

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 October 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](http://libguides.bodleian.ox.ac.uk/Keeping_up_to_date))

I had a request to add a section on NEWS and NEWS 2. Please let me know if there is anything you would like to see highlighted in the bulletin

Please also pass the bulletin on to other interested people and encourage them to sign up. Anyone can be added to the mailing list.

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## SEPSIS BULLETIN September 2019

### NEWS

[Using sepsis scores in emergency department and ward patients.](#)

Steele L, Hill S

**Br J Hosp Med (Lond).** 2019 Aug 2;80(8):C120-C123. Sepsis-3, published in 2016, defined sepsis as 'life-threatening organ dysfunction caused by a dysregulated host response to infection'. Instead of systemic inflammatory response syndrome (SIRS), calculating the Sequential Organ Failure Assessment (SOFA) score was recommended. The complexity of SOFA also led to the introduction of quick SOFA (qSOFA) as a bedside tool. The simultaneous removal of SIRS and introduction of qSOFA belies their significant differences, with SIRS having a high sensitivity but very low specificity, and qSOFA being very specific for a poor

### Adult sepsis

[Effect of a Recombinant Human Soluble Thrombomodulin on Mortality in Patients With Sepsis-Associated Coagulopathy: The SCARLET Randomized Clinical Trial.](#)

Vincent JL, et al

**JAMA.** 2019 May 28;321(20):1993-2002.

Previous research suggested that soluble human recombinant thrombomodulin may reduce mortality among patients with sepsis-associated coagulopathy. To determine the effect of human recombinant thrombomodulin vs placebo on 28-day all-cause mortality among patients with sepsis-associated coagulopathy. Among patients with sepsis-associated coagulopathy, administration of a human recombinant thrombomodulin, compared with placebo, did not

outcome, but having a lower sensitivity than SIRS. In the UK, the variables within qSOFA are collected on a regular and repeated basis, along with additional variables, as part of the National Early Warning Score (NEWS). A knowledge of SIRS, qSOFA and NEWS is of value in assessing patients with suspected sepsis, as discussed in this article.

[Clinical Scores and Formal Triage for Screening of Sepsis and Adverse Outcomes on Arrival in an Emergency Department All-Comer Cohort.](#)

Nieves Ortega R, et al

**J Emerg Med.** 2019 Sep 6. pii: S0736-4679(19)30552-9.

Early recognition of sepsis remains a major challenge. The clinical utility of the Quick Sepsis-Related Organ Failure Assessment (qSOFA) score is still undefined. Several studies have tested its prognostic value. However, its ability to diagnose sepsis is still unknown. Our aim was to compare the performance of qSOFA, systemic inflammatory response syndrome (SIRS) criteria, National Early Warning Score (NEWS), and formal triage with the Emergency Severity Index (ESI) algorithm to identify patients with sepsis and predict adverse outcomes on arrival in an emergency department (ED) all-comer cohort. qSOFA offered high specificity for the prediction of sepsis and adverse outcomes. However, its low sensitivity does not support widespread use as a screening tool for sepsis. NEWS outperformed qSOFA for prediction of adverse outcomes and screening for sepsis.

[Early identification of severe community-acquired pneumonia: a retrospective observational study.](#)

Grudzinska FS, et al

**BMJ Open Respir Res.** 2019 Jun 5;6(1):e000438.

Community-acquired pneumonia (CAP) is a leading cause of sepsis worldwide. Prompt identification of those at high risk of adverse outcomes improves survival by enabling early escalation of care. There are multiple severity assessment tools recommended for risk stratification; however, there is no consensus as to which tool should be used for those with CAP. We sought to assess whether pneumonia-specific, generic sepsis or early warning scores were most accurate at predicting adverse outcomes. All four scoring systems can stratify according to increasing risk in CAP; however, when a confident diagnosis of pneumonia can be made, these data support the use of pneumonia-specific tools rather than generic sepsis or early warning scores.

significantly reduce 28-day all-cause mortality.

[Vitamin C and Thiamine for Sepsis and Septic Shock.](#)

Mitchell et al

**Am J Med.** 2019 Aug 27. pii: S0002-9343(19)30699-0.

Sepsis and septic shock are medical emergencies resulting in significant morbidity and mortality. Intravenous (IV) vitamin C, thiamine, and hydrocortisone have shown promise in reducing hospital mortality. The Memphis Veterans Affairs Medical Center (VAMC) similarly implemented this regimen, called the vitamin C protocol, for patients presenting in sepsis or septic shock in the intensive care unit (ICU). Although no significant mortality benefit was observed, the vitamin C protocol was not associated with patient harm. In this Veteran population, there was reduced ICU length of stay, suggesting possible benefit. Though further investigation is warranted, utilization of IV vitamin C, thiamine, and hydrocortisone in patients with sepsis or septic shock may be a treatment option worth considering.

[Real World Patterns of Antimicrobial Use and Microbiology Investigations in Patients with Sepsis outside the Critical Care Unit: Secondary Analysis of Three Nation-Wide Point Prevalence Studies.](#)

Kopczynska M, et al

**J Clin Med.** 2019 Aug 29;8(9). pii: E1337. doi:

10.3390/jcm8091337.

Recent description of the microbiology of sepsis on the wards or information on the real-life antibiotic choices used in sepsis is lacking. There is growing concern of the indiscriminate use of antibiotics and omission of microbiological investigations in the management of septic patients. We performed a secondary analysis of three annual 24-h point-prevalence studies on the general wards across all Welsh acute hospitals in years 2016-2018. Our study shows that antibiotics prescription practice is not accompanied by microbiological investigations. A significant proportion of sepsis patients are still at risk of not receiving appropriate antibiotics treatment and microbiological investigations; this may be improved by a more thorough implementation of sepsis screening tools.

[Evaluation and Predictors of Fluid Resuscitation in Patients With Severe Sepsis and Septic Shock.](#)

Kuttab HI, et al

**Crit Care Med.** 2019 Aug 7.

[Computer-aided National Early Warning Score to predict the risk of sepsis following emergency medical admission to hospital: a model development and external validation study.](#)

Faisal M, et al

**CMAJ.** 2019 Apr 8;191(14):E382-E389.

In hospitals in England, patients' vital signs are monitored and summarized into the National Early Warning Score (NEWS); this score is more accurate than the Quick Sepsis-related Organ Failure Assessment (qSOFA) score at identifying patients with sepsis. We investigated the extent to which the accuracy of the NEWS is enhanced by developing and comparing 3 computer-aided NEWS (cNEWS) models (M0 = NEWS alone, M1 = M0 + age + sex, M2 = M1 + subcomponents of NEWS + diastolic blood pressure) to predict the risk of sepsis. From the 3 cNEWS models, model M2 is the most accurate. Given that it places no additional burden of data collection on clinicians and can be automated, it may now be carefully introduced and evaluated in hospitals with sufficient informatics infrastructure.

[Persistently elevated early warning scores and lactate identifies patients at high risk of mortality in suspected sepsis.](#)

Hargreaves DS, et al

**Eur J Emerg Med.** 2019 Aug 28.

In the UK, the National early warning score (NEWS) is recommended as part of screening for suspicion of sepsis. Is a change in NEWS a better predictor of mortality than an isolated score when screening for suspicion of sepsis? Persistently elevated NEWS, from prehospital through the ED to the time of ward admission, combined with an elevated ED lactate identifies patients with suspicion of sepsis at highest risk of in-hospital mortality.

**Neonatal and paediatric sepsis**

[Presepsin as a diagnostic marker of sepsis in children and adolescents: a systemic review and meta-analysis.](#)

Yoon SH, et al.

**BMC Infect Dis.** 2019 Aug 30;19(1):760. doi: 10.1186/s12879-019-4397-1.

Early diagnosis of sepsis in pediatric patients is vital but remains a major challenge. Previous studies showed that presepsin is potentially a reliable diagnostic biomarker for sepsis in adult and neonates. However,

Rapid fluid resuscitation has become standard in sepsis care, despite "low-quality" evidence and absence of guidelines for populations "at risk" for volume overload. Our objectives include as follows: 1) identify predictors of reaching a 30 mL/kg crystalloid bolus within 3 hours of sepsis onset (30by3); 2) assess the impact of 30by3 and fluid dosing on clinical outcomes; 3) examine differences in perceived "at-risk" volume-sensitive populations, including end-stage renal disease, heart failure, obesity, advanced age, or with documentation of volume "overload" by bedside examination. Failure to reach 30by3 was associated with increased odds of in-hospital mortality, irrespective of comorbidities. Predictors of inadequate resuscitation can be identified, potentially leading to interventions to improve survival. These findings are retrospective and require future validation.

