



Here is the latest edition of the Sepsis Bulletin. The bulletin covers the latest information on sepsis and comes out monthly. Next edition is due February 2020. 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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<p>Adult sepsis</p>
<p>Circulating Complement C3-Alpha Chain Levels Predict Survival of Septic Shock Patients. Cheng TH; et al Shock (Augusta, Ga.); Dec 2019 Circulating complement C3 fragments released during septic shock might contribute to the development of complications such as profound hypotension and disseminated intravascular coagulation. The role of C3 in the course of septic shock varies in the literature, possibly because circulating C3 exists in different forms indistinguishable via traditional ELISA-based methods. We sought to test the relationship between C3 forms, measured by Western blotting with its associated protein size differentiation feature, and clinical outcomes. Circulating C3-alpha chain levels is a significant independent predictor of survival in septic shock patients.</p>
<p>Complement Activation in Human Sepsis is Related to Sepsis-Induced Disseminated Intravascular Coagulation. Abe T; et al Shock (Augusta, Ga.); Jan 2020 In human sepsis, little is known about the relationships between complement activation and the clinical</p>

characteristics of sepsis, including disseminated intravascular coagulation (DIC), interventions, and prognosis. The degree of complement activation is related to DIC, severity, intensive interventions, and mortality. Further studies are needed to confirm the usefulness of SC5b-9 for stratifying sepsis patients.

[C-reactive protein as a prognostic factor in intensive care admissions for sepsis: A Swedish multicenter study.](#)

Koozi H; et al

Journal of critical care; Dec 2019; vol. 56 ; p. 73-79

C-reactive protein (CRP) is not included in the major intensive care unit (ICU) prognostic tools such as the Simplified Acute Physiology Score (SAPS). We assessed CRP on ICU admission as a SAPS-3 independent risk marker for short-term mortality and length of stay (LOS) in ICU patients with sepsis. An admission CRP level >100 mg/L is associated with an increased risk of ICU and 30-day mortality as well as prolonged LOS in survivors, irrespective of morbidity measured with SAPS-3. Thus, CRP may be a simple, early marker for prognosis in ICU admissions for sepsis.

[Delay in Antibiotic Administration Is Associated With Mortality Among Septic Shock Patients With Staphylococcus aureus Bacteremia.](#)

Corl KA; et al

Critical care medicine; Dec 2019

The relationship between the timing of antibiotics and mortality among septic shock patients has not been examined among patients specifically with Staphylococcus aureus bacteremia. The results of this study further support the importance of prompt appropriate antibiotic administration for patients with septic shock. Physicians should consider acting quickly to administer antibiotics with S. aureus coverage to any patient suspected of having septic shock.

[Double inter-hospital transfer in Sepsis patients presenting to the ED does not worsen mortality compared to single inter-hospital transfer.](#)

Arulraja MD; et al

Journal of critical care; Nov 2019; vol. 56 ; p. 49-57

Sepsis is a leading cause of hospital deaths. Inter-hospital transfer is frequent in sepsis and is associated with increased mortality. Some sepsis patients undergo two inter-hospital transfers (double transfer). This study assessed the (1) prevalence, (2) associated risk factors, (3) associated mortality, and (4) hospital length-of-stay and costs of double-transfer of sepsis patients. Double-transfer occurs in 2.1% of low-sepsis patients. Double-transfers had similar mortality and increased length of stay and costs compared to single-transfers.

[Effect of Pravastatin Pretreatment and Hypercapnia on Intestinal Microvascular Oxygenation and Blood Flow During Sepsis.](#)

Schulz J et al

Shock (Augusta, Ga.); Jan 2020; vol. 53 (no. 1); p. 88-94

In septic patients, adequate microvascular oxygenation (μHbO_2) of the intestine is vital for their outcome. Recent studies suggest that statins can ameliorate septic microcirculation in a variety of tissues. However, the effect on intestinal microvascular oxygenation and blood flow is largely unknown. Furthermore, there are indications that statin therapy might not be beneficial in the presence of hypercapnia, as observed in septic acute respiratory distress syndrome (ARDS) patients. Therefore, the present study explores the effect of pravastatin with and without additional moderate acute hypercapnia on intestinal microvascular oxygenation and blood flow in experimental sepsis. Pravastatin pretreatment ameliorates the intestinal microvascular oxygenation in sepsis and thus seems to prevent intestinal hypoxia. Furthermore, we demonstrated that additional hypercapnia abolishes this effect, indicating why septic ARDS patients might not benefit from pravastatin therapy.

