

Here is the latest edition. The bulletin covers the latest information on sepsis and comes out monthly. Next edition is due very shortly for March 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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SEPSIS BULLETIN February 2020

Adult sepsis

[Xenobiotic receptors in mediating the effect of sepsis on drug metabolism.](#)

Lv C, Huang L.

Acta Pharm Sin B. 2020 Jan;10(1):33-41.

Sepsis is an infection-induced systemic inflammatory syndrome. The immune response in sepsis is characterized by the activation of both proinflammatory and anti-inflammatory pathways. When sepsis occurs, the expression and activity of many inflammatory cytokines are markedly affected. Xenobiotic receptors are chemical-sensing transcription factors that play essential roles in the transcriptional regulation of drug-metabolizing enzymes (DMEs). Xenobiotic receptors mediate the functional crosstalk between sepsis and drug metabolism because the inflammatory cytokines released during sepsis can affect the expression and activity of xenobiotic receptors and thus impact the expression and activity of DMEs. Xenobiotic receptors in turn may affect the clinical outcomes of sepsis. This review focuses on the sepsis-induced inflammatory response and xenobiotic receptors such as pregnane X receptor (PXR), aryl hydrocarbon receptor (AHR), glucocorticoid receptor (GR), and constitutive androstane receptor (CAR), DMEs such as CYP1A, CYP2B6, CYP2C9, and CYP3A4, and drug transporters such as p-glycoprotein (P-gp), and multidrug resistance-associated protein (MRPs) that are affected by sepsis. Understanding the xenobiotic receptor-mediated effect of sepsis on drug metabolism will help to improve the safe use of drugs in sepsis patients and the development of new xenobiotic receptor-based therapeutic strategies for sepsis.

[Potential of glucocorticoids to treat intestinal inflammation during sepsis.](#)

Van Looveren K, Wallaey C, Libert C.

Curr Opin Pharmacol. 2020 Jan 25;53:1-7.

Glucocorticoids (GCs) are steroid hormones characterized by their anti-inflammatory and immunosuppressive nature. Although GCs are very commonly prescribed, in several diseases, including sepsis, their clinical treatment is hampered by side effects and by the occurrence of glucocorticoid resistance (GCR). Sepsis is defined as a life-threatening organ dysfunction, initiated by a dysregulated systemic host response to infections. With at least 19 million cases per year and a lethality rate of about 25%, sepsis is one of the most urgent unmet medical needs. The gut is critically affected during sepsis and is considered as a driving force in this disease. Despite there is no effective treatment for sepsis, pre-clinical studies show promising results by preserving or restoring gut integrity. Since GC treatment reveals therapeutic effects in Crohn's disease (CD) and in pre-clinical sepsis models, we hypothesize that targeting GCs to the gut or stimulating local GC production in the gut forms an interesting strategy for sepsis treatment. According to recent findings that show that dimerization of the glucocorticoid receptor (GR) is essential in inducing anti-inflammatory effects in pre-clinical sepsis models, we predict that new generation GCs that selectively dimerize the GR, can therefore positively affect the outcome of sepsis treatment.

[Sepsis and septic shock: Guideline-based management.](#)

Dugar S, Choudhary C, Duggal A.

Cleve Clin J Med. 2020 Jan;87(1):53-64.

Sepsis is a life-threatening organ dysfunction that results from the body's response to infection. It requires prompt recognition, appropriate antibiotics, careful hemodynamic support, and control of the source of infection. With the trend in management moving away from protocolized care in favor of appropriate usual care, an understanding of sepsis physiology and best practice guidelines is critical.

[Lower vs Higher Fluid Volumes During Initial Management of Sepsis: A Systematic Review With Meta-Analysis and Trial Sequential Analysis.](#)

Meyhoff TS, et al.

Chest. 2020 Jan 23:S0012-3692(20)30123-9.

IV fluids are recommended during the initial management of sepsis, but the quality of evidence is low, and clinical equipoise exists. We aimed to assess patient-important benefits and harms of lower vs higher fluid volumes in adult patients with sepsis. In this systematic review, we found very low quantity and quality of evidence supporting the decision on the volumes of IV fluid therapy in adults with sepsis.