[Association Between Sepsis and Microvascular Brain Injury.](#)

Ehlenbach WJ, et al

**Crit Care Med.** 2019 Aug 5.

Many survivors of sepsis suffer long-term cognitive impairment, but the mechanisms of this association remain unknown. The objective of this study was to determine whether sepsis is associated with cerebral microinfarcts on brain autopsy. Sepsis was specifically associated with moderate to severe vascular brain injury as assessed by microvascular infarcts. This association was stronger for microinfarcts within the cerebral cortex, with those who experienced severe sepsis hospitalization being more than twice as likely to have evidence of moderate to severe cerebral cortical injury in adjusted analyses. Further study to identify mechanisms for the association of sepsis and microinfarcts is needed.

[A Machine Learning Algorithm to Predict Severe Sepsis and Septic Shock: Development, Implementation, and Impact on Clinical Practice.](#)

Giannini HM, et al

**Crit Care Med.** 2019 Aug 5.

Develop and implement a machine learning algorithm to predict severe sepsis and septic shock and evaluate the impact on clinical practice and patient outcomes. Our machine learning algorithm can predict, with low sensitivity but high specificity, the impending occurrence of severe sepsis and septic shock. Algorithm-generated predictive alerts modestly impacted clinical measures. Next steps include

there is no pooled analysis of its efficacy as a diagnostic biomarker for sepsis in children. The aims of the present meta-analysis were to assess the overall diagnostic accuracy of presepsin in pediatric sepsis and compare it to those for C-reactive protein (CRP) and procalcitonin (PCT). Currently available evidence indicates that presepsin has higher sensitivity and diagnostic accuracy, but lower specificity, than PCT or CRP in detecting sepsis in children. However, these results must be carefully interpreted as the number of studies included was small and the studies were statistically heterogeneous.

[Serial Carboxyhemoglobin Levels and Its Relationship with Late Onset Sepsis in Preterm Infants: An Observational Cohort Study.](#)

Guney Varal I, Dogan P.

**Fetal Pediatr Pathol.** 2019 Aug 20:1-11.

This study aimed at assessing the serial carboxyhemoglobin (COHb) levels in preterm infants during the first week of life and their variation with late-onset sepsis (LOS). In this study, we demonstrated an increase in COHb levels at the onset of LOS and a decrease with response to antibiotherapy.

[Global Divergence From World Health Organization Treatment Guidelines for Neonatal and Pediatric Sepsis.](#)

Jackson C, et al

**Pediatr Infect Dis J.** 2019 Aug 12.

We used data from 2 global point prevalence surveys of antibiotic prescribing to describe the treatment of sepsis in hospitalized neonates and children. One hundred eighty-five of 824 neonates (22.5%) and 9/786 children (1.1%) received a World Health Organization-recommended first-line treatment; of the remainder, 9/639 neonates (1.4%) and 102/777 children (13.1%) received a World Health Organization-recommended second-line treatment. Reasons for this low adherence to guidance should be explored.

[Reducing Variability in the Infant Sepsis Evaluation \(REVISE\): A National Quality Initiative.](#)

Biondi EA, et al.

**Pediatrics.** 2019 Sep;144(3). pii: e20182201.

Substantial variability exists in the care of febrile, well-appearing infants. We aimed to assess the impact of a national quality initiative on appropriate hospitalization and length of stay (LOS) in this population. Reducing Variability in the Infant Sepsis Evaluation noted improvement in key aspects of febrile infant

describing clinical perception of this tool and optimizing algorithm design and delivery.

[Subcostal TAPSE: a retrospective analysis of a novel right ventricle function assessment method from the subcostal position in patients with sepsis.](#)

Main AB et al

**Ultrasound J.** 2019 Aug 27;11(1):19.

Tricuspid annular plane systolic excursion (TAPSE) is frequently used as an objective measure of right-ventricular dysfunction. Abnormal TAPSE values are associated with poor prognosis in a number of disease states; however, the measure is not always easy to obtain in the critically ill. The purpose of this study is to assess the feasibility and accuracy of using a subcostal view and TAPSE measurement as a measure of right-ventricular dysfunction. A secondary aim was to perform a pilot study to assess whether right-ventricular dysfunction was associated with adverse outcomes including mortality. Subcostal TAPSE is a feasible and accurate alternative to conventional TAPSE from the apical view in critically ill patients. Further research is required to elucidate the relationship between RV dysfunction and outcomes in sepsis.

