Here is the latest edition of the Sepsis Bulletin. The bulletin covers the latest information on sepsis and comes out fortnightly. Next edition is due 25 October 2018. Older editions are available as pdfs on the Keeping Up To Date library guide (http://libguides.bodleian.ox.ac.uk/Keeping_up_to_date)

Please also pass the bulletin on to other interested people and encourage them to sign up. Anyone can be added to the mailing list.

To support you further in keeping up to date, we have a current awareness service, **KnowledgeShare**. You let us know about the different areas you are interested in (for example lung cancer, leadership, orthopaedics, infection control, patient safety, etc.) and we send out an email fortnightly with any new high-level reports, studies, guidelines which match. This is a free service. For more information see our guide. To sign up, fill out our form: https://ox.libguides.com/ld.php?content_id=31673730

SEPSIS BULLETIN
11 October 2018

Neonatal, paediatric and maternal sepsis

Suspected or known neonatal sepsis and neurodevelopmental delay by 5 years.
Savioli K. et al
J Perinatol. 2018 Sep 10. [Epub ahead of print]
Evaluates the impact of known and suspected neonatal sepsis in the term and preterm infant on neurodevelopmental delay by 5 years. Concludes that neonatal sepsis and suspected sepsis are associated with neurodevelopmental delay by 5 years of age.

Expression Levels of Candidate Circulating microRNAs in Early-Onset Neonatal Sepsis Compared With Healthy Newborns
Dhas B.B. et al
Genomics Insights. 2018 Sep 2;11:1178631018797079.
The high mortality rate of neonatal sepsis is directly connected with time-consuming diagnostic methods that have low sensitivity and specificity. The need of the hour is to develop novel diagnostic techniques that are rapid and more specific. In this study, we estimated the expression levels of circulating microRNAs (miRNAs) that are involved in regulating immune

Adult sepsis (cont.)

Suspicion of Sepsis (SOS) Insights Dashboard
Imperial College Health Partners
The AHSN Network and NHS Improvement 2018
Sepsis is a life-threatening condition that claims approximately 37,000 lives a year, although the exact figure is difficult to determine. It is caused when the body responds poorly to a bacterial infection and attacks its own tissues and organs. Sepsis is notoriously difficult to spot because there is no clear diagnostic test for the condition. For the first time, the NHS will now be able to track improvements – such as rates of survival and length of hospitals stays. Now all hospitals across England are being asked to use a tool which will allow them to identify how many patients are at risk of sepsis. This NHS tool will for the first time measure the number of patients coming into hospital as an emergency with a severe bacterial infection categorised as of "suspicion of sepsis". Previously the measurement for sepsis has fluctuated but this tool gives serious infections a defined category that all organisations in the NHS will use, identifying patients

response genes and underlying inflammatory responses, which may be used for sepsis diagnosis.

[Use of melatonin as adjunctive therapy in neonatal sepsis: A systematic review and meta-analysis](#)
Henderson, R ; Kim, S ; Lee, E
Complementary Therapies In Medicine, 2018 Aug, Vol.39, pp.131-136
Sepsis remains one of the major causes of neonatal mortality and morbidity. Increased production of free radicals and pro-inflammatory cytokines, combined with the innately low levels of plasma antioxidants in neonates, have been implicated in the pathogenesis and complications of neonatal sepsis. To date, few clinical trials on the beneficial effects of exogenous melatonin on improvement of clinical outcomes in septic neonates have been conducted. Findings showed that administration of melatonin as adjunctive therapy significantly reduced an inflammatory biomarker and improved sepsis status in neonate. Larger scale studies with higher validity are needed to demonstrate clear clinical benefits of the therapy.

[Late onset sepsis: comparison between coagulase-negative staphylococci and other bacteria in the neonatal intensive care unit](#)
Berlak, N. et al
Infectious Diseases, 29 June 2018, pp.1-7
This study compares demographic and clinical features of neonates with late-onset sepsis due to coagulase-negative-staphylococcus with those due to other bacterial pathogens. Initial empiric treatment for suspected sepsis should be targeted for other pathogens than coagulase-negative-staphylococci and vancomycin treatment should be reserved for infants with specific risk factors and according to local antimicrobial susceptibility.

[The cut-off levels of procalcitonin and C-reactive protein and the kinetics of mean platelet volume in preterm neonates with sepsis](#)
Aydemir, C. et al
BMC Pediatrics, 1 August 2018, Vol.18(1)
Sepsis is a leading cause of morbidity and mortality among newborns. C-reactive protein (CRP) and procalcitonin (PCT) have some limitations in the diagnosis of preterm neonatal sepsis. In this study, the cut-offs of PCT and CRP, and the efficacy of mean platelet volume (MPV) were investigated. Optimal cut-off levels of CRP 1 and PCT 1 may differ in preterm sepsis subgroups. The diagnostic performances of CRP 1 and PCT 1 didn't differ however, they were more efficacious than MPV.

who should be screened for sepsis and giving clinicians the most accurate picture yet for how many people are at risk of developing sepsis.

[Evaluation of Repeated Quick Sepsis-Related Organ Failure Assessment Measurements Among Patients With Suspected Infection.](#)
Kievlan, D.R. et al
Critical Care Med. 2018 Aug 20.
Among patients with suspected infection, a single measurement of the quick Sepsis-related Organ Failure Assessment has good predictive validity for sepsis, yet the increase in validity from repeated measurements is unknown. We sought to determine the incremental predictive validity for sepsis of repeated quick Sepsis-related Organ Failure Assessment measurements over 48 hours compared with the initial measurement. Repeated measurements of quick Sepsis-related Organ Failure Assessment improve predictive validity for sepsis using in-hospital mortality compared with a single measurement of quick Sepsis-related Organ Failure Assessment at the time a clinician suspects infection.

[Heart rate variability as predictor of mortality in sepsis: A systematic review](#)
de Castilho, F.M. et al
PLoS One. 2018 Sep 11;13(9):e0203487.
Autonomic dysregulation is one of the recognized pathophysiological mechanisms in sepsis, generating the hypothesis that heart rate variability (HRV) can be used to predict mortality in sepsis. Several HRV parameters are reduced in nonsurviving septic patients in short-term recording. Two studies have found that SDNN is associated with mortality in sepsis, even after adjusting for possible confounding factors.

[HDL inflammatory index correlates with and predicts severity of organ failure in patients with sepsis and septic shock](#)
Guirgis, F.W. et al
PLoS One. 2018 Sep 14;13(9):e0203813
High density lipoprotein (HDL) is important for defense against sepsis but becomes dysfunctional (Dys-HDL) during inflammation. We hypothesize that Dys-HDL correlates with organ dysfunction (sequential organ failure assessment (SOFA) score) early sepsis. HII correlated with SOFA and predicted 48-hour SOFA score in early sepsis. Future studies are needed to delineate potential mechanisms.

[Deficiency of receptor-interacting protein kinase 3 (RIPK3) attenuates inflammation and organ injury in neonatal sepsis](#)
Hansen, L.W. et al
Journal of Pediatric Surgery, September 2018, Vol.53(9), pp.1699-1705
Sepsis is the third leading cause of morbidity and mortality in neonates. Sepsis in neonates is characterized as the systemic inflammation owing to infection within the first 28 days after birth. The molecular mechanism causing the exaggerated inflammation phenotype in neonates has not been completely elucidated. Receptor interacting protein kinase 3 (RIPK3) is a protein identified as a mediator in programmed necrosis or necroptosis. We hypothesize that RIPK3 could be responsible for the inflammatory response in neonates and that deficiency in the RIPK3 protein attenuates inflammation and organ injury in neonatal sepsis. The deficiency in RIPK3 attenuated serum and lung cytokines, lung injury and neutrophil infiltration and lung and gut apoptosis. These data suggest that RIPK3, in part, is responsible for the systemic inflammatory response in neonatal sepsis.

[A Quality Improvement Collaborative for Pediatric Sepsis: Lessons Learned](#)
Paul, R. et al
Pediatric Quality and Safety: January/February 2018 - Volume 3 - Issue 1 - p e051
Sepsis is a leading cause of morbidity and mortality in children worldwide. Barriers exist for timely recognition and management in emergency care settings. This 1-year quality improvement collaborative sought to reduce mortality from sepsis. A quality improvement collaborative focused on improving timely recognition and management of pediatric sepsis to septic shock led to some process improvements but did not show improvement in mortality. Future national efforts should standardize definitions and processes of care for sepsis to septic shock, including the identification of a "time zero" for measuring the timeliness of treatment.

[Assessment of clinical outcome of children with sepsis outside the intensive care unit.](#)
Zallocco F et al
Eur J Pediatr. 2018 Sep 17.
In 2016, in order to identify adult patients with sepsis who are likely to have poor outcomes, the Third International Consensus Definitions Task Force introduced a new bedside index, called the quick Sepsis-related Organ Failure Assessment (qSOFA) score. However, these new criteria have not been validated in

[Association between early serum cholinesterase activity and 30-day mortality in sepsis-3 patients: A retrospective cohort study](#)
Peng, Z.L. et al
PLoS One. 2018 Aug 30;13(8):e0203128.
Low serum cholinesterase (SCHE) activity has been associated with poor prognoses in a variety of conditions, including sepsis. However, such an association has not been well characterized since the Third International Consensus Definitions Task Force modified the definition of sepsis to "life-threatening organ dysfunction due to a dysregulated host response to infection" (known as sepsis-3) in 2016. In the current retrospective cohort study, we examined whether 30-day mortality in sepsis-3 patients is associated with SCHE activity. These data suggest that lower SCHE activity is an independent risk factor for 30-day mortality in sepsis-3 patients.

[Recurrent bacterial translocation from gut and sepsis in Head and neck cancer patients and its prevention by probiotics.](#)
Gunduz M. et al
Med Hypotheses. 2018 Nov;120:124-127. Epub 2018 Aug 27.
Head and neck cancers are the 6th most common cancer type in human malignant tumors and treated with chemoradiotherapy and surgery. Chemotherapy during these treatment modalities leads to damage of intestinal epithelial barriers and results in translocation of intestinal bacteria in bloodstream through invasion in these damaged regions. In this report, we report two cases of hypopharyngeal cancer patients, both of whom received chemotherapy before surgery. The patients demonstrated repeated sepsis before and after surgery, supporting translocation of intestinal bacteria. Proper continuous probiotic use prevented proliferation and intestinal bacterial translocation. Hypothesis of bacterial translocation and prevention by probiotics are discussed.

[Sepsis: Personalized Medicine Utilizing 'Omic' Technologies-A Paradigm Shift?](#)
Itenov T.S. et al
Healthcare (Basel). 2018 Sep 7;6(3). pii: E111.
Sepsis has over the years proven a considerable challenge to physicians and researchers. Numerous pharmacological and non-pharmacological interventions have been tested in trials, but have unfortunately failed to improve the general prognosis. This has led to the speculation that the sepsis population may be too heterogeneous to be targeted with the traditional one treatment suits all' approach.

the pediatric population. In this study, we sought to assess the qSOFA score for children with sepsis, who are being treated outside the pediatric intensive care units. The qSOFA score showed a low accuracy to identify children in the pediatric ward at risk for severe sepsis. Clinical tools are needed to facilitate the diagnosis of impending organ dysfunction in pediatric infection outside of the ICU.

Adult sepsis
[Sepsis Core Measures - Are They Worth the Cost?](#)
Esposito A. et al
J Emerg Med. 2018 Sep 22. pii: S0736-4679(18)30751-0
In 2015, the Centers for Medicare and Medicaid Services (CMS) and the Joint Commission launched the sepsis core measures in an attempt to decrease sepsis morbidity and mortality. Recent studies call into question the multiple treatment measures in early goal-directed therapy on which these CMS measures are based. There was no difference in the mortality rate of patients with a final diagnosis of sepsis. However, there was a significant increase in the utilization of resources to care for these patients. As a result of the overutilization of these resources, the cost for both patients and hospitals has increased without improvement in mortality.

[A Comparison of Mortality From Sepsis in Brazil and England: The Impact of Heterogeneity in General and Sepsis-Specific Patient Characteristics.](#)
Ranzani O.T. et al.
Crit Care Med. 2018 Sep 20.
Tests whether differences in both general and sepsis-specific patient characteristics explain the observed differences in sepsis mortality between countries, using two national critical care (ICU) databases. Patients with sepsis admitted to ICUs in Brazil and England have important differences in general and sepsis-specific characteristics, from source of admission to organ dysfunctions. We show that comparing crude mortality from sepsis patients admitted to the ICU between countries, as currently performed, is not reliable and that the adjustment for both general and sepsis-specific patient characteristics is essential for valid international comparisons of mortality amongst sepsis patients admitted to critical care units.

[Symmetrical (SDMA) and asymmetrical dimethylarginine (ADMA) in sepsis: high plasma levels as combined risk markers for sepsis survival](#)
Winkler, M.S. et al
Critical Care 201822:216

Recent advances in genetic and biochemical analyses now allow genotyping and biochemical characterisation of large groups of patients via the 'omics' technologies. These new opportunities could lead to a paradigm shift in the approach to sepsis towards personalised treatments with interventions targeted towards specific pathophysiological mechanisms activated in the patient. In this article, we review the potentials and pitfalls of using new advanced technologies to deepen our understanding of the clinical syndrome of sepsis.
Renin-angiotensin-aldosterone system inhibition and outcome of sepsis

[Baycare Health System's Approach to Implement an Evidence-Based Sepsis Mortality Reduction Program](#)
Gupta, C. et al
Performance Improvement, September 2018, Vol.57(8), pp.31-35
Sepsis is the 10th leading cause of death in the United States. A 14-hospital health system formed a multidisciplinary team to build an evidence-based sepsis-mortality reduction program (SMRP). SMRP leads to a statistically significant decrease in sepsis mortality, significant improvement in compliance with SEP-1 (core measure), and statistically significant negative correlation between SEP-1 bundle compliance rates and the sepsis-mortality rates. Patients who received the SEP-1 bundle were 51 more likely to survive.

[Not all organ dysfunctions are created equal – Prevalence and mortality in sepsis](#)
Capan M. et al
J Crit Care. 2018 Sep 13;48:257-262.
While organ dysfunctions within sepsis have been widely studied, interaction between measures of organ dysfunction remains an understudied area. The objective of this study is to quantify the impact of organ dysfunction on in-hospital mortality in infected population. There exist differences in measures of organ dysfunction occurrence and their association with mortality. These findings support increased clinical efforts to identify sepsis patients to inform diagnostic decisions.

[Antibiotics has more impact on mortality than other early goal-directed therapy components in patients with sepsis: An instrumental variable analysis](#)
Londoño J. et al
J Crit Care. 2018 Aug 30;48:191-197.
This study estimates the effect of each of the EGDT components, as well as of the antibiotics, on length-of-

Nitric oxide (NO) regulates processes involved in sepsis progression, including vascular and immune function. NO is generated by nitric oxide synthases (NOS) from L-arginine. Cellular L-arginine uptake is inhibited by symmetric dimethylarginine (SDMA) and asymmetric dimethylarginine (ADMA) is a competitive inhibitor of NOS. Increased inhibitor blood concentrations lead to reduce NO bioavailability. The aim of this study was to determine whether plasma concentrations of SDMA and ADMA are markers for sepsis survival. Increased plasma concentrations of SDMA and ADMA are associated with sepsis severity. Therefore, our findings suggest reduced NO bioavailability in non-survivors of sepsis. One may use individual SDMA and ADMA levels to identify patients at risk. In view of the pathophysiological role of NO we conclude that the vascular system and immune response are most severely affected when SDMA and ADMA levels are high.

