently required.

Association of septic shock definitions and standardized mortality ratio in a contemporary cohort of critically ill patients
Kashyap, R. et al
Journal of Critical Care; Apr 2019; vol. 50 ; p. 269
The newly proposed septic shock definition has provoked a substantial controversy in the emergency and critical care communities. We aim to compare new (SEPSIS-III) versus old (SEPSIS-II) definitions for septic shock in a contemporary cohort of critically ill patients. Compared to SEPSIS-II, SEPSIS-III definition of septic shock identifies patients further along disease trajectory with higher likelihood of poor outcome.

Bolus therapy with 3% hypertonic saline or 0.9% saline in emergency department patients with suspected sepsis: A pilot randomised controlled trial.
Smart L. et al
J Crit Care. 2019 Mar 28;52:33-39.
Hypertonic saline administered during fluid resuscitation may mitigate endothelial glycocalyx (EG) shedding and inflammation. The objective of this pilot

J Neonatal Perinatal Med. 2019 Mar 30.
Neonatal antibiotic use is associated with a greater risk of nosocomial infection, necrotizing enterocolitis, and mortality. It can induce drug-resistant pathogens that contribute to increased neonatal morbidity/mortality, healthcare costs, and length of stay. Prior to the antibiotic stewardship program, decisions to obtain blood cultures and empiric antibiotics for possible Early-onset Sepsis (EOS) in late preterm and term infants upon NICU admission were provider-dependent rather than algorithm-based. We aimed to decrease empiric antibiotic prescription from 70% to 56% (20% decrease) in infants ≥34 weeks gestation admitted to the NICU. A significant reduction in antibiotic use and sepsis evaluations was achieved for late preterm and term infants upon NICU admission. No clinical deterioration occurred in post-intervention infants who did not receive antibiotics. There is significant overlap between CDC guidelines and SRC recommendations.

Prenatal and postnatal inflammation-related risk factors for retinopathy of prematurity.
Goldstein GP. et al
J Perinatol. 2019 Apr 1.
To evaluate the relationship between prenatal and postnatal inflammation-related risk factors and severe retinopathy of prematurity (ROP). Postnatal inflammation-related factors were associated with severe ROP more strongly than prenatal factors. The association between prenatal inflammation-related factors and ROP was explained by earlier gestational age in infants exposed to prenatal inflammation.

Serum Level of Antithrombin III (ATIII) Could Serve as a Prognostic Biomarker in Neonatal Sepsis.
Samra N et al
Fetal Pediatr Pathol. 2019 Mar 31:1-9.
Neonatal sepsis syndrome continues to have a high morbidity and mortality rate despite the progress in neonatal intensive care. There is no single diagnostic test which can reliably diagnose sepsis in the newborn, beside blood culture. Antithrombin III may be one promising single marker for sepsis syndrome diagnosis and prognosis. Antithrombin III is lower in sepsis syndrome neonates and may be a useful biomarker in neonatal sepsis.

Adult sepsis
Characteristics and Outcomes of Patients With and Without Type 2 Diabetes Mellitus and Pulmonary Sepsis
Sathananthan, M. et al.

randomised controlled trial was to measure the effect of hypertonic saline, compared to isotonic saline, on biomarkers of EG shedding and inflammation in emergency department patients with suspected sepsis. Although a single bolus of hypertonic saline increased serum osmolality, it did not reduce biomarkers of EG shedding or inflammation, compared to patients that received isotonic saline.

Association of dermatomyositis with systemic and opportunistic infections in the United States.
Ren Z. et al
Arch Dermatol Res. 2019 Apr 6.
Patients with dermatomyositis have multiple risk factors for serious and opportunistic infections, including immune dysregulation, long-term systemic corticosteroid treatment and comorbid health conditions. We sought to determine whether dermatomyositis is associated with increased odds and burden of systemic, opportunistic and antibiotic-resistant infections. In conclusion, dermatomyositis is associated with higher odds, costs and inpatient mortality from serious and opportunistic infections.