[Endotoxin Removal in Septic Shock with the Alteco® LPS Adsorber was Safe But Showed No Benefit Compared to Placebo in the Double-Blind Randomized Controlled Trial - the Asset Study.](#)

Lipcsey M; et al

Shock (Augusta, Ga.); Dec 2019

Lipopolysaccharides (LPS) are presumed to contribute to the inflammatory response in sepsis. We

investigated if extracorporeal Alteco® LPS Adsorber for LPS removal in early Gram-negative septic shock was feasible and safe. Also, effect on endotoxin level, inflammatory response and organ function were assessed. In a small cohort of patients with presumed Gram-negative septic shock, levels of circulating endotoxin were low and no adverse effects within 28 days after LPS adsorber-treatment were observed. No benefit compared to a sham device was seen when using a LPS adsorber in addition to standard care.

[Fluid resuscitation in patients with end-stage renal disease on hemodialysis presenting with severe sepsis or septic shock: A case control study.](#)

Rajdev K; et al

Journal of critical care; Feb 2020; vol. 55 ; p. 157-162

Due to the potential risk of volume overload, physicians are hesitant to aggressively fluid-resuscitate septic patients with end-stage renal disease (ESRD) on hemodialysis (HD). Our study indicates that aggressive fluid resuscitation appears to be safe in ESRD patients.

[From a pressure-guided to a perfusion-centered resuscitation strategy in septic shock: Critical literature review and illustrative case.](#)

Gazmuri RJ; de Gomez CA

Journal of critical care; Nov 2019

We support a paradigm shift in the management of septic shock from pressure-guided to perfusion-centered, expected to improve outcome while reducing adverse effects from vasopressor therapy and aggressive fluid resuscitation. We propose focusing the hemodynamic management of septic shock on reversing organ hypoperfusion instead of attaining a predefined MAP target as the key strategy for improving outcome.

[Impact of insufficient admission vitamin D serum concentrations on sepsis incidence and clinical outcomes in patients with thermal injury.](#)

Zavala S; et al

Burns ; journal of the International Society for Burn Injuries; Dec 2019

In burn patients, vitamin D has been studied primarily in the pediatric population and focused mainly on the correlation with bone marker measurements and incidence of fractures. There is an association between vitamin D deficiency and the development of sepsis in non-burn critically-ill patients. However, there is limited data on vitamin D concentrations and clinical outcomes in burn patients, such as sepsis. The objective of this study is to evaluate the impact of vitamin D concentrations on the incidence of sepsis in adult burn patients. Patients with adequate vitamin D concentrations on admission had a reduction in the incidence of sepsis as compared to patients with insufficient vitamin D concentrations. Insufficient vitamin D concentrations may contribute to other worsened clinical outcomes in burn patients. Our findings set the stage for future, multicenter studies to determine the role of vitamin D supplementation in burn patients.

[Impaired B-Cell Maturation Contributes to Reduced B Cell Numbers and Poor Prognosis in Sepsis.](#)

Duan S; et al

Shock (Augusta, Ga.); Nov 2019

Reduced B cell numbers plays a critical role in sepsis immunosuppression. The role of B-cell maturation regulated by T follicular helper (Tfh) cells in reduced B cell numbers during sepsis remains unclear. We tested the hypothesis that impaired B-cell maturation contributes to reduced B cell numbers. Impaired B-cell maturation contributes to reduced B cell numbers, while the numbers of cTfh cell, acting as a warning indicator for sepsis prognosis, may be a new therapeutic target for treating sepsis.

