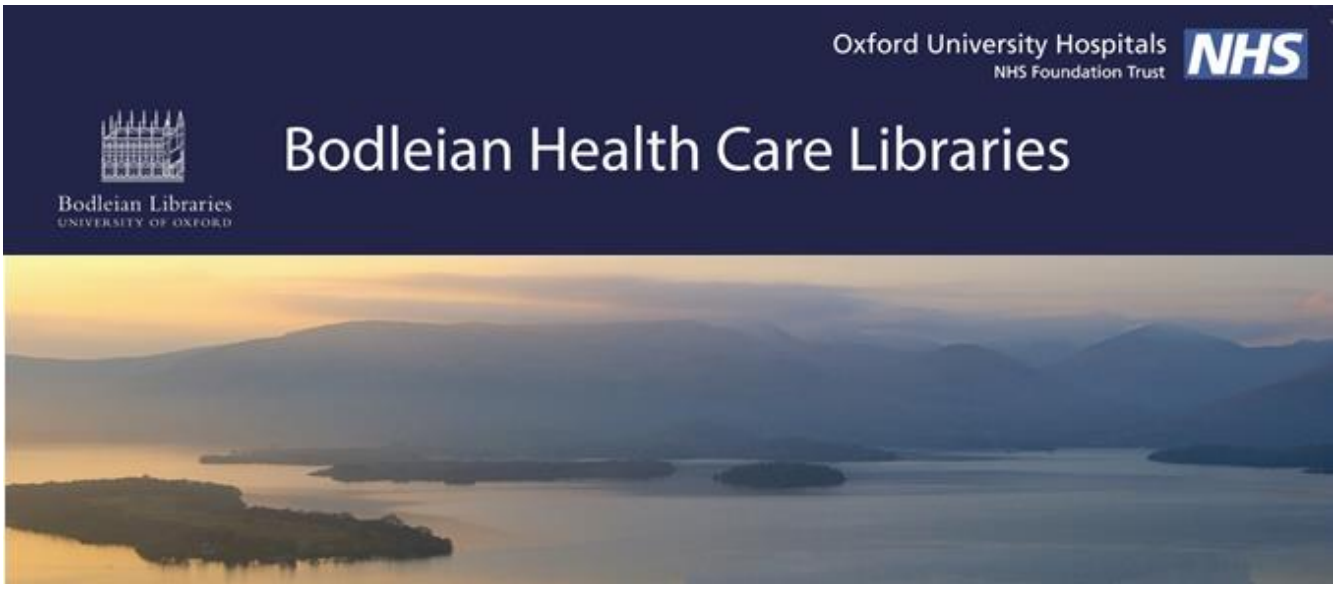
Here is the latest edition of the Sepsis Bulletin. The bulletin covers the latest information on sepsis and comes out monthly. Older editions are available as pdfs on the Keeping Up To Date library guide (http://libguides.bodleian.ox.ac.uk/Keeping_up_to_date)



SEPSIS BULLETIN
June 2021

Sepsis

A Prediction Model for Assessing Prognosis in Critically Ill Patients With Sepsis-Associated Acute Kidney Injury
Hu, H et al
Shock (Augusta, Ga.), 2021,
BACKGROUND: Sepsis-associated acute kidney injury (SA-AKI) is a common problem in critically ill patients and is associated with high morbidity and mortality. Early prediction of the survival of hospitalized patients with SA-AKI is necessary, but a reliable and valid prediction model is still lacking. CONCLUSIONS: Our SAKI model has predictive value for in-hospital mortality of SA-AKI in critically ill patients and outperforms generic scores.

Calpain Activation and Organ Failure in Sepsis: Molecular Insights and Therapeutic Perspectives
Huang, Y et al
Shock (Augusta, Ga.), 2021, 56, May-15
ABSTRACT: Sepsis is a severe systemic response to infection; its ensuing organ failure commonly portends an unfavorable prognosis. Despite the fact that sepsis has been studied for decades, the molecular mechanisms underlying sepsis-induced organ dysfunction remain elusive and more complex than previously thought, and effective therapies are extremely limited. Calpain is a type of calcium-dependent cysteine protease that includes dozens of isoforms. Calpain, as well as its endogenous-specific inhibitor calpastatin, have been implicated in the pathogenesis of sepsis-induced organ dysfunction. Further, there is an accumulating body of evidence supporting the beneficial effect of calpain inhibition or regulation on multiple organ failure in sepsis. Better understanding of the underlying molecular mechanisms is helpful in the development of calpain/calpastatin-targeted therapeutic strategies to protect against sepsis-induced organ injury. The aim of this review is to summarize the recent literature and evidence surrounding the role

of the calpain/calpastatin system in the process of organ dysfunction caused by sepsis-including regulation of cell death, modulation of inflammatory response, and disruption of critical proteins-to provide guidance for future research and therapy development.

