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 19 July 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)

I would like to make this bulletin as relevant as possible to you. Please let me know what you would like to see in the content.

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SEPSIS BULLETIN
2 July 2018

Neonatal and paediatric sepsis
Risk factors and inpatient outcomes associated with acute kidney injury at pediatric severe sepsis presentation
Fitzgerald, J.C. et al.
Pediatr Nephrol (2018).
Little data exist on acute kidney injury (AKI) risk factors in pediatric sepsis. We identified risk factors and inpatient outcomes associated with AKI at sepsis recognition in children with severe sepsis. In pediatric severe sepsis, AKI is associated with age, comorbidities, infection characteristics, and hypotension. Future evaluation of risk factors for AKI progression during sepsis is warranted to minimize AKI progression in this high-risk population.

Reviewing the WHO guidelines for antibiotic use for sepsis in neonates and children
Fuchs, A. et al

Adult sepsis (cont.)
Automated monitoring compared to standard care for the early detection of sepsis in critically ill patients.
Warttig, S. et al
Cochrane Database of Systematic Reviews 2018, Issue 6. Art. No.: CD012404
Sepsis is a life-threatening condition that is usually diagnosed when a patient has a suspected or documented infection, and meets two or more criteria for systemic inflammatory response syndrome (SIRS). The incidence of sepsis is higher among people admitted to critical care settings such as the intensive care unit (ICU) than among people in other settings. If left untreated sepsis can quickly worsen; severe sepsis has a mortality rate of 40% or higher, depending on definition. Recognition of sepsis can be challenging as it usually requires patient data to be combined from multiple unconnected sources, and interpreted correctly, which can be complex and time consuming to do. Electronic systems that are designed to connect information sources together, and automatically collate,

Paediatrics and International Child Health 2018, 38 (sup1): S3-S15

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. Current WHO guidelines supporting the use of gentamicin and penicillin for hospital-based patients or gentamicin (IM) and amoxicillin (oral) when referral to a hospital is not possible are in accordance with currently available evidence and other international guidelines, and there is no strong evidence to change this. The benefit of a cephalosporin alone or in combination as a second-line therapy in regions with known high rates of non-susceptibility is not well established. Further research into hospital-acquired sepsis in neonates and children is required.

[Late-onset Sepsis in Preterm Infants Can Be Detected Preclinically by Fecal Volatile Organic Compound Analysis: A Prospective, Multicenter Cohort Study](#)

Berkhout, D.J.C. et al.

Clinical Infectious Diseases, ciy383

The intestinal microbiota has increasingly been considered to play a role in the etiology of late-onset sepsis (LOS). We hypothesize that early alterations in fecal volatile organic compounds (VOCs), reflecting intestinal microbiota composition and function, allow for discrimination between infants developing LOS and controls in a preclinical stage. Fecal VOC analysis allowed for preclinical discrimination between infants developing LOS and matched controls. Early detection of LOS may provide clinicians a window of opportunity for timely initiation of individualized therapeutic strategies aimed at prevention of sepsis, possibly improving LOS-related morbidity and mortality.

[Beneficial effect of melatonin in the treatment of neonatal sepsis](#)

El-Gendy, F.M. et al.

Journal of Maternal-fetal & Neonatal Medicine 2018, 31 (17): 2299-2303

OBJECTIVE: To study the effect of melatonin as an adjuvant therapy in the treatment of neonatal

analyse, and continuously monitor the information, as well as alerting healthcare staff when pre-determined diagnostic thresholds are met, may offer benefits by facilitating earlier recognition of sepsis and faster initiation of treatment, such as antimicrobial therapy, fluid resuscitation, inotropes, and vasopressors if appropriate. However, there is the possibility that electronic, automated systems do not offer benefits, or even cause harm. This might happen if the systems are unable to correctly detect sepsis (meaning that treatment is not started when it should be, or it is started when it shouldn't be), or healthcare staff may not respond to alerts quickly enough, or get 'alarm fatigue' especially if the alarms go off frequently or give too many false alarms.

[Comparison of qSOFA with current emergency department tools for screening of patients with sepsis for critical illness](#)

Rodriguez, R. M. et al

Emerg Med J 2018;35:350-356.

We sought to compare the quick sequential organ failure assessment (qSOFA) to systemic inflammatory response syndrome (SIRS), severe sepsis criteria and lactate levels for their ability to identify ED patients with sepsis with critical illness. For patients admitted from the ED with infectious disease diagnoses, qSOFA criteria performed as well or better than SIRS criteria, severe sepsis criteria and lactate levels in predicting critical illness.

[Fluid therapy and shock: an integrative literature review](#).

Silva, J. et al

British Journal of Nursing 2018; 27(8): 449-454.

Shock refers to a physiological situation that puts life at risk. Its early identification and the timely institution of therapeutic measures can avoid death. Despite the frequent administration of fluid therapy as a treatment for shock, the type and dose of fluids to be delivered remain undetermined. Hypotensive resuscitation, with blood, is the most appropriate approach in haemorrhagic shock. There remains a question regarding the best approach in septic shock. However, conservative fluid therapy seems to be appropriate, with preference given to the administration of balanced crystalloids or albumin as an alternative.

[Health-related outcomes of critically ill patients with and without sepsis](#)

Thompson, K. et al

Intensive Care Medicine 2018 June 27

Purpose is to determine differences in health-related quality of life (HRQoL), survival and healthcare resource use of critically ill adults with and without sepsis. Critically ill patients with sepsis have higher healthcare

sepsis. METHODS: This study is a prospective nonrandomized nonblind case-control study and was carried on 40 neonates with neonatal sepsis diagnosed by both clinical and laboratory criteria. They were enrolled from the Neonatal Intensive Care Unit, Menoufia University Hospitals. These cases were selected during the study period from November 2015 to May 2016 and were divided into two groups: intervention group (number 20 neonates) received melatonin 20 mg as single dose and antibiotics and control group (number 20 neonates) received antibiotics only and then both groups followed by physical examination, complete blood count (CBC), and high sensitive C-reactive protein (hs-CRP) to evaluate the improvement in both groups. RESULTS: Before melatonin administration, there was no significant difference between intervention group and control group with regard to clinical condition, hs-CRP, and other serum parameters. After 24 and 72 hours of melatonin administration, both groups improved with regard to clinical condition, hs-CRP, and serum parameters with significant improvement in intervention group than control group. CONCLUSION: Melatonin could be used in the treatment of neonatal sepsis in both preterm and full-term neonates beside the conventional treatment.

[The relative resistance of children to sepsis mortality: from pathways to drug candidates](#)
Joachim, R.B. et al
Molecular Systems Biology (2018) 14, e7998
Attempts to develop drugs that address sepsis based on leads developed in animal models have failed. We sought to identify leads based on human data by exploiting a natural experiment: the relative resistance of children to mortality from severe infections and sepsis. Using public datasets, we identified key differences in pathway activity (Pathprint) in blood transcriptome profiles of septic adults and children. To find drugs that could promote beneficial (child) pathways or inhibit harmful (adult) ones, we built an in silico pathway drug network (PDN) using expression correlation between drug, disease, and pathway gene signatures across 58,475 microarrays. Specific pathway clusters from children or adults were assessed for correlation with drug-based signatures. Validation by literature curation and by direct testing in an endotoxemia model of murine sepsis of the most correlated drug candidates demonstrated that the Pathprint-PDN methodology is more effective at generating positive drug leads than gene-level methods (e.g., CMap). Pathway-centric Pathprint-PDN is a

resource use and costs but similar survival and HRQoL compared to matched patients without sepsis.

[Glycocalyx biomarker syndecan-1 is a stronger predictor of respiratory failure in patients with sepsis due to pneumonia, compared to endocan.](#)
Smart, L. et al
J Crit Care. 2018 Jun 18;47:93-98. [Epub ahead of print]
Endocan, a component of the endothelial glycocalyx (EG), has been linked with respiratory failure in sepsis. This study explored the temporal patterns of three EG biomarkers, including endocan, and their relationships with inflammation and respiratory failure. Syndecan-1, but not endocan, was associated with neutrophil activation and was the best EG biomarker predictor of adverse clinical outcomes.

[Surviving Sepsis Campaign: Research Priorities for Sepsis and Septic Shock](#)
Coopersmith, C.M. et al
Critical Care Medicine 2018 June 27
OBJECTIVE: To identify research priorities in the management, epidemiology, outcome and underlying causes of sepsis and septic shock. CONCLUSIONS: While the Surviving Sepsis Campaign guidelines give multiple recommendations on the treatment of sepsis, significant knowledge gaps remain, both in bedside issues directly applicable to clinicians, as well as understanding the fundamental mechanisms underlying the development and progression of sepsis. The priorities identified represent a roadmap for research in sepsis and septic shock.

