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 11 October 2018. 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
27 September 2018

Neonatal, paediatric and maternal sepsis

Health-Related Quality of Life after Pediatric Severe Sepsis
Syngal, P.
Healthcare 2018, 6(3), 113
Pediatric severe sepsis is a public health problem with significant morbidities in those who survive. In this article, we aim to present an overview of the important studies highlighting the limited data available pertaining to long-term outcomes of survivors of pediatric severe sepsis. There is significant and longstanding morbidity seen in children and their families following a severe sepsis illness. Further prospective data are required to study the long-term outcomes of sepsis in the pediatric population.

Suspected or known neonatal sepsis and neurodevelopmental delay by 5 years
Savioli, K. et al
Journal of Perinatology 10 September 2018
Objective: Evaluate impact of known and suspected neonatal sepsis in the term and preterm infant on neurodevelopmental delay by 5 years. Conclusion:

Adult sepsis (cont.)

THE SEPTIC HEART Current Understanding of Molecular Mechanisms and Clinical Implications.
Martin, L. et al.
Chest. 2018 Aug 29. pii: S0012-3692(18)32284-0
Septic cardiomyopathy is a key feature of sepsis-associated cardiovascular failure. Despite the lack of consistent diagnostic criteria, patients typically exhibit ventricular dilatation, reduced ventricular contractility and/or both right and left ventricular dysfunction with a reduced response to volume infusion. Although there is solid evidence that the presence of septic cardiomyopathy is a relevant contributor to organ dysfunction and an important factor in the already-complicated therapeutic management of septic patients, there are still several questions to be asked: Which factors/mechanisms cause a cardiac dysfunction associated with sepsis? How do we diagnose septic cardiomyopathy? How do we treat septic cardiomyopathy? How does septic cardiomyopathy influence the long-term outcome of the patient?

Neonatal sepsis and suspected sepsis are associated with neurodevelopmental delay by 5 years of age.

Respiratory Viral Infections in Infants with Possible Sepsis.
Aykac, K. et al
J Med Virol. . September 2018
Knowledge of infections leading sepsis is needed to develop comprehensive infection prevention and sepsis early recognition and treatment strategies.The aim of this study was to investigate the etiology of sepsis and evaluate the proportion of respiratory viral pathogens in infants under two years of age with possible sepsis. Our results suggest that respiratory tract viruses may play an important role in patients with sepsis and they should be kept in mind especially in winter and spring seasons. With an overall viral respiratory viruses as a single pathogen detection rate of 36.6% in sepsis etiology.

Virulence Factors and Antibiotic Resistance of Klebsiella pneumoniae Strains Isolated From Neonates With Sepsis
Khalit S. K. et al
Front Med (Lausanne). 2018; 5: 225.
Klebsiella pneumoniae is one of the most important infectious agents in neonates. There are “classic” and hypervirulent strains of K. pneumoniae. The “classic” non-virulent strain of K. pneumoniae, producing extended-spectrum beta-lactamases (ESBLs), is associated with nosocomial infections. Hypervirulent K. pneumoniae strains are associated with invasive infections in previously healthy adult people, and most of them exhibit antimicrobial susceptibility. The role of virulent strains of K. pneumoniae (including hv-KP) in neonatal infections is unknown. The aim of the study was the assessment of the impact of virulence factors and antibiotic resistance of K. pneumoniae strains on clinical features and outcomes of neonatal infection. The prevalence of virulent strains of K. pneumoniae among neonates with sepsis and other neonatal infection is higher than we think. The most severe forms of neonatal sepsis with an unfavorable outcome in our study were due to virulent strains of K. pneumoniae.

Microbiological comparison of blood culture and amplification of 16S rDNA methods in combination with DGGE for detection of neonatal sepsis in blood samples
García-Gudiño, I. et al
European Journal of Pediatrics January 2018, Volume 177, Issue 1, pp 85–93 | Cite as
It is estimated that 15% of all newborns admitted to the neonatal intensive care unit (NICU) for suspected

Emergency department sepsis screening tool decreases time to antibiotics in patients with sepsis
Shah, T. et al
American Journal of Emergency Medicine 36 (2018) 1745– 1748
Recent literature has highlighted the importance of early identification and treatment of sepsis; however, limited data exists to help recognize sepsis in the emergency department (ED) through use of a screening tool. The purpose of this study was to evaluate the impact of a sepsis screening tool implemented in an academic medical center ED on compliance with the 3-hour sepsis bundle. Although implementation of an ED sepsis screening tool did not increase 3-hour bundle compliance, it did increase the proportion of patients receiving timely antimicrobial therapy and demonstrated a trend towards decreased mortality.