[The Emerging Role of Vitamin C as a Treatment for Sepsis.](#)

Kashiouris MG, et al.

Nutrients. 2020 Jan 22;12(2):E292.

Sepsis, a life-threatening organ dysfunction due to a dysregulated host response to infection, is a leading cause of morbidity and mortality worldwide. Decades of research have failed to identify any specific therapeutic targets outside of antibiotics, infectious source elimination, and supportive care. More recently, vitamin C has emerged as a potential therapeutic agent to treat sepsis. Vitamin C has been shown to be deficient in septic patients and the administration of high dose intravenous as opposed to oral vitamin C leads to markedly improved and elevated serum levels. Its physiologic role in sepsis includes attenuating oxidative stress and inflammation, improving vasopressor synthesis, enhancing immune cell function, improving endovascular function, and epigenetic immunologic modifications. Multiple clinical trials have demonstrated the safety of vitamin C and two recent studies have shown promising data on mortality improvement. Currently, larger randomized controlled studies are underway to validate these findings. With further study, vitamin C may become standard of care for the treatment of sepsis, but given its safety profile, current treatment can be justified with compassionate use.

[Effect of alkaline phosphatase on sepsis-associated acute kidney injury patients: A systematic review and meta-analysis.](#)

Tang W, et al.

Medicine (Baltimore). 2020 Jan;99(4):e18788.

This systematic review and meta-analysis were performed to evaluate kidney function in patients with sepsis-associated acute kidney injury (SA-AKI) on alkaline phosphatase (AP) therapy. In patients with SA-AKI, AP showed a relatively late protective effect by improving ECC at days 7, 14, and 28. ECC level improved when patients received AP dose of 0.212 mg/kg. Mortality improved at days 28 and 90, respectively, when patients received AP dose of 1.6 mg/kg. Levels of overall AKI biomarkers were improved in short term.

[Rate and risk factors for rehospitalisation in sepsis survivors: systematic review and meta-analysis.](#)

Shankar-Hari M, et al.

Intensive Care Med. 2020 Jan 23.

Sepsis survivors have a higher risk of rehospitalisation and of long-term mortality. We assessed the rate, diagnosis, and independent predictors for rehospitalisation in adult sepsis survivors. Rehospitalisation events are common in sepsis survivors, with one in five rehospitalisation events occurring within 30 days of hospital discharge following an index sepsis admission. The generic and sepsis-specific characteristics at index sepsis admission are commonly reported risk factors for rehospitalisation.

[Hypoxia-inducible factors in metabolic reprogramming during sepsis.](#)

Vanderhaeghen T, et al.

FEBS J. 2020 Jan 23.

Sepsis is a highly heterogeneous syndrome that is caused by an imbalanced host response to infection. Despite huge investments, sepsis remains a contemporary threat with significant burden on health systems. Vascular dysfunction and elevated oxygen consumption by highly metabolically active immune cells result in tissue hypoxia during inflammation. The transcription factor hypoxia-inducible factor-1 α (HIF1 α), and its family members, plays an important role in cellular metabolism and adaptation to cellular stress caused by hypoxia. In this review, we discuss the role of HIF in sepsis. We show possible mechanisms by which the inflammatory response activated during sepsis affects the HIF pathway. The activated HIF pathway in turn changes the metabolism of both innate and adaptive immune cells. As HIF expression in leukocytes of septic patients can be directly linked with mortality, we discuss multiple ways of interfering with the HIF signaling pathway.

[Machine learning for the prediction of sepsis: a systematic review and meta-analysis of diagnostic test accuracy.](#)

Fleuren LM, et al.

Intensive Care Med. 2020 Mar;46(3):383-400.

Early clinical recognition of sepsis can be challenging. With the advancement of machine learning, promising real-time models to predict sepsis have emerged. We assessed their performance by carrying out a systematic review and meta-analysis. This systematic review and meta-analysis show that on retrospective data, individual machine learning models can accurately predict sepsis onset ahead of time. Although they present alternatives to traditional scoring systems, between-study heterogeneity limits the assessment of pooled results. Systematic reporting and clinical implementation studies are needed to bridge the gap between bytes and bedside.

