SEPSIS BULLETIN
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Sepsis

Complement as a Major Inducer of Harmful Events in Infectious Sepsis

Fattahi F et al

Shock. 2020;54(5):595-605

There is abundant evidence that infectious sepsis both in humans and mice with polymicrobial sepsis results in robust activation of complement. Major complement activation products involved in sepsis include C5a anaphylatoxin and its receptors (C5aR1 and C5aR2) and, perhaps, the terminal complement activation product, C5b-9. These products (and others) also cause dysfunction of the innate immune system, with exaggerated early proinflammatory responses, followed by decline of the innate immune system, leading to immunosuppression and multiorgan dysfunction. Generation of C5a during sepsis also leads to activation of neutrophils and macrophages and ultimate appearance of extracellular histones, which have powerful proinflammatory and prothrombotic activities. Small molecular blocking agents for C5aRs are currently in development and may be therapeutically effective for treatment of sepsis.

Phagocytosis-Inflammation Crosstalk in Sepsis: New Avenues for Therapeutic Intervention

Hortova-Kohoutkova M et al

Shock. 2020;54(5):606-14

Phagocytosis is a complex process by which cells within most organ systems remove pathogens and cell debris. Phagocytosis is usually followed by inflammatory pathway activation, which promotes pathogen elimination and inhibits pathogen growth. Delayed pathogen elimination is the first step in sepsis development and a key factor in sepsis resolution. Phagocytosis thus has an important role during sepsis and likely contributes to all of its clinical stages. However, only a few studies have specifically explored and characterized phagocytic activity during sepsis. Here, we describe the phagocytic processes that occur as part of the immune response preceding sepsis onset and identify the elements of phagocytosis that might constitute a predictive marker of sepsis outcomes.

Combination therapy of vitamin C and thiamine for septic shock: a multi-centre, double-blinded randomized, controlled study

Hwang SY et al

Intensive Care Med. 2020;46(11):2015-25

PURPOSE: To evaluate the effects of early combination therapy with intravenous vitamin C and thiamine on recovery from organ failure in patients with septic shock. CONCLUSION: In this study, vitamin C and thiamine administration in the early phase of septic shock did not improve organ function compared with placebo, despite improvements in vitamin C and thiamine levels.

National Trends and Variation of Functional Status Deterioration in the Medically Critically Ill

Ingraham NE et al

Crit Care Med. 2020;48(11):1556-64

OBJECTIVES: Physical and psychologic deficits after an ICU admission are associated with lower quality of life, higher mortality, and resource utilization. This study aimed to examine the prevalence and secular changes of functional status deterioration during hospitalization among nonsurgical critical illness survivors over the past decade. CONCLUSIONS: Following nonsurgical critical illness, the prevalence of functional status deterioration and magnitude increased in a nationally representative cohort, despite efforts to reduce ICU dysfunction over the past decade. Identifying the prevalence of functional status deterioration and primary etiologies associated with functional status deterioration will elucidate vital areas for further research and targeted interventions. Reducing ICU debilitation for key disease processes may improve ICU survivor mortality, enhance quality of life, and decrease healthcare utilization.

Could lung bacterial dysbiosis predict ICU mortality in patients with extra-pulmonary sepsis? A proof-of-concept study

Sepsis Lung Microbiome Study G

Intensive Care Med. 2020;46(11):2118-20

Sepsis is a major cause of mortality worldwide. However, prognosis in these critically ill patients is based on severity scores, in combination with plasma biomarkers, which have shown a limited power to predict patient severity; thus, novel and more accurate biomarkers are needed. Alterations of the microbial diversity (commonly known as dysbiosis) have been linked to sepsis development and severity. Interestingly, enrichment of gut bacteria in the lung microbiome has been found in patients with sepsis and acute respiratory distress syndrome (ARDS), likely by translocation of intestinal microbes. However, although it is known that the lung microbiome is severely altered in critically ill patients, a specific association of the lung dysbiosis with sepsis mortality remains to be determined.

A Hyperdynamic Left Ventricle on Echocardiogram: Not Always Sepsis

Singer DJ and Oropello J

Chest. 2020;158(5):e263-e5

POCUS is commonly used in EDs and ICUs. The diagnosis of right ventricle failure, often caused by massive PE, is a potentially life-saving diagnosis that can be made immediately at the bedside using POCUS.

Pentraxin-3, Troponin T, N-Terminal Pro-B-Type Natriuretic Peptide in Septic Patients

Vassalli F et al

Shock. 2020;54(5):675-80

OBJECTIVE: To investigate the behavior of pentraxin-3 (PTX3), troponin T (hsTnT), N-terminal pro-B type Natriuretic Peptide (NT-proBNP) in sepsis and their relationships with sepsis severity and oxygen transport/utilization impairment. CONCLUSIONS: The selected biomarkers seem related to different mechanisms during sepsis: PTX3 to sepsis severity, hsTnT to impaired oxygen transport, NT-proBNP to sepsis severity, oxygen transport, and aggressive fluid strategy.

An Explainable Artificial Intelligence Predictor for Early Detection of Sepsis

Yang M et al

Crit Care Med. 2020;48(11):e1091-e6

OBJECTIVES: Early detection of sepsis is critical in clinical practice since each hour of delayed treatment has been associated with an increase in mortality due to irreversible organ damage. This study aimed to develop an explainable artificial intelligence model for early predicting sepsis by analyzing the electronic health record data from ICU provided by the PhysioNet/Computing in Cardiology Challenge 2019. DESIGN: Retrospective observational study. CONCLUSIONS: Explainable artificial intelligence sepsis predictor model achieves superior performance for predicting sepsis risk in a real-time way and provides interpretable information for understanding sepsis risk in ICU.

Sepsis, the Administration of Intravenous Fluids and Respiratory failure: A Retrospective analysis - SAIFR Study
Jagan N et al
Chest. 2020
BACKGROUND: Although resuscitation with intravenous fluids (IVF) 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 intravenous fluid bolus of 30 cc/kg or more conservative resuscitation of fewer than 30 cc/kg? INTERPRETATION: In this single-center retrospective study we found by broadly defining respiratory failure as an increase in oxygen requirements, a conservative initial IVF resuscitation strategy did not correlate with decreased rates of hypoxemic respiratory failure.

The Hematopoietic Stem/Progenitor Cell Response to Hemorrhage, Injury and Sepsis: A Review of Pathophysiology
Kelly LS et al
Shock. 2020;Publish Ahead of Print
Hematopoietic stem/progenitor cells (HSPC) have both unique and common responses following hemorrhage, injury, and sepsis. 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.

A non-inferiority study comparing efficacy of preoperative prophylactic antibiotics for preventing infectious complications in patients with less severe burns
Hill DM et al
Burns. 2020
While international burn injury guidelines discourage prophylactic antibiotics on admission, current surgery guidelines focusing on antimicrobial prophylaxis place thermal injury under a general plastics procedure umbrella, and require significant evidential extrapolation. The purpose of this study was to determine if withholding systemic antibiotics in patients with <20% total body surface area (TBSA) burns without invasive wound infections and undergo wound excision is non-inferior to patients that receive preoperative antibiotics. Success was defined as lack of graft loss, bacteremia, or surgical site infection. In patients with <20% TBSA burns and without active wound infections, withholding preoperative systemic antibiotics will preserve unneeded antimicrobial exposure without increasing risk of infection-related complications.

Serum Levels of Branched Chain Amino Acids Predict Duration of Cardiovascular Organ Failure in Septic Shock
Puskarich MA et al
Shock. 2020;Publish Ahead of Print
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.

Identifying Septic Shock Populations Benefitting From Polymyxin B Hemoperfusion: A Prospective Cohort Study Incorporating a Restricted Cubic Spline Regression Model
Nakata H et al
Shock. 2020;54(5):667-74
INTRODUCTION: Polymyxin B hemoperfusion (PMX-HP) is an adjuvant therapy for sepsis or septic shock that removes circulating endotoxin. However, PMX-HP has seldom achieved expectations in randomized trials targeting nonspecific overall sepsis patients. If used in an optimal population, PMX-HP may be beneficial. This study aimed to identify the optimal population for PMX-HP in patients with septic shock. CONCLUSIONS: Our results suggested that although PMX-HP did not reduce in-hospital mortality among overall septic shock patients, it may benefit a limited population with high age and higher disease severity.

Changes in Self-Rated Health After Sepsis in Older Adults: A Retrospective Cohort Study
Carey MR et al

Chest. 2020;158(5):1958-66
BACKGROUND: As more individuals survive sepsis, there is an urgent need to understand its effects on patient-reported outcomes. RESEARCH QUESTION: What is the effect of sepsis on self-rated health, and what role, if any, does functional disability play in mediating this effect? INTERPRETATION: Self-rated health worsened initially after sepsis but returned to the level of that of nonhospitalized control subjects by year 6. Mitigating sepsis-related functional disability may play a key role in improving self-rated health after sepsis.

NEWS2

The performance of the National Early Warning Score and National Early Warning Score 2 in hospitalised patients infected by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
Kostakis I et al
Resuscitation. 2020
INTRODUCTION: Since the introduction of the UK's National Early Warning Score (NEWS) and its modification, NEWS2, coronavirus disease 2019 (COVID-19), has caused a worldwide pandemic. NEWS and NEWS2 have good predictive abilities in patients with other infections and sepsis, however there is little evidence of their performance in COVID-19. CONCLUSIONS: The finding that NEWS or NEWS2 performance was good and similar in all five cohorts (range=0.842-0.894) suggests that amendments to NEWS or NEWS2, such as the addition of new covariates or the need to change the weighting of existing parameters, are unnecessary when evaluating patients with COVID-19. Our results support the national and international recommendations for the use of NEWS or NEWS2 for the assessment of acute-illness severity in patients with COVID-19.

Neonatal, paediatric and maternal sepsis

A Quality Improvement Initiative To Optimize Antibiotic Use in a Level 4 NICU
Meyers JM et al
Pediatrics. 2020;146(5)
BACKGROUND: Given the risks associated with antibiotics, efforts to reduce unnecessary antibiotic use in the NICU have become increasingly urgent. In 2016, a comprehensive 3-year quality improvement (QI) initiative was conducted in a level 4 NICU that sought to decrease the antibiotic use rate (AUR) by 20%. CONCLUSIONS: Our efforts significantly reduced antibiotic use and exposure in our NICU. Our comprehensive, rigorous approach to QI is applicable to teams focused on improvement.

Poor postnatal weight growth is a late finding after sepsis in very preterm infants
Flannery DD et al
Arch Dis Child Fetal Neonatal Ed. 2020
OBJECTIVE: To characterise the association between sepsis and postnatal weight growth when accounting for the degree of growth restriction present at birth CONCLUSION: Infants with sepsis had similar early weight growth trajectories as infants without sepsis but developed significant deficits in weight that were not apparent until several weeks after the onset of sepsis.

Ampicillin and Gentamicin in Infants With Suspected Sepsis: Long Live Amp and Gent-But for How Long? JAMA Pediatr
Weissman SJ and Stoll B
JAMA Pediatr. 2020
Continued surveillance of antibiotic susceptibility of neonatal pathogens is essential. At present, the empirical regimen of ampicillin and gentamicin remains appropriate for term infants with suspected sepsis and for most preterm infants, but in the most severely ill VLBW infants, we are obliged to consider broader-spectrum antibiotics—agents that can save lives but also reshape microbial ecology at local and global levels.

Comparison of the management recommendations of the Kaiser Permanente neonatal early-onset sepsis risk calculator (SRC) with NICE guideline CG149 in infants >/=34 weeks' gestation who developed early-onset sepsis
Morris R et al
Arch Dis Child Fetal Neonatal Ed. 2020;105(6):581-6
OBJECTIVE: To compare the management recommendations of the Kaiser Permanente neonatal early-onset sepsis risk calculator (SRC) with National Institute for Health and Care Excellence (NICE) guideline CG149 in infants >/=34

weeks' gestation who developed early-onset sepsis (EOS). CONCLUSION: While both tools were poor in identifying EOS within 4 hours, NICE was superior to SRC in identifying asymptomatic cases. Currently, four out of five EOS have symptoms at first identification, the majority of whom present within 24 hours of birth. Antibiotic stewardship programmes using SRC should include enhanced observation for infants currently treated within NICE guidance.

Low risk of necrotising enterocolitis in enterally fed neonates with critical heart disease: an observational study

Nordenstrom K et al

Arch Dis Child Fetal Neonatal Ed. 2020;105(6):609-14

OBJECTIVE: We aimed to investigate the frequency of necrotising enterocolitis (NEC) in infants with critical congenital heart disease (CCHD) hypothesising that preoperative enteral feeding does not increase the risk of NEC. BACKGROUND: When NEC affects term infants, underlying risk factors such as asphyxia, sepsis or CCHD are often found. Due to fear of NEC development in infants with CCHD great caution is practised in many countries to defer preoperative enteral feeding, but in Sweden this is routinely provided. CONCLUSIONS: This study showed a low risk of NEC in term infants fed enterally before cardiac surgery. We speculate that preoperative enteral feeding of neonates with CCHD does not increase the risk of NEC development.

Prospective, randomized, double-blind, placebo-controlled evaluation of the Pharmacokinetics, Safety and Efficacy of Recombinant Antithrombin Versus Placebo in Preterm Preeclampsia

Paidas MJ et al

Am J Obstet Gynecol. 2020;223(5):739 e1- e13

BACKGROUND: Despite expectant management, preeclampsia remote from term usually results in preterm delivery. Antithrombin, which displays antiinflammatory and anticoagulant properties, may have a therapeutic role in treating preterm preeclampsia, a disorder characterized by endothelial dysfunction, inflammation, and activation of the coagulation system. OBJECTIVE: This randomized, placebo-controlled clinical trial aimed to evaluate whether intravenous recombinant human antithrombin could prolong gestation and therefore improve maternal and fetal outcomes. CONCLUSION: The administration of recombinant human antithrombin in preterm preeclampsia neither prolonged pregnancy nor improved neonatal or maternal outcomes.

The practice of blood volume submitted for culture in a neonatal intensive care unit

Singh MP et al

Arch Dis Child Fetal Neonatal Ed. 2020;105(6):600-4

BACKGROUND: Neonatal sepsis is the leading cause of mortality and morbidity in neonatal intensive care units. The volume of blood taken for culture remains one of the most important factors in isolating microorganisms. OBJECTIVES: To evaluate the impact of the intervention on the blood volume submitted for culture and to identify factors influencing the volume as determined by the phlebotomist. CONCLUSION: The study underscores the role of educational intervention in improving the blood culture volume in newborn infants. Poor backflow from the cannula is an important cause of inadequate volume collection.

COVID-19 and sepsis

Predicting intensive care unit admission and death for COVID-19 patients in the emergency department using early warning scores

Covino M et al

Resuscitation. 2020;156:84-91

AIMS: To identify the most accurate early warning score (EWS) for predicting an adverse outcome in COVID-19 patients admitted to the emergency department (ED). CONCLUSION: In our single-centre cohort of COVID-19 patients, NEWS and REMS measured on ED arrival were the most sensitive predictors of 7-day ICU admission or death. EWS could be useful to identify patients with low risk of clinical deterioration.

Pulmonary embolism in hospitalised patients with COVID-19

Whyte MB et al

Thromb Res. 2020;195:95-9

BACKGROUND: Coronavirus disease 2019 (COVID-19) is characterised by dyspnoea and abnormal coagulation parameters, including raised D-dimer. Data suggests a high incidence of pulmonary embolism (PE) in ventilated patients with COVID-19. OBJECTIVES: To determine the incidence of PE in hospitalised patients with COVID-19 and the diagnostic yield of Computer Tomography Pulmonary Angiography (CTPA) for PE. We also examined the utility of

D-dimer and conventional pre-test probability for diagnosis of PE in COVID-19. CONCLUSIONS: Even outside of the critical care environment, PE in hospitalised patients with COVID-19 is common. Of note, approaching half of PE events were diagnosed on hospital admission. More data are needed to identify an optimal diagnostic pathway in patients with COVID-19. Randomised controlled trials of intensified thromboprophylaxis are urgently needed.

Characterisation of 22445 patients attending UK emergency departments with suspected COVID-19 infection: Observational cohort study

Goodacre S et al

PLoS One. 2020;15(11):e0240206

BACKGROUND: Hospital emergency departments play a crucial role in the initial assessment and management of suspected COVID-19 infection. This needs to be guided by studies of people presenting with suspected COVID-19, including those admitted and discharged, and those who do not ultimately have COVID-19 confirmed. We aimed to characterise patients attending emergency departments with suspected COVID-19, including subgroups based on sex, ethnicity and COVID-19 test results. CONCLUSIONS: Important differences exist between patient groups presenting to the emergency department with suspected COVID-19. Adults and children differ markedly and require different approaches to emergency triage. Admission and adverse outcome rates among adults suggest that policies to avoid unnecessary ED attendance achieved their aim. Subsequent COVID-19 confirmation confers a worse prognosis and greater need for organ support.

Coronavirus Disease 2019 Sepsis: A Nudge Toward Antibiotic Stewardship

Coz Yataco AO and Simpson SQ

Chest. 2020;158(5):1833-4

Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection; such infections can be caused by bacteria, fungi, or in the case of coronavirus disease 2019 (COVID-19), a virus (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]). In bacterial sepsis, which is the most common variety, early and appropriate antibiotics are crucial to decrease mortality rates and the progression to more severe forms of disease.

International Survey to Establish Prioritized Outcomes for Trials in People With Coronavirus Disease 2019

Evangelidis N et al

Crit Care Med. 2020;48(11):1612-21

OBJECTIVES: There are over 4,000 trials conducted in people with coronavirus disease 2019. However, the variability of outcomes and the omission of patient-centered outcomes may diminish the impact of these trials on decision-making. The aim of this study was to generate a consensus-based, prioritized list of outcomes for coronavirus disease 2019 trials. CONCLUSIONS: Life-threatening respiratory and other organ outcomes were consistently highly prioritized by all stakeholder groups. Patients/family members gave higher priority to many patient-reported outcomes compared with health professionals.