Here is the latest edition of the Sepsis Bulletin. The bulletin covers the latest information on sepsis and comes out monthly. Next edition is due December 2019. 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 let me know if there is anything you would like to see highlighted in the bulletin

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SEPSIS BULLETIN November 2019

NEWS2

Accuracy of National Early Warning Score 2 (NEWS2) in Prehospital Triage on In-Hospital Early Mortality: A Multi-Center Observational Prospective Cohort Study.

Martín-Rodríguez F. et al

Prehosp Disaster Med. 2019 Oct 25:1-9.

In cases of mass-casualty incidents (MCIs), triage represents a fundamental tool for the management of and assistance to the wounded, which helps discriminate not only the priority of attention, but also the priority of referral to the most suitable center. The objective of this study was to evaluate the capacity of different prehospital triage systems based on physiological parameters (Shock Index [SI], Glasgow-Age-Pressure Score [GAP], Revised Trauma Score [RTS], and National Early Warning Score 2 [NEWS2]) to predict early mortality (within 48 hours) from the index event for use in MCIs. Prehospital scores of the NEWS2 are

Adult sepsis

Predicting Prolonged Intensive Care Unit Stay Among Patients With Sepsis-Induced Hypotension

Murphy, D. L. et al

Am J Crit Care. 2019 Nov;28(6):e1-e7.

Sepsis risk stratification tools typically predict mortality, although stays in the intensive care unit (ICU) of 24 hours or longer may be more clinically relevant for emergency department disposition. We explore predictors of ICU stay of 24 hours or longer among infected, hypotensive emergency department patients. These exploratory results show that heart failure, bicarbonate level of less than 20 mEq/L, tachypnea, or creatinine level greater than 2.0 mg/dL increases the likelihood of an ICU stay of 24 hours or longer among infected, hypotensive emergency department patients.

easy to obtain and represent a reliable test, which make it an ideal system to help in the initial assessment of high-risk patients, and to determine their level of triage effectively and efficiently. The Prehospital Emergency Medical System (PhEMS) should evaluate the inclusion of the NEWS2 as a triage system, which is especially useful for the second triage (evacuation priority).

Predicting need for intensive care unit admission in adult emphysematous pyelonephritis patients at emergency departments: comparison of five scoring systems.

Yap X.H. et al

Sci Rep. 2019 Nov 12;9(1):16618.

This study assesses the performance of National Early Warning Score (NEWS), Quick Sepsis-related Organ Failure Assessment (qSOFA), Modified Early Warning Score (MEWS), Rapid Emergency Medicine Score (REMS), and Rapid Acute Physiology Score (RAPS) in predicting emphysematous pyelonephritis (EPN) patients' need for intensive care unit (ICU) admission. A retrospective analysis was conducted at four training and research hospitals' emergency departments (EDs) on all EPN adult patients from January 2007 to August 2017. In this multicentre ED EPN series, we recommend using NEWS in early identification of critical EPN patients and advance planning for ICU admission. This would reduce delays in ICU transfer and ultimately improve patient outcomes.

Accuracy and interobserver-agreement of respiratory rate measurements by healthcare professionals, and its effect on the outcomes of clinical prediction/diagnostic rules.

Latten G.H.P. et al

PLoS One. 2019 Oct 3;14(10):e0223155.

In clinical prediction/diagnostic rules aimed at early detection of critically ill patients, the respiratory rate plays an important role. We investigated the accuracy and interobserver-agreement of respiratory rate measurements by healthcare professionals, and the potential effect of incorrect measurements on the scores of 4 common clinical prediction/diagnostic rules: Systemic Inflammatory Response Syndrome (SIRS) criteria, quick Sepsis-related Organ Failure Assessment (qSOFA), National Early Warning Score (NEWS), and Modified Early Warning Score (MEWS). The accuracy and interobserver-agreement of respiratory rate measurements by healthcare professionals are

Effects of Sepsis on Morbidity and Mortality in Critically III Patients 2 Years After Intensive Care Unit Discharge

Biason, L. et al

Am J Crit Care. 2019 Nov;28(6):424-432. Morbidity and mortality after discharge from an intensive care unit appear to be higher in patients with sepsis than in patients without sepsis. We evaluate

sepsis than in patients without sepsis. We evaluate morbidity and mortality in patients with and without sepsis within 2 years after intensive care unit discharge. Compared with patients without sepsis, those with sepsis have higher mortality in the intensive care unit and have more pain, hospital readmissions, and functional decline within 2 years after discharge.

DAMPs and NETs in Sepsis

Denning, N-L et al.

Front Immunol. 2019; 10: 2536.

Sepsis is a deadly inflammatory syndrome caused by an exaggerated immune response to infection. Much has been focused on host response to pathogens mediated through the interaction of pathogenassociated molecular patterns (PAