SEPSIS BULLETIN
January 2021

Sepsis
NEWS2
Neonatal, paediatric and maternal sepsis
COVID-19 and sepsis

Sepsis

Norepinephrine, Dopamine, and Vasopressin in Patients with Sepsis and Preexisting or Acute Heart Failure: A Retrospective Cohort Study

Zhou D, Zhu B, Jiang J, Zhou G, Zhou S

Med Sci Monit 2021;27:e927716

The aim of this study was to assess the impact of norepinephrine (NE), norepinephrine plus vasopressin (NE+VAS) and dopamine in patients with sepsis and heart failure. Compared with NE or dopamine alone, NE+VAS can reduce survival in patients with sepsis and heart failure who need vasopressors. Compared with the other 2 treatment options, dopamine can shorten ICU and hospital stays for these patients.

Semiquantitative Power Doppler Ultrasound Score to Predict Acute Kidney Injury in Patients With Sepsis or Cardiac Failure: A Prospective Observational Study

Zhi HJ, Zhao J, Nie S, Ma YJ, Cui XY, Zhang M, et al

J Intensive Care Med 2021;36(1):115-22

Diagnosing acute kidney injury (AKI) stage 3 in critically ill patients may help physicians in making treatment decisions. This diagnosis relies chiefly on urinary output and serum creatinine, which may be of limited value. This study aimed to explore the diagnostic performance of renal resistive index (RRI) and semiquantitative power Doppler ultrasound (PDU) scores in predicting AKI stage 3 in patients with sepsis or cardiac failure. Power Doppler ultrasound scores could effectively predict AKI stage 3 in patients with cardiac failure but not in patients with sepsis. Renal resistive index is a poor predictor of AKI stage 3 in patients with sepsis or cardiac failure.

Sex- and Gender-Dependent Differences in Clinical and Preclinical Sepsis

Zhang M, Macala KF, Fox-Robichaud A, Mendelson AA, Lalu MM

Shock 2021;Publish Ahead of Print

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 in 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. Clinical evidence of sex-dependent differences in sepsis is equivocal. Since clinical studies are limited to observational data and confounded by a multitude of factors, preclinical studies provide a unique opportunity to investigate sex-differences in a controlled, experimental environment. Numerous preclinical studies have suggested that females may experience favourable outcomes in comparison to males. The underlying mechanistic evidence for sex-dependent differences in sepsis and other models of shock (e.g. trauma-hemorrhage) largely centres around the beneficial effects of estrogen. Other mechanisms, such as the immunosuppressive role of testosterone and X-linked mosaicism are also thought to contribute to observed sex- and gender-dependent differences in sepsis. 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.

Outcomes of new-onset atrial fibrillation in patients with sepsis: A systematic review and meta-analysis of 225,841 patients

Xiao FP, Chen MY, Wang L, He H, Jia ZQ, Kuai L, et al

Am J Emerg Med 2021;42:23-30

The outcomes of new-onset atrial fibrillation (AF) during sepsis are inconsistent and inconclusive. This meta-analysis aims to provide a comprehensive description of the impact of new-onset AF on the prognosis of sepsis. New-onset AF is frequently associated with adverse outcomes in patients with sepsis. This is a clinical issue that warrants more attention and should be managed appropriately to prevent poor prognosis.

Accuracy of Heparin-Binding Protein in Diagnosing Sepsis: A Systematic Review and Meta-Analysis

Wu YL, Yo CH, Hsu WT, Qian F, Wu BS, Dou QL, et al

Crit Care Med 2021;49(1):e80-e90

Existing studies evaluating the accuracy of heparin-binding protein for the diagnosis of sepsis have been inconsistent. We conducted a systematic review and meta-analysis to assess the totality of current evidence regarding the utility of heparin-binding protein to diagnose sepsis in patients with presumed systemic infection. The diagnostic ability of heparin-binding protein is favorable, demonstrating both high sensitivity and specificity in predicting progression to sepsis in critically ill patients. Future studies could assess the incremental value that heparin-binding protein may add to a multimodal sepsis identification and prognostication algorithm for critically ill patients.

Measurement of Sepsis in a National Cohort Using Three Different Methods to Define Baseline Organ Function

Wayne MT, Molling D, Wang XQ, Hogan CK, Seelye S, Liu VX, et al

Ann Am Thorac Soc 2021

In 2017, the U.S. Centers for Disease Control and Prevention (CDC) developed a new surveillance definition of sepsis, the adult sepsis event (ASE), to better track sepsis epidemiology. The ASE requires evidence of acute organ dysfunction and defines baseline organ function pragmatically as the best in-hospital value. This approach may undercount sepsis if new organ dysfunction does not resolve by discharge. We look to understand how sepsis identification and outcomes differ when using the best laboratory values during hospitalization versus methods that use historical look-backs to define baseline organ function. Among Veterans hospitalized with potential infection, the majority had laboratory values in the prior 6 months. Using 3- and 6-month look-backs to define baseline organ function resulted in an 11% and 17% relative increase, respectively, in the number of sepsis hospitalizations identified.

A novel procalcitonin-based score for detecting sepsis among critically ill patients

Tsui TL, Huang YT, Kan WC, Huang MS, Lai MY, Ueng KC, et al

PLoS One 2021;16(1):e0245748

Procalcitonin (PCT) has been widely investigated as an infection biomarker. The study aimed to prove that serum PCT, combining with other relevant variables, has an even better sepsis-detecting ability in critically ill patients. We proposed a novel PCT-based score that performs better in detecting sepsis than serum PCT levels alone, C-reactive protein, and infection probability score.

Early prolonged neutrophil activation in critically ill patients with sepsis

Törnblom S, Nisula S, Vaara ST, Poukkanen M, Andersson S, Pettilä V, et al

Innate Immun 2021:1753425920980078

We hypothesised that plasma concentrations of biomarkers of neutrophil activation and pro-inflammatory cytokines differ according to the phase of rapidly evolving sepsis. In an observational study, we measured heparin-binding protein (HBP), myeloperoxidase (MPO), IL-6 and IL-8 in 167 sepsis patients on intensive care unit admission. Elevation of neutrophil activation markers HBP and MPO was an early event in the evolution of sepsis, lasting beyond the subsidence of the pro-inflammatory cytokine reaction. Thus, as sepsis biomarkers, HBP and MPO were not as prone as IL-6 and IL-8 to the effect of sample timing.

The effects of a limited infusion rate of fluid in the early resuscitation of sepsis on glycocalyx shedding measured by plasma syndecan-1: a randomized controlled trial

Saoraya J, Wongsamita L, Srisawat N, Musikatavorn K

J Intensive Care 2021;9(1):1

Aggressive fluid administration is recommended in the resuscitation of septic patients. However, the delivery of a rapid fluid bolus might cause harm by inducing degradation of the endothelial glycocalyx. This research aimed to examine the effects of the limited infusion rate of fluid on glycocalyx shedding as measured by syndecan-1 in patients with sepsis-induced hypoperfusion. In sepsis resuscitation, the limited rate of fluid resuscitation compared to the standard rate did not significantly reduce changes in syndecan-1 at 6 h.

