

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 14 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

1 April 2019

Neonatal, paediatric and maternal sepsis

[Peripheral blood neutrophil-to-lymphocyte ratio in preterm infants with intraventricular hemorrhage.](#)

Stein A.A. et al.

Clin Neurol Neurosurg. 2019 Mar 16;180:52-56
Intraventricular hemorrhage (IVH) remains a major complication of prematurity, affecting 20-25% of

Adult sepsis (cont.)

[Terlipressin for septic shock patients: a meta-analysis of randomized controlled study.](#)

Zhu Y. et al

J Intensive Care. 2019 Mar 12;7:16.
Catecholamines are commonly used in septic shock but face limitations of their hypo-responsiveness and

premature infants of very low birth weight. Preterm infants with IVH are at risk for developing significant complications, including posthemorrhagic hydrocephalus and seizures. Multiple studies have reported an association between the neutrophil-to-lymphocyte ratio (NLR) in peripheral blood and outcomes after acute intracranial hemorrhage in adults. However, the prognostic value of the NLR in preterm infants, particularly those with IVH, has not been investigated previously. The development of seizures in preterm infants with IVH is known to significantly increase morbidity. In this study, higher peripheral blood NLR (>3) correlated with the development of seizures, independent of sepsis or meningitis. Further prospective validation of the role of NLR as a predictive marker for seizures in preterm infants is warranted.

[Staphylococcus capitis and NRCS-A clone: the story of an unrecognized pathogen in neonatal intensive care units.](#)

Laurent F. and Butin M.

Clin Microbiol Infect. 2019 Mar 27. pii: S1198-743X(19)30111-9.

In neonatal ICUs, nosocomial late-onset sepsis (LOS), mostly due to coagulase negative staphylococci, constitute a major cause of death or impairment. *Staphylococcus capitis*, usually considered as a poorly virulent species, has been reported as a cause of LOS. *S. capitis* must be considered as a true pathogen in neonates. The decreased susceptibility to vancomycin may be involved in failure of vancomycin therapy. Further studies are needed to better manage its diffusion inside each NICU but also worldwide.

[Procalcitonin versus C-reactive protein: review of kinetics and performance for diagnosis of neonatal sepsis.](#)

adverse events due to high dose. Terlipressin is a synthetic vasopressin analog with greater selectivity for the V1-receptor. A meta-analysis was conducted to evaluate the efficacy and safety of terlipressin in septic shock. Current results suggest terlipressin did not show added survival benefit in septic shock therapy when compared with catecholamines.

[Cost-effectiveness of rapid diagnostic assays that perform directly on blood samples for the diagnosis of septic shock.](#)

Shehadeh F. et al

Diagn Microbiol Infect Dis. 2019 Mar 3. pii: S0732-8893(18)30384-5.

Molecular diagnostic assays that test directly whole blood provide the ability to decrease inappropriate antimicrobial therapy and improve survival in patients with septic shock. We developed a decision analysis model to evaluate the cost-effectiveness of the addition of molecular assays to blood cultures in adults admitted to medical ICUs with septic shock.

[Comparison of the accuracy of three early warning scores with SOFA score for predicting mortality in adult sepsis and septic shock patients admitted to intensive care unit.](#)

Khwannimit B. et al

Heart Lung. 2019 Mar 19. pii: S0147-9563(18)30334-0

The purpose of this study was to compare the accuracy of the Modified Early Warning Score (MEWS), National Early Warning Score (NEWS) and Search Out Severity (SOS), with the quick Sequential Organ Failure Assessment (qSOFA) and SOFA scores, to predict outcomes in sepsis patients. The SOS presents nearly as good as the SOFA score, to predict mortality among sepsis patients admitted to the ICU. The early warning score is another, alternative tool to use for risk

Eschborn S and Weitkamp JH

J Perinatol. 2019 Mar 29.

Procalcitonin (PCT) and C-reactive protein (CRP) are commonly used biomarkers, but their diagnostic advantage for neonatal early-onset (EOS) or late-onset (LOS) sepsis is controversial. In a comprehensive literature review we found significant heterogeneity between studies in sample timing, cut-off values, consideration of blood culture results for sepsis classification, and definition of EOS versus LOS. More studies directly comparing both biomarkers for EOS and LOS, especially in extremely and very-low-birth-weight infants, are needed to determine their clinical value for guidance of antibiotic therapy in neonatal sepsis.