[The REDS score: a new scoring system to risk-stratify emergency department suspected sepsis: a derivation and validation study.](#)

Sivayoham N, et al.

**BMJ Open.** 2019 Aug 26;9(8):e030922.

To derive and validate a new clinical prediction rule to risk-stratify emergency department (ED) patients admitted with suspected sepsis. The REDS score is a simple and objective score to risk-stratify ED patients with suspected sepsis.

[Balanced Crystalloids Versus Saline in Sepsis: A Secondary Analysis of the SMART Trial](#)

Brown RM, et al.

**Am J Respir Crit Care Med.** 2019 Aug 27.

Administration of intravenous crystalloid solutions is a fundamental therapy for sepsis, but the effect of crystalloid composition on patient outcomes remains unknown. To compare the effect of balanced crystalloids versus saline on 30-day in-hospital mortality among critically ill adults with sepsis. Among patients with sepsis in a large randomized trial, use of balanced crystalloids was associated with a lower 30-day in-hospital mortality compared to use of saline

management. Similar projects may be used to improve care in other clinical conditions.

[Efficacy of pentoxifylline treatment for neonatal sepsis: a meta-analysis of randomized controlled studies.](#)

Tian J, et al

**Ital J Pediatr.** 2019 Aug 22;45(1):108.

Pentoxifylline may be an important approach to treat neonatal sepsis. However, its use has not been well established. We conduct a systematic review and meta-analysis to evaluate the efficacy of pentoxifylline treatment for neonatal sepsis. Pentoxifylline treatment may be associated with reduced mortality and hospital stay in neonatal sepsis.

[Towards understanding global patterns of antimicrobial use and resistance in neonatal sepsis: insights from the NeoAMR network](#)

Li G, et al

**Arch Dis Child.** 2019 Aug 24. pii: archdischild-2019-316816.

To gain an understanding of the variation in available resources and clinical practices between neonatal units (NNUs) in the low-income and middle-income country (LMIC) setting to inform the design of an observational study on the burden of unit-level antimicrobial resistance (AMR). AMR is already a significant issue in NNUs worldwide. The apparent burden of AMR in a given NNU in the LMIC setting can be influenced by a range of factors which will vary substantially between NNUs. These variations must be considered when designing interventions to improve neonatal mortality globally.

[Severe Sepsis-Associated Morbidity and Mortality among Critically Ill Children with Cancer.](#)

Aljabari S, et al

**J Pediatr Intensive Care.** 2019 Sep;8(3):122-129.

Severe sepsis (SS) in pediatric oncology patients is a leading cause of morbidity and mortality. We investigated the incidence of and risk factors for morbidity and mortality among children diagnosed with cancer from 2008 to 2012, and admitted with SS during the 3 years following cancer diagnosis. A total of 1,002 children with cancer were included, 8% of whom required pediatric intensive care unit (PICU) admission with SS. Death and/or multiple organ dysfunction syndrome occurred in 34 out of 99 PICU encounters (34%). Lactate level and history of stem-cell transplantation were significantly associated with the

[Impaired vascular reactivity in sepsis - a systematic review with meta-analysis](#)

Kazune S, et al

**Arch Med Sci Atheroscler Dis.** 2019 Jul 18;4:e151-e161.

Vascular dysfunction due to reduced nitric oxide bioavailability plays an important role in the pathogenesis of sepsis. This meta-analysis examines evidence from published literature to evaluate whether in the adult population the presence/severity of sepsis is associated with impaired vasoreactivity. Septic patients have attenuated vascular reactivity when compared to healthy volunteers. There are insufficient data indicating that these changes can identify patients at risk of worsening organ failure or death.

[Comparison of the sepsis-2 and sepsis-3 definitions in severely injured trauma patients](#)

Eriksson J, et al.

**J Crit Care.** 2019 Aug 9;54:125-129.

To evaluate the performance of the new SOFA-based sepsis definition in trauma patients. The sepsis-3 definition identifies much fewer patients and is more strongly associated with adverse outcomes than the sepsis-2 definition. The sepsis-3 definition seems to be useful in the post trauma setting.