Sepsis Awareness to Enhance Early Identification of Sepsis in Emergency Departments

Rajan JJ, Rodzevik T

J Contin Educ Nurs 2021;52(1):39-42

Early identification of sepsis continues to be a challenge for nurses in the acute care setting. Often, a gap exists between existing policies for sepsis identification and structured education to support these policies. Using a sepsis standing order set combined with education helped to identify and elevate the care of sepsis patients. Resources such as the Surviving Sepsis Campaign screening tool to identify sepsis helped emergency department nurses to identify sepsis in a timely manner

Heart Dysfunction in Sepsis

Poveda-Jaramillo R

J Cardiothorac Vasc Anesth 2021;35(1):298-309

Cardiac involvement during sepsis frequently occurs. A series of molecules induces a set of changes at the cellular level that result in the malfunction of the myocardium. The understanding of these molecular alterations has simultaneously promoted the implementation of diagnostic strategies that are much more precise and allowed the advance of the therapeutics. The heart is a vital organ for survival. Its well-being ensures the adequate supply of essential elements for organs and tissues.

Post-mortem diagnosis of sepsis: when it's too late

Passaro G, dell'Aquila M, De Filippis A, Baronti A, Costantino A, Iannaccone F, et al

Clin Ter 2021;171(1):e60-e2

Post-mortem diagnosis of sepsis is often very difficult to make, especially in the elderly affected by multiple comorbidities. However, clinical evaluation following histology, immunohistochemistry, microbiological tests, immunoassays and proteomics can improve reliability of this post-mortem diagnosis.

Association between low body mass index and increased 28-day mortality of severe sepsis in Japanese cohorts

Oami T, Karasawa S, Shimada T, Nakada TA, Abe T, Ogura H, et al

Sci Rep 2021;11(1):1615

Current research regarding the association between body mass index (BMI) and altered clinical outcomes of sepsis in Asian populations is insufficient. We investigated the association between BMI and clinical outcomes using two Japanese cohorts of severe sepsis. In conclusion, patients with a BMI < 18.5 had a significantly increased 28-day mortality compared to those with a BMI ≥ 18.5 in Japanese cohorts with severe sepsis.

Combination of Procalcitonin Value on Hospital Admission and Its Subsequent Change in Value Is Associated With the Prognosis of Sepsis

Muratsu A, Muroya T, Katayama Y, Shimizu K, Ogura H, Kuwagata Y, et al
Crit Care Explor 2021;3(1):e0298
We evaluate the relationship between the procalcitonin value in blood on hospital admission and its subsequent change and prognosis among sepsis patients. Our study showed the sepsis patients with a procalcitonin value in blood of less than 33.2 ng/mL on hospital admission and change in serum procalcitonin of less than 0.0 ng/mL had high mortality at 28 days after hospital admission.

TELEmedicine as an intervention for sepsis in emergency departments: a multicenter, comparative effectiveness study (TELEvISED Study)
Mohr NM, Harland KK, Okoro UE, Fuller BM, Campbell K, Swanson MB, et al
J Comp Eff Res 2021
Sepsis is a life-threatening infection that affects over 1.7 million Americans annually. Low-volume rural hospitals have worse sepsis outcomes, and emergency department (ED)-based telemedicine (tele-ED) has been one promising strategy for improving rural sepsis care. The objective of this study is to evaluate the impact of tele-ED consultation on sepsis care and outcomes in rural ED patients. The TELEvISED study is a multicenter (n = 25) retrospective propensity-matched comparative effectiveness study of tele-ED care for rural sepsis patients in a mature tele-ED network. Telemedicine-exposed patients will be matched with non telemedicine patients using a propensity score to predict tele-ED use. The primary outcome is 28-day hospital free days, and secondary outcomes include adherence with guidelines, mortality and organ failure. ClinicalTrials.gov: NCT04441944.

Splenic volume on computed tomography scans is associated with mortality in patients with sepsis
Mitsuyama Y, Shimizu K, Hirayama A, Komukai S, Kitamura T, Ogura H, et al
Int J Infect Dis 2021
The spleen is a key organ of the immune system. Asplenia has been reported to increase the risk of sepsis from overwhelming post-splenectomy infection. However, there are few reports on the association between splenic volume and mortality in patients with no history of splenectomy. In this study, we focused on splenic volume of patients with sepsis and evaluated the association between splenic volume and mortality. Splenic volume appeared to be an independent predictor of poor prognosis.

Mortality prediction using a novel combination of biomarkers in the first day of sepsis in intensive care units
Liu J, Bai C, Li B, Shan A, Shi F, Yao C, et al
Sci Rep 2021;11(1):1275
Early identification of infection severity and organ dysfunction is crucial in improving outcomes of patients with sepsis. We aimed to develop a new combination of blood-based biomarkers that can early predict 28-day mortality in patients with sepsis or septic shock. The combination of IL-6, NT-proBNP, and INR may serve as a potential predictor of 28-day mortality in critically ill patients with sepsis or septic shock.

Clostridium perfringens sepsis in three patients with acute leukemia and review of the literature
Liu F, Xue S, Zhang Y, Yang J, Hu J, Li D, et al
Int J Hematol 2021:1-10
In this study, we aimed to improve understanding of the clinical manifestations, laboratory findings, and risk factors of Clostridium perfringens sepsis in patients with acute leukemia and to analyze treatment strategies for improving prognosis. We analyzed clinical manifestations, laboratory data, diagnosis, and treatment strategies in three cases of C. perfringens sepsis in patients with acute leukemia. We also reviewed and analyzed the relevant literature, incorporating our findings into the discussion. Multimodal treatments, including fluid resuscitation, antibiotics, organ support, and blood purification, are essential for success.

International normalised ratio as an independent predictor of mortality in limb necrotising fasciitis with sepsis
Ling XW, Lin K, Jiang XQ, Wu Q, Liu ZJ, Li S, et al
Ann R Coll Surg Engl 2021;103(1):35-40
Necrotising fasciitis with sepsis is a life threatening disease. The aim of this study was to analyse the association between international normalised ratio (INR) and mortality in sepsis patients with necrotising fasciitis. INR is a significant independent predictor of mortality in sepsis patients diagnosed with necrotising fasciitis.

The Association between Dynamic Changes in Serum Presepsin Levels and Mortality in Immunocompromised Patients with Sepsis: A Prospective Cohort Study

Lee J, Kim S, Kim KH, Jeong NR, Kim SC, Oh EJ

Diagnostics (Basel) 2021;11(1)

Presepsin is a subtype of soluble CD14 that is increased in the blood of septic patients. We investigated the role of dynamic changes in serum presepsin levels in critically ill, immunocompromised patients with sepsis. These findings suggest that dynamic changes in presepsin levels between day 1 and day 3 are associated with in-hospital mortality in patients with sepsis, especially in immunocompromised patients.

Emerging benefits and drawbacks of alpha(2) -adrenoceptor agonists in the management of sepsis and critical illness

Lankadeva YR, Shehabi Y, Deane AM, Plummer MP, Bellomo R, May CN

Br J Pharmacol 2021

Alpha(2) -adrenoceptor agonists are increasingly being used for the provision of comfort, sedation and the management of delirium in critically ill patients with and without sepsis. In this context, increased sympathetic and inflammatory activity are common pathophysiological features linked to multi-organ dysfunction, particularly in patients with sepsis or those undergoing cardiac surgery requiring cardiopulmonary bypass. Experimental and clinical studies support the notion that the alpha(2) -adrenoceptor agonists, dexmedetomidine and clonidine, mitigate sympathetic and inflammatory overactivity in sepsis and cardiac surgery requiring cardiopulmonary bypass. These effects can protect vital organs, including the cardiovascular system, kidneys and brain. We review the pharmacodynamic mechanisms by which alpha(2) -adrenoceptor agonists might mitigate multi-organ dysfunction arising from pathophysiological conditions associated with excessive inflammatory and adrenergic stress in experimental studies. We also outline recent clinical trials that have examined the use of dexmedetomidine in critically ill patients with and without sepsis and in patients undergoing cardiac surgery.

Procalcitonin to Reduce Long-Term Infection-associated Adverse Events in Sepsis

Kyriazopoulou E, Liaskou-Antoniou L, Adamis G, Panagaki A, Melachroinopoulos N, Drakou E, et al

Am J Respir Crit Care Med Jan 2021

Although early antimicrobial discontinuation guided by procalcitonin (PCT) has shown decreased antibiotic consumption in lower respiratory tract infections, the outcomes in long-term sepsis sequelae remain unclear. We investigate if PCT guidance may reduce the incidence of long-term infection-associated adverse events in sepsis. In sepsis, PCT guidance was effective in reducing infection-associated adverse events, 28-day mortality, and cost of hospitalization.

Omega-3 Fatty Acid Lipid Emulsions are Safe and Effective in Reducing Endotoxemia and Sepsis in Acute-on-Chronic Liver Failure-an open-label randomized controlled trial

Kulkarni AV, Anand L, Vyas AK, Premkumar M, Choudhury AK, Trehanpati N, et al

J Gastroenterol Hepatol 2021

Sepsis is an important determinant of the outcome of acute-on-chronic liver failure (ACLF) patients. Omega-3 fatty acids (FAs) are known to suppress inflammation, reduce morbidity, and mortality in postoperative and critically ill patients. We aimed to evaluate the effect of intravenous omega-6 and omega-3 FA lipid emulsions in ACLF patients. Omega-3 FAs are safe and effective in reducing systemic inflammation, endotoxemia, and sepsis in patients with ACLF. These lipid emulsions could also be considered as effective sources of immunonutrition in such sick patients.

Recent advances in the research and management of sepsis-associated DIC

Iba T, Connors JM, Nagaoka I, Levy JH

Int J Hematol 2021;113(1):24-33

Disseminated intravascular coagulation (DIC) is a common and life-threatening complication in sepsis. Sepsis-associated DIC is recognized as the systemic activation in coagulation with suppressed fibrinolysis that leads to organ dysfunction in combination with systemic intravascular inflammation. In this process, thrombin contributes a key role in connecting both coagulation and inflammation. Endothelial injury, a result of sepsis, causes DIC due to the effect of multiple activated factors that include neutrophils, platelets, and damage-associated molecular patterns. Recent advances in the understanding of pathophysiology have made it possible to diagnose sepsis-associated DIC at earlier timing with better accuracy. However, progress in the treatment is still limited, and new therapeutics for sepsis-associated DIC are needed.

Counting the cost of major infection and sepsis in New Zealand: an exploratory study using the National Minimum Data Set

Huggan PJ, Helms TA, Gibbons V, Reid K, Hutchins H, Sheerin I

N Z Med J 2021;134(1528):10-25

We explore the population-at-risk and potential cost of a sepsis episode in New Zealand. Infectious diseases with the potential to cause sepsis are common among hospital inpatients. Direct treatment costs are high for those who present with or progress to sepsis due to these infections.

Pathophysiology of sepsis-induced cardiomyopathy

Hollenberg SM, Singer M

Nat Rev Cardiol 2021

Sepsis is the life-threatening organ dysfunction caused by a dysregulated host response to infection and is the leading cause of death in intensive care units. Cardiac dysfunction caused by sepsis, usually termed sepsis-induced cardiomyopathy, is common and has long been a subject of interest. In this Review, we explore the definition, epidemiology, diagnosis and pathophysiology of septic cardiomyopathy, with an emphasis on how best to interpret this condition in the clinical context. Advances in diagnostic techniques have increased the sensitivity of detection of myocardial abnormalities but have posed challenges in linking those abnormalities to therapeutic strategies and relevant clinical outcomes. Sophisticated methodologies have elucidated various pathophysiological mechanisms but the extent to which these are adaptive responses is yet to be definitively answered. Although the indications for monitoring and treating septic cardiomyopathy are clinical and directed towards restoring tissue perfusion, a better understanding of the course and implications of septic cardiomyopathy can help to optimize interventions and improve clinical outcomes.

Improving Antibiotic Administration Rate for Patients With Sepsis in the Emergency Department

Hatozaki C, Sakuramoto H, Okamoto M, Nakajima H, Shimojo N, Inoue Y

J Nurs Care Qual 2021

Previous studies have demonstrated that delayed antibiotic administration increases the risk of mortality in patients with sepsis. In the emergency department, the antibiotic administration rate within 1 and 3 hours for patients with suspected sepsis was low. Nurse-initiated quality improvement improved the early administration of antibiotics for patients with suspected sepsis.

Beta-Blockers, Tachycardia and Survival Following Sepsis- An Observational Cohort Study

Guz D, Buchritz S, Guz A, Ikan A, Babich T, Daitch V, et al

Clin Infect Dis 2021

Sepsis is associated with excessive release of catecholamines which causes tachycardia and correlates with poor clinical outcome. Beta blockers (BB) may blunt this effect on heart rate (HR). The objective of this study is to assess whether chronic BB therapy is associated with better clinical outcomes in patients with sepsis admitted to internal medicine wards. Chronic BB therapy was associated with decreased mortality in patients hospitalized with sepsis in internal medicine wards exhibiting absolute and relative tachycardia.

Usefulness of Sepsis-3 in diagnosing and predicting mortality of ventilator-associated lower respiratory tract infections

Gaudet A, Devos M, Keignart S, Pouly O, Lecailtel S, Wallet F, et al

PLoS One 2021;16(1):e0245552

Early distinguishing ventilator-associated tracheobronchitis (VAT) and ventilator-associated pneumonia (VAP) remains difficult in the daily practice. However, this question appears clinically relevant, as treatments of VAT and VAP currently differ. In this study, we assessed the accuracy of sepsis criteria according to the Sepsis-3 definition in the early distinction between VAT and VAP. Sepsis criteria according to the Sepsis-3 definition show a high specificity but a low sensitivity for the diagnosis of VAP. Our results do not support the use of these criteria for the early diagnosis of VAP in patients with VA-LRTI.

Validity of "Sepsis-3" criteria in identifying patients with community-onset sepsis in Internal Medicine wards; a prospective, multicenter study

Fortini A, Faraone A, Meini S, Bettucchi M, Longo B, Valoriani B, et al

Eur J Intern Med 2021

Few data are available on the validity of "Sepsis-3" criteria in identifying patients with sepsis in internal medicine wards (IMWs). Real-life data about this topic and on the prevalence of sepsis in IMWs could be useful for improving hospital organization. OBJECTIVES: To assess the validity of "Sepsis-3" criteria in identifying patients with community-onset sepsis in IMWs. Secondary objectives: to evaluate the prevalence of these patients in IMWs and to compare "Sepsis-3" and "Sepsis-1" criteria. "Sepsis-3" criteria are able to identify patients with community-onset sepsis in IMWs, whose prevalence and in-hospital mortality are remarkably high. Medical departments should adapt their organization to the needs for care of these complex patients.

Early ICU-mortality in sepsis - causes, influencing factors and variability in clinical judgement: a retrospective cohort study

Driessen RGH, Heijnen NFL, Hulsewe R, Holtkamp JWM, Winkens B, van de Poll MCG, et al

Infect Dis (Lond) 2021;53(1):61-8

Sepsis is a global health care problem with a high mortality. Early death seems common; however, data are sparse. The objective of the present study was to report causes and influencing factors of early death in sepsis and septic shock. Early death after ICU admission in sepsis is common and primarily caused by multiple organ failure, mesenteric ischaemia and death after unsuccessful CPR. Influencing factors were delay in ICU admission and futile ICU admission. Fleiss kappa indicates substantial variability in clinical judgement between intensivists, strengthening the necessity for shared decision making.

The effects of sepsis on endothelium and clinical implications

Dolmatova EV, Wang K, Mandavilli R, Griendling KK

Cardiovasc Res 2021;117(1):60-73

Sepsis accounts for nearly 700 000 deaths in Europe annually and is caused by an overwhelming host response to infection resulting in organ failure. The endothelium is an active contributor to sepsis and as such represents a major target for therapy. During sepsis, endothelial cells amplify the immune response and activate the coagulation system. They are both a target and source of inflammation and serve as a link between local and systemic immune responses. In response to cytokines produced by immune cells, the endothelium expresses adhesion molecules and produces vasoactive compounds, inflammatory cytokines, and chemoattractants, thus switching from an anticoagulant to procoagulant state. These responses contribute to local control of infection, but systemic activation can lead to microvascular thrombosis, capillary permeability, hypotension, tissue hypoxia, and ultimately tissue damage. This review focuses on the role of the endothelium in leucocyte adhesion and transmigration as well as production of reactive oxygen and nitrogen species, microRNAs and cytokines, formation of signalling microparticles, and disseminated intravascular coagulation. We also discuss alterations in endothelial permeability and apoptosis. Finally, we review the diagnostic potential of endothelial markers and endothelial pathways as therapeutic targets for this devastating disease.

Addressing Gaps in Nurses' Knowledge of Sepsis: A Literature Review

Coiner SE, Wingo NP

J Contin Educ Nurs 2021;52(1):43-6

Sepsis is a dangerous and costly health care condition requiring prompt identification and emergency treatment. Bedside nurses have a crucial role in these early steps. Nurses should receive effective and timely education on identifying and treating sepsis in their patient populations. The purpose of this article is to review the literature and to identify how current sepsis education methods are addressing the gaps in nursing knowledge of sepsis. PubMed and CINAHL databases were used to search the literature. After inclusion and exclusion criteria were applied, nine articles were chosen for synthesis. Synthesis revealed three major themes: (a) assessing nurse sepsis knowledge, (b) using electronic learning methods for education, and (c) incorporating simulation into sepsis training. Gaps in the literature were also identified. [J Contin Educ Nurs. 2021;52(1):43-46.].

Secondary Peritonitis and Intra-Abdominal Sepsis: An Increasingly Global Disease in Search of Better Systemic Therapies

Clements TW, Tolonen M, Ball CG, Kirkpatrick AW

Scand J Surg 2021:1457496920984078

Secondary peritonitis and intra-abdominal sepsis are a global health problem. The life-threatening systemic insult that results from intra-abdominal sepsis has been extensively studied and remains somewhat poorly understood. While local surgical therapy for perforation of the abdominal viscera is an age-old therapy, systemic therapies to

control the subsequent systemic inflammatory response are scarce. Advancements in critical care have led to improved outcomes in secondary peritonitis. The understanding of the effect of secondary peritonitis on the human microbiome is an evolving field and has yielded potential therapeutic targets. This review of secondary peritonitis discusses the history, classification, pathophysiology, diagnosis, treatment, and future directions of the management of secondary peritonitis. Ongoing clinical studies in the treatment of secondary peritonitis and the open abdomen are discussed.

The Impact of Statin Use prior to intensive Care Unit (icu) Admission on critically Ill Patients with sepsis

Chinaeke EE, Love BL, Magagnoli J, Yunusa I, Reeder G

Pharmacotherapy 2021

We evaluate the impact of pre-intensive care unit admission (pre-ICU) statin use on all-cause in-hospital mortality and ICU length of stay (LOS). Among patients with sepsis admitted to the medical ICU, pre-ICU statin use is causally associated with a decrease in 30-day ICU mortality, ICU LOS, and 30-day in-hospital mortality compared to non-use. This study adds to the totality of evidence on the pleiotropic effect of statin use in patients with sepsis.

A randomized trial to compare procalcitonin and C-reactive protein in assessing severity of sepsis and in guiding antibacterial therapy in Egyptian critically ill patients

Ali WA, Bazan NS, Elberry AA, Hussein RRS

Ir J Med Sci 2021

Procalcitonin (PCT) and C-reactive protein (CRP) are the main used biomarkers for sepsis and in guiding antibiotic therapy, although PCT high cost limits its use in developing countries. We are comparing between PCT and CRP in assessing severity of sepsis and in guiding antibacterial therapy in critically ill patients. PCT is a more accurate diagnostic and prognostic biomarker than CRP in patients with sepsis. PCT significantly shortened patients' exposure to antibacterial therapy and hospital length of stay.