[Improved Outcomes After Regional Implementation of Sepsis Alert: A Novel Triage Model.](#)

Rosenqvist M; et al

Critical care medicine; Jan 2020

We assess whether the triage model Sepsis Alert for Emergency Departments results in improved initial care of patients with severe infections. The implementation of the new triage model Sepsis Alert with special attention to severe sepsis patients led to faster and more accurate antibiotic treatment and improved diagnostic procedures and supportive care.

[Incidence, risk factors, and outcomes for sepsis-associated delirium in patients with mechanical](#)

[ventilation: A sub-analysis of a multicenter randomized controlled trial.](#)

Yamamoto T; et al

Journal of critical care; Dec 2019; vol. 56 ; p. 140-144

This study aimed to investigate incidence, risk factors, and outcomes for sepsis-associated delirium (SAD) in mechanically ventilated patients. SAD was associated with a less number of ventilator-free days and longer length of ICU stay. Emergency surgery, more doses of midazolam, and fentanyl may be independent risk factors for SAD in mechanically ventilated patients with sepsis.

[Inhibition of Aerobic Glycolysis Promotes Neutrophil to Influx to the Infectious Site Via CXCR2 in Sepsis.](#)

Tan C; et al

Shock (Augusta, Ga.); Jan 2020; vol. 53 (no. 1); p. 114-123

Recent evidences suggest that metabolic reprogramming plays an important role in the regulation of innate inflammatory response; however, the specific mechanism is unclear. Together, we found a novel mechanism for the migration of neutrophils regulated by metabolism and suggested that aerobic glycolysis might be a potential target of intervention in sepsis.

[Lubricin as a Therapeutic and Potential Biomarker in Sepsis.](#)

Richendrfer H; Jay GD

Critical care clinics; Jan 2020; vol. 36 (no. 1); p. 55-67

Proteoglycan 4 (or lubricin), a mucin-like glycoprotein, was originally classified as a lubricating substance within diarthrodial joints. More recently, lubricin has been found in other tissues and has been implicated in 2 inflammatory pathways within the cell, via the Toll-like receptors (TLRs) and CD44. Lubricin is an antagonist of TLR2 and TLR4, and appears to enter cells via the CD44 receptor. Because of lubricin's action on these receptors, downstream processes of inflammation are halted, thereby preventing release of cytokines (a hallmark of inflammation and sepsis) from the cell, indicating lubricin's role as a biomarker and possible therapeutic for sepsis.

[Methane-Rich Saline Protects Against Sepsis-Induced Liver Damage by Regulating the PPAR- \$\gamma\$ /NF- \$\kappa\$ B Signaling Pathway.](#)

Li Z; et al

Shock (Augusta, Ga.); Dec 2019; vol. 52 (no. 6); p. e163-e172

Sepsis, a life-threatening organ dysfunction due to a dysregulated response to infection, is a common complication of major surgery. Previous studies have shown that methane possesses protective properties. This study aims to investigate the protective effect of methane-rich saline (MRS) on sepsis-induced liver injury. Our data indicated that methane treatment prevented liver damage in sepsis via anti-inflammatory, anti-oxidative, and anti-apoptotic properties that involved the PPAR- γ /NF- κ B signaling pathway.

[Muscle degradation, vitamin D and systemic inflammation in hospitalized septic patients.](#)

Borges RC; et al

Journal of critical care; Dec 2019; vol. 56 ; p. 125-131

To date, the relationship between systemic inflammation and muscle changes observed by ultrasonography in septic patients in clinical studies is not known. Furthermore, the role of vitamin D on muscle changes in these patients needs to be investigated. In septic patients, there is an association between inflammation and changes in muscle mass and strength during ICU stay, which is similar to those observed in experimental studies. In addition, there was an association of vitamin D with recovery of muscle strength during hospitalization.

[Performance of a quick sofa-65 score as a rapid sepsis screening tool during initial emergency department assessment: A propensity score matching study.](#)

Lee J; Song JU

Journal of critical care; Feb 2020; vol. 55 ; p. 1-8

We sought to elucidate the performance of a Quick Sequential Organ Function Assessment-65 (qSOFA-65) score in recognizing sepsis and to compare the qSOFA-65 score to systemic inflammatory response syndrome (SIRS) and qSOFA scores. We found that qSOFA-65 was more likely to identify patients with sepsis on the initial ED visit relative to qSOFA or SIRS. This may have quality improvement implications in

predicting sepsis.