[Association of Deferred vs Immediate Cord Clamping With Severe Neurological Injury and Survival in Extremely Low-Gestational-Age Neonates.](#)

Lodha A. et al

JAMA Netw Open. 2019 Mar 1;2(3):e191286.

Deferred cord clamping (DCC) is recommended for term and preterm neonates to reduce neonatal complications. Information on the association of DCC with outcomes for extremely low-gestational-age neonates is limited. In this study of extremely low-gestational-age neonates who received DCC or ICC, DCC was associated with reduced risk for the composite outcome of severe neurological injury or mortality.

[Intrapartum antibiotics for prolonged rupture of membranes at term to prevent Group B Streptococcal sepsis.](#)

Geethanath R.M. et al

J Obstet Gynaecol. 2019 Mar 27:1-4.

The timely administration of intrapartum antibiotic prophylaxis (IAP) to eligible pregnant mothers reduces the risk of early onset Group B Streptococcus (GBS) neonatal sepsis. The incidence of neonatal GBS sepsis is

stratification and sepsis screening for ICU sepsis patients.

[Effects of norepinephrine and vasopressin discontinuation order in the recovery phase of septic shock: a systematic review and individual patient data meta-analysis.](#)

Hammond D.A. et al

Pharmacotherapy. 2019 Mar 20.

The impact of vasopressin and norepinephrine discontinuation order in the recovery phase of septic shock remains controversial. This systematic review and patient-level meta-analysis was performed to determine the impact of vasopressin and norepinephrine discontinuation order on clinically significant outcomes in the recovery phase of septic shock. Discontinuation of norepinephrine prior to vasopressin during the recovery phase of septic shock resulted in less clinically significant hypotension but no difference in mortality or lengths of stay. Larger, prospective studies evaluating the impact of relative vasopressin deficiency and norepinephrine and vasopressin discontinuation order and timing on patient-centered outcomes are needed.

[Reporting of Organ Support Outcomes in Septic Shock Randomized Controlled Trials: A Methodologic Review-The Sepsis Organ Support Study.](#)

Bourcier S. et al

Crit Care Med. 2019 Mar 19.

Many recent randomized controlled trials in the field of septic shock failed to demonstrate a benefit on mortality. Randomized controlled trials increasingly report organ support duration and organ support-free days as primary or secondary outcomes. We conducted a methodologic systematic review to assess how organ support outcomes were defined and reported in septic shock randomized controlled trials.

increasing, in spite of national guidelines for its prevention. This retrospective cohort study was undertaken to assess the incidence of culture-proven GBS sepsis before and after a change of practice on intrapartum management of GBS sepsis in babies born at Sunderland Royal Hospital between January 1 2008 and December 31 2017. The timely administration of IAP to all eligible women is possible if the national guidelines are consistent and interpreted correctly. Our national guideline on the prolonged rupture of membranes at term is not clear and is interpreted differently. If IAP is provided in all those with risk factors irrespective of gestation, this would involve additional costs to the NHS; but in the long term, it will benefit as it reduces morbidity.

[The Utility of Soluble CD14 Subtype in Early Diagnosis of Culture-Proven Early-Onset Neonatal Sepsis and Prediction of Outcome.](#)

Gad G.I. et al.

Am J Perinatol. 2019 Mar 21.

To evaluate soluble cluster of differentiation 14 subtype (sCD14-ST), also named presepsin, as an early marker for the diagnosis of culture-proven early-onset sepsis (EOS) in neonates and to assess its relation to disease severity and mortality. sCD14-ST could be used as a powerful diagnostic and prognostic marker of EOS. Its quantitative measurement at birth could be a good predictor of sepsis severity and mortality.

[Preventing early-onset group B streptococcal sepsis: is there a role for rescreening near term?](#)

Mirsky R. et al

J Matern Fetal Neonatal Med. 2019 Mar 19:1-7.

The Centers for Disease Control and Prevention 2010 guidelines recommend group B streptococcus (GBS) screening at 35-37-week gestation to identify women with positive cultures who should receive intrapartum

This study highlights the heterogeneity and infrequency of organ support duration/organ support-free days outcome reporting in septic shock trials. When reported, the definitions of these outcome measures and methods of calculation are also infrequently reported, in particular how nonsurvivors were accounted for, which may have an important impact on interpretation.

[Cardiovascular clusters in septic shock combining clinical and echocardiographic parameters: a post hoc analysis.](#)

Geri G.e t al

Intensive Care Med. 2019 Mar 19.

Mechanisms of circulatory failure are complex and frequently intricate in septic shock. Better characterization could help to optimize hemodynamic support. Our clustering approach on a large population of septic shock patients, based on clinical and echocardiographic parameters, was able to characterize five different cardiovascular phenotypes. How this could help physicians to optimize hemodynamic support should be evaluated in the future.

[The association between autoimmune disease and 30-day mortality among sepsis ICU patients: a cohort study.](#)

Sheth M. et al

Crit Care. 2019 Mar 18;23(1):93.

Sepsis results from a dysregulated host response to an infection that is associated with an imbalance between pro- and anti-inflammatory cytokines. This imbalance is hypothesized to be a driver of patient mortality. Certain autoimmune diseases modulate the expression of cytokines involved in the pathophysiology of sepsis. However, the outcomes of patients with autoimmune disease who develop sepsis have not been studied in

antibiotics and notes that the predictive value of a negative culture declines after 5 weeks. However, despite the lack of evidence, current guidelines do not recommend rescreening for those screened between 35 and 37 weeks. Our objectives were to investigate the rate of conversion from negative to positive results in women rescreened after appropriate screening at 35-37-week gestation and to examine the impact of rescreening on the use of intrapartum antibiotics. Additionally, we examined cases of early-onset group B streptococcal sepsis (early-onset GBS) in term neonates. Our results provide support for the current CDC recommendation against rescreening near term for those women already screened at 35-37-week gestation given the low rate of conversion from negative to positive, and the extremely low rate of early-onset GBS in the screened population.

[Unusual presentation of late-onset disseminated staphylococcal sepsis in a preterm infant.](#)

Khattak S.G. et al

BMJ Case Rep. 2019 Mar 15;12(3). pii: e226325.

An ex-30-week gestation, preterm male baby was admitted to a tertiary neonatal unit and noted to have increased ventilator requirements and diagnosed with sepsis. The baby also developed an abscess over the left elbow and over the xiphisternum along with a decrease in movement of the left hand and the right leg. Pantone-Valentine leukocidin (PVL)-producing *Staphylococcus aureus* (SA) was isolated from the blood culture. A whole body MRI showed disseminated abscess with multiple foci in the lung, left elbow and over the xiphisternum. Disseminated sepsis with multiple septic foci has not been previously reported in neonates. We would like to highlight the fact that sepsis due to PVL toxin-producing SA can cause significant morbidity and mortality in neonates. Proper screening should be done to rule out septic foci in

detail. The objective of this study is to determine whether patients with autoimmune diseases have different sepsis outcomes than patients without these comorbidities. We demonstrated that autoimmune diseases are associated with a lower 30-day mortality risk in sepsis. Our findings suggest that autoimmune diseases affect 30-day mortality through a mechanism unrelated to the chronic use of immunomodulation medications. Since this study was conducted within a single study center, research using data from other medical centers will provide further validation.

[Pulmonary infections prime the development of subsequent ICU-acquired pneumonia in septic shock.](#)

Llitjos J.F. et al

Ann Intensive Care. 2019 Mar 15;9(1):39.

To investigate the determinants and the prognosis of intensive care unit (ICU)-acquired pneumonia in patients with septic shock. Septic shock of pulmonary origin may represent a risk factor for subsequent ICU-acquired pneumonia without affecting mortality.

[The Correlation between Serum Level of Vitamin D and Outcome of Sepsis Patients; a Cross-Sectional Study](#)

Shojaei, M. et al

Archives of Academic Emergency Medicine, 2019, Vol.7(1)

The effect of vitamin D deficiency in manifestation of sepsis and its role as an important mediator in the immune system has received attention. The present study was done with the aim of evaluating the correlation between serum levels of vitamin D and outcome of sepsis patients. Based on the results of the present study, the prevalence of vitamin D deficiency in sepsis patients presenting to the ED was estimated as 61.6%. A significant and indirect correlation was found between the serum level of vitamin D3 and mortality as well as older age. It seems that

neonates. MRI is a good non-invasive investigation to document septic foci in a neonate and rule out multiorgan involvement.

[Asymptomatic bacteriuria in pregnancy: systematic reviews of screening and treatment effectiveness and patient preferences.](#)

Wingert A. et al

BMJ Open. 2019 Mar 13;9(3):e021347.

To systematically review screening and treatment effectiveness, and patient preferences, to inform recommendations by the Canadian Task Force on Preventive Health Care on screening for asymptomatic bacteriuria in pregnancy. Antibiotic treatment for women having significant bacteriuria likely reduces the incidence of pyelonephritis and low birth weight, but we are uncertain about the magnitude of the effect and about the extent to which we can apply these results to asymptomatic populations and screening programmes.

[Effect of chlorhexidine cord application on prevention of neonatal sepsis in developing countries: Systematic review and meta-analysis](#)

Gelano, T.F. et al

International Journal of Health Sciences, 2019, Vol.13(1), p.40-51

The aim of this review was to identify the pooled effect of chlorhexidine cord application on prevention of neonatal sepsis in developing countries. Chlorhexidine cord application significantly reduces neonatal sepsis and mortality in developing countries. Therefore, we stress the importance of including chlorhexidine cord application into the essential newborn care in the setting with high burden of neonatal mortality.

consumption of vitamin D supplements might be helpful in decreasing the prevalence of infection, sepsis, and mortality caused by it, especially in older age.

[Quick Sequential \(Sepsis Related\) Organ Failure Assessment: A high performance rapid prognostication tool in patients having acute pyelonephritis with upper urinary tract calculi](#)

Pandey, S. et al

Investigative and Clinical Urology, 2019, Vol.60(2), p.120-126

Analyzes the utility of quick Sequential Organ Failure Assessment (qSOFA) in patients with uro-sepsis due to acute pyelonephritis (APN) with upper urinary tract calculi, we conducted this study. The role of qSOFA as a tool for rapid prognostication in patients with sepsis is emerging. But there has been a great debate on its utility. Literature regarding utility of qSOFA in uro-sepsis is scarce. qSOFA is a reliable and rapid bedside tool in patients with sepsis with accuracy more than SIRS in predicting inhospital mortality and ICU admissions.

[Association of Lymphopenia with Short Term Outcomes of Sepsis Patients; a Brief Report](#)

Sheikh M. V. et al

Archives of Academic Emergency Medicine, 2019, Vol.7(1)

Studies have claimed that low lymphocyte count is independently correlated with 28-day survival of sepsis patients. Therefore, this study aimed to evaluate the value of lymphopenia in predicting the short-term outcome of sepsis patients. Based on the findings, lymphopenia was independently associated with higher 28-day mortality and lymphopenic patients were older than the control group and had a significantly higher need for ICU admission, higher

[Nested case-control study of multiple serological indexes and Brighton pediatric early warning score in predicting death of children with sepsis](#)

Xie, X. et al

World Journal of Clinical Cases, 2019, Vol.7(4), p.431-440

Currently, it is difficult to predict the complications of children at the early stage of sepsis. Brighton pediatric early warning score (PEWS) is a disease risk assessment system that is simple and easy to operate, which has good sensitivity and specificity in disease recognition among children. Because detection indicators vary widely in children, a single indicator is difficult to assess the post-treatment status of children with sepsis. Antibacterial treatments within 1 h, shock, MODS, PCT, ALB, and PEWS are independent risk factors for the death of children with sepsis. The predictive accuracy of the combination of PCT, ALB, and PEWS for the prognosis of children with sepsis is the best.

[Early Onset Neonatal E.Coli Sepsis](#)

O'Rahelly, M. et al.

Irish medical journal, 14 February 2019, Vol.112(2), pp.868

This was a retrospective case-control study over 14 years comparing characteristics of neonates who developed E.coli bacteraemia with matched infant controls whose mothers were colonised with E.coli on high vaginal swab but who did not develop bacteraemia. Data was obtained from maternal and neonatal charts, the laboratory data-base was analysed to identify possible risk factors for E.coli bacteraemia. 21 cases and 38 controls were identified. The data showed no difference in gender, maternal age, white cell count, or cord pH. Significant differences were found in gestation (33 vs. 39.5wks p5 days is advised.

probability of 28-day septic shock and readmission due to sepsis, and higher SOFA score.

[Relation of neutrophil-to-lymphocyte ratio to acute kidney injury in patients with sepsis and septic shock: A retrospective study](#)

Bu, X. et al

International Immunopharmacology, May 2019, Vol.70, pp.372-377

The purpose of this study was to determine the association of the neutrophil-to-lymphocyte ratio (NLR) measured at the time of admission to intensive unit (ICU) with acute kidney injury (AKI) in patients with sepsis and septic shock. In addition, we investigated whether the NLR affects in-hospital mortality in septic AKI patients. NLR, a laboratory variable that is simple, widely available and inexpensive, was associated with the development of septic AKI and may be potential for risk stratification of septic AKI. •The NLR of the AKI group was higher than that of the non-AKI group in patients with sepsis and septic shock. •The NLR was independent predictors of septic AKI. •The NLR may be a useful marker in septic AKI risk stratification.

[Metformin Affects Serum Lactate Levels in Predicting Mortality of Patients with Sepsis and Bacteremia](#)

Chen, F-C. et al

Journal of clinical medicine, 06 March 2019, Vol.8(3)

This study determined if the use of metformin affected the prognostic value of hyperlactatemia in predicting 28-day mortality among patients with sepsis and bacteremia. Metformin users had higher lactate levels than nonusers in increasing sepsis severity. Serum lactate levels could be useful in predicting mortality in patients using metformin, but higher levels are required to obtain more precise results.

Adult sepsis

[Troponin Testing for Assessing Sepsis-Induced Myocardial Dysfunction in Patients with Septic Shock](#)

Kim, J-S. et al

Journal of Clinical Medicine, 2/2019, Vol.8(2), p.239

Myocardial dysfunction in patients with sepsis is not an uncommon phenomenon, yet reported results are conflicting and there is no objective definition.

Measurement of troponin may reflect the state of the heart and may correlate with echocardiographically derived data. This study aimed to evaluate the role of admission and peak troponin-I testing for the identification of sepsis-induced myocardial dysfunction (SIMD) by transthoracic echocardiography (TTE). About two-thirds of patients with an elevated hs-TnI level have various cardiac dysfunctions in terms of TTE. Rather than the initial level, the peak hs-TnI and ST-T change may be considered as a risk factor of SIMD.

[Does use of Electronic Alerts for Systemic Inflammatory Response Syndrome \(SIRS\) to Identify Patients with Sepsis Improve Mortality?](#)

Seetharaman, S. et al

The American journal of medicine, 01 March 2019

The objective of this study was to assess if earlier antibiotic administration in patients with Systemic Inflammatory Response Syndrome (SIRS) and evidence of organ dysfunction identified through electronic alerts improves patient mortality. The use of alerts in the electronic medical record may misclassify patients with SIRS as having sepsis. Time to antibiotic administration in patients meeting SIRS criteria and evidence of end-organ dysfunction through BPA alerts did not affect 30-day mortality rates across a health system. Patient severity of illness, gender and facility also independently predicted mortality. There were higher rates of antibiotic use and Clostridium difficile infection in patients with BPA alerts.

[Epidemiology and Predictors of 30-Day Readmission in Patients With Sepsis](#)

Gadre, S.K. et al

Chest, March 2019, Vol.155(3), pp.483-490

Patients with sepsis are particularly vulnerable to readmissions. We describe the associated etiology and risk factors for readmission in patients with sepsis using a large administrative database inclusive of patients of all ages and insurance status. Our study cohort was derived from the Healthcare Cost and Utilization Project's National Readmission Data from 2013 to 2014 by identifying patients admitted with sepsis. We describe that readmission after a sepsis hospitalization is common and costly. The majority of readmissions were associated with infectious etiologies. The striking rate of readmission demands efforts to further clarify the determinants of readmission and develop strategies in terms of quality of care and care transitions to prevent this outcome.

[Risk factors for infection and evaluation of Sepsis-3 in patients with trauma](#)

Eguia, E. et al

The American Journal of Surgery 2019 Mar 8

We aim to examine the risk factors associated with infection in trauma patients and the Sepsis-3 definition. Patients with trauma often arrive with organ dysfunction, which adds complexity and inaccuracy to the operational definition of Sepsis-3 using changes in SOFA scores. Injury severity score, comorbidities, SOFA score, and sex are risk factors associated with developing an infection after trauma.

- Injured patients arrive with organ dysfunction, which adds inaccuracy to the operational definition of Sepsis-3.
- Injury severity score, comorbidities, SOFA score, and sex are risk factors associated with developing an infection after an injury.
- The admission SOFA score

[The ATP-binding cassette gene ABCF1 functions as an E2 ubiquitin-conjugating enzyme controlling macrophage polarization to dampen lethal septic shock.](#)

Arora, H. et al.

Immunity 50, 418–431 (2019)

Sepsis is a bi-phasic inflammatory disease that threatens approximately 30 million lives and claims over 14 million annually, yet little is known regarding the molecular switches and pathways that regulate this disease. Here, we have described ABCF1, an ATP-Binding Cassette (ABC) family member protein, which possesses an E2 ubiquitin enzyme activity, through which it controls the Lipopolysaccharide (LPS)- Toll-like Receptor-4 (TLR4) mediated gram-negative insult by targeting key proteins for K63-polyubiquitination. Ubiquitination by ABCF1 shifts the inflammatory profile from an early phase MyD88-dependent to a late phase TRIF-dependent signaling pathway, thereby regulating TLR4 endocytosis and modulating macrophage polarization from M1 to M2 phase. Physiologically, ABCF1 regulates the shift from the inflammatory phase of sepsis to the endotoxin tolerance phase, and modulates cytokine storm and interferon- β (IFN- β)-dependent production by the immunotherapeutic mediator, SIRT1. Consequently, ABCF1 controls sepsis induced mortality by repressing hypotension-induced renal circulatory dysfunction.

[ED Door-to-Antibiotic Time and Long-term Mortality in Sepsis](#)

Peltan, I.D. et al

Chest 2019 Feb 16.

The impact of antibiotic timing on sepsis outcomes remains controversial due to conflicting results from previous studies. This study investigated the association of door-to-antibiotic time with long-term

was greater than the SOFA score at the time of infection in 17% of infected cases.

[Global impact of World Sepsis Day on digital awareness of sepsis: an evaluation using Google Trends](#)

Savelkoel, J. et al

Critical Care, 12/2018, Vol.22(1)

World Sepsis Day (WSD) was established by the Global Sepsis Alliance in 2012 and is held every 13th of September. One of the objectives is to raise global awareness of sepsis. Despite its high mortality rate, an international survey reported that 80–90% of the public in western countries are unfamiliar with sepsis. Anno 2018, public knowledge is no longer solely obtained via television and newspapers, but is largely acquired via the Internet and social media. These resources therefore contribute to digital awareness, and can be used to share knowledge. We aimed to investigate whether WSD is indeed associated with a global increase in digital information-seeking behaviour.

[Manifold beneficial effects of acetyl salicylic acid and nonsteroidal anti-inflammatory drugs on sepsis](#)

Eisen, Damon P.

Intensive Care Medicine, 8/2012, Vol.38(8), pp.1249-1257

Acetyl salicylic acid (ASA) and nonsteroidal anti-inflammatory drugs (NSAIDs) may have potential as adjunctive agents for sepsis. This review considers the large body of literature that indicates a basis for sepsis therapy with ASA and suggests an agenda for future intervention studies in sepsis prevention and treatment. Low-dose ASA appears to be beneficial in the prevention and treatment of sepsis and SIRS. If proven, this intervention would have a major, cost-effective impact on sepsis care.

mortality in ED patients with sepsis. Delays in ED antibiotic initiation time are associated with clinically important increases in long-term, risk-adjusted sepsis mortality.

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