[Health economic evaluations of sepsis interventions in critically ill adult patients: a systematic review.](#)

Higgins AM, et al.

J Intensive Care. 2020 Jan 8;8:5.

Sepsis is a global health priority. Interventions to reduce the burden of sepsis need to be both effective and cost-effective. We performed a systematic review of the literature on health economic evaluations of sepsis treatments in critically ill adult patients and summarised the evidence for cost-effectiveness. There is wide variation in the cost-effectiveness of sepsis interventions. There remain important gaps in the literature, with no economic evaluations identified for several interventions routinely used in sepsis. Given the high economic and social burden of sepsis, high-quality economic evaluations are needed to increase our understanding of the cost-effectiveness of these interventions in routine clinical practice and to inform decision makers.

[2020 exceptional surveillance of neutropenic sepsis: prevention and management in people with cancer \(NICE guideline CG151\).](#)

London: National Institute for Health and Care Excellence (UK); 2020 Jan 14.

The NICE guideline on neutropenic sepsis recommends offering fluoroquinolones for primary

prophylaxis. The guideline committee came to this conclusion after examining over 200 randomised controlled trials of primary prophylaxis, basing their decision on clinical evidence that fluoroquinolones are more effective than placebo for reducing mortality and neutropenic sepsis. Additionally, an economic model built for the guideline showed that primary prophylaxis with fluoroquinolones in solid tumours is more cost effective than other strategies, which was robust to sensitivity analysis. Risks of fluoroquinolones were noted by the committee, such as side effects and bacterial resistance, but it was agreed that the benefit of saving lives outweighed potential harms.

[Immunotherapy in sepsis - brake or accelerate?](#)

Steinhagen F, et al

Pharmacol Ther. 2020 Jan 10;107476.

Sepsis, a life threatening syndrome characterized by organ failure after infection, is the most common cause of death in hospitalized patients. The treatment of sepsis is generally supportive in nature, involving the administration of intravenous fluids, vasoactive substances and oxygen plus antibiotics to eliminate the pathogen. No drugs have been approved specifically for the treatment of sepsis, and clinical trials of potential therapies have failed to reduce mortality - suggesting that new approaches are needed. Abnormalities in the immune response elicited by the pathogen, ranging from excessive inflammation to immunosuppression, contribute to disease pathogenesis. Although hundreds of immunomodulatory agents are potentially available, it remains unclear which patient benefits from which immune therapy at a given time point. Results indicate the importance of personalized therapy, specifically the need to identify the type of intervention required by each individual patient at a given point in the disease process. To address this issue will require using biomarkers to stratify patients based on their individual immune status. This article reviews recent and ongoing clinical investigations using immunostimulatory or immunosuppressive therapies against sepsis including non-pharmacological and novel preclinical approaches.

[Sepsis-associated encephalopathy: a vicious cycle of immunosuppression.](#)

Ren C, et al.

J Neuroinflammation. 2020 Jan 10;17(1):14.

Sepsis-associated encephalopathy (SAE) is commonly complicated by septic conditions, and is responsible for increased mortality and poor outcomes in septic patients. Uncontrolled neuroinflammation and ischemic injury are major contributors to brain dysfunction, which arises from intractable immune malfunction and the collapse of neuroendocrine immune networks, such as the cholinergic anti-inflammatory pathway, hypothalamic-pituitary-adrenal axis, and sympathetic nervous system. Dysfunction in these neuromodulatory mechanisms compromised by SAE jeopardizes systemic immune responses, including those of neutrophils, macrophages/monocytes, dendritic cells, and T lymphocytes, which ultimately results in a vicious cycle between brain injury and a progressively aberrant immune response. Deep insight into the crosstalk between SAE and peripheral immunity is of great importance in extending the knowledge of the pathogenesis and development of sepsis-induced immunosuppression, as well as in exploring its effective remedies.

[Publication Trends of Research on Sepsis and Host Immune Response during 1999-2019: A 20-year Bibliometric Analysis.](#)

Yao RQ, et al.

Int J Biol Sci. 2020 Jan 1;16(1):27-37.

