



SEPSIS BULLETIN

07 June 2018

Neonatal and paediatric sepsis

[Adaptive response of neonatal sepsis-derived Group B Streptococcus to bilirubin](#)

Hansen, R. et al

Scientific Reports volume 8, Article number: 6470 (2018)

Hyperbilirubinemia is so common in newborns as to be termed physiological. The most common bacteria involved in early-onset neonatal sepsis are *Streptococcus agalactiae*, commonly called Group B *Streptococcus* (GBS). Whilst previous studies show bilirubin has antioxidant properties and is beneficial in endotoxic shock, little thought has been given to whether bilirubin might have antibacterial properties. The data improve our understanding of the mechanisms modulating GBS survival in neonatal hyperbilirubinemia and suggest physiological jaundice may have an evolutionary role in protection against early-onset neonatal sepsis. Public-friendly article also available in [The Conversation](#).

[Mortality and morbidity in community-acquired sepsis in European pediatric intensive care units: a](#)

Adult Sepsis (cont)

[Emergency management of sepsis: The simple stuff saves lives](#)

Sweet, D. et al

BCMJ, vol. 54 , No. 4 , May 2012 , Pages 176-182

Many emergency departments have implemented sepsis protocols since the 2001 publication of results from the early goal-directed therapy trial, which showed early targeted resuscitation lowers mortality. As part of an attempt to improve clinical and operational outcomes for emergency departments across British Columbia, we reviewed sepsis management literature and considered sepsis protocol implementation in the province's emergency departments. During the literature review we found that many observational studies confirmed an association between implementation of emergency sepsis protocols and decreased mortality. The literature also confirmed that septic patients who have elevated serum lactate and do not clear serum lactate rapidly have increased mortality, and that delay in administration of antibiotics after onset of septic shock was associated with increased mortality. Two BC-based initiatives, the Evidence to Excellence Sepsis Collaborative and Clinical Care Management, support

[prospective cohort study from the European Childhood Life-threatening Infectious Disease Study \(EUCLIDS\)](#)

Boeddha, N.P. et al

Crit Care. 2018 May 31;22(1):143.

Sepsis is one of the main reasons for non-elective admission to pediatric intensive care units (PICUs), but little is known about determinants influencing outcome. We characterized children admitted with community-acquired sepsis to European PICUs and studied risk factors for mortality and disability. Concludes that despite widespread immunization campaigns, invasive bacterial disease remains responsible for substantial morbidity and mortality in critically ill children in high-income countries. Almost one third of sepsis survivors admitted to the PICU were discharged with some disability. More research is required to delineate the long-term outcome of pediatric sepsis and to identify interventional targets. Our findings emphasize the importance of improved early sepsis-recognition programs to address the high burden of disease.

[Biomarkers for diagnosis of neonatal sepsis: a literature review.](#)

Fuchs, A. et al

Paediatrics and International Child Health Volume 38, 2018 - Issue sup1

Guidelines from 2005 for treating suspected sepsis in low- and middle-income countries (LMIC) recommended hospitalisation and prophylactic intramuscular (IM) or intravenous (IV) ampicillin and gentamicin. In 2015, recommendations when referral to hospital is not possible suggest the administration of IM gentamicin and oral amoxicillin. In an era of increasing antimicrobial resistance, an updated review of the appropriate empirical therapy for treating sepsis (taking into account susceptibility patterns, cost and risk of adverse events) in neonates and children is necessary.

improvements in management of sepsis in BC emergency departments, which should include early identification of septic patients, rapid and appropriate fluid resuscitation, lab tests (serum lactate and blood cultures), antibiotic administration, and source control of infection. Close clinical monitoring and biomarker (lactate) monitoring are also necessary during resuscitation to optimize safety and efficacy.

[Procalcitonin as a diagnostic marker for sepsis/septic shock in the emergency department; a study based on Sepsis-3 definition](#)

Kim, S.J. et al

The American Journal of Emergency Medicine. May 2018 ahead of print

The recent definition of sepsis was modified based on a scoring system focused on organ failure (Sepsis-3). It would be a time-consuming process to detect the sepsis patient using Sepsis-3. Procalcitonin (PCT) is a well-known biomarker for diagnosing sepsis/septic shock and monitoring the efficacy of treatment. We conducted a study to verify the predictability of PCT for diagnosing sepsis based on Sepsis-3 definition. Conclusion: PCT is a reliable biomarker to predict sepsis or septic shock according to the Sepsis-3 definitions.

[Haplotypes composed of minor frequency single nucleotide polymorphisms of the TNF gene protect from progression into sepsis: A study using the new sepsis classification.](#)

Retsas, T. et al

Int J Infect Dis. 2018 Feb; 67:102-106.