[P(v-a)CO2/C(a-v)O2-directed resuscitation does not improve prognosis compared with SvO2 in severe sepsis and septic shock: A prospective multicenter randomized controlled clinical study](#)
Longxiang S. et al
Journal of Critical Care, Volume 48, December 2018, Pages 314-320
The present study examined the value of P(v-a)CO2/C(a-v)O2 compared with ScvO2 as a target for clinical resuscitation of severe sepsis/septic shock. P(v-a)CO2/C(a-v)O2-directed resuscitation did not improve prognosis compared with ScvO2 in severe sepsis and septic shock.

[CRRT for sepsis-induced acute kidney injury.](#)
Romagnoli S. et al
Curr Opin Crit Care. 2018 Sep 18.
Sepsis-induced acute kidney injury (SI-AKI) represents the first cause of AKI in ICUs, and renal replacement therapy (RRT) is frequently applied in advanced AKI stages. The debate between 'rescue' indications for RRT start in patients with severe AKI (acidosis, hyperkalemia, uremia, oliguria/anuria, volume overload) and a proactive RRT initiation is still ongoing. In addition, current SI-AKI pathophysiologic theory has identified the toxic effects of soluble middle-molecules released during sepsis and inflammation (pathogen and damaged associated molecular patterns).The purpose of the present review is to summarize the recent literature on RRT for patients with SI-AKI. Supportive or replacement measures for severe stages of renal dysfunction and blood purification techniques for sepsis syndrome will be reviewed.In the present

stay and mortality. Among patients entering ER with infection and shock or hypoperfusion criteria, the use of appropriate antibiotics in the first 3 h is the measure that has the greatest impact on survival. In addition, among patients with hyperlactatemia >4 mmol/L, the clearance of >10% of lactate during resuscitation is associated with better outcomes.

[Derivation of a screen to identify severe sepsis and septic shock in the Emergency Department-BOMBARD vs. SIRS and qSOFA](#)
Rothrock S.G. et al
Am J Emerg Med. 2018 Sep 15. pii: S0735-6757(18)30757-5.
This study looks to predict severe sepsis/septic shock in ED patients. They conducted a retrospective case-control study of patients ≥18 admitted to two urban hospitals with a combined ED census of 162,000. Study cases included patients with severe sepsis/septic shock admitted via the ED. Controls comprised admissions without severe sepsis/septic shock. Using multivariate logistic regression, a prediction rule was constructed - BOMBARD. The model's AUROC was internally validated using 1000 bootstrap samples. BOMBARD was more accurate than SIRS and qSOFA at predicting severe sepsis/septic shock and sepsis mortality.

[Smartphone-based pathogen diagnosis in urinary sepsis patients](#)
Barnes, Lucien et al.
EBioMedicine 2018
There is an urgent need for rapid, sensitive, and affordable diagnostics for microbial infections at the point-of-care. Although a number of innovative systems have been reported that transform mobile phones into potential diagnostic tools, the translational challenge to clinical diagnostics remains a significant hurdle to overcome. A smartphone-based real-time loop-mediated isothermal amplification (smaRT-LAMP) system was developed for pathogen ID in urinary sepsis patients. The free, custom-built mobile phone app allows the phone to serve as a stand-alone device for quantitative diagnostics, allowing the determination of genome copy-number of bacterial pathogens in real time. The smaRT-LAMP system is effective against diverse Gram-negative and -positive pathogens and biological specimens, costs less than $100 US to fabricate (in addition to the smartphone), and is configurable for the simultaneous detection of multiple pathogens. SmaRT-LAMP thus offers the potential to deliver rapid diagnosis and treatment of urinary tract infections and urinary sepsis

review, the recent insights and results from large randomized and nonrandomized trials in the area of RRT applied both as supportive measures for kidney failure and blood purification techniques are described.