Association of Household Income Level and In-Hospital Mortality in Patients With Sepsis: A Nationwide Retrospective Cohort Analysis.
Rush, B. et al
Journal of Intensive Care Medicine, 33(10), 551-556. (2018).
Associations between low socioeconomic status (SES) and poor health outcomes have been demonstrated in a variety of conditions. However, the relationship in patients with sepsis is not well described. We investigated the association of lower household income with in-hospital mortality in patients with sepsis across the United States. After adjustment for severity of illness, patients with sepsis who live in the lowest median income quartile had a higher risk of mortality compared to residents of the highest income quartile. The association between SES and mortality in sepsis warrants further investigation with more comprehensive measures of SES.

ICU Admission Source as a Predictor of Mortality for Patients With Sepsis
Motzkus, C.A. et al
Journal of Intensive Care Medicine Vol 33, Issue 9, pp. 510 - 516
Sepsis is the leading noncardiac cause of intensive care unit (ICU) death. Pre-ICU admission site may be associated with mortality of ICU patients with sepsis. This study quantifies mortality differences among patients with sepsis admitted to an ICU from a hospital ward, emergency department (ED), or an operating room (OR). Patients with sepsis admitted to an ICU from a hospital ward experienced greater mortality than patients with sepsis admitted to an ICU from an

sepsis receive multiple broad-spectrum antibiotics without pathogen identification. The gold standard for bacterial sepsis detection is blood culture, but the sensitivity of this method is very low. Recently, amplification and analysis of the 16S ribosomal DNA (rDNA) bacterial gene in combination with denaturing gradient gel electrophoresis (DGGE) has proven to be a useful approach for identifying bacteria that are difficult to isolate by standard culture methods. The main goal of this study was to compare two methods used to identify bacteria associated with neonatal sepsis: blood culture and broad range 16S rDNA-DGGE. Our study shows that the molecular approach with 16S rDNA-DGGE identifies twofold more pathogenic bacteria than bacteriological culture, including complex bacterial communities associated with the development of bacterial sepsis in neonates.

Comparison between presepsin and procalcitonin in early diagnosis of neonatal sepsis
Iskandar, A. et al
The Journal of Maternal-Fetal & Neonatal Medicine, May 2018
Neonatal sepsis remains worldwide one of the leading causes of morbidity and mortality in both term and preterm infants. Lower mortality rates are related to timely diagnostic evaluation and prompt initiation of empiric antibiotic therapy. Blood culture, as gold standard examination for sepsis, has several limitations for early diagnosis, so that sepsis biomarkers could play an important role in this regard. This study was aimed to compare the value of the two biomarkers presepsin and procalcitonin in early diagnosis of neonatal sepsis. In early diagnosis of neonatal sepsis, compared with procalcitonin, presepsin seems to provide better early diagnostic value with consequent possible faster therapeutical decision making and possible positive impact on outcome of neonates.

Comparison of antibiotic dosing recommendations for neonatal sepsis from established reference sources
Liem, T. B. Y. et al
Int J Clin Pharm. 2018; 40(2): 436–443.
Incorrect dosing is the most frequent prescribing error in neonatology, with antibiotics being the most frequently prescribed medicines. Computer physician order entry and clinical decision support systems can create consistency contributing to a reduction of medication errors. Although evidence-based dosing recommendations should be included in such systems, the evidence is not always available and subsequently, dosing recommendations mentioned in guidelines and textbooks are often based on expert opinion. Antibiotic dosage recommendations for neonates with sepsis can

ED. These findings indicate that there may be systematic differences in the selection of patient care locations, recognition, and management of patients with sepsis that warrant further investigation.

Understandability and Actionability of the CDC'S Printable Sepsis Patient Education Material
Schorr, C. et al
Am J Crit Care September 2018 vol. 27 no. 5 418-427
Quality improvement efforts in sepsis management have increased patients' survival rates. Many sepsis survivors experience sequelae leading to unplanned hospital readmissions and subsequent mortality, especially when survivors delay seeking medical attention because they do not recognize the signs and symptoms of recurrent sepsis. Thus, increasing knowledge of sepsis among patients and caregivers before initial hospital discharge is essential. The Sepsis Fact Sheet provides useful patient information as evaluated using established recommendations for printed materials and expert content validation. Areas for improvement include providing a summary, modifying images, and simplifying language. Results may be useful for sepsis education and discharge teaching.