[Factors associated with post-operative sepsis following surgery for spinal tumors: An analysis of the ACS-NSQIP database](#)
Malik, A.T. et al
Clinical Neurology and Neurosurgery Volume 172, September 2018, Pages 1-7
Sepsis is a rare but potentially devastating complication when it occurs after surgery for spinal tumors. Given the morbidity associated with sepsis, we sought to collate evidence using a large national surgical database to identify the incidence, pre-operative predictors and post-operative factors associated with sepsis following spinal tumor surgery. Three percent of patients following surgery for spinal tumor experience an episode of sepsis within 30 days. The most likely sources of sepsis include UTI, pneumonia and SSI. Pre- and post-operative targeted interventions in these high risk patients will be most beneficial in reducing the incidence, morbidity and mortality from sepsis after surgery for spinal tumors.

[The use of IgM-enriched immunoglobulin in adult patients with sepsis.](#)

powerful new way to identify drug candidates for intervention against sepsis and provides direct insight into pathways that may determine survival.

Adult sepsis
Sepsis and septic shock
Maurizio Cecconi, Laura Evans, Mitchell Levy, Andrew Rhodes
Lancet 2018 June 21

Sepsis is a common condition that is associated with unacceptably high mortality and, for many of those who survive, long-term morbidity. Increased awareness of the condition resulting from ongoing campaigns and the evidence arising from research in the past 10 years have increased understanding of this problem among clinicians and lay people, and have led to improved outcomes. The World Health Assembly and WHO made sepsis a global health priority in 2017 and have adopted a resolution to improve the prevention, diagnosis, and management of sepsis. In 2016, a new definition of sepsis (Sepsis-3) was developed. Sepsis is now defined as infection with organ dysfunction. This definition codifies organ dysfunction using the Sequential Organ Failure Assessment score. Ongoing research aims to improve definition of patient populations to allow for individualised management strategies matched to a patient's molecular and biochemical profile. The search continues for improved diagnostic techniques that can facilitate this aim, and for a pharmacological agent that can improve outcomes by modifying the disease process. While waiting for this goal to be achieved, improved basic care driven by education and quality-improvement programmes offers the best hope of increasing favourable outcomes.

Six subphenotypes in septic shock: Latent class analysis of the PROWESS Shock study
Gårdlund, B. et al
J Crit Care. 2018 Jun 3;47: 70–79. [Epub ahead of print]

Septic shock is a highly heterogeneous condition which is part of the challenge in its diagnosis and treatment. In this study we aim to identify clinically relevant subphenotypes of septic shock using a novel statistic al approach. Latent class analysis (LCA) can be used to identify subphenotypes within a complex phenomenon like septic shock. LCA identified six distinctive subphenotypes of septic shock with a high degree of separation. Each subphenotype has its specific, clinically relevant, characteristics. LCA appears to be an applicable statistical tool in analysing a heterogenous clinical

Kakoullis L1
J Crit Care. 2018 Jun 3;47:30-35. [Epub ahead of print]

The administration of intravenous immunoglobulins (IVIG) is one of the adjunct therapies investigated and applied to sepsis patients, with the first studies being published nearly four decades ago. Intravenous immunoglobulin preparations have several mechanisms of action e.g. antigen neutralization, Fc-receptor blockade on phagocytic cells, modulation of cytokine responses and modulation of immune cell functions. The currently available evidence suggesting the use of intravenous immunoglobulins in sepsis is weak, but results from recent trials and systematic metanalyses seem more promising for the use of intravenous IgM-enriched immunoglobulins (IVIgGM) in septic patients. Nevertheless, the results of studies examining its value are contradicting. The purpose of this review is to summarize and present, clearly and thoroughly, the currently available data regarding established and future potential clinical uses of IVIgGM in patients with sepsis.

Current aspects in sepsis approach. Turning things around
Candel, F.J. et al
Revista Española de Quimioterapia 2018 June 25

The incidence and prevalence of sepsis depend on the definitions and records that we use and we may be underestimating their impact. Up to 60% of the cases come from the community and in 30-60% we obtain microbiological information. Sometimes its presentation is ambiguous and there may be a delay in its detection, especially in the fragile population. Developing ultra-fast Point-of-Care tests (less than 30 minutes), implementing technologies based on omics, big data or massive sequencing or restoring "healthy" microbiomes in critical patients after treatment are the main focuses of research in sepsis. The main benefits of establishing a sepsis code are to decrease the time to achieve diagnosis and treatment, improve organization, unify criteria, promote teamwork to achieve common goals, increase participation, motivation and satisfaction among team members, and reduce costs.

cohort of septic shock. The results may lead to a better understanding of septic shock complexity and form a basis for considering targeted therapies and selecting patients for future clinical trials.