Candida colonization as a predictor of invasive candidiasis in non-neutropenic ICU patients with sepsis: A systematic review and meta-analysis

Alenazy H, Alghamdi A, Pinto R, Daneman N

Int J Infect Dis 2021;102:357-62

Candida colonization is a risk factor for the development of invasive candidiasis. This study sought to estimate the magnitude of this association, and determine if this information can be used to guide empirical antifungal therapy initiation in critically ill septic patients. Candida colonization is strongly associated with the likelihood of invasive candidiasis among ICU patients with sepsis. Available data argue against initiating empirical antifungal treatment in non-neutropenic septic patients without prior documented Candida colonization.

Diabetes on sepsis outcomes in non-ICU patients: A cohort study and review of the literature

Akinosoglou K, Kapsokosta G, Mouktaroudi M, Rovina N, Kaldis V, Stefos A, et al

J Diabetes Complications 2021;35(1):107765

We sought to determine whether primary outcomes differ between non-ICU septic patients with and without type 2 diabetes (T2D). DM does not appear to negatively affect outcomes in septic patients not requiring ICU.

NEWS2 top

The utility of the rapid emergency medicine score (REMS) compared with SIRS, qSOFA and NEWS for Predicting in-hospital Mortality among Patients with suspicion of Sepsis in an emergency department

Ruangsomboon O, Boonmee P, Limsuwat C, Chakorn T, Monsomboon A

BMC Emerg Med 2021;21(1):2

Many early warning scores (EWSs) have been validated to prognosticate adverse outcomes secondary to sepsis in the Emergency Department (ED). These EWSs include the Systemic Inflammatory Response Syndrome criteria (SIRS), the quick Sequential Organ Failure Assessment (qSOFA) and the National Early Warning Score (NEWS). However, the Rapid Emergency Medicine Score (REMS) has never been validated for this purpose. We aimed to assess and compare the prognostic utility of REMS with that of SIRS, qSOFA and NEWS for predicting mortality in patients with suspicion of sepsis in the ED. REMS was an early warning score with higher accuracy than sepsis-related scores (qSOFA and SIRS), similar to NEWS, and had the highest utility in terms of net benefit compared to SIRS, qSOFA and NEWS in predicting in-hospital mortality in patients presenting to the ED with suspected sepsis.

Sepsis Screening: Combining Early Warning Scores and SIRS Criteria

Kangas C, Iverson L, Pierce D

Clin Nurs Res 2021;30(1):42-9

Providing effective screening tools to nurses is necessary to improve patient outcomes and health care quality. This research examines if the modification of two electronic health record sepsis screening tools using a combined systemic inflammatory response syndrome (SIRS), modified early warning score (MEWS), and national early warning score (NEWS) criteria improves the recognition of sepsis by nurses. The updated criteria showed significant improvement toward correctly identifying sepsis and presents the opportunity to develop an effective tool that balances sensitivity with specificity.

Neonatal, paediatric and maternal sepsis

top

Vitamin D status was associated with sepsis in critically ill children: A PRISMA compliant systematic review and meta-analysis

Yu W, Ying Q, Zhu W, Huang L, Hou Q

Medicine (Baltimore) 2021;100(2):e23827

Sepsis leads to the high mortality in critically ill infants and children. It is still controversial whether vitamin D deficiency was associated with the incidence of sepsis. Thus we designed the systematic review and meta-analysis. We demonstrated that critically ill infants and children with sepsis could have a lower 25-OHD level and severe vitamin D deficiency comparing to those without sepsis. Future studies should focus on the association of vitamin D supplement and the occurrence of sepsis in critically ill children.

Is there a relationship between causative microorganisms and hearing loss in neonatal sepsis?

Yilmaz FH, Emiroğlu N, Oflaz MB, Yücel M, Keçeci R, Arbağ H, et al

Birth Defects Res 2021

The aim of the present study was to determine the possible relationship between cultured microorganisms and hearing loss in infants admitted to the neonatal intensive care unit (NICU) who could not pass a standard hearing test. The relationship between hearing loss and microorganisms causing sepsis could not be determined in this research.

Biomarkers for Estimating Risk of Hospital Mortality and Long-Term Quality-of-Life Morbidity After Surviving Pediatric Septic Shock: A Secondary Analysis of the Life After Pediatric Sepsis Evaluation Investigation

Wong HR, Reeder RW, Banks R, Berg RA, Meert KL, Hall MW, et al

Pediatr Crit Care Med 2021;22(1):8-15

The Life After Pediatric Sepsis Evaluation investigation recently reported that one-third of children who survive sepsis experience significant health-related quality-of-life impairment compared with baseline at 1 year after hospitalization. Pediatric Sepsis Biomarker Risk Model is a multibiomarker tool for estimating baseline risk of mortality among children with septic shock. We determined if the Pediatric Sepsis Biomarker Risk Model biomarkers have predictive capacity for estimating the risk of hospital mortality and long-term health-related quality-of-life morbidity among children with community-acquired septic shock. Pediatric Sepsis Biomarker Risk Model had modest performance for estimating hospital mortality in an external cohort of children with community-acquired septic shock. The Pediatric Sepsis Biomarker Risk Model biomarkers appear to have utility for estimating the risk of persistent, serious deterioration of health-related quality of life up to 3 months after surviving septic shock. These findings suggest an opportunity to develop a clinical tool for early assignment of risk for long-term health-related quality-of-life morbidity among children who survive septic shock.

Vancomycin in neonatal sepsis: predictive performance of a Chinese neonatal population pharmacokinetic model and clinical efficacy evaluation

Weng XH, Zhu CQ, Duan LF, Li L, Yang ZM, Wang SN, et al

Eur J Hosp Pharm 2021

In the neonatal population, individual calculation and adjustment of vancomycin (VCM) doses has been recommended based on population pharmacokinetics (PPK) methods. Our previous study established a Chinese neonatal VCM PPK model. The main goal of this study was to evaluate the predictive performance of this PPK model for VCM trough concentration. This PPK model has good predictive performance in Chinese neonatal patients. Both AUC(0-24)/MIC and trough concentration can predict the clinical efficacy of antibacterial treatment.

Pharmacokinetics of meropenem in children with sepsis undergoing extracorporeal life support: A prospective observational study

Wang Y, Li Z, Chen W, Yan G, Wang G, Lu G, et al

J Clin Pharm Ther 2021

Meropenem, a broad-spectrum carbapenem, is frequently used to treat severe bacterial infections in critically ill children. Recommendations for meropenem doses in adult infections are available; however, few studies have been published regarding the use of meropenem in children with sepsis, especially in those receiving continuous renal replacement therapy (CRRT) and extracorporeal membrane oxygenation (ECMO). We aimed to investigate the pharmacokinetic (PK) parameters of meropenem in children with sepsis receiving extracorporeal life support (ECLS). No significant alterations in the PK parameters of meropenem occurred in children with sepsis administered ECMO and/or CRRT. Further investigations including PK modelling could provide evidence for appropriate meropenem dosing regimens during ECLS administration.