Sepsis, the Administration of IV Fluids, and Respiratory Failure: A Retrospective Analysis-SAIFR Study
Jagan, N et al
Chest, 2021, 159, 1437-1444
BACKGROUND: Although resuscitation with IV fluids is the cornerstone of sepsis management, consensus regarding their association with improvement in clinical outcomes is lacking. RESEARCH QUESTION: Is there a difference in the incidence of respiratory failure in patients with sepsis who received guideline-recommended initial IV fluid bolus of 30 mL/kg or more conservative resuscitation of less than 30 mL/kg? INTERPRETATION: In this single-center retrospective study, we found that by broadly defining respiratory failure as an increase in oxygen requirements, a conservative initial IV fluid resuscitation strategy did not correlate with decreased rates of hypoxemic respiratory failure.

Elevated Plasma Levels of Matrix Metalloproteinase-3 and Tissue-Inhibitor of Matrix Metalloproteinases-1 Associate with Organ Dysfunction and Mortality in Sepsis
Jones, T. K. et al
Shock (Augusta, Ga.), 2021,
BACKGROUND: Matrix Metalloproteinases (MMP) respond to tissue damage during sepsis. Higher plasma concentrations of MMPs and the tissue-inhibitor of matrix metalloproteinases (TIMP) have been reported in sepsis compared to healthy controls. The objective of this study was to examine if plasma levels of MMP-3, MMP-9, and TIMP-1 associate with mortality and organ dysfunction during sepsis. CONCLUSION: Elevated plasma concentrations of TIMP-1 associate with organ dysfunction and mortality in sepsis. Higher plasma levels of MMP-3 associate with shock and mortality. Plasma MMP and TIMP-1 may warrant further investigation as emerging sepsis theragnostic biomarkers.

The Hematopoietic Stem/Progenitor Cell Response to Hemorrhage, Injury, and Sepsis: A Review of Pathophysiology
Kelly, L. S. et al
Shock (Augusta, Ga.), 2021, 56, 30-41
ABSTRACT: Hematopoietic stem/progenitor cells (HSPC) have both unique and common responses following hemorrhage, injury, and sepsis. HSPCs from different lineages have a distinctive response to these "stress" signals. Inflammation, via the production of inflammatory factors, including cytokines, hormones, and interferons, has been demonstrated to impact the differentiation and function of HSPCs. In response to injury, hemorrhagic shock, and sepsis, cellular phenotypic changes and altered function occur, demonstrating the rapid response and potential adaptability of bone marrow hematopoietic cells. In this review, we summarize the pathophysiology of emergency myelopoiesis and the role of myeloid-derived suppressor cells, impaired erythropoiesis, as well as the mobilization of HSPCs from the bone marrow. Finally, we discuss potential therapeutic options to optimize HSPC function after severe trauma or infection.

Immunomodulatory and Therapeutic Effects of Mesenchymal Stem Cells on Organ Dysfunction in Sepsis
Khosrojerdi, A et al
Shock (Augusta, Ga.), 2021, 55, 423-440
ABSTRACT: Sepsis is a life-threatening disorder that is caused by a dysregulated inflammatory response during an infection. The disease mostly affects pregnant women, newborns, and patients in intensive care units. Sepsis treatment is a significant part of a country's health budgets. Delay in the therapy causes irreversible failure of various organs due to the lack of blood supply and reduction of oxygen in the tissues and eventually increased mortality. The involvement of four or five organs by sepsis has been attributed to an increased risk of death to over 90%. Although antibiotics are at the first line of sepsis treatment, they do not possess enough potency to control the disease and prevent subsequent organ failure. The immunomodulatory, anti-inflammatory, anti-apoptotic, and anti-microbial properties of mesenchymal stem cells (MSCs) have been reported in various studies. Therefore, the application of MSCs has been considered

a potentially promising therapeutic strategy. In preclinical studies, the administration of MSCs has been associated with reduced bacterial load and decreased levels of pro-inflammatory factors as well as the improved function of the different vital organs, including heart, kidney, liver, and lungs. The current study provides a brief review of sepsis and its pathophysiology, and then highlights recent findings in the therapeutic effects of MSCs and MSC-derived secretome in improving sepsis-induced organ dysfunction. Besides, eligible sepsis candidates for MSC-therapy and the latest clinical findings in these areas have been reviewed.