Several articles have provided conflicting results regarding the role of single nucleotide polymorphisms (SNPs) in the promoter region of the TNF gene in susceptibility to sepsis. Former articles have been based on previous definitions of sepsis. This study investigated the influence of TNF haplotypes on the development of sepsis using the new Sepsis-3 definitions. CONCLUSIONS:

[Reconciling conflicting results from pediatric sepsis studies: the need for context-specific sepsis bundles](#)

Kortz, T. et al

Pediatric Critical Care Medicine: June 2018 - Volume 19 - Issue 6 - p 594–595

Reports on sepsis bundle adherence and outcomes in children with severe sepsis and septic shock at a referral hospital in Colombia before and after an educational intervention. The bundle, based on the 2010 PALS algorithm (6), included: 1) identifying sepsis within 5 minutes, 2) securing vascular access within 15 minutes, 3) administering fluid boluses within 60 minutes, 4) starting antibiotics within 60 minutes, and 5) initiating vasoactives, if indicated, within 60 minutes. The intervention was a 40-minute lecture- and case-based program that reinforced PALS guidelines and bundle elements with emergency department staff.

Adult sepsis

[Long-Term Survival of Young Patients Surviving ICU Admission With Severe Sepsis](#)

Abu-Kaf, H. et al

Critical Care Medicine: May 7, 2018 - Volume Online First

Sepsis remains a disease with a high mortality rate. The study goal was to assess long-term survival of severe sepsis in young patients. A total of 409 patients less than 45 years who survived to hospital discharge were age and sex matched with 818 patients with infectious disease without sepsis selected from internal medicine or surgical department admissions. Young patients experiencing an episode of severe sepsis continue to be at higher risk of long-term mortality. The highest mortality rates were observed during the first 24 months following discharge.

[Vitamin C: should we supplement?](#)

Spoelstra-de Man, A

Haplotypes containing minor frequency SNP alleles of TNF protect against the development of sepsis without affecting the outcome.

[Prompt Administration of Antibiotics and Fluids in the Treatment of Sepsis: A Murine Trial](#)

Lewis, A. et al

Critical Care Medicine: May 2018 - Volume 46 - Issue 5 - p e426–e434

Sepsis, the acute organ dysfunction caused by a dysregulated host response to infection, poses a serious public health burden. Current management includes early detection, initiation of antibiotics and fluids, and source control as necessary. Although observational data suggest that delays of even a few hours in the initiation of antibiotics or IV fluids is associated with survival, these findings are controversial. There are no randomized data in humans, and prior animal studies studied time from experimental manipulation, not from the onset of clinical features of sepsis. Using a recently developed murine cecal ligation and puncture model that precisely monitors physiologic deterioration, we hypothesize that incremental hourly delays in the first dose of antibiotics, in the first bolus of fluid resuscitation, or a combination of the two at a clinically relevant point of physiologic deterioration during polymicrobial sepsis will shorten survival.

[Association of the Quick Sequential \(Sepsis-Related\) Organ Failure Assessment \(qSOFA\) Score With Excess Hospital Mortality in Adults With Suspected Infection in Low- and Middle-Income Countries](#)

Rudd, K.E. et al

JAMA. Published online May 20, 2018

The quick Sequential (Sepsis-Related) Organ Failure Assessment (qSOFA) score has not been well-evaluated in low- and middle-income countries (LMICs). Article looks at how to assess the association of qSOFA with excess hospital death among patients with suspected infection in LMICs and to compare

Current Opinion in Critical Care: June 1, 2018 - Volume
Publish Ahead of Print

Hypovitaminosis C and vitamin C deficiency are very common in critically ill patients due to increased needs and decreased intake. Because vitamin C has pleiotropic functions, deficiency can aggravate the severity of illness and hamper recovery. A short course of intravenous vitamin C in pharmacological dose seems a promising, well tolerated, and cheap adjuvant therapy to modulate the overwhelming oxidative stress in severe sepsis, trauma, and reperfusion after ischemia. Large randomized controlled trials are necessary to provide more evidence before wide-scale implementation can be recommended.

[Derivation and Validation of a Biomarker-Based Clinical Algorithm to Rule Out Sepsis From Noninfectious Systemic Inflammatory Response Syndrome at Emergency Department Admission: A Multicenter Prospective Study](#)

Mearelli, F. et al

Critical Care Medicine: May 7, 2018 - Volume Online
First

Objectives were to derive and validate a predictive algorithm integrating a nomogram-based prediction of the pretest probability of infection with a panel of serum biomarkers, which could robustly differentiate sepsis/septic shock from noninfectious systemic inflammatory response syndrome. Conclusions: We have developed and validated a high-performing, reproducible, and parsimonious algorithm to assist emergency department physicians in distinguishing sepsis/septic shock from noninfectious systemic inflammatory response syndrome.

[Sepsis-induced myocardial dysfunction](#)

Keith R Walley

Current Opinion in Critical Care 2018 May 24

Sepsis leads to a complex intramyocardial inflammatory response that results in sepsis-induced myocardial dysfunction. Here, recent findings are reviewed in a

qSOFA with the systemic inflammatory response syndrome (SIRS) criteria. Finds that when assessed among hospitalized adults with suspected infection in 9 LMIC cohorts, the qSOFA score identified infected patients at risk of death beyond that explained by baseline factors. However, the predictive validity varied among cohorts and settings, and further research is needed to better understand potential generalizability.