[Sepsis information-seeking behaviors via Wikipedia between 2015 and 2018: A mixed methods retrospective observational study.](#)

Jabaley CS, et al

**PLoS One.** 2019 Aug 22;14(8):e0221596.

Raising public awareness of sepsis, a potentially life-threatening dysregulated host response to infection, to hasten its recognition has become a major focus of physicians, investigators, and both non-governmental and governmental agencies. While the internet is a common means by which to seek out healthcare information, little is understood about patterns and drivers of these behaviors. We sought to examine traffic to Wikipedia, a popular and publicly available online encyclopedia, to better understand how, when, and why users access information about sepsis. Clickstream analysis suggests that most sepsis and septic shock Wikipedia pageviews originate from external referrals, namely search engines. Owing to its granular and publicly available traffic data, Wikipedia holds promise as a means by which to better understand global drivers of online sepsis information seeking. Further characterization of user engagement with this information may help to elucidate means by

development of death and/or organ dysfunction ( $p < 0.05$ ).

[A neonatal sequential organ failure assessment score predicts mortality to late-onset sepsis in preterm very low birth weight infants.](#)

Wynn JL, et al

**Pediatr Res.** 2019 Aug 8.

An operational definition of organ dysfunction applicable to neonates that predicts mortality in the setting of infection is lacking. We determined the utility of an objective, electronic health record (EHR)-automated, neonatal sequential organ failure assessment (nSOFA) score to predict mortality from late-onset sepsis (LOS) in premature, very low birth weight (VLBW) infants. The nSOFA scoring system predicted mortality in VLBW infants with LOS and this automated system was integrated into our EHR. Prediction of LOS mortality is a critical step toward improvements in neonatal sepsis outcomes.

[Practice variations and rates of late onset sepsis and necrotizing enterocolitis in very preterm born infants, a review.](#)

Adams M, et al

**Transl Pediatr.** 2019 Jul;8(3):212-226.

The burden of late onset sepsis (LOS) and necrotizing enterocolitis (NEC) remains high for newborns in low- and high-income countries. Very preterm born infants born below 32 weeks gestation are at highest risk because their immune system is not yet adapted to ex-utero life, providing intensive care frequently compromises their skin or mucosa and they require a long duration of hospital stay. An epidemiological overview is difficult to provide because there is no mutually accepted definition available for either LOS or NEC. LOS incidence proportions are generally reported based on identified blood culture pathogens. However, discordance in minimum day of onset and whether coagulase negative staphylococci or fungi should be included into the reported proportions lead to variation in reported incidences. Complicating the comparison are the absence of biomarkers, ancillary lab tests or prediction models with sufficiently high positive and/or negative predictive values. The only high negative predictive values result from negative blood culture results with negative lab results allowing to discontinue antibiotic treatment. Similar difficulties exist in reporting and diagnosing NEC. Although most publications base their proportions on a modified

which to optimize the visibility, content, and delivery of awareness promotion efforts.

[Overall systematic approach to sepsis damages on urogenital tissues: protective power of lacosamide.](#)

Gunyeli I, et al

**Arch Gynecol Obstet.** 2019 Aug 21.

The aim of the study was to evaluate the harmful effects of sepsis on the urogynecological tissues and the ability of Lacosamide (LCM) on Lipopolysaccharide (LPS)-induced cytokine production, oxidative stress and apoptotic pathways, in the experimental rat sepsis model. These findings demonstrated that sepsis caused oxidative stress, apoptosis and inflammation in the urogenital tissues. We revealed that LCM ameliorated the damage caused by sepsis in urogenital tissue.

[Incidence and impact of sepsis on long-term outcomes after subarachnoid hemorrhage: a prospective observational study.](#)

Gonçalves B, et al.

**Ann Intensive Care.** 2019 Aug 20;9(1):94.

Aneurysmal subarachnoid hemorrhage (SAH) is an acute cerebrovascular disease associated with high mortality and long-term functional impairment among survivors. Systemic inflammatory responses after acute injury and nosocomial infections are frequent complications, making the management of these patients challenging. Here, we hypothesized that sepsis might be associated with early and long-term mortality and functional outcomes. Our objective was to define the incidence of sepsis, diagnosed prospectively with the Sepsis-3 criteria, and to determine its impact on mortality and functional outcomes of patients with SAH. Sepsis plays a significant role in the outcomes of patients with SAH, affecting both mortality and long-term functional outcomes. Combining high-level neurocritical care management of neurological complications and the optimal diagnosis and management of sepsis may effectively reduce secondary brain injury and improve patients' outcomes after SAH.

[Lactate Predicts Both Short- and Long-Term Mortality in Patients With and Without Sepsis.](#)

Villar J, et al

**Infect Dis (Auckl).** 2019 Aug 6;12:1178633719862776.

To measure the relationship between lactate and mortality in hospital inpatients. Main outcomes of interest were 3-day, 30-day, and 1-year all-cause

version of Bell's stage 2 or 3, comparisons are made difficult by the multifactorial nature of the disease reflecting several pathways to intestinal necrosis, the absence of a reliable biomarker and the unclear differentiation from spontaneous intestinal perforations. Comparable reports in very low birthweight infants range between 5% and 30% for LOS and 1.6% to 7.1% for NEC. Evidence based guidelines to support treatment are missing. Treatment for LOS remains largely empirical and focused mainly on antibiotics. In the absence of a clear diagnosis, even unspecific early warning signals need to be met with antibiotic treatment. Cessation after negative blood culture is difficult unless the child was asymptomatic from the beginning. As a result, antibiotics are the most commonly prescribed medications, but unnecessary exposure may result in increased risk for mortality, NEC, further infections and childhood obesity or asthma. Finding ways to limit antibiotic use are thus important and have shown a large potential for improvement of care and limitation of cost. Over recent decades, none of the attempts to establish novel therapies have succeeded. LOS and NEC proportions remained mostly stable. During the past 10 years however, publications emerged reporting a reduction, sometimes by almost 50%. Most concern units participating in a surveillance system using quality improvement strategies to prevent LOS or NEC (e.g., hand hygiene, evidence based "bundles", feeding onset, providing own mother's milk). We conclude that these approaches display a potential for wider spread reduction of LOS and NEC and for a subsequently more successful development of novel therapies as these often address the same pathways as the prevention strategies.

[Persistent Mitochondrial Dysfunction Linked to Prolonged Organ Dysfunction in Pediatric Sepsis.](#)

Weiss SL, et al

**Crit Care Med.** 2019 Aug 2.

Limited data exist about the timing and significance of mitochondrial alterations in children with sepsis. We therefore sought to determine if alterations in mitochondrial respiration and content within circulating peripheral blood mononuclear cells were associated with organ dysfunction in pediatric sepsis. Mitochondrial respiration was acutely decreased in peripheral blood mononuclear cells in pediatric sepsis despite an increase in mitochondrial content. Over time, a rise in mitochondrial DNA tracked with

mortality. Lactate predicts risk of death in all patients, although patients with sepsis have a higher mortality for any given lactate level. We report the novel finding that serum lactate, including normal values, is associated with long-term mortality.

[Hypoxia and HIF activation as a possible link between sepsis and thrombosis.](#)

Evans CE et al

**Thromb J.** 2019 Aug 14;17:16.

Risk factors for thrombosis include hypoxia and sepsis, but the mechanisms that control sepsis-induced thrombus formation are incompletely understood. A recent article published in Thrombosis Journal: (i) reviews the role of endothelial cells in the pathogenesis of sepsis-associated microthrombosis; (ii) describes a novel 'two-path unifying theory' of hemostatic disorders; and (iii) refers to hypoxia as a consequence of microthrombus formation in sepsis patients. The current article adds to this review by describing how sepsis and thrombus formation could be linked through hypoxia and activation of hypoxia-inducible transcription factors (HIFs). In other words, hypoxia and HIF activation may be a cause as well as a consequence of thrombosis in sepsis patients. While microthrombosis reduces microvascular blood flow causing local hypoxia and tissue ischemia, sepsis-induced increases in HIF1 activation could conversely increase the expression of coagulant factors and integrins that promote thrombus formation, and stimulate the formation of pro-thrombotic neutrophil extracellular traps. A better understanding of the role of cell-specific HIFs in thrombus formation could lead to the development of novel prophylactic therapies for individuals at risk of thrombosis.