Sepsis is an intractable disorder, which is associated with high risk of organ dysfunction and even death, while its pathogenesis remains largely unclear. Our study aims to study the research trend on sepsis and host immune response, and compare the contribution of publications from different countries, institutions, journals and authors. The United States made the most outstanding contribution within this important field. There is a mismatch between the quantity and quality of publications from China. Latest progress can be tracked in journal of Shock. Immunosuppression related researches may be hotspots in the near future.

[Efficacy of vitamin C in patients with sepsis: An updated meta-analysis.](#)

Wei XB, et al.

Eur J Pharmacol. 2020 Feb 5;868:172889.

Previous studies have suggested the beneficial effects of vitamin C in patients with sepsis. However, the

results could not be reproduced in the subsequent studies. This meta-analysis aimed to reevaluate the value of vitamin C treatment in patients with sepsis. Electronic databases were searched from inception to August 2019 for the studies comparing the effect of vitamin C versus non-vitamin C infusion in patients with sepsis. Retrospective meta-analysis could not reveal the beneficial effect of vitamin C on patients with sepsis. Therefore, in order to clarify the role of vitamin C in sepsis the high-quality RCTs will be required in the future study.

[Recent advances in the study of progranulin and its role in sepsis.](#)

Tian Get al

Int Immunopharmacol. 2020 Feb;79:106090.

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. The mortality rate of in-hospital patients whose conditions are complicated by sepsis remains high in spite of intensive-care treatment, therefore placing a significant financial burden on the health care system. In recent years, progranulin (PGRN), a cysteine-rich secretory protein (CRISP), has been found to play a crucial role in sepsis. PGRN participates in the pathogenesis of sepsis via diverse pathways, including bacterial clearance, cell growth and survival, tissue repair, and the regulation of inflammation. PGRN knockout mice suffer from serious infectious processes, whereas therapeutic administration of recombinant PGRN to such mice enhances bacterial clearance and reduces organ injury and mortality rate. Even though PGRN plays an important role in regulating sepsis, its potential mechanisms have not been completely clarified. In this review, we summarize the most recent research advances in the study of PGRN and its role in sepsis.

[A Systematic Review of Preexisting Sepsis and Extracorporeal Membrane Oxygenation.](#)

Sangli SS, et al.

ASAIO J. 2020 Jan;66(1):1-7

We retrospectively reviewed all pertinent extracorporeal membrane oxygenation (ECMO) studies (January 1995 to September 2017) of adults with sepsis as a primary indication for intervention and its association with morbidity and mortality. Collected data included study type, ECMO configuration, outcomes, effect size, and other features. Overall survival varied substantially among studies (15.38-71.43%). Existing studies do not present well-defined patterns supporting use of ECMO in sepsis because of sample sizes and disparate study designs.

[The role of *Vibrio vulnificus* virulence factors and regulators in its infection-induced sepsis.](#)

Li G, Wang MY.

Folia Microbiol (Praha). 2020 Apr;65(2):265-274

Due to the development of Marine aquaculture, infections caused by *Vibrio vulnificus* are common all over the world. Symptoms of *V. vulnificus* infection vary from gastrointestinal illness to septicemia. After infection with *V. vulnificus*, some patients showed gastrointestinal symptoms, including vomiting, fever, diarrhea, and so on. Others appeared wound infection at the site of contact with bacteria, and even developed sepsis. Once it develops into sepsis, the prognosis of patients is very poor. However, its underlying pathogenic mechanism remains largely undetermined. Growing evidence shows that it can induce primary septicemia mainly via essential virulence factors and regulators. Therefore, it is important to identify the factors that play roles in sepsis. In this review, we systematically expounded the role of *V. vulnificus* virulence factors and regulators in its infection-induced sepsis in order to provide useful information for the treatment and prevention of *V. vulnificus*.

[Mobilization of endothelial progenitor cells in sepsis.](#)

Sun R, Huang J, Sun B.

Inflamm Res. 2020 Jan;69(1):1-9.