[Plasma Mitochondrial DNA Levels Are Associated With ARDS in Trauma and Sepsis Patients.](#)

Faust HE; et al

Chest; Jan 2020; vol. 157 (no. 1); p. 67-76

Critically ill patients who develop ARDS have substantial associated morbidity and mortality. Circulating mitochondrial DNA (mtDNA) released during critical illness causes endothelial dysfunction and lung injury in experimental models. This study hypothesized that elevated plasma mtDNA is associated with ARDS in critically ill patients with trauma and sepsis. Plasma mtDNA levels were associated with incident ARDS in two critical illness populations. Given supportive preclinical data, our findings suggest a potential link between circulating mtDNA and lung injury and merit further investigation as a potentially targetable mediator of ARDS.

[Plasma sRAGE Acts as a Genetically Regulated Causal Intermediate in Sepsis-associated Acute Respiratory Distress Syndrome.](#)

Jones TK; et al

American journal of respiratory and critical care medicine; Jan 2020; vol. 201 (no. 1); p. 47-56

Acute respiratory distress syndrome (ARDS) lacks known causal biomarkers. Plasma concentrations of sRAGE (soluble receptor for advanced glycation end products) strongly associate with ARDS risk. However, whether plasma sRAGE contributes causally to ARDS remains unknown. Plasma sRAGE is genetically regulated during sepsis, and MR analysis indicates that increased plasma sRAGE leads to increased ARDS risk, suggesting plasma sRAGE acts as a causal intermediate in sepsis-related ARDS.

[Predictive Accuracy of the Quick Sepsis-Related Organ Failure Assessment Score in Brazil: A Prospective Multicenter Study.](#)

Machado FR; et al

American journal of respiratory and critical care medicine; Jan 2020

Although proposed as a clinical prompt to sepsis based on predictive validity for mortality, the quick Sequential Organ Failure Assessment (qSOFA) score is often used as a screening tool, which requires high sensitivity. We assessed the predictive accuracy of qSOFA for mortality in Brazil, focusing on sensitivity. qSOFA ≥ 2 has low sensitivity for predicting death in patients with suspected infection in a developing country. Using qSOFA ≥ 2 as a screening tool for sepsis may miss patients that ultimately die. Using qSOFA ≥ 1 or adding lactate to qSOFA ≥ 1 may improve sensitivity.

[Regulatory Roles of Human Surfactant Protein B Variants on Genetic Susceptibility to Pseudomonas Aeruginosa Pneumonia-Induced Sepsis.](#)

Yang F; et al

Shock (Augusta, Ga.); Dec 2019

Surfactant protein B (SP-B) is essential for life and plays critical roles in host defense and lowering alveolar surface tension. A single nucleotide polymorphism (SNP rs1130866) of human SP-B (hSP-B) alters the N-linked glycosylation, thus presumably affecting SP-B function. This study has investigated the regulatory roles of hSP-B genetic variants on lung injury in pneumonia-induced sepsis. hSP-B variants differentially regulate susceptibility through modulating the surface activity of surfactant, cell death and inflammatory signaling in sepsis.

[Rescue stem cell allograft in intensive care unit patients during septic shock with multi-organ failure.](#)

Leprêtre P; et al

Journal of critical care; Dec 2019; vol. 54 ; p. 122-124

We describe what we believe to be the first two cases of patients who received an allograft in intensive care unit (ICU) despite severe septic shock with multi-organ failure (MOF). Allograft should be considered as a rescue therapy in ICU for patients with aplasia, during septic shock with multi-organ failure, however close multidisciplinary discussion is required between intensivists and onco-hematologists.

[Sepsis quality in safety-net hospitals: An analysis of Medicare's SEP-1 performance measure.](#)

Barbash IJ; Kahn JM

Journal of critical care; Dec 2019; vol. 54 ; p. 88-93

Newly enacted policies at the state and federal level in the United States require acute care hospitals to

engage in sepsis quality improvement. However, responding to these policies requires considerable resources and may disproportionately burden safety-net hospitals. To better understand this issue, we analyzed the relationship between hospital safety-net status and performance on Medicare's SEP-1 quality measure. Existing sepsis policies may harm safety-net hospitals and widen health disparities. Our findings suggest that strategies to promote collaboration among hospitals may be an avenue for sepsis performance improvement in safety-net hospitals.