Assessment of fluid resuscitation on time to hemodynamic stability in obese patients with septic shock
Kiracofe-Hoyte, B. R. et al
Journal of critical care, 2021, 63, 196-201
PURPOSE: Assess time to hemodynamic stability (HDS) in obese patients with septic shock who received <30 vs. =30 ml/kg of initial fluid resuscitation based on actual body weight (ABW). CONCLUSIONS: Obese patients given =30 ml/kg based on ABW had a shorter time to HDS and a lower risk of in-hospital death. Exploratory results suggest improved outcomes resuscitating by ABW vs. IBW; ABW showed no strong benefit over AdjBW. Further prospective studies are needed to confirm the optimal fluid dosing in obese patients.

Frequency and risk factors of post-intensive care syndrome components in a multicenter randomized controlled trial of German sepsis survivors
Kosilek, R. P. et al
Journal of critical care, 2021, 65, 268-273
BACKGROUND: Post-intensive care syndrome (PICS) is a combination of cognitive, psychiatric and physical impairments in survivors of critical illness and intensive care. There is little data on long-term co-occurrence of associated impairments. CONCLUSIONS: Almost all study participants showed impairments associated with PICS in at least one domain. The proposed classification models for PICS appear to be too broad to identify specific risk factors beyond its individual components.

Association between sepsis survivorship and long-term cardiovascular outcomes in adults: a systematic review and meta-analysis
Kosyakovsky, L. B. et al
Intensive care medicine, 2021,
PURPOSE: We aimed to determine the association between sepsis and long-term cardiovascular events. CONCLUSIONS: Surviving sepsis may be associated with a long-term, excess hazard of late cardiovascular events which may persist for at least 5 years following hospital discharge.

Right Ventricular Dysfunction in Early Sepsis and Septic Shock
Lanspa, M. J. et al
Chest, 2021, 159, 1055-1063
Background: Sepsis is a frequently lethal state, commonly associated with left ventricular (LV) dysfunction. Right ventricular (RV) dysfunction in sepsis is less well understood. Research Question: In septic patients, how common is RV dysfunction, and is it associated with worse outcomes? Interpretation: Right ventricular dysfunction is present in nearly half of studied septic patients and is associated with over threefold higher 28-day mortality. Copyright © 2020 American College of Chest Physicians

Effectiveness of polymyxin B-immobilized hemoperfusion against sepsis and septic shock: A systematic review and meta-analysis
Li, X et al
Journal of critical care, 2021, 63, 187-195
PURPOSE: To evaluate the efficacy and safety of Polymyxin B-immobilized hemoperfusion (PMX-HP) against sepsis or septic shock. CONCLUSION: Using PMX-HP to treat patients with less severe sepsis can reduce overall mortality and is safe. Treatment efficacy may benefit from the reduction of endotoxin level and the improvement of hemodynamics. More high quality RCTs are required to further evaluate the clinical role of PMX-HP against severe sepsis or septic shock.

Sepsis-Associated Acute Kidney Injury
Manrique-Caballero, C. L. et al
Critical care clinics, 2021, 37, 279-301
Sepsis-associated acute kidney injury (S-AKI) is a common and life-threatening complication in hospitalized and critically ill patients. It is characterized by rapid deterioration of renal function associated with sepsis. The pathophysiology of S-AKI remains incompletely understood, so most therapies remain reactive and nonspecific. Possible pathogenic mechanisms to explain S-AKI include microcirculatory dysfunction, a dysregulated inflammatory response, and cellular metabolic reprogramming. In addition, several biomarkers have been developed in an attempt to improve diagnostic sensitivity and specificity of S-AKI. This article discusses the current understanding of S-AKI, recent advances in pathophysiology and biomarker development, and current preventive and therapeutic approaches.

Treatment with IgM-enriched immunoglobulin in sepsis: a matched case-control analysis
Martinez, J. I. et al
Journal of critical care, 2021, 64, 120-124
The therapeutic potential of IgM-enriched immunoglobulin preparations (IgGAM) in sepsis remains a field of debate. The use of polyclonal immunoglobulins as adjuvant therapy (Esen & Tugrul, 2009; Kaukonen et al., 2014; Molnár et al., 2013; Taccone et al., 2009) has been shown to improve clinical outcomes in terms of mortality. This study analyze the impact of IgM-enriched IgG (IgGM) as additional immunomodulation. This study showed that treatment with IgGM in patients with sepsis was an independent modulator of the 28-day associated with a lower mortality.