[Procalcitonin as a prognostic marker for sepsis based on SEPSIS-3.](#)

Jekarl DW, et al

**J Clin Lab Anal.** 2019 Aug 16:e22996.

The revised definition of sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection (SEPSIS-3). The objective of this study was to evaluate procalcitonin (PCT) for the diagnosis and prognosis of sepsis using SEPSIS-3. PCT could support and predict the unfavorable prognosis of sepsis based on SEPSIS-3, whereas diagnostic potential of PCT requires further evaluations.

[Identifying Sepsis Populations Benefitting from](#)

improved respiration. Although initial mitochondrial alterations in peripheral blood mononuclear cells were unrelated to organ dysfunction, persistently low respiration was associated with slower recovery from organ dysfunction.

[Effects of immunotherapy on mortality in neonates with suspected or proven sepsis: a systematic review and network meta-analysis.](#)

Li Y, et al

**BMC Pediatr.** 2019 Aug 5;19(1):270.

To investigate the efficacies of different immunotherapies in neonates with suspected or proven sepsis. No significant differences in all-cause mortality or the duration of hospital stay were found in neonates with suspected or proven sepsis treated with the four types of immunotherapies and those treated with placebo.

[Factors influencing awareness of healthcare providers on maternal sepsis: a mixed-methods approach.](#)

Brizuela V, et al

**BMC Public Health.** 2019 Jun 3;19(1):683.

An awareness campaign set to accompany the Global Maternal Sepsis Study (GLOSS) was launched in 2017. In order to better develop and evaluate the campaign, we sought to understand the factors that influence awareness of maternal sepsis by exploring healthcare providers' knowledge, perception of enabling environments, and perception of severity of maternal sepsis. Awareness on maternal sepsis, while acknowledged as important, remains low. Healthcare providers need resources and support to feel confident about the correct identification and management of sepsis, as a prerequisite for the improvement of awareness of maternal sepsis. Similarly, providers need to know about maternal sepsis and its severity to understand the importance of reducing sepsis-related mortality and morbidity. Awareness raising campaigns can help bring neglected maternal health conditions, such as sepsis, to the forefront of global and local agendas.

[Using an eLearning Module to Facilitate Sepsis Knowledge Acquisition Across Multiple Institutions and Learner Disciplines.](#)

Woods JM, et al

**Pediatr Emerg Care.** 2019 Aug 23.

Guidelines exist for care of pediatric sepsis, but no study has assessed the benefit of electronic learning

[Anticoagulant Therapy: A Prospective Cohort Study Incorporating a Restricted Cubic Spline Regression Model.](#)

Yamakawa K, et al

**Thromb Haemost.** 2019 Aug 13. doi: 10.1055/s-0039-1693740. [Epub ahead of print]

Anticoagulant therapy has seldom been achieved in randomized trials targeting nonspecific overall sepsis patients. Although the key components to identify the appropriate target in sepsis may be disseminated intravascular coagulation (DIC) and high disease severity, the interaction and relation of these two components for the effectiveness of therapy remain unknown. This article identifies the optimal target of anticoagulant therapy in sepsis. Anticoagulant therapy was associated with better outcome according to the deterioration of both DIC and disease severity, suggesting that anticoagulant therapy should be restricted to patients having DIC and high disease severity simultaneously.

[Sepsis in patients with cirrhosis awaiting liver transplantation: new trends and management.](#)

Martin Mateos R, et al

**Liver Transpl.** 2019 Aug 13

Bacterial infections are more frequent and severe in patients with advanced liver disease and, therefore, in liver transplant candidates. The increased risk of infection in these patients parallels the severity of the immune dysfunction associated with cirrhosis, featured by systemic inflammation and progressive immunodeficiency. Other factors contribute to this risk, such as genetic polymorphisms, proton-pump inhibitor overuse, the numerous invasive procedures and hospitalizations these patients go through, or the immunosuppressive effects of malnutrition or alcohol abuse. Bacterial infections have a great impact on disease progression and significantly increase mortality rates before and after liver transplantation. Mechanisms leading to organ failure in sepsis are associated not only with the hemodynamic derangement but also with an excessive inflammatory response triggered by infection. Further, prophylactic and empirical antibiotic treatment strategies in patients with cirrhosis are being modified according to the growing prevalence of multi-drug resistant bacteria in the past decade. Also, new criteria have been introduced for the diagnosis of sepsis and septic shock. These new definitions have been validated in cirrhotic patients and show a better accuracy to predict in-



(eLearning) in this topic area. The objective of this multicenter study was to assess knowledge acquisition and retention for pediatric sepsis across multiple health care provider roles, using an adaptive and interactive eLearning module. An eLearning module improved immediate and delayed pediatric sepsis knowledge in pediatric health care providers across multiple institutions and provider roles. Immediate knowledge gain was meaningful as indicated by effect sizes, although by the time of the delayed test, the effect was smaller. This module fills an important gap in currently available pediatric sepsis education.