The Vitamin C, Thiamine and Steroids in Sepsis (VICTAS) Protocol: a prospective, multi-center, double-blind, adaptive sample size, randomized, placebo-controlled, clinical trial.
Hager DN et al
Trials. 2019 Apr 5;20(1):197.
Sepsis accounts for 30% to 50% of all in-hospital deaths in the United States. Other than antibiotics and source control, management strategies are largely supportive with fluid resuscitation and respiratory, renal, and circulatory support. Intravenous vitamin C in conjunction with thiamine and hydrocortisone has recently been suggested to improve outcomes in patients with sepsis in a single-center before-and-after study. However, before this therapeutic strategy is adopted, a rigorous assessment of its efficacy is needed. VICTAS is a large, multi-center, double-blind, adaptive sample size, randomized, placebo-controlled trial that will test the efficacy of vitamin C, thiamine, and hydrocortisone as a combined therapy in patients with respiratory or circulatory dysfunction (or both) resulting from sepsis. Because the components of this therapy are inexpensive and readily available and have very favorable risk profiles, demonstrated efficacy would have immediate implications for the management of sepsis worldwide.

Biomarker-assisted identification of sepsis-related acute liver impairment: a frequent and deadly condition in critically ill patients.

Journal of Intensive Care Medicine, 03/06/2019, p.088506661983391
To date, studies have provided conflicting results regarding the impact of type 2 diabetes mellitus (DM) on sepsis-related outcomes. Our objective is to understand the impact of type 2 DM in bacterial pneumonia and sepsis-related intensive care unit (ICU) outcomes. Our findings demonstrated that type 2 DM does not increase the overall mortality. Our findings of increased mortality in both type 2 DM patients with lower admission glucose, and non-DM patients with higher mean glucose during the hospital stay needs to be further evaluated. Future studies in regards to this could lead to personalized glucose treatment goals for patients.

Caspse-11-GSDMD pathway is required for serum ferritin secretion in sepsis
Wang D et al
Clin Immunol. 2019 Feb 5. pii: S1521-6616(18)30488-1
Ferritin is the major iron storage molecule of vertebrates, which can be detected in serum under numerous conditions, including inflammatory, neurodegenerative, and malignant diseases. Given this character, serum ferritin is frequently used as a biomarker in clinical settings. How the ferritin secreted to the serum has attracted much attention. Although some studies have found ferritin was mediated via the endoplasmic reticulum (ER)-Golgi secretion pathway or secretory lysosomes trafficking pathway under normal conditions, the secretion pathway of ferritin under pathological conditions, especially in sepsis is not very clear. In this report, we adopt a murine sepsis model to study the secretion pathway of ferritin in sepsis. We demonstrated caspase-11-GSDMD pathway and associated pyroptosis are required for secretion of ferritin in vitro and in vivo in sepsis. Moreover, our work connects pyroptosis to serum ferritin secretion and suggests a passive release process of ferritin, enhancing our understanding of the mechanism of ferritin secretion.

Sepsis caused by bacterial colonization of migrated distal ventriculoperitoneal shunt catheter into the pulmonary artery: a first case report and literature review
Hajdarpašić E et al
World Neurosurg. 2019 Mar 9. pii: S1878-8750(19)30599-6
Migration of distal ventriculoperitoneal (VP) shunt catheter into another body part has been described as a potentially serious surgical complication. We present the first case of sepsis caused by transcardial and pulmonary migration of distal catheter into the heart

Jensen JS et al
Clin Chem Lab Med. 2019 Apr 5. pii:
The prognostic impact of mild/moderate liver impairment among critically ill patients is not known. We aimed to determine whether acute liver impairment, as measured by several biomarkers, (i) is frequent, (ii) influences prognosis and (iii) to determine whether such an effect is specific for infected critically ill patients. Among infected critically ill patients, subtle liver impairment, (elevated HA and bilirubin), was associated with a progressive and highly increased risk of death for the patient; this was robust to adjustment for other predictors of mortality. HA can identify patients at high risk.

Risk Factors for Post-Operative Sepsis and Septic Shock in Patients Undergoing Emergency Surgery.
Gabriel V. et al
Surg Infect (Larchmt). 2019 Apr 5.
Sepsis after emergency surgery is associated with a higher mortality rate than elective surgery, and total hospital costs increase by 2.3 times. This study aimed to identify risk factors for post-operative sepsis or septic shock in patients undergoing emergency surgery. Risk factors for the development of sepsis or septic shock are ASA PS class 2 or higher, partially or totally dependent functional status, and male gender. Emergency pancreatic or small intestinal procedures may confer a higher risk. Greater vigilance and early post-operative screening may be of benefit in patients with these risk factors.