Sepsis, an intractable clinical syndrome, is often accompanied by severe vascular endothelial injury and barrier dysfunction. Previous evidence has shown that the endogenous repair mechanism of damaged vascular endothelium requires the proliferation of local endothelial cells (ECs), but processes of re-endothelialization and angiogenesis after endothelial injury are also affected by bone marrow-derived endothelial progenitor cells (EPCs). EPC mobilization has been linked to the mechanism of vascular endothelial repair in various chronic diseases. However, the potential value of EPC mobilization in the treatment of sepsis has not been explored. EPC mobilization plays an important role in endothelial repair; this may guide the discovery of novel methods to treat sepsis.

[Prognosis of \$\beta\$ -adrenergic blockade therapy on septic shock and sepsis: A systematic review and meta-analysis of randomized controlled studies.](#)

Li J, et al

Cytokine. 2020 Feb;126:154916.

β -adrenoceptor antagonist (β -blocker) may have potential in the treatment of septic shock and sepsis. However, the relevant research findings are still controversial. β -blocker of esmolol is safe and effective in improving 28-day mortality and controlling ventricular rate in patients with sepsis after fluid resuscitation, and has no significant adverse effect on tissue perfusion.

[The NLRP3 Inflammasome and Its Role in Sepsis Development.](#)

Danielski LG, et al

Inflammation. 2020 Feb;43(1):24-31.

The pathophysiology of sepsis is extremely complex. During this disease, the exacerbation of the inflammatory response causes oxidative stress, alterations in mitochondrial energy dynamics, and multiple organ failure. Some studies have highlighted the important role of the NLRP3 inflammasome in sepsis. This inflammasome is a macromolecular protein complex that finely regulates the activation of caspase-1 and the production and secretion of potent pro-inflammatory cytokines such as IL-1 β and IL-18. In this review, we elucidate evidences to understand the connection between sepsis development and the NLRP3 inflammasome, the most widely investigated member of this class of receptor.

[Sepsis roadmap: What we know, what we learned, and where we are going.](#)

Kumar V.

Clin Immunol. 2020 Jan;210:108264.

Sepsis is a life-threatening condition originating as a result of systemic blood infection causing, one or more organ damage due to the dysregulation of the immune response. In 2017, the world health organization (WHO) declared sepsis as a disease of global health priority, needing special attention due to its high prevalence and mortality around the world. Most of the therapeutics targeting sepsis have failed in the clinics. The present review highlights the history of the sepsis, its immunopathogenesis, and lessons learned after the failure of previously used immune-based therapies. The subsequent section, where to go describes in details the importance of the complement system (CS), autophagy, inflammasomes, and microbiota along with their targeting to manage sepsis. These systems are interconnected to each other, thus targeting one may affect the other. We are in an urgent need for a multi-targeting therapeutic approach for sepsis.

[Diagnosing acute brain dysfunction due to sepsis.](#)

Esen F, et al

Neurol Sci. 2020 Jan;41(1):25-33.

Developments in the management of critically ill patients suffering organ dysfunctions have demonstrated that brain is the prominent organ to be effected during critical illness. Acute brain dysfunction due to pathologic neuroinflammatory processes associated with sepsis is commonly seen and related to morbidity and mortality in the ICU treatment. Studies reported that survivors of sepsis may suffer long-term cognitive dysfunction that affects quality of life. However, there are no specific approaches to diagnose acute brain dysfunction in the early phase to target protective measures. In recent years, imaging methods and biomarkers are the most important issues of studies. This review will address the current diagnostic approaches to acute brain dysfunction related to sepsis.

[A Review on The Protective Effects of Metformin in Sepsis-Induced Organ Failure.](#)

Ismail Hassan F et al

Cell J. 2020 Jan;21(4):363-370

[Heart failure and sepsis: practical recommendations for the optimal management.](#)

Arfaras-Melainis A, Polyzogopoulou E, Triposkiadis F, Xanthopoulos A, Ikonomidis I, Mebazaa A, Parissis J. Heart Fail Rev. 2020 Mar;25(2):183-194.

