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 15 August 2018 (due to staff holidays). 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 19 July 2018

Neonatal, paediatric and maternal sepsis

Successful Termination of Sustained Transmission of Resident MRSA Following Extensive Neonatal Intensive Care Unit Refurbishment: An Intervention Study.

Semple, A. et al

Journal of Hospital Infection: July 12, 2018
Neonatal sepsis is a leading cause of morbidity and mortality in neonatal units worldwide. Meticillin resistant Staphylococcus aureus (MRSA) has become a leading causative pathogen. Many neonatal units experience endemic colonization and infection of their infants, which is often very challenging to successfully eradicate. We report successful termination of sustained transmission of endemic strains of MRSA from our neonatal unit following complete unit redesign and refurbishment.

Adult sepsis (cont.)

Meningococcal Working Group report

The Meningococcal Working Group for UK Government **Department of Health and Social Care.** 2 July 2018 This is a report on raising awareness of the signs and symptoms, and ensuring early diagnosis and treatment, of sepsis and meningococcal disease. This report sets out 12 recommendations aimed at organisations and bodies that have a role to play in improving awareness and early diagnosis of sepsis and meningococcal disease.

<u>Viewpoint: The role of glucocorticoids as adjunctive treatment for sepsis in the modern era</u>

Marik, P.E.

<u>The golden hour of sepsis: An in-depth analysis of sepsis-related maternal mortality in middle-income country Suriname</u>

Kodan, L.R. et al

PloS One 2018, 13 (7): e0200281

Sepsis was the main cause of maternal mortality in Suriname, a middle-income country. Objective of this study was to perform a qualitative analysis of the clinical and management aspects of sepsis-related maternal deaths with a focus on the 'golden hour' principle of antibiotic therapy. n Suriname, a middle-income country, maternal mortality could be reduced by improving early recognition and timely diagnosis of sepsis, vital signs monitoring and immediate antibiotic infusion (within the golden hour).

<u>Distribution</u>, antimicrobial resistance and predictors of mortality in neonatal sepsis.

Bandyopadhyay, T. et al.

J Neonatal Perinatal Med. 2018;11(2):145-153. The aim of this study is to investigate etiological agents, patterns of antimicrobial resistance and predictors of mortality in culture proven neonatal sepsis. A high degree of antimicrobial resistance underscores the need to understand the pathogenesis of resistance, curtail the irrational prescription of antibiotics in neonates and the requirement for measures to prevent it in low-income and middle-income countries.

<u>Association of vitamin D deficiency with an increased risk of late-onset neonatal xepsis</u>

Dhandai, R. et al.

Paediatrics and International Child Health 2018 July 13,: 1-5

Vitamin D deficiency in mothers and neonates is being recognised increasingly as a leading cause of many adverse health effects in the newborn infant, including sepsis. A prospective observational study was conducted at a tertiary care Paediatric teaching hospital in northern India to assess vitamin D deficiency as a possible risk factor for late-onset sepsis (LOS) in term and late preterm neonates and also to examine the correlation between maternal and infant vitamin D levels during the neonatal period. Neonates with vitamin D deficiency are at greater risk of LOS than those with sufficient vitamin D levels.

<u>Clinical Significance of Interleukin-6 in the Diagnosis of Sepsis and Discriminating Sepsis Induced by Gramnegative Bacteria</u>

Shao, W-X. et al

The Lancet Respiratory Medicine. Available online 11 July 2018

Glucocorticoids have been used as adjunctive therapy in patients with sepsis and septic shock for more than four decades. The rationale for the use of glucocorticoids is that this class of drugs downregulates the proinflammatory response and limits the antiinflammatory response while preserving innate immunity. Between 1976 and 2017, 22 randomised placebo-controlled trials have been published evaluating the benefit of glucocorticoids in patients with community-acquired pneumonia, sepsis, and septic shock. These studies produced conflicting results. In 2018, two large randomised controlled trials (RCTs) were published evaluating the role of hydrocortisone in patients with septic shock. The Activated Protein C and Corticosteroids for Human Septic Shock (APROCCHSS) trial reported a reduction in 90-day mortality whereas the Adjunctive Corticosteroid Treatment in Critically III Patients with Septic Shock (ADRENAL) trial reported no mortality benefit. This Viewpoint critically appraises these two RCTs and evaluates the use of glucocorticoids in the treatment of sepsis and septic shock in the modern era.

Repeated vital sign measurements in the emergency department predict patient deterioration within 72 hours: a prospective observational study

Quinten, V.M. et al

Scandinavian Journal of Trauma, Resuscitation and

Emergency Medicine 2018 July 13, 26 (1): 57

More than one in five patients presenting to the emergency department (ED) with (suspected) infection or sepsis deteriorate within 72 h from admission. Surprisingly little is known about vital signs in relation to deterioration, especially in the ED. The aim of our study was to determine whether repeated vital sign measurements in the ED can differentiate between patients who will deteriorate within 72 h and patients who will not deteriorate. Repeated vital sign measurements in the ED are better at identifying patients at risk for deterioration within 72 h from admission than single vital sign measurements at ED admission.