Temporal Differential Expression of Physiomarkers Predicts Sepsis in Critically Ill Adults
Mohammed, A et al
Shock (Augusta, Ga.), 2021, 56, 58-64
BACKGROUND: Sepsis is a life-threatening condition with high mortality rates. Early detection and treatment are critical to improving outcomes. Our primary objective was to develop artificial intelligence capable of predicting sepsis earlier using a minimal set of streaming physiological data in real time. CONCLUSIONS: This study demonstrates that salient physiomarkers derived from continuous bedside monitoring are temporally and differentially expressed in septic patients. Using this information, minimalistic artificial intelligence models can be developed to predict sepsis earlier in critically ill patients.

Thromboelastograph:A prognostic marker in sepsis with organ dysfunction without overt bleeding
Ninan, K. F. et al
Journal of critical care, 2021, 65, 177-183
BACKGROUND: Coagulation abnormalities are not infrequent in sepsis. It is unclear if abnormalities in thromboelastogram (TEG) are associated with mortality in patients with severe sepsis without overt bleeding. CONCLUSION: A subset of patients with severe sepsis without overt bleeding are hypocoagulable. Hypocoagulability is associated with mortality and need for transfusion.

Depression and Long-Term Survival Among South Korean Sepsis Survivors: A Nationwide Cohort Study From 2011 to 2014
Oh, T. K. et al
Critical care medicine, 2021,
OBJECTIVES: We investigated the prevalence of pre- and postsepsis depression and examined the association between diagnosis of pre- and postsepsis depression and 5-year all-cause mortality among survivors of sepsis. CONCLUSIONS: Among sepsis survivors in South Korea, 2.4%% were newly diagnosed with depression within 1 year after their sepsis diagnosis. In addition, postsepsis depression was independently associated with higher 5-year all-cause mortality among sepsis survivors. Our results suggest that patients with a history of sepsis and associated depression may be a high-risk group that interventions may be directed toward.

Quality of life after sepsis and its association with mortality among sepsis survivors in South Korea: A population level cohort study
Oh, T. K. et al

Journal of critical care, 2021, 64, 193-198
PURPOSE: This study aimed to investigate the incidence and effect of quality of life (QOL) change in Korean sepsis survivors. CONCLUSIONS: We found that most sepsis survivors experienced a worsening in their QOL, which was associated with a higher risk of long-term mortality.

Serum Levels of Branched Chain Amino Acids Predict Duration of Cardiovascular Organ Failure in Septic Shock
Puskarich, M. A. et al
Shock (Augusta, Ga.), 2021, 56, 65-72
BACKGROUND: Sepsis shifts cardiac metabolic fuel preference and this disruption may have implications for cardiovascular function. A greater understanding of the role of metabolism in the development and persistence of cardiovascular failure in sepsis could serve to identify novel pharmacotherapeutic approaches. CONCLUSIONS: Among patients with septic shock, BCAA concentrations independently predict time to shock resolution. This study provides hypothesis generating data into the potential contribution of BCAAs to the pathophysiology of cardiovascular failure in sepsis, opening areas for future investigations.

Prognosis and Risk Factors of Sepsis Patients in Chinese Icus: A Retrospective Analysis of A Cohort Database
Qu, Z et al
Shock (Augusta, Ga.), 2021,
BACKGROUND: Sepsis-3 proposed a new definition of septic shock that excluded patients without hyperlactacidemia. The data from China might help to elucidate the prognosis of this special patient group. OBJECTIVE: To study the clinical prognosis and factors affecting patients with sepsis based on data from Chinese intensive care units (ICUs). CONCLUSIONS: Patients with hypotension but without hyperlactacidemia in the ICU also show a high 28-day mortality, and some clinical factors may affect their prognosis and must be treated carefully in the future.

Evaluation of the Initiation Timing of Hydrocortisone in Adult Patients With Septic Shock
Sacha, G. L. et al
Shock (Augusta, Ga.), 2021, 55, 488-494
INTRODUCTION: Clinical studies evaluating the use of hydrocortisone in patients with septic shock are heterogeneous in design with conflicting results. The appropriate time in which to initiate hydrocortisone after shock onset is unknown. This study sought to compare clinical outcomes including vasopressor duration and mortality in patients with septic shock who received hydrocortisone based on timing of initiation after shock onset. CONCLUSIONS: In patients in whom hydrocortisone is prescribed for vasopressor-dependent septic shock, timing is crucial and hydrocortisone should be started within the first 12?h after shock onset.