[Vascular Endothelium in Neonatal Sepsis: Basic Mechanisms and Translational Opportunities.](#)

Pietrasanta C, et al

**Front Pediatr.** 2019 Aug 13;7:340.

Neonatal sepsis remains a major health issue worldwide, especially for low-birth weight and premature infants, with a high risk of death and devastating sequelae. Apart from antibiotics and supportive care, there is an unmet need for adjunctive treatments to improve the outcomes of neonatal sepsis. Strong and long-standing research on adult patients has shown that vascular endothelium is a key player in the pathophysiology of sepsis and sepsis-associated organ failure, through a direct interaction with pathogens, leukocytes, platelets, and the effect of soluble circulating mediators, in part produced by endothelial cells themselves. Despite abundant evidence that the neonatal immune response to sepsis is distinct from that of adults, comparable knowledge on neonatal vascular endothelium is much more limited. Neonatal endothelial cells express lower amounts of adhesion molecules compared to adult ones, and present a reduced capacity to neutralize reactive oxygen species. Conversely, available evidence on biomarkers of endothelial damage in neonates is not as robust as in adult patients, and endothelium-targeted therapeutic opportunities for neonatal sepsis are almost unexplored. Here, we summarize current knowledge on the structure of neonatal vascular endothelium, its interactions with neonatal immune system and possible endothelium-targeted diagnostic and therapeutic tools for neonatal sepsis. Furthermore, we outline areas of basic and translational research worthy of further study, to shed light on the role of vascular endothelium in the context of neonatal sepsis.

hospital mortality than previous criteria based on the systemic inflammatory response syndrome. Accurate prophylaxis and early identification and treatment of bacterial infections are key to reduce the burden of sepsis in patients with cirrhosis awaiting liver transplantation.

[Regional trends in In-hospital Cardiac Arrest following sepsis-related admissions and subsequent mortality.](#)

Desai R, et al

**Resuscitation.** 2019 Aug 10;143:35-41.

Previous studies have reported regional variation in either the incidence or outcomes of sepsis or In-hospital Cardiac Arrest (IHCA) discretely; however, regional variations in the incidence and outcomes of sepsis-associated IHCA (SA-IHCA) have never been studied. This nationwide analysis demonstrates that the highest incidence of SA-IHCA is in the Southern region of the US whereas the associated in-hospital mortality was highest in the West. The incidence of SA-IHCA is rising in the Midwest and South from 2007 to 2014. Despite significant advances in the treatment of sepsis and IHCA, there has been no significant improvement in the incidence of SA-IHCA and subsequent survival in any US geographic region from 2007 to 2014.

[Prehospital characteristics among patients with sepsis: a comparison between patients with or without adverse outcome.](#)

Olander A, et al

**BMC Emerg Med.** 2019 Aug 6;19(1):43

The prehospital care of patients with sepsis are commonly performed by the emergency medical services. These patients may be critically ill and have high in-hospital mortality rates. Unfortunately, few patients with sepsis are identified by the emergency medical services, which can lead to delayed treatment and a worse prognosis. Therefore, early identification of patients with sepsis is important, and more information about the prehospital characteristics that can be used to identify these patients is needed. Based on this lack of information, the objectives of this study were to investigate the prehospital characteristics that are identified while patients with sepsis are being transported to the hospital by the emergency medical services, and to compare these values to those of the patients with and without adverse outcomes during their hospital stays. The findings suggests that patients having a decreased oxygen saturation and body

temperature, increased serum glucose level and altered mental status during prehospital care are at risk of a poorer patient prognosis and adverse outcome. Recognizing these prehospital characteristics may help to identify patients with sepsis early and improve their long-term outcomes. However further research is required to predict limit values of saturation and serum glucose and to validate the use of prehospital characteristics for adverse outcome in patients with sepsis.

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