<u>Corticosteroids in Sepsis: An Updated Systematic</u> <u>Review and Meta-Analysis.</u>

Rochwerg, B. et al.

Crit Care Med. 2018 Jul 2. [Epub ahead of print] This systematic review and meta-analysis addresses the efficacy and safety of corticosteroids in critically ill patients with sepsis. We updated a comprehensive search of MEDLINE, EMBASE, CENTRAL, and LILACS, and

Pediatric Infectious Disease Journal 2018, 37 (8): 801-805

A total of 379 children with sepsis were involved in this study to discuss the clinical significance of interleukin (IL)-6 in the differential diagnosis of sepsis and its capability of differentiating the sepsis induced by Gram-negative bacteria from that induced by Grampositive bacteria. They formed the case group, and their C-reactive protein (CRP), procalcitonin (PCT) and IL-6 levels before antibiotics and after recovery were checked. CRP, IL-6 and PCT are applicable to the differential diagnosis of sepsis and differentiating the sepsis induced by Gram-negative bacteria from Grampositive bacteria. Appropriate combinations of these indicators are capable of increasing differential diagnosis efficiency. These indicators can be used as markers of antibiotics usage, but whether they can be used as markers to withdraw antibiotics is still needed to be observed.

Adult sepsis

Skin mottling score and capillary refill time to assess mortality of septic shock since pre-hospital setting Jouffroy, R. et al.

American Journal of Emergency Medicine 2018 July 6 The early identification of septic shock patients at high risk of poor outcome is essential to early initiate optimal treatments and to decide on hospital admission. Biomarkers are often used to evaluate the severity. In prehospital settings, the availability of biomarkers, such as lactate, is restricted. In this context, clinical tools such as skin mottling score (SMS) and capillary refill time (CRT) are more suitable. In this study, we describe prehospital SMS and CRT's ability to predict mortality of patients with septic shock initially cared in the prehospital setting by a mobile intensive care unit. In this study, we report an association between prehospital SMS and CRT, and mortality of patients with septic shock. SMS and CRT are simple tools that could be used to optimize the triage and to decide early intensive care admission.

<u>Arguing for Adaptive Clinical Trials in Sepsis</u> Talisa, V.B. et al.

Frontiers in Immunology 2018, 9: 1502
Sepsis is life-threatening organ dysfunction due to dysregulated response to infection. Patients with sepsis exhibit wide heterogeneity stemming from genetic, molecular, and clinical factors as well as differences in pathogens, creating challenges for the development of effective treatments. In this review, we discuss challenges in the evaluation of treatments

unpublished sources for randomized controlled trials that compared any corticosteroid to placebo or no corticosteroid in critically ill children and adults with sepsis. Conclusions: In critically ill patients with sepsis, corticosteroids possibly result in a small reduction in mortality while also possibly increasing the risk of neuromuscular weakness.

Plasma myeloperoxidase-conjugated DNA level predicts outcomes and organ dysfunction in patients with septic shock

Maruchi, Y. et al.

Critical Care: the Official Journal of the Critical Care Forum 2018 July 13, 22 (1): 176

Recent studies have suggested that excessive formation of neutrophil extracellular traps (NETs) plays a critical role in the pathogenesis of sepsis. Although elevation of the plasma level of cell-free DNA (cf-DNA) has been reported in sepsis patients, there has been little direct measurement of circulating free NETs such as myeloperoxidase-conjugated DNA (MPO-DNA). The objectives of this study were to detect NETs in the bloodstream of patients with septic shock, and to assess the correlations of circulating NET levels with organ dysfunction, disease severity, and mortality. Conclusion: The increase in circulating MPO-DNA in patients with septic shock indicates acceleration of NET formation in the early stages of sepsis. High MPO-DNA levels are associated with the severity of organ dysfunction and 28-day mortality due to septic shock, but not with the DIC score. These results suggest that excessive NET formation contributes to the pathogenesis of septic shock.

[Fluid Resuscitation and Management in Patients with Sepsis and Septic Shock]. [Article in German] Kochanek M. et al

Dtsch Med Wochenschr. 2018 Jul;143(14):1039-1049. Sepsis and septic shock are common diseases with high mortality rates. Although volume therapy has been a central component of sepsis therapy for decades, the choice of optimal fluid and fluid intake is unclear. This paper summarizes findings on pathophysiology, clinical trial results, and current recommendations for optimal volume and fluid management in sepsis.

Early enteral nutrition is associated with reduced inhospital mortality from sepsis in patients with sarcopenia

Koga, Y. et al.