Acute heart failure (AHF) is a common clinical challenge that a wide spectrum of physicians encounters in every practice. In many cases, AHF is due to decompensation of chronic heart failure. This

decompensation may be triggered by various reasons, with sepsis being a notable one. Sepsis is defined as a life-threatening organ dysfunction caused by the dysregulated host response to infection and is associated with a very high mortality, which may reach 25%. Alarmingly, the increase in the mortality rate of patients with combined cardiac dysfunction and sepsis is extremely high (may reach 90%). Thus, these patients need urgent intervention. Management of patients with AHF and sepsis is challenging since cornerstone interventions for AHF may be contraindicated in sepsis and vice versa (e.g., diuretic treatment). Unfortunately, no relevant guidelines are yet available, and treatment remains empirical. This review attempts to shed light on the intricacies of the available interventions and suggests routes of action based on the existing bibliography.

Neonatal, paediatric and maternal 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. 2020 Jan;105(1):26-31.

We aim 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

[Mean platelet volume in preterm: a predictor of early onset neonatal sepsis.](#)

Shaaban HA, Safwat N.

J Matern Fetal Neonatal Med. 2020 Jan;33(2):206-211.

Early onset sepsis (EOS) is potentially life-threatening problem especially in preterm. EOS diagnosis is challenging due to its non-specific signs and laboratory tests. Mean platelet volume (MPV) has been used as predictor of many inflammatory diseases. Here we aim to assess the correlation between serial MPV measurement and EOS occurrence in preterm infants and to determine MPV effectiveness in combination with C reactive protein (CRP) to diagnose EOS and mortality prediction. High cord blood and day 3 MPV can be used as surrogate marker for prediction of EOS and associated mortality in preterm neonates.

[Early onset sepsis calculator implementation is associated with reduced healthcare utilization and financial costs in late preterm and term newborns.](#)

Achten NB, et al.

Eur J Pediatr. 2020 Jan 2

The neonatal early onset sepsis (EOS) calculator is a novel tool for antibiotic stewardship in newborns, associated with a reduction of empiric antibiotic treatment for suspected EOS. We studied if implementation of the EOS calculator results in less healthcare utilization and lower financial costs of suspected EOS. In newborns at risk for EOS, EOS calculator implementation is associated with a significant reduction in laboratory investigations related to suspected EOS and significantly shorter stay in those born term. EOS calculator implementation in term newborns is associated with a mean reduction of €207 in costs for EOS-related care per admitted newborn.

[Standardizing the approach to late onset sepsis in neonates through antimicrobial stewardship: a quality improvement initiative.](#)

Lamba V, et al.

J Perinatol. 2020 Jan 6;

Antibiotics are the most prescribed medication in the neonatal intensive care unit (NICU) and there is marked variation in their use. While they are vital for treatment of infections, they put infants at risk for infections with drug resistant organisms, alteration in their microbiome and several other morbidities.

Specific guidelines for neonates are often lacking and our NICU is not compliant with late onset sepsis (LOS) guidelines. Developing and engaging a NICU ASP team improves compliance with late onset sepsis guidelines through the implementation of a LOS bundle of care.

[Markers of NETosis Do Not Predict Neonatal Early Onset Sepsis: A Pilot Study.](#)

Stiel CU, et al

Front Pediatr. 2019;7:555.

Early-onset sepsis in neonates potentially results in substantial morbidity and mortality. A key player in sepsis is a neutrophil extracellular trap (NET) to limit dissemination of pathogens. Aim of this study was to evaluate markers of NET formation in umbilical cord blood as a predictor of neonatal sepsis. NET markers in umbilical cord blood appear to not predict the onset of neonatal sepsis. These findings probably result from the neonates' inability or delayed ability to form NETs, which is suspected to be a main reason for the increased risk of severe infections in neonates, but is also assumed to prevent negative NET-mediated consequences during perinatal adaptation.

[A Retrospective Review of Neonatal Sepsis among GBS-Colonized Women Undergoing Planned Cesarean Section after Labor Onset or Rupture of Membranes.](#)

Yahya FB, Hathcock MA.

Infect Dis Obstet Gynecol. 2020;2020:4365259.

Sepsis is a leading cause of mortality and morbidity in neonates, with group B streptococcus (GBS) remaining the most frequent pathogen isolated from term infants. Surveillance data showed that the majority of cases of early-onset GBS disease were neonates born to women who either received no or suboptimal intrapartum antibiotic prophylaxis with a notable portion of those women having a missed opportunity to receive ≥ 4 hours of chemoprophylaxis. Women planning delivery by cesarean section who present in labor or rupture of membranes prior to their scheduled surgery are unlikely to receive optimal GBS chemoprophylaxis and thus their neonates are at risk of having sepsis. This study suggests that neonates of GBS-colonized women having a planned cesarean section after onset of labor or rupture of membranes are at increased risk of having a sepsis diagnosis. This finding suggests the need for additional studies to assess the risk of sepsis among neonates of women in this group.

[Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study.](#)

Rudd KE, et al

Lancet. 2020 Jan 18;395(10219):200-211.

Sepsis is life-threatening organ dysfunction due to a dysregulated host response to infection. It is considered a major cause of health loss, but data for the global burden of sepsis are limited. As a syndrome caused by underlying infection, sepsis is not part of standard Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) estimates. Accurate estimates are important to inform and monitor health policy interventions, allocation of resources, and clinical treatment initiatives. We estimated the global, regional, and national incidence of sepsis and mortality from this disorder using data from GBD 2017. Despite declining age-standardised incidence and mortality, sepsis remains a major cause of health loss worldwide and has an especially high health-related burden in sub-Saharan Africa.

[Neonatal early onset sepsis in Middle Eastern countries: a systematic review.](#)

Khalil N, Blunt HB, Li Z, Hartman T.

Arch Dis Child. 2020 Jan 22;.

Early onset neonatal sepsis (EOS) accounts for a significant portion of neonatal mortality, which accounts for 46% of global under five child mortality. This systematic review studies the bacterial aetiology of EOS in the Middle East, susceptibility patterns to recommended empirical antibiotic therapy and whether this differs between high-income and middle-income countries in the region. EOS in middle-income countries was more likely to be due to Gram-negative pathogens and less likely to be susceptible to empirical antibiotic therapy. This has important public health implications regarding neonatal mortality in the Middle East region.

[Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children.](#)

Weiss SL, et al

Pediatr Crit Care Med. 2020 Feb;21(2):e52-e106.

We aim to develop evidence-based recommendations for clinicians caring for children (including infants, school-aged children, and adolescents) with septic shock and other sepsis-associated organ dysfunction. A large cohort of international experts was able to achieve consensus regarding many recommendations for the best care of children with sepsis, acknowledging that most aspects of care had relatively low quality of evidence resulting in the frequent issuance of weak recommendations. Despite this challenge, these recommendations regarding the management of children with septic shock and other sepsis-associated organ dysfunction provide a foundation for consistent care to improve outcomes and inform future research.

[Identification of Pediatric Sepsis for Epidemiologic Surveillance Using Electronic Clinical Data.](#)

Weiss SL, et al

Pediatr Crit Care Med. 2020 Feb;21(2):113-121.

This is a method to identify pediatric sepsis episodes that is not affected by changing diagnosis and claims-based coding practices does not exist. We derived and validated a surveillance algorithm to identify pediatric sepsis using routine clinical data and applied the algorithm to study longitudinal trends in sepsis epidemiology. An algorithm using routine clinical data provided an objective, efficient, and reliable method for pediatric sepsis surveillance. An increased sepsis incidence and stable mortality, free from influence of changes in diagnosis or billing practices, were evident.

Lissauer D, et al

[Development of the FAST-M maternal sepsis bundle for use in low-resource settings: a modified Delphi process.](#)

BJOG. 2020 Feb;127(3):416-423.

We develop a sepsis care bundle for the initial management of maternal sepsis in low resource settings. We reviewed the literature to identify all potential interventions and practices around the initial management of sepsis that could be bundled together. A modified Delphi process, using an online questionnaire and in-person meetings, was then undertaken to gain consensus on bundle items. Participants ranked potential bundle items in terms of perceived importance and feasibility, considering their use in both hospitals and health centres. Findings from the healthcare practitioners were then triangulated with those of the experts. A clinically relevant maternal sepsis bundle for low resource settings has been developed by international consensus.

[Surviving Sepsis in a Referral Neonatal Intensive Care Unit: Association between Time to Antibiotic Administration and In-Hospital Outcomes.](#)

Schmatz M, et al

J Pediatr. 2020 Feb;217:59-65.e1.