A comparison of machine learning models versus clinical evaluation for mortality prediction in patients with sepsis

van Doorn W, Stassen PM, Borggreve HF, Schalkwijk MJ, Stoffers J, Bekers O, et al

PLoS One 2021;16(1):e0245157

Patients with sepsis who present to an emergency department (ED) have highly variable underlying disease severity, and can be categorized from low to high risk. Development of a risk stratification tool for these patients is important for appropriate triage and early treatment. The aim of this study was to develop machine learning models predicting 31-day mortality in patients presenting to the ED with sepsis and to compare these to internal medicine physicians and clinical risk scores. Machine learning models outperformed internal medicine physicians and clinical risk scores in predicting 31-day mortality. These models are a promising tool to aid in risk stratification of patients presenting to the ED with sepsis.

Peritoneal dialysis in children with sepsis associated AKI (SA-AKI): an experience in a low to middle income country

Tomar A, Kumar V, Saha A

Paediatr Int Child Health 2021:1-8

In critically ill children, sepsis-associated acute kidney injury (SA-AKI) has significant morbidity and mortality. Aim: To estimate whether early initiation of peritoneal dialysis (PD) has a better short-term outcome than standard PD. Compared with standard PD, early PD in SA-AKI resulted in a favourable renal outcome, decreased duration of PD and early discontinuation of dialysis.

Neutrophil-to-Lymphocyte Ratio as an Alternative Marker of Neonatal Sepsis in Developing Countries

Sumitro KR, Utomo MT, Widodo ADW

Oman Med J 2021;36(1):e214

We sought to analyze the neutrophil-to-lymphocyte ratio (NLR) as an alternative marker of neonatal sepsis. NLR, calculated from complete blood count, can be used as an alternative marker of easy and relatively inexpensive neonatal sepsis, especially in developing countries, and detection of proven neonatal sepsis to be better when combined with CRP.

Term newborns at risk for early-onset neonatal sepsis: Clinical surveillance versus systematic paraclinical test

Schmitt C, Novy M, Hascoët JM

Arch Pediatr 2021

Early-onset neonatal sepsis is a rare but potentially lethal infection that is very often suspected in daily practice. Previous national guidelines recommended the use of systematic paraclinical tests for healthy term newborns with suspected infection. These guidelines were updated in 2017 by the French Health Authority (Haute Autorité de santé), and promote initial clinical monitoring taking into account the infectious risk level for term and near-term born infants. We assess the impact of the new recommendations on antibiotic therapy prescription and invasive tests, and on the outcomes of infants born from 36weeks' gestation. In this study, the application of the new guidelines enabled a reduction of antibiotic exposure and a reduction of invasive tests without additional risk.

Functional Outcomes at 1 Year After PICU Discharge in Critically Ill Children With Severe Sepsis

Sankar J, Moodu S, Kumar K, Sankar MJ, Kabra SK, Lodha R

Pediatr Crit Care Med 2021;22(1):40-9

We evaluate the functional outcomes in critically ill children with severe sepsis using the Pediatric Overall

Performance Category scale and Pediatric Cerebral Performance Category scale and to evaluate the risk factors for "worse outcomes." Children with severe sepsis had significant "new onset" mild to moderate functional disability at PICU discharge, and most of these children recovered within 1 year after PICU discharge. Day 1 pediatric Sequential Organ Failure Assessment score and patient receiving cardiopulmonary resuscitation during the ICU stay were found to be the significant risk factors of "worse outcomes."

Early-onset sepsis in term infants admitted to neonatal intensive care units (2011-2016)

Polcwiartek LB, Smith PB, Benjamin DK, Zimmerman K, Love A, Tiu L, et al

J Perinatol 2021;41(1):157-63

We investigate characteristics of term infants culture-evaluated for early-onset sepsis (EOS) in neonatal intensive care units (NICUs), frequencies of organisms causing EOS, and factors associated with EOS. GBS was the most frequent cause of EOS. Early risk factor recognition may help daily management of term infants in NICUs.

Resource Use and Outcomes for Children Hospitalized With Severe Sepsis or Septic Shock

Odetola FO, Gebremariam A

J Intensive Care Med 2021;36(1):89-100

We describe patient and hospital characteristics associated with in-hospital mortality, length of stay (LOS), and charges for children with severe sepsis or septic shock who often require specialized organ-supportive technology to enhance outcomes, availability of which might vary across hospitals. Efforts to mitigate the substantial in-hospital mortality and resource use observed in pediatric severe sepsis or septic shock should be age-specific and focused on the influence of comorbidities and organ dysfunction on outcomes. Future research should elucidate reasons for higher resource use at urban hospitals.

Neurodevelopmental outcomes following neonatal late-onset sepsis and blood culture-negative conditions

Mukhopadhyay S, Puopolo KM, Hansen NI, Lorch SA, DeMauro SB, Greenberg RG, et al

Arch Dis Child Fetal Neonatal Ed 2021

We determine risk of death or neurodevelopmental impairment (NDI) in infants with late-onset sepsis (LOS) versus late-onset, antibiotic-treated, blood culture-negative conditions (LOCNC). Infants with LOS had higher risk of death, but not NDI, compared with infants with LOCNC. Surviving infants with LOCNC had higher risk of NDI compared with unaffected infants. Improving outcomes for infants with LOCNC requires study of the underlying conditions and the potential impact of antibiotic exposure.

Development of a Quality Improvement Learning Collaborative to Improve Pediatric Sepsis Outcomes

Larsen GY, Brilli R, Macias CG, Niedner M, Auletta JJ, Balamuth F, et al

Pediatrics 2021;147(1)

Pediatric sepsis is a major public health problem. Published treatment guidelines and several initiatives have increased adherence with guideline recommendations and have improved patient outcomes, but the gains are modest, and persistent gaps remain. The Children's Hospital Association Improving Pediatric Sepsis Outcomes (IPSO) collaborative seeks to improve sepsis outcomes in pediatric emergency departments, ICUs, general care units, and hematology/oncology units. We developed a multicenter quality improvement learning collaborative of US children's hospitals. We reviewed treatment guidelines and literature through 2 in-person meetings and multiple conference calls. We defined and analyzed baseline sepsis-attributable mortality and hospital-onset sepsis and developed a key driver diagram (KDD) on the basis of treatment guidelines, available evidence, and expert opinion.

Association of inflammatory biomarkers with subsequent clinical course in suspected late onset sepsis in preterm neonates

Kurul Ş, Simons SHP, Ramakers CRB, De Rijke YB, Kornelisse RF, Reiss IKM, et al

Crit Care 2021;25(1):12

Sepsis is a major health issue in preterm infants. Biomarkers are used to diagnose and monitor patients with sepsis, but C-reactive protein (CRP) is proven not predictive at onset of late onset neonatal sepsis (LONS) diagnosis. The aim of this study was to evaluate the association of interleukin-6(IL-6), procalcitonin (PCT) and CRP with subsequent sepsis severity and mortality in preterm infants suspected of late onset neonatal sepsis. Our findings show that serum IL-6 and PCT levels at moment of suspected late onset neonatal sepsis offer valuable information about sepsis severity and mortality risk in infants born below 32 weeks of gestation. The discriminative value was superior to that

of CRP. Determining these biomarkers in suspected sepsis may help identify patients with imminent severe sepsis, who may require more intensive monitoring and therapy.

Occurrence of Hyperbilirubinemia in Neonates Given a Short-term Course of Ceftriaxone versus Cefotaxime for Sepsis
Hile GB, Musick KL, Dugan AJ, Bailey AM, Howington GT
J Pediatr Pharmacol Ther 2021;26(1):99-103
Ceftriaxone and cefotaxime are appealing options for the treatment of neonatal infections. Guidelines recommend cefotaxime as the cephalosporin of choice in neonates because of ceftriaxone's potential to cause hyperbilirubinemia. Unfortunately, due to cefotaxime discontinuation, providers must choose between alternative antibiotics. Clinicians at our institution adopted a protocol allowing for the utilization of cefepime and ceftriaxone for the management of neonatal sepsis. The objective of this study was to compare the incidence of hyperbilirubinemia between ceftriaxone and cefotaxime in the treatment of neonatal infections beyond the first 14 days of life. Patients who received a short-term course of ceftriaxone did not have a higher likelihood of developing hyperbilirubinemia compared with those who received a short-term course of cefotaxime during their hospital stay.

C-reactive protein and the neonatal early-onset sepsis calculator for the diagnosis of neonatal sepsis
Friedman N, Yochpaz S, Zirkin S, Herzlich J, Marom R
Eur J Clin Microbiol Infect Dis 2021
Our aim was to evaluate the utility of the neonatal early-onset sepsis risk calculator (NEOSC) to the utility of C-reactive protein (CRP) for diagnosing neonatal EOS. This retrospective study reviewed the records of neonates who underwent sepsis workups due to equivocal symptoms and compared their CRP values to the calculator's recommendations and their cultures. The calculator's high specificity enables safe avoidance of multiple blood tests and antibiotic treatments for suspected neonates who are not infected. CRP tests can reduce the number of infected newborns the calculator may miss, at the cost of unnecessary blood tests and antibiotic therapy to many newborns.

Association of Acute Kidney Injury With Subsequent Sepsis in Critically Ill Children
Formeck CL, Joyce EL, Fuhrman DY, Kellum JA
Pediatr Crit Care Med 2021;22(1):e58-e66: Acute kidney injury is a major cause of morbidity and mortality in critically ill children. A growing body of evidence has shown that acute kidney injury affects immune function, yet little is known about the association between acute kidney injury and subsequent infection in pediatric patients. Our objective was to examine the association of non-septic acute kidney injury with the development of subsequent sepsis in critically ill children. Acute kidney injury is associated with an increased risk for subsequent infection in critically ill children. These results further support the concept of acute kidney injury as a clinically relevant immunocompromised state.

Global incidence and mortality of neonatal sepsis: a systematic review and meta-analysis
Fleischmann C, Reichert F, Cassini A, Horner R, Harder T, Markwart R, et al
Arch Dis Child 2021
Neonates are at major risk of sepsis, but data on neonatal sepsis incidence are scarce. We aimed to assess the incidence and mortality of neonatal sepsis worldwide. Neonatal sepsis is common and often fatal. Its incidence remains unknown in most countries and existing studies show marked heterogeneity, indicating the need to increase the number of epidemiological studies, harmonise neonatal sepsis definitions and improve the quality of research in this field. This can help to design and implement targeted interventions, which are urgently needed to reduce the high incidence of neonatal sepsis worldwide.

Comparison of Manual and Automated Sepsis Screening Tools in a Pediatric Emergency Department
Eisenberg M, Freiman E, Capraro A, Madden K, Monuteaux MC, Hudgins J, et al
Pediatrics 2021
We compare the performance and test characteristics of an automated sepsis screening tool with that of a manual sepsis screen in patients presenting to a pediatric emergency department (ED). An automated sepsis screening algorithm had higher sensitivity and specificity than a widely used manual sepsis screen and was performed on 100% of patients in the ED, ensuring continuous sepsis surveillance throughout the ED stay.

Diagnostic accuracy of interleukin-6 for early-onset sepsis in preterm neonates
Ebenebe CU, Hesse F, Blohm ME, Jung R, Kunzmann S, Singer D

J Matern Fetal Neonatal Med 2021;34(2):253-8
Early-onset sepsis (EOS) is a leading cause of morbidity and mortality among neonates. Yet, accurate diagnosis remains a major challenge in clinical routine. The aim of this study was to evaluate the diagnostic accuracy of Interleukin-6 (IL-6) in combination with other objective perinatal data for early-onset sepsis (EOS) in preterm neonates. The combination of IL-6 with other perinatal factors can significantly increase specificity and sensitivity in the diagnosis of EOS. However, overall diagnostic accuracy cannot be notably improved as there is a tradeoff between sensitivity and specificity. Although these findings do not necessarily apply in clinical routine, they can be of substantial value in the assistance of individual decision making.

Early-onset sepsis: can we screen fewer babies safely?
Eason J, Ward H, Danko O, Richardson K, Vaitkute R, McKeon-Carter R
Arch Dis Child 2021;106(1):86-8
Over the past 2-3 years at the Southwest Peninsula tertiary neonatal unit in Plymouth, the authors have observed an increase in the number of clinically well term infants being screened and treated with antibiotics for infection in accordance with NICE guidance. The aim of our study was to assess the safety of implementing the Kaiser Permanente Early Onset Sepsis (KPEOS) calculator to minimise antibiotic usage in term infants in line with antimicrobial stewardship, reducing separation from mother at birth and facilitating earlier discharge. These results demonstrated a potentially safe and effective quality improvement (QI) in our hospital with fewer babies treated and a reduced length of stay for this cohort. Considering individual hospitals rates for term Group B Streptococcal sepsis, this QI may be a safe and economical alternative to current practices for screening well term infants.