[Tenascin C Plasma Levels in Critically Ill Patients with or Without Sepsis: A Multicentre Observational Study.](#)

Meijer MT; et al

Shock (Augusta, Ga.); Nov 2019

Tenascin C (TNC) is an extracellular matrix protein able to modulate the immune response. Knowledge regarding its role during sepsis and general critical illness is still limited. We here assessed the temporal dynamics of plasma TNC during sepsis and non-septic critical illness, its capacity to predict patient outcome, and its specificity towards infection. Although admission TNC was higher in CAP than in no-CAP patients, it performed poorly in distinguishing the two groups. TNC plasma levels are persistently elevated during sepsis and non-septic critical illness. In sepsis patients they are reflective of disease severity more than independent predictors of mortality. Despite higher levels in patients with infection compared with non-infectious controls, TNC does not perform sufficiently to be used as a standalone biomarker discriminating sepsis from non-infectious critical illness.

[The Epidemiology of Sepsis in Chinese ICUs: A National Cross-Sectional Survey.](#)

Xie J; et al

Critical care medicine; Dec 2019

We performed a national cross-sectional survey to determine the epidemiologic characteristics of patients with sepsis in ICU in China. Sepsis affects a fifth of patients admitted to ICUs in mainland China with a 90-day mortality rate of 35.5%. Our findings indicate that a large burden of sepsis, and we need to focus on sepsis as a quality improvement target in China given the high mortality. In addition, further studies are needed to delineate the epidemiology of sepsis outside the ICU.

[Therapeutic and Adverse Effects of Thrombomodulin Alfa to Treat Sepsis-Induced Disseminated Intravascular Coagulation.](#)

Imaura M; et al

Shock (Augusta, Ga.); Nov 2019

In the treatment of disseminated intravascular coagulation (DIC), which is a complication of underlying diseases such as infections and malignant tumors, effective plasma concentrations of thrombomodulin (TM) alfa range from 300-900 ng/mL; however, appropriate concentrations when treating sepsis-induced DIC are unknown. Thus, our aim was to determine the relationship between plasma concentrations of TM alfa and its therapeutic effects, and hemorrhagic adverse events. The recommended plasma concentration of TM alfa in the treatment of septic DIC was determined to be higher than 600 ng/mL, and a dose of 380 U/kg (0.06 mg/kg) was necessary to achieve this concentration.

Neonatal, paediatric and maternal sepsis

[PERSEVERE Biomarkers Predict Severe Acute Kidney Injury and Renal Recovery in Pediatric Septic Shock.](#)

Stanski NL; et al

American journal of respiratory and critical care medicine; Jan 2020

Acute kidney injury (AKI), a common complication of sepsis, is associated with substantial morbidity and mortality and lacks definitive disease-modifying therapy. Early, reliable identification of at risk patients is important for targeted implementation of renal protective measures. PERSEVERE-II is a validated, multi-biomarker prognostic enrichment strategy to estimate baseline mortality risk in pediatric septic shock. Among children with septic shock, the PERSEVERE biomarkers predict severe D3 SA-AKI and identify patients with early AKI who are likely to recover.

[Mitochondrial dysfunction is associated with an immune paralysis phenotype in pediatric sepsis.](#)

Weiss SL; et al

Shock (Augusta, Ga.); Nov 2019

Immune dysregulation is a defining feature of sepsis, but the role for mitochondria in the development of immunoparalysis in pediatric sepsis is not known. We sought to determine if mitochondrial dysfunction measured in peripheral blood mononuclear cells (PBMCs) is associated with immunoparalysis and systemic inflammation in children with sepsis. Children with sepsis had lower PBMC mitochondrial respiration when immunoparalysis was present compared to those without immunoparalysis. The subsets with immune paralysis and low mitochondrial respiration exhibited the highest levels of systemic inflammation.