Systolic dysfunction as evaluated by tissue Doppler imaging echocardiography and mortality in septic patients: A systematic review and meta-analysis
Sanfilippo, F et al
Journal of critical care, 2021, 62, 256-264
PURPOSE: Septic induced cardiomyopathy has a wide spectrum of presentation, being associated with systolic and/or diastolic dysfunction. There is currently no evidence of association between left ventricular (LV) systolic dysfunction and mortality in septic patients. CONCLUSIONS: There is no association between mortality and LV systolic function as evaluated by TDI s' wave in septic patients.

Towards Understanding the Effective Use of Antibiotics for Sepsis
Schinkel, M et al
Chest, 2021,
BACKGROUND: The benefits of early antibiotics for sepsis have recently been questioned. Evidence for this mainly comes from observational studies. The only randomized trial on this subject, the Prehospital Antibiotics Against Sepsis (PHANTASi) trial, did not find significant mortality benefits from early antibiotics. That subgroups of patients benefit from this practice is still plausible, given the heterogeneous nature of sepsis. RESEARCH QUESTION: Do subgroups of sepsis patients experience 28-day mortality benefits from early administration of antibiotics in a prehospital setting? And what key traits drive these

benefits? INTERPRETATION: An interaction between age and benefits of early antibiotics for sepsis has not been reported before. When validated, it can have major implications for clinical practice. This new insight into benefits of early antibiotic treatment for younger sepsis patients may enable more effective care.

High-dose CytoSorb hemoadsorption is associated with improved survival in patients with septic shock: A retrospective cohort study
Schultz, P et al
Journal of critical care, 2021, 64, 184-192
BACKGROUND AND PURPOSE: Hemoadsorption with CytoSorb® offers a possible therapeutic approach in septic shock, but modes of application and dosing are still undetermined. CONCLUSIONS: The application of CytoSorb® seems to be effective in various conditions of septic shock. In a cohort of most severely ill patients the observed mortality was lower than predicted and decreased linearly with blood purification volumes inadvertently exceeding 6 l/kg BW. These results suggest that hemoadsorption might improve survival provided that the applied dose is high enough.

A Randomized Trial of Mycobacterium w in Severe Presumed Gram-Negative Sepsis
Sehgal, I. S. et al
Chest, 2021,
BACKGROUND: Mycobacterium w, an immunomodulator, has been shown to resolve early organ failure in severe sepsis. RESEARCH QUESTION: Does Mw improve survival in patients with severe presumed gram-negative sepsis? : The use of Mw was associated with a significant reduction in mortality in patients with severe presumed gram-negative sepsis. Further studies are required to confirm our findings. TRIAL REGISTRY: ClinicalTrials.gov; No.: NCT02330432; URL: www.clinicaltrials.gov.

Clinical Effect of Systemic Steroids in Patients With Cirrhosis and Septic Shock
Serafim, L. P. et al
Shock (Augusta, Ga.), 2021,
PURPOSE: Evidence regarding the utility of systemic steroids in treating patients with cirrhosis and septic shock remains equivocal. This study aimed to evaluate and elucidate the association of steroid use with outcomes and adverse effects in a cohort of patients with cirrhosis and septic shock. CONCLUSION: The use of systemic steroids was more prevalent in cirrhotic patients with higher vasopressor requirements. It was not associated with decreased mortality or increased ICU- and hospital-free days, or to adverse effects.

Descriptors of Sepsis Using the Sepsis-3 Criteria: A Cohort Study in Critical Care Units Within the U.K. National Institute for Health Research Critical Care Health Informatics Collaborative
Shah, A. D. et al
Critical care medicine, 2021,
OBJECTIVES: To describe the epidemiology of sepsis in critical care by applying the Sepsis-3 criteria to electronic health records. CONCLUSIONS: We successfully operationalized the Sepsis-3 criteria to an electronic health record dataset to describe the characteristics of critical care patients with sepsis. This may facilitate sepsis research using electronic health record data at scale without relying on human coding.

Race Does Not Impact Sepsis Outcomes When Considering Socioeconomic Factors in Multilevel Modeling
Vazquez Guillamet, M. C. et al
Critical care medicine, 2021,
OBJECTIVES: To determine whether race is a major determinant of sepsis outcomes when controlling for socioeconomic factors. CONCLUSIONS: Our study demonstrates that race is not an independent risk factor for sepsis mortality, as well as sepsis-related length of stay. We should expand our inquiry into determinants of sepsis outcomes by including socioeconomic variables.