Prehospital sepsis alert notification decreases time to initiation of CMS sepsis core measures
Hunter, Christopher L. et al.
The American Journal of Emergency Medicine 2018, Objective to determine if prehospital identification of sepsis will affect time to Centers for Medicare and Medicaid services (CMS) sepsis core measures and improve clinical outcomes. Methods were to conduct a retrospective cohort study among septic patients who were identified as "sepsis alerts" in the emergency department (ED). Metrics including time from ED registration to fluid resuscitation, blood cultures, serum lactate draws, and antibiotics administration were compared between those who had pre-arrival notification by EMS versus those that did not. Additionally, outcomes such as mortality and intensive care unit (ICU) admission were recorded. Conclusion that prehospital sepsis alert notification may decrease time to specific metrics shown to improve outcomes in sepsis.

Association of Neighborhood Socioeconomic Status With Risk of Infection and Sepsis.
Donnelly JP et al
Clin Infect Dis. 2018 Jun 1;66(12):1940-1947.
Prior studies suggest disparities in sepsis risk and outcomes based on place of residence. We sought to examine the association between neighborhood socioeconomic status (nSES) and hospitalization for infection and sepsis. Our study shows that differential infection risk may explain nSES disparities in sepsis incidence, as higher nSES is associated with lower infection hospitalization rates, but there is no association with sepsis among those hospitalized. Mediation analysis showed that nSES may influence infection hospitalization risk at least partially through physical weakness, individual income, and comorbid diabetes.

with a simple test that can be performed at low cost at the point-of-care.

Raising Awareness for Sepsis, Sepsis Screening, Early Recognition, and Treatment in the Emergency Department
Walters, E.
Journal of Emergency Nursing. Volume 44, Issue 3, May 2018, Pages 224-227
Early recognition and initiation of treatment is vital to patient outcomes and survival from sepsis. Sepsis screening in triage should be completed by nurses on all patients with suspected infection. Initiation of sepsis protocol and/or standing orders for positive sepsis screens should be implemented. Education of staff, patients, and families should be done regarding signs and symptoms of sepsis, severe sepsis, and severe sepsis with shock; raise awareness.

The global burden of sepsis: barriers and potential solutions.
Rudd KE et al
Crit Care. 2018 Sep 23;22(1):232.
Sepsis is a major contributor to the global burden of disease. The majority of sepsis cases and deaths are estimated to occur in low and middle-income countries. Barriers to reducing the global burden of sepsis include difficulty quantifying attributable morbidity and mortality, low awareness, poverty and health inequity, and under-resourced and low-resilience public health and acute health care delivery systems. Important differences in the populations at risk, infecting pathogens, and clinical capacity to manage sepsis in high and low-resource settings necessitate context-specific approaches to this significant problem. We review these challenges and propose strategies to overcome them. These strategies include strengthening health systems, accurately identifying and quantifying sepsis cases, conducting inclusive research, establishing data-driven and context-specific management guidelines, promoting creative clinical interventions, and advocacy.

01865 221936
hcl-enquiries@bodleian.ox.ac.uk
www.bodleian.ox.ac.uk/nhs

Register for OpenAthens to access e-resources:
https://openathens.nice.org.uk/

Bulletin content based partly on CASH (Current Awareness Service for Health) here

To subscribe/unsubscribe from this bulletin please email library@ouh.nhs.uk or reply to this email.

Please see our privacy notice https://libguides.bodleian.ox.ac.uk/Keeping_up_to_date/privacynotice