[Bet 2: Does intravenous vitamin C improve mortality in patients with severe sepsis? \[Best evidence topic report\].](#)

Sheikh M. et al

Emergency Medicine Journal 2018;35(4):272-274.

A shortcut review was carried out to establish whether the use of intravenous vitamin C can reduce mortality or morbidity in patients diagnosed in the early phases of severe sepsis. Three directly relevant papers were found using the reported search strategy. The author, date and country of publication; patient group studied; study type; relevant outcomes; results and study weaknesses of the best papers are tabulated. It is concluded that there is insufficient high-quality research to justify the routine use of vitamin C in severe sepsis. Further multicentre, double-blinded randomised controlled trials are required in order to establish the role of vitamin C in sepsis.

[Pro-inflammatory Th1 and Th17 cells are suppressed during human experimental endotoxemia whereas anti-inflammatory IL-10 producing T-cells are unaffected](#)

Brinkhoff, A. et al

Frontiers in Immunology 2018, 9: 1133

Sepsis is one of the leading causes of the deaths in hospitals. During sepsis, patients are exposed to endotoxemia, which may contribute to the dysregulation of the immune system frequently observed in sepsis. This dysregulation leads to impaired pro-inflammatory responses and may

physiologic context. Sepsis-induced myocardial dysfunction is increasingly recognized as a major contributor to outcome of septic shock. Significant strides have been made in understanding the intramyocardial inflammatory response that causes myocardial dysfunction. A number of novel approaches show promise by modulating the intramyocardial inflammatory response.

[Predictive Validity of Sepsis-3 Definitions and Sepsis Outcomes in Critically Ill Patients: A Cohort Study in 49 ICUs in Argentina](#)

Estenssoro, E. et al

Critical Care Medicine: May 8, 2018 - Volume Online First

The new Sepsis-3 definitions have been scarcely assessed in low- and middle-income countries; besides, regional information of sepsis outcomes is sparse. Our objective was to evaluate Sepsis-3 definition performance in Argentina. Increasing severity of Sepsis-3 categories adequately tracks mortality; cardiovascular dysfunction subgroup, not included in Sepsis-3, has distinct characteristics. Sequential Organ Failure Assessment score shows adequate prognosis accuracy, contrary to systemic inflammatory response syndrome. This study supports the predictive validity of Sepsis-3 definitions.

[Pathophysiology of Septic Shock](#)

Russell, J.A. et al

Crit Care Clin. 2018 Jan;34(1):43-61

Fundamental features of septic shock are vasodilation, increased permeability, hypovolemia, and ventricular dysfunction. Vasodilation owing to increased nitric oxide and prostaglandins is treated with vasopressors (norepinephrine first). Increased permeability relates to several pathways (Slit/Robo4, vascular endothelial growth factor, angiopoietin 1 and 2/Tie2 pathway, sphingosine-1-phosphate, and heparin-binding protein), some of which are targets for therapies. Hypovolemia is common and crystalloid is

increase the risk for secondary infections in sepsis. The experimental human endotoxemia model is widely used as a model system to study the acute effects of endotoxemia. Under physiological circumstances, the immune system is tightly regulated. Effector T-cells exert pro-inflammatory function and are restrained by regulatory T-cells (Tregs), which modulate pro-inflammatory effector responses. Endotoxemia may induce inadequate Treg activity or render effector T-cells dysfunctional. It was the aim of the study to investigate effector T-cell and Treg responses in an experimental human endotoxemia model.

[Adherence to a procalcitonin-guided antibiotic treatment protocol in patients with severe sepsis and septic shock](#)

Hohn, A. et al

Ann Intensive Care. 2018 Jun 4;8(1):68.

In randomised controlled trials, procalcitonin (PCT)-guided antibiotic treatment has been proven to significantly reduce length of antibiotic therapy in intensive care unit (ICU) patients. However, concern was raised on low protocol adherence and high rates of overruling, and thus the value of PCT-guided treatment in real clinical life outside study conditions remains unclear. In this study, adherence to a PCT protocol to guide antibiotic treatment in patients with severe sepsis and septic shock was analysed. In patients with severe sepsis and septic shock, procalcitonin testing was irregular and adherence to a local PCT protocol was low in real clinical life. However, adherently treated patients had a shorter duration of antibiotic treatment without negative clinical outcomes. Procalcitonin peak values and kinetics had a clear impact on the regularity of PCT testing.

recommended for fluid resuscitation. Cardiomyocyte-inflammatory interactions decrease contractility and dobutamine is recommended to increase cardiac output. There is benefit in decreasing heart rate in selected patients with esmolol. Ivabradine is a novel agent for heart rate reduction without decreasing contractility.

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