Presepsin Values Predict Septic Acute Kidney Injury, Acute Respiratory Distress Syndrome, Disseminated Intravascular Coagulation, and Shock
Shimoyama, Y et al
Shock (Augusta, Ga.), 2021, 55, 501-506
BACKGROUND: Sepsis remains a major cause of mortality in critically ill patients. This study aimed to

determine whether presepsin is a predictor of septic acute kidney injury (AKI), acute respiratory distress syndrome (ARDS), disseminated intravascular coagulation (DIC), and shock. CONCLUSION: Presepsin is a predictor of septic AKI, ARDS, and DIC. Combining presepsin values with GPS improved the specificity for predicting septic ARDS relative to using baseline presepsin values alone.

Variations in insulin requirements can be an early indicator of sepsis in burn patients
Singh, S. R. et al
Burns : journal of the International Society for Burn Injuries, 2021,
INTRODUCTION: A >25% increase in daily insulin dosing is suggestive of possible sepsis in burn patients, however, no conclusive evidence is available regarding the time point at which insulin dosing begins to increase. The purpose of this study is to determine the exact time point at which the insulin requirement increases among non-diabetic burn patients with sepsis. CONCLUSION: Daily insulin dosing increases 48 h prior to development of other clinical signs of sepsis and can be used as a sensitive early marker.

Association Between Premorbid Beta-Blocker Exposure and Sepsis Outcomes-The Beta-Blockers in European and Australian/American Septic Patients (BEAST) Study
Tan, K et al
Critical care medicine, 2021,
OBJECTIVES: To examine the effect of premorbid ß-blocker exposure on mortality and organ dysfunction in sepsis. CONCLUSIONS: This study suggests that ß-blocker exposure prior to sepsis, especially to noncardioselective ß blockers, may be associated with better outcome. The findings suggest prospective evaluation of ß-blocker use in the management of sepsis.

Heparin prevents caspase-11-dependent septic lethality independent of anticoagulant properties
Tang, Y et al
Immunity, 2021, 54, 454-467.e6
Heparin, a mammalian polysaccharide, is a widely used anticoagulant medicine to treat thrombotic disorders. It is also known to improve outcomes in sepsis, a leading cause of mortality resulted from infection-induced immune dysfunction. Whereas it is relatively clear how heparin exerts its anticoagulant effect, the immunomodulatory mechanisms enabled by heparin remain enigmatic. Here, we show that heparin prevented caspase-11-dependent immune responses and lethality in sepsis independent of its anticoagulant properties. Survival was higher in septic patients treated with heparin than those without heparin treatment. The identification of this previously unrecognized heparin function establishes a link between innate immune responses and coagulation.

The Association Between Antibiotic Delay Intervals and Hospital Mortality Among Patients Treated in the Emergency Department for Suspected Sepsis
Taylor, S. P. et al
Critical care medicine, 2021, 49, 741-747
OBJECTIVES: Rapid delivery of antibiotics is a cornerstone of sepsis therapy, although time targets for specific components of antibiotic delivery are unknown. We quantified time intervals comprising the task of antibiotic delivery and evaluated the association between interval delays and hospital mortality among patients treated in the emergency department for suspected sepsis. CONCLUSIONS: Both recognition delays and administration delays were associated with increased hospital mortality, but only for longer delays. These results suggest that both metrics may be important to measure and improve for patients with suspected sepsis but do not support targets less than 1 hour.

Impact of Right Ventricular Dysfunction on Short-term and Long-term Mortality in Sepsis: A Meta-analysis of 1,373 Patients
Vallabhajosyula, S et al
Chest, 2021, 159, 2254-2263
BACKGROUND: Right ventricular (RV) dysfunction in sepsis and septic shock has been infrequently studied and has uncertain prognostic significance. RESEARCH QUESTION: Does RV function impact mortality in sepsis and septic shock? STUDY DESIGN AND INTERPRETATION: In this meta-analysis of observational

studies, RV dysfunction was associated with higher short-term and long-term mortality in sepsis and septic shock.

Age-related incidence and outcomes of sepsis in California, 2008-2015
Wardi, G et al
Journal of critical care, 2021, 62, 212-217
PURPOSE: Sepsis remains amongst the most common causes of death worldwide. It has been described as a disease of the elderly, but contemporary data on risk factors and mortality is lacking. CONCLUSION: Age remains an important sepsis risk factor, but other conditions correlated more closely with sepsis-associated death. Patients over 85 years of age suffering from septic shock may have a better chance of survival than previously thought.