Application of HAS 2017 guidelines for asymptomatic neonates born at ≥34 weeks' gestation at risk of early-onset neonatal sepsis in a level-2 maternity department
Cabaret B, Latry V
Arch Pediatr 2021
The 2017 Haute Autorité de santé (HAS) guidelines for the medical care of neonates born at≥34 weeks' gestation (WG) at risk of early-onset neonatal sepsis (EONS) placed emphasis on clinical examination rather than laboratory tests. Were these guidelines relevant in our level-2 maternity department, and how can they affect our professional practice? The HAS guidelines, emphasising repeated clinical assessment of newborns at risk of EONS rather than laboratory, were considered to be feasible in our maternity department. They led to an improvement in our professional practices and a reduction in laboratory procedures.

Treatment outcomes, antibiotic use and its resistance pattern among neonatal sepsis patients attending Bahawal Victoria Hospital, Pakistan
Atif M, Zia R, Malik I, Ahmad N, Sarwar S
PLoS One 2021;16(1):e0244866
Sepsis is one of the major causes of neonatal mortality in Pakistan. This study aimed to investigate the treatment outcomes, antibiotic use and its resistance pattern among neonatal sepsis patients attending a tertiary care hospital in Pakistan. We also aimed to identify the factors affecting mortality in neonatal sepsis patients. The mortality rate associated with sepsis was high in our study cohort. The bacterial isolates showed high level of resistance against the antibiotics started as the empiric therapy. Rational use of antibiotics can decrease the adverse outcomes in neonatal sepsis patients.

The Use of Daptomycin in the Treatment of Persistent Coagulase-Negative Staphylococcal Sepsis in Premature Infants: A Case Series
Asfour SS, Asfour RS, Khalil TM, Al-Mouqdad MM
J Pediatr Pharmacol Ther 2021;26(1):92-8
Daptomycin is a lipopeptide antibiotic with rapid bactericidal activity against Gram-positive bacteria. Reports regarding the use of daptomycin in infants are still limited. Thus, the objective of this report is to describe the safety and efficacy of daptomycin in premature infants with persistent coagulase-negative staphylococci (CoNS) infection. Large and randomized studies are necessary to ensure daptomycin's safety and efficacy for the treatment of infants with persistent sepsis caused by Gram-positive bacteria.

Role of repeat procalcitonin estimation at 48 hours for outcome in pregnancy associated sepsis: a prospective observational study

Agarwal R, Sharma K, Mehndiratta M, Mohta M, Srivastava H, Anthonio AE
Obstet Gynecol Sci 2021;64(1):27-33
We assessed whether repeat procalcitonin (PCT) estimation has a role in detecting organ dysfunctions and mortality in pregnancy associated sepsis (PAS). Repeat PCT estimation at 48 hours could complement the clinical findings and enhance the prognostic value for PAS.

COVID-19 and sepsis top

Severe COVID-19 and Sepsis: Immune Pathogenesis and Laboratory Markers
Zafer MM, El-Mahallawy HA, Ashour HM
Microorganisms 2021;9(1)
The ongoing outbreak of the novel coronavirus disease 2019 (COVID-19), induced by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has taken a significant toll on people and countries all over the world. The pathogenesis of COVID-19 has not been completely elucidated yet. This includes the interplay between inflammation and coagulation which needs further investigation. The massive production of proinflammatory cytokines and chemokines results in the so-called cytokine storm, leading to plasma leakage, vascular hyperpermeability, and disseminated vascular coagulation. This is usually accompanied by multiorgan failure. The extensive changes in the serum levels of cytokines are thought to play a crucial role in the COVID-19 pathogenesis. Additionally, the viral load and host inflammation factors are believed to have a significant role in host damage, particularly lung damage, from SARS-CoV-2. Interestingly, patients exhibit quantitative and qualitative differences in their immune responses to the virus, which can impact the clinical manifestation and outcomes of COVID-19. There needs to be a better understanding of the dynamic events that involve immune responses, inflammatory reactions, and viral replication in the context of the COVID-19 infection. Here, we discuss the main aspects of COVID-19 pathogenesis while supporting the hypothesis that inflammatory immune responses are involved in the progression of the disease to a more critical and fatal phase. We also explore the similarities and differences between severe COVID-19 and sepsis. A deeper understanding of the COVID-19 clinical picture as it relates to better-known conditions such as sepsis can provide useful clues for the management, prevention, and therapy of the disease.

Therapeutic approaches targeting renin-angiotensin system in sepsis and its complications
Ning L, Rong J, Zhang Z, Xu Y
Pharmacol Res 2021:105409
Sepsis, caused by the inappropriate host response to infection, is characterized by excessive inflammation response and organ dysfunction, continues to be a critical clinical problem. Commonly, sepsis may progress to septic shock and have a high risk of complications, including acute kidney injury (AKI), acute respiratory distress syndrome (ARDS), sepsis-induced myocardial dysfunction (SIMD), liver dysfunction, cerebral dysfunction, and skeletal muscle atrophy, predominantly contributing to high mortality. Additionally, viral sepsis may be critical for the pathogenesis of coronavirus disease 2019 (COVID-19). Renin-angiotensin system (RAS) may represent as an effective therapeutic target for sepsis therapies. The role of RAS involved in the pathogenesis of sepsis has been spotlighted and some preclinical and clinical trials studies targeted at RAS for sepsis treatment have shown promising results. Herein, we attempt to review the effects and mechanisms of RAS manipulation on sepsis and provide new insights into optimization RAS modulation for this terrible heterogeneous syndrome.

B cell depletion and signs of sepsis-acquired immunodeficiency in bone marrow and spleen of COVID-19 deceased
Ihlow J, Michaelis E, Greuel S, Heynol V, Lehmann A, Radbruch H, et al
Int J Infect Dis 2021;103:628-35
In coronavirus disease 2019 (COVID-19), the adaptive immune response is of considerable importance, and detailed cellular immune reactions in the hematological system of patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection are yet to be clarified. The results of this study suggest the presence of sepsis-related immunodeficiency in severe COVID-19 pneumonia with superinfection. Furthermore, our findings indicate that lymphocytopenia in COVID-19 is accompanied by B cell depletion in hematopoietic tissue, which might impede the durability of the humoral immune response to SARS-CoV-2.

Advanced echocardiographic phenotyping of critically ill patients with coronavirus-19 sepsis: a prospective cohort study
Bagate F, Masi P, d'Humières T, Al-Assaad L, Chakra LA, Razazi K, et al

J Intensive Care 2021;9(1):12

Sepsis is characterized by various hemodynamic alterations which could happen concomitantly in the heart, pulmonary and systemic circulations. A comprehensive demonstration of their interactions in the clinical setting of COVID-19 sepsis is lacking. This study aimed at evaluating the feasibility, clinical implications, and physiological coherence of the various indices of hemodynamic function and acute myocardial injury (AMI) in COVID-19 sepsis. In this comprehensive hemodynamic evaluation in critically ill COVID-19 septic patients, we identified four homogeneous and coherent clusters with a good feasibility. AMI was common and associated with alteration of LV and RV functions. Echocardiographic assessment had a clinical impact on patient management in most cases.