We look to determine if time to antibiotic administration is associated with mortality and in-hospital outcomes in a neonatal intensive care unit (NICU) population. Among infants with sepsis, delayed time to antibiotic administration was an independent risk factor for death and prolonged cardiovascular dysfunction. Further study is needed to define optimal timing of antimicrobial administration in high-risk NICU populations.

[Clinical Effects and Outcomes After Polymyxin B-Immobilized Fiber Column Direct Hemoperfusion Treatment for Septic Shock in Preterm Neonates.](#)

Nishizaki N, et al

Pediatr Crit Care Med. 2020 Feb;21(2):156-163

We compare the effectiveness and mortality of early-onset sepsis or late-onset sepsis treatments with polymyxin B-immobilized fiber column direct hemoperfusion in terms of effectiveness and mortality in

preterm infants with septic shock. Polymyxin B-immobilized fiber column direct hemoperfusion treatment for preterm infants with septic shock due to early-onset sepsis is associated with earlier hemodynamic and respiratory status improvements and with lower mortality than that due to late-onset sepsis. Early neonatal septic shock detection and polymyxin B-immobilized fiber column direct hemoperfusion induction may improve the prognosis of affected infants.

[Staphylococcus epidermidis in feedings and feces of preterm neonates.](#)

Moles L, et al

PLoS One. 2020;15(2):e0227823

Staphylococcus epidermidis has emerged as the leading agent causing neonatal late-onset sepsis in preterm neonates; although the severity of the episodes caused by this species is often underestimated, it might exert relevant short- and long-term detrimental effects on neonatal outcomes. In this context, the objective of this study was to characterize a collection of S. epidermidis strains obtained from meconium and feces of preterm infants, and to assess the potential role of the enteral feeding tubes as potential reservoirs for this microorganism. Our results indicates the existence of a complex and genetically diverse S. epidermidis population in the NICU environment. A better knowledge of S. epidermidis strains may help to devise strategies to avoid their conversion from symbiont to pathobiont microorganisms in the NICUs.

NEWS2

[Can the prehospital National Early Warning Score 2 identify patients at risk of in-hospital early mortality? A prospective, multicenter cohort study.](#)

Martín-Rodríguez F, et al

Heart Lung. 2020 Mar 11:S0147-9563(20)30086-8.

The National Early Warning Score 2 (NEWS2) scores can help identify clinical deterioration. We assess the predictive capacity of the NEWS2 at prehospital level for the detection of early mortality in the hospital. The NEWS2 performed at prehospital level is a bedside tool for predicting early hospital mortality.

[Scores for sepsis detection and risk stratification - construction of a novel score using a statistical approach and validation of RETTS.](#)

Mellhammar L, et al

PLoS One. 2020 Feb 20;15(2):e0229210.

We look to allow early identification of patients at risk of sepsis in the emergency department (ED), a variety of risk stratification scores and/or triage systems are used. The first aim of this study was to develop a risk stratification score for sepsis based upon vital signs and biomarkers using a statistical approach. Second, we aimed to validate the Rapid Emergency Triage and Treatment System (RETTS) for sepsis. RETTS combines vital signs with symptoms for risk stratification. Even with a statistical approach, we could not construct better risk stratification scores for sepsis than NEWS2. RETTS was inferior to NEWS2 for screening for sepsis.

[Implementing the National Early Warning Score 2 into pre-registration nurse education.](#)

Butler ZA.

Nurs Stand. 2020 Feb 28;35(3):70-75.

Recognising signs of deteriorating health in patients and responding to them appropriately are crucial nursing competencies. In acute care, failure to detect and act promptly on deterioration can lead to the patient's death. To achieve clinical competence, nursing students require training in the use of techniques for monitoring physiological observations as well as protocols that enable them to respond to deterioration. The use of early warning scores has been advocated to standardise the methods and frequency of patient monitoring in acute care settings. In 2012, the Royal College of Physicians developed the National Early Warning Score (NEWS), which was updated in 2017 and known as NEWS2. This early warning score is used in acute hospitals in England, Scotland, Wales and Northern Ireland. This

article explores the benefits and challenges of using NEWS2 as an educational tool in pre-registration nursing programmes to support nursing students in recognising and responding to deteriorating health.

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