NEWS2 top

No articles

Neonatal, paediatric and maternal sepsis top

Effect of obesity on mortality among hospitalized paediatric patients with severe sepsis
Thavamani, A et al
Pediatric obesity, 2021, 16, e12777
INTRODUCTION: Severe sepsis is one of the leading causes of mortality among children. Studies in adults have suggested a protective effect of obesity on mortality among patients hospitalized with sepsis. Paediatric studies evaluating similar relationship is lacking. CONCLUSIONS: Paediatric obesity is associated with reduced mortality among patients with PSS, with the exception of morbid obesity. Further prospective studies are needed to better understand the relationship between obesity and outcomes in PSS.

Metric Development for the Multicenter Improving Pediatric Sepsis Outcomes (IPSO) Collaborative
Paul, R et al
Pediatrics, 2021, 147,
BACKGROUND: A 56 US hospital collaborative, Improving Pediatric Sepsis Outcomes, has developed variables, metrics and a data analysis plan to track quality improvement (QI)-based patient outcomes over time. Improving Pediatric Sepsis Outcomes expands on previous pediatric sepsis QI efforts by improving electronic data capture and uniformity across sites. CONCLUSIONS: A comprehensive data dictionary was developed for the largest pediatric sepsis QI collaborative, optimizing automation and ensuring sustainable reporting. These approaches can be used in other large-scale sepsis QI projects in which researchers seek to leverage EHR data abstraction.

Absence of relationship between serum cortisol and critical illness in premature infants
Prelipcean, I et al
Archives of disease in childhood. Fetal and neonatal edition, 2021, 106, 408-412
BACKGROUND: Inadequate cortisol production in response to critical illness in extremely preterm infants may exacerbate poor outcomes. Despite commonly measuring cortisol concentration and administering hydrocortisone for presumed adrenal insufficiency, the relationship between serum cortisol concentration and illness severity remains unclear in this unique population. OBJECTIVE: To determine the relationship between cortisol concentrations and illness severity as measured by the Score for Neonatal Acute Physiology II, neonatal Sequential Organ Failure Assessment and Vasoactive-Inotropic Score in premature infants. CONCLUSIONS: Cortisol concentrations in extremely preterm infants did not correlate with illness severity regardless of gestational age. Further studies are needed to identify clinically useful mediators of adrenal dysfunction and to guide clinical management.

Outcomes of very preterm infants with neonatal hyperglycaemia: a systematic review and meta-analysis
Rath, C. P. et al
Archives of disease in childhood. Fetal and neonatal edition, 2021,
OBJECTIVE: To explore the association between hyperglycaemia and adverse outcomes in very preterm infants. CONCLUSION: Hyperglycaemia in very preterm infants is associated with higher odds of mortality,

any-grade IVH and any-stage ROP. A limitation was lack of availability of adjusted ORs from many of the included studies. PROSPERO REGISTRATION NUMBER: CRD42020193016.

Top 10 Pearls for the Recognition, Evaluation, and Management of Maternal Sepsis
Shields, A et al
Obstetrics and gynecology, 2021, 138, 289-304
Maternal sepsis is an obstetric emergency and a leading cause of maternal morbidity and mortality. Early recognition in a pregnant or postpartum patient can be a challenge as the normal physiologic changes of pregnancy may mask the signs and symptoms of sepsis. Bedside assessment tools may aid in the detection of maternal sepsis. Timely and targeted antibiotic therapy and fluid resuscitation are critical for survival in patients with suspected sepsis. Once diagnosed, a search for etiologies and early application of source control measures will further reduce harms. If the patient is in septic shock or not responding to initial treatment, multidisciplinary consultation and escalation of care is necessary. Health care professionals should be aware of the unique complications of sepsis in critically ill pregnant and postpartum patients, and measures to prevent poor outcomes in this population. Adverse pregnancy outcomes may occur in association with sepsis, and should be anticipated and prevented when possible, or managed appropriately when they occur. Using a standardized approach to the patient with suspected sepsis may reduce maternal morbidity and mortality.

Plasma Nucleosomes Are Associated With Mortality in Pediatric Acute Respiratory Distress Syndrome
Yehya, N et al
Critical care medicine, 2021, 49, 1149-1158
OBJECTIVES: Circulating nucleosomes and their component histones have been implicated as pathogenic in sepsis and acute respiratory distress syndrome in adults. However, their role in pediatric acute respiratory distress syndrome is unknown. CONCLUSIONS: Plasma nucleosomes are associated with acute respiratory distress syndrome severity, nonpulmonary organ failures, and worse outcomes in pediatric acute respiratory distress syndrome.