Journal of Critical Care 2018 June 30, 47: 153-158 To determine whether the association of early enteral nutrition (EEN) with mortality from sepsis differs for sepsis, and explore potential benefits and weaknesses of recent advances in adaptive trial methodologies to address these challenges.

<u>Gut-origin sepsis in the critically ill patient:</u> pathophysiology and treatment

Assimakopoulos, S.F. et al.

Infection 2018 July 12

Gut permeability is increased in critically ill patients, and associated with the development of the systemic inflammatory response syndrome and multiple organ dysfunction syndrome (MODS). The pathogenetic link(s) and potential therapies are an area of intense research over the last decades. There is an emerging need for application of sensitive non-invasive and easily measured biomarkers of early intestinal injury (e.g., citrulline, intestinal fatty acid protein, and zonulin) in our everyday clinical practice, guiding the early pharmacological intervention in critically ill patients to restore or prevent intestinal injury and improve their outcomes.

<u>CE: A Review of the Revised Sepsis Care Bundles</u> Lester, D. et al

American Journal of Nursing 2018 July 12
Sepsis is an extreme response to infection that can cause tissue damage, organ failure, and death if not treated promptly and appropriately. Each year in the United States, sepsis affects more than 1.5 million people and kills roughly 250,000. Prompt recognition and treatment of sepsis are essential to saving lives, and nurses play a critical role in the early detection of sepsis, as they are often first to recognize the signs and symptoms of infection. Here, the authors review recent revisions to the sepsis care bundles and discuss screening and assessment tools nurses can use to identify sepsis in the ICU, in the ED, on the medical-

<u>Pediatric Sepsis: A Primer for the Pediatrician</u> Conway, E.E.

surgical unit, and outside the hospital.

Pediatric Annals; Vol. 47, Iss. 7, (Jul 2018)
Sepsis is the body's systemic response to infection and is a serious health care concern that affects neonatal, pediatric, and adult populations worldwide. Severe sepsis (sepsis that has progressed to cellular dysfunction and organ damage or evidence of hypoperfusion) and septic shock (sepsis with persistent hypotension despite adequate fluid resuscitation) are still associated with high mortality rates despite improvements in the management of infectious processes. The cellular processes that occur as a result of the inflammatory response in sepsis, including

between patients with and without sarcopenia, we retrospectively reviewed septic patients treated at our centre between January 2010 and August 2017. Conclusions: EEN may be more beneficial in sarcopenic patients.

<u>Time-related association between fluid balance and mortality in sepsis patients: interaction between fluid balance and haemodynamics</u>

Shen, Y. et al.

Scientific Reports 2018 July 10, 8 (1): 10390 This study aimed to investigate the time-related association between cumulative fluid balance (FB) and mortality. In conclusion, the positive FB during the second but not the first 24 hours was associated with increased mortality in sepsis. Achieving more negative FB was associated with decreased mortality only in the second 24 hours.

Risk Factors and Outcomes Associated With Sepsis After Coronary Artery Bypass and Open Heart Valve Surgeries Karamnov, S. et al.

Seminars in Cardiothoracic and Vascular Anesthesia 2018 July 1,

Sepsis causes significant morbidity and mortality after cardiac surgery and carries a significant burden on health care costs. There is a general association of increased risk of post-cardiac surgery sepsis in patients with postoperative complications. We sought to investigate significant patient and procedural risk factors and outcomes associated with sepsis after cardiac surgery. We identified multiple patient and surgical characteristics as well as postoperative outcomes associated with postoperative sepsis development in the high-risk population of patients undergoing cardiac surgery. Early identification of patients who are at high risk for postoperative sepsis can facilitate early treatment interventions.

Head-to-head comparison of qSOFA and SIRS criteria in predicting the mortality of infected patients in the emergency department: a meta-analysis

Jianjun Jiang, J.Y. et al

Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine 2018 July 11, 26 (1): 56
Recently, the concept of sepsis was redefined by an international task force. This international task force of experts recommended using the quick Sequential Organ Failure Assessment (qSOFA) criteria instead of the systemic inflammatory response syndrome (SIRS) criteria to classify patients at high risk for death. However, the added value of these new criteria in the emergency department (ED) remains unclear. Thus, we

impaired perfusion and microcirculatory coagulation, can lead to organ system dysfunction. Early recognition of sepsis can help prompt treatment to improve patient care. Current pediatric guidelines emphasize early recognition, aggressive fluid resuscitation, and administration of antibiotics within the first hour for a better outcome. The practitioner needs to always be mindful of the possibility of sepsis when examining a patient with potential symptoms.

performed this meta-analysis to determine the diagnostic accuracy of the qSOFA criteria in predicting mortality in ED patients with infections and compared the performance with that of the SIRS criteria. A qSOFA score ≥ 2 and SIRS score ≥ 2 are strongly associated with mortality in ED patients with infections. However, it is also clear that qSOFA and SIRS have limitations as risk stratification tools for ED patients with infections.

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