Open abdominal management for perforative peritonitis with septic shock: a retrospective analysis on usefulness of a standardized treatment protocol.
Inukai K. et al
Eur J Trauma Emerg Surg. 2019 Apr 4.
Damage control surgery (DCS) with open abdominal management (OAM) has been increasingly expanded to include critically ill non-trauma patients. However, there is limited data regarding the usefulness of this protocol for the treatment of severe perforative peritonitis (PP), especially with septic shock (SS). Here, we retrospectively evaluated the usefulness of our OAM protocol for PP with SS. A standardized protocol for OAM may improve the outcomes of patients with SS due to PP. This damage control approach can be applied for the treatment of severe abdominal sepsis.

Targeting Complement Pathways in Polytrauma- and Sepsis-Induced Multiple-Organ
Dysfunction.
Karasu E. et al
Front Immunol. 2019 Mar 21;10:543.

and pulmonary artery, which was subsequently colonized by Klebsiella pneumoniae. Migration of a distal VP shunt catheter into the heart should be considered in patients with a previously placed VP shunt presenting with cardiopulmonary problems, arrhythmia, and/or fever. Neurosurgeons should be involved as soon as possible, and a multidisciplinary approach is warranted.

Elevated serum IL-37 concentrations in patients with sepsis.
Wang YC et al
Medicine (Baltimore). 2019 Mar;98(10):e14756
To investigate the changes and significance of IL-37 in patients with sepsis. The level of IL-37 observed in sepsis was found to correlate with the severity of the inflammatory reaction. IL-37 could be an important cytokine in the control of sepsis by suppressing the production of pro-inflammatory cytokines.

Phenylephrine Attenuated Sepsis-Induced Cardiac Inflammation and Mitochondrial Injury Through an Effect on the PI3K/Akt Signaling Pathway
Li HM et al
J Cardiovasc Pharmacol. 2019 Mar;73(3):186-194
o investigate whether phenylephrine (PE) inhibits sepsis-induced cardiac dysfunction, cardiac inflammation, and mitochondrial injury through the PI3K/Akt signaling pathway. PE attenuated sepsis-induced cardiac dysfunction, cardiac inflammation, and mitochondrial injury through the PI3K/Akt signaling pathway.

Location is the key to function: HMGB1 in sepsis and trauma-induced inflammation.
Deng M et al.
J Leukoc Biol. 2019 Apr 4.
High mobility group box 1 (HMGB1) is a multifunctional nuclear protein, probably known best as a prototypical alarmin or damage-associated molecular pattern (DAMP) molecule when released from cells. This review highlights some of the mechanisms that contribute to location and functions of HMGB1, and focuses on some recent insights on important intracellular effects of HMGB1 during sepsis and trauma.

Exposure to traumatic or infectious insults results in a rapid activation of the complement cascade as major fluid defense system of innate immunity. The complement system acts as a master alarm system during the molecular danger response after trauma and significantly contributes to the clearance of DAMPs and PAMPs. However, depending on the origin and extent of the damaged macro- and micro -milieu, the complement system can also be either excessively activated or inhibited. In both cases, this can lead to a maladaptive immune response and subsequent multiple cellular and organ dysfunction. The arsenal of complement-specific drugs offers promising strategies for various critical conditions after trauma, hemorrhagic shock, sepsis, and multiple organ failure. The imbalanced immune response needs to be detected in a rational and real-time manner before the translational therapeutic potential of these drugs can be fully utilized. Overall, the temporal-spatial complement response after tissue trauma and during sepsis remains somewhat enigmatic and demands a clinical triad: reliable tissue damage assessment, complement activation monitoring, and potent complement targeting to highly specific rebalance the fluid phase innate immune response.

Cortisol and adrenal androgens as independent predictors of mortality in septic patients.
De Castro R. et al
PLoS One. 2019 Apr 4;14(4):e0214312.
We look to determine the prognostic value of cortisol, Dehydroepiandrosterone (DHEA) and Dehydroepiandrosterone-sulfate (DHEAS), together with their ratios (cortisol/DHEA and cortisol/DHEAS), as independent predictors of mortality in septic patients. Basal cortisol measured within the first 24 hours of the septic process was the best prognostic factor for in-hospital and 28-day mortality, even superior to the Sequential Organ Failure Assessment (SOFA) or Acute Physiology and Chronic Health Evaluation II (APACHE II) scores. The cortisol/DHEAS ratio was an independent predictor of long-term mortality.

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