Childhood Mortality After Fluid Bolus With Septic or Severe Infection Shock: A Systematic Review and Meta-Analysis
Yue, J et al
Shock (Augusta, Ga.), 2021, 56, 158-166
BACKGROUND: A considerable debate on whether fluid bolus could decrease childhood mortality in pediatric patients with septic or severe infection shock is still unresolved. A systematic review and meta-analysis was conducted to investigate the mortality rates after fluid bolus among children with septic or severe infection shock. CONCLUSION: For the mortality at 48?h, the no bolus group showed decreased mortality when compared with the bolus group, especially in the malaria group. Similar results were found in the colloids and crystalloids solution in patients with malaria shock. Meta-analysis studies with long-term follow-up period and larger sample size are warranted to address the conclusion in the future.

Sex- and Gender-Dependent Differences in Clinical and Preclinical Sepsis
Zhang, M. Q. et al
Shock (Augusta, Ga.), 2021, 56, 178-187
ABSTRACT: In this mini-review we provide an overview of sex- and gender-dependent issues in both clinical and preclinical sepsis. The increasing recognition for the need to account for sex and gender in biomedical research brings a unique set of challenges and requires researchers to adopt best practices when conducting and communicating sex- and gender-based research. This may be of particular importance in sepsis, given the potential contribution of sex bias in the failures of translational sepsis research in adults and neonates. Significant knowledge gaps still exist in this field. Future investigations can address these gaps through careful consideration of sex and gender in clinical studies, and the use of clinically accurate preclinical models that reflect sex differences. A better understanding of sex-and gender-dependent differences may serve to increase translational research success.

COVID-19 and sepsis top

Coronavirus Disease 2019 as Cause of Viral Sepsis: A Systematic Review and Meta-Analysis
Karakike, E et al
Critical care medicine, 2021,
OBJECTIVE: Coronavirus disease 2019 is a heterogeneous disease most frequently causing respiratory tract infection, which can induce respiratory failure and multiple organ dysfunction syndrome in its severe forms. The prevalence of coronavirus disease 2019-related sepsis is still unclear; we aimed to describe this in a systematic review. CONCLUSIONS: The majority of coronavirus disease 2019 patients hospitalized in the ICU meet Sepsis-3 criteria and present infection-associated organ dysfunction. The medical and scientific community should be aware and systematically report viral sepsis for prognostic and treatment implications.

Comparison of Circulating Immune Cells Profiles and Kinetics Between Coronavirus Disease 2019 and Bacterial Sepsis
de Roquetaillade, C et al
Critical care medicine, 2021,
OBJECTIVES: Although clinical presentation of coronavirus disease 2019 has been extensively described, immune response to severe acute respiratory syndrome coronavirus 2 remains yet not fully understood. Similarities with bacterial sepsis were observed; however, few studies specifically addressed differences of immune response between both conditions. Here, we report a longitudinal analysis of the immune response in coronavirus disease 2019 patients, its correlation with outcome, and comparison between severe coronavirus disease 2019 patients and septic patients. CONCLUSIONS: Circulating immune cells profile differs between mild and severe coronavirus disease 2019 patients. Severe coronavirus disease 2019 is associated with a unique immune profile as compared with sepsis. Several immune features are associated with outcome. Thus, immune monitoring of coronavirus disease 2019 might be of help for patient management.

Core Outcome Measures for Trials in People With Coronavirus Disease 2019: Respiratory Failure, Multiorgan Failure, Shortness of Breath, and Recovery
Tong, A et al
Critical care medicine, 2021, 49, 503-516
OBJECTIVES: Respiratory failure, multiple organ failure, shortness of breath, recovery, and mortality have been identified as critically important core outcomes by more than 9300 patients, health professionals, and the public from 111 countries in the global coronavirus disease 2019 core outcome set initiative. The aim of this project was to establish the core outcome measures for these domains for trials in coronavirus disease 2019. CONCLUSIONS: The coronavirus disease 2019 core outcome set recommended core outcome measures have content validity and are considered the most feasible and acceptable among existing measures. Implementation of the core outcome measures in trials in coronavirus disease 2019 will ensure consistency and relevance of the evidence to inform decision-making and care of patients with coronavirus disease 2019.

The Surviving Sepsis Campaign: Research Priorities for Coronavirus Disease 2019 in Critical Illness
Coopersmith, C. M. et al
Critical care medicine, 2021, 49, 598-622
OBJECTIVES: To identify research priorities in the management, pathophysiology, and host response of coronavirus disease 2019 in critically ill patients. CONCLUSIONS: Although knowledge of both biology and treatment has increased exponentially in the first year of the coronavirus disease 2019 pandemic, significant knowledge gaps remain. The research priorities identified represent a roadmap for investigation in coronavirus disease 2019.

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