Evaluation of Thromboelastometry in Sepsis in Correlation With Bleeding During Invasive Procedures
Lukas, P. et al
Clinical and Applied Thrombosis/Hemostasis Vol 24, Issue 6, pp. 993 - 997
Prolongation of prothrombin time (PT) is often encountered in patients with sepsis. On the other hand, thromboelastometry as a global coagulation test might yield normal results. The aim of our study was to evaluate whether prolonged PT in the presence of normal thromboelastometry parameters is associated with severe bleeding in patients with sepsis undergoing invasive procedures. In patients with sepsis undergoing low-risk bleeding invasive procedures (central venous catheter placement, dialysis catheter insertion, drain insertion, and so on) or high-risk bleeding invasive procedures (surgical tracheostomy, surgical laparotomy, thoracotomy, and so on), coagulation was assessed by thromboelastometry using EXTEM test (test for evaluation of the extrinsic pathway of coagulation, contains activator of extrinsic pathway) and with PT. Despite prolonged INR/PR, no severe bleeding was observed during invasive procedures. Our data show that sepsis may be accompanied by normal thromboelastometry results, despite prolonged values of PT, and invasive procedures were performed without severe bleeding. This approach to coagulation

be derived from important reference sources and guidelines. Further exploration to overcome variation in dosage recommendations is necessary to obtain standardized dosage regimens.

C-reactive protein for late-onset sepsis diagnosis in very low birth weight infants
Marc Beltempo
BMC Pediatr. 2018; 18: 16.
Late-onset sepsis in very low birth weight (VLBW) infants is a diagnostic challenge. We aimed to evaluate the diagnostic utility of the C-Reactive protein (CRP) and the complete blood count (CBC) for late-onset sepsis in VLBW infants. At initial sepsis evaluation (T0), both CBC and CRP should be performed to increase sensitivity. A highly negative predictive value is reachable with only two tests: a CBC at T0 and a CRP a T24.

Is MPV a Predictive Marker for Neonatal Sepsis? A Pilot Study
Hanaganahalli, S. et al
Journal of Pediatric Hematology/Oncology. Issue: Volume 40(7), October 2018, p 548–552
Neonatal sepsis (NS) continues to be a diagnostic challenge and a prime cause of mortality. Forage for a lucid, cost-effective yet highly sensitive and specific marker in diagnosing this entity is an incessant task. This study aimed to evaluate the predictive value of mean platelet volume (MPV) in diagnosing NS. Strikingly higher values of platelet count, immature-to-mature neutrophil ratio, MPV, plateletcrit, and C-reactive protein were found in group I in contrast to those in groups II and III (P<0.05). The baseline MPV of patients with culture-proven sepsis was comparatively higher than controls and was found to be statistically significant. Hence, MPV can be a simple, economical, and specific predictor of NS.

Interleukin 17 is an important pathogenicity gene in pediatric sepsis.
Han Y, Li X, Gao S, et al.
J Cell Biochem. 2018;1-8.
Sepsis represents a complex disease with the dysregulated inflammatory response. The purpose of this study is to explore the role of interleukin 17 (IL-17, also known as IL-17A) in the occurrence and development of pediatric sepsis. IL-17A might be a potential therapeutic target for pediatric sepsis.

assessment in sepsis may reduce administration of fresh frozen plasma to the patients.

Sepsis Bundle Adherence Is Associated with Improved Survival in Severe Sepsis or Septic Shock
Milano, P.K. et al
West J Emerg Med. 2018 Sep; 19(5): 774–781.
There have been conflicting data regarding the relationship between sepsis-bundle adherence and mortality. Moreover, little is known about how this relationship may be moderated by the anatomic source of infection or the location of sepsis declaration. In a large public healthcare system, adherence with severe sepsis/septic shock management bundles was found to be associated with improved survival. Bundle adherence seems to be most beneficial for patients with pneumonia. The overall improved survival in patients who received bundle-adherent care was driven by patients declaring in the ICU. Adherence was not associated with lower mortality in the large subset of patients who declared in the ED, nor in the smaller subset of patients who declared in the ward.

Increasing Sepsis Rates in the United States: Results From National Inpatient Sample, 2005 to 2014
Rubens, M. et al
Journal of Intensive Care Medicine First Published September 2, 2018
Objectives: To examine the trends in hospitalization rates, mortality, and costs for sepsis during the years 2005 to 2014. Conclusions: Hospitalizations for sepsis increased during the years 2005 to 2014. Our study paradoxically found declining rates of in-hospital mortality, length of stay, and mean hospitalization cost for sepsis. These findings could be due to biases introduced by International Classification of Diseases, Ninth Revision, Clinical Modification coding rules and increased readmission rates or alternatively due to increased awareness and surveillance and changing disposition status. Standardized epidemiologic registries should be developed to overcome these biases.

Review: the Role and Mechanisms of Macrophage Autophagy in Sepsis
Qiu, P. et al
Inflammation pp 1–14 07 September 2018
Sepsis is a systemic inflammatory response syndrome caused by infection. The core mechanism underlying sepsis is immune dysfunction, with macrophages, as important cells of the innate immune system, playing an essential role. Autophagy has been shown to be closely related to inflammation and immunity, and

Adult sepsis

[Incidence and variables associated with short and long-term mortality in patients with systemic lupus erythematosus and sepsis admitted in intensive care units]

Abramovich, E. et al

Lupus First Published September 5, 2018

Infections are common among patients with systemic lupus erythematosus (SLE), and are associated with increased morbidity and mortality. SLE is not an independent risk factor for 30-day or 3-year mortality following ICU admission with sepsis. Increased late mortality was associated with congestive heart failure within the SLE patients alone. None of the SLE-related variables were statistically different between the living and deceased SLE patients.

[Mortality Changes Associated with Mandated Public Reporting for Sepsis: The Results of the New York State Initiative]

Levy, M.M. et al

American Journal of Respiratory and Critical Care Medicine September 07, 2018

In 2013, the New York State Department of Health (NYSDOH) began a mandatory, state-wide initiative to improve early recognition and treatment of severe sepsis and septic shock. This study examines protocol initiation, 3-hour and 6-hour sepsis bundle completion, and risk-adjusted hospital mortality among adult patients with severe sepsis and septic shock. New York's statewide initiative increased compliance with sepsis-performance measures. Risk-adjusted sepsis mortality decreased during the initiative and was associated with increased hospital-level compliance

[Impact of body mass index on survival of medical patients with sepsis: a prospective cohort study in a university hospital in China]

Qingtao Zhou

BMJ Open. 2018; 8(9): e021979.

Objective: To evaluate the impact of body mass index (BMI) on survival of a Chinese cohort of medical patients with sepsis. Conclusions: BMI was an independent factor associated with 90-day survival in a Chinese cohort of medical patients with sepsis, with patients having a lower BMI at a higher risk of death.

autophagy enhancement in sepsis can play a protective role by negatively regulating abnormal macrophage activation, modulating macrophage polarization phenotype, reducing activation of the inflammasome and release of inflammatory factors, and affecting macrophage apoptosis. However, excessive autophagy may also lead to autophagic death of macrophages, which further aggravates the inflammatory response. The mechanisms underlying these functions are relatively complex and remain unclear, but may be related to a variety of signaling pathways such as NF-κB, mTOR, and PI3K/AKT. The administration of drugs to assist in the regulation of macrophage autophagy has become a novel treatment for sepsis. The present review focuses on the role and the potential mechanisms of macrophage autophagy in sepsis.

[Effect of Audit and Feedback on Physician Adherence to Clinical Practice Guidelines for Pneumonia and Sepsis]

Trent, S.A. et al

American Journal of Medical Quality First Published September 12, 2018

The objective was to estimate the effect of feedback with blinded peer comparison on emergency physician adherence to guidelines for appropriate antibiotic administration for inpatient pneumonia and completion of the 3-hour Surviving Sepsis Bundle for severe sepsis. Feedback with blinded peer comparison significantly improved emergency physician guideline adherence.

[The association between pre-operative sepsis and 30-day mortality in hip fracture patients—A cohort study.]

Mørch, S.S. et al.

Acta Anaesthesiol Scand. 2018;62:1209–1214.

Post-operative sepsis considerably increases mortality, but the extent of pre-operative sepsis in hip fracture patients and its consequences are sparsely elucidated. The aim of this study was to assess the association between pre-operative sepsis and 30-day mortality after hip fracture surgery. Pre-operative sepsis in hip fracture patients was associated with an increased length of hospital stay and tended to increase mortality. Pre-operative sepsis in hip fracture patients merits more intensive surveillance and increased attention to timely treatment.

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