['Intermittent' versus 'continuous' ScvO2 monitoring in children with septic shock: a randomised, non-inferiority trial.](#)

Sankar J; et al

Intensive care medicine; Jan 2020; vol. 46 (no. 1); p. 82-92

We compare the effect of 'intermittent' central venous oxygen saturation (ScvO2) monitoring with 'continuous' ScvO2 monitoring on shock resolution and mortality in children with septic shock. Given that a greater proportion of children attained therapeutic end points in the first 6 h, continuous monitoring of ScvO2 should preferably be used to titrate therapy in the first few hours in children with septic shock. In the absence of such facility, intermittent monitoring of ScvO2 can be used to titrate therapy in these children, given the lack of difference in the proportion of patients achieving shock resolution at 24 h or in risk of mortality between the intermittent and continuous groups.

[Bacterial and Fungal Etiology of Sepsis in Children in the United States: Reconsidering Empiric Therapy.](#)

Prout AJ; et al

Critical care medicine; Nov 2019

Timely empiric antimicrobial therapy is associated with improved outcomes in pediatric sepsis, but minimal data exist to guide empiric therapy. We sought to describe the prevalence of four pathogens that are not part of routine empiric coverage (e.g., *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Clostridium difficile*, and fungal infections) in pediatric sepsis patients in a contemporary nationally representative sample. In this nationally representative administrative database, the most common identified pathogen was *S. aureus* in previously healthy and chronically ill children. In addition, a high proportion of children with sepsis and select chronic diseases had infections with methicillin-resistant *S. aureus*, fungal infections, *Pseudomonas* infections, and *C. difficile*. Clinicians caring for pediatric patients should consider coverage of these organisms when administering empiric antimicrobials for sepsis.

[Universal screening versus risk-based protocols for antibiotic prophylaxis during childbirth to prevent early-onset Group B streptococcal disease: a systematic review and meta-analysis.](#)

Hasperhoven GF et al

BJOG : an international journal of obstetrics and gynaecology; Jan 2020

Early-onset group B streptococcal (EOGBS) disease (including sepsis, meningitis, and pneumonia) causes significant morbidity and mortality in newborn infants worldwide. Antibiotic prophylaxis can prevent vertical streptococcal transmission, yet no uniform criteria to identify eligible women for prophylaxis exist. Some guidelines recommend universal GBS screening to pregnant women in their third trimester (screening-based protocol), while others employ risk-based protocols. We compare the effectiveness of screening-based vs risk-based protocols in preventing EOGBS disease. Screening-based protocols were associated with lower incidences of EOGBS disease compared to risk-based protocols, while not clearly overexposing women to antibiotics. This information is of relevance for future policymaking.

[Measurement of gut oxygenation in the neonatal population using near-infrared spectroscopy: a clinical tool?](#)

Seager E; et al

Archives of disease in childhood. Fetal and neonatal edition; Jan 2020; vol. 105 (no. 1); p. 76-86

Near-infrared spectroscopy (NIRS) is a non-invasive bedside monitor of tissue oxygenation that may be a useful clinical tool in monitoring of gut oxygenation in newborn infants. We systematically review literature to determine whether NIRS is a reliable tool to monitor gut oxygenation on neonatal units. NIRS may prove to be a useful bedside tool on the neonatal unit, working alongside current clinical tools in the monitoring of newborn infants (preterm and term) and inform clinical management. We recommend further studies including randomised controlled trials looking at specific measurements and

cut-offs for abdominal NIRS for use in further clinical practice.

[Core outcomes in neonatology: development of a core outcome set for neonatal research.](#)

Webbe JWH; et al.

Archives of disease in childhood. Fetal and neonatal edition; Nov 2019

Neonatal research evaluates many different outcomes using multiple measures. This can prevent synthesis of trial results in meta-analyses, and selected outcomes may not be relevant to former patients, parents and health professionals. A COS for clinical trials and other research studies involving infants receiving neonatal care in a high-income setting has been identified. This COS for neonatology will help standardise outcome selection in clinical trials and ensure these are relevant to those most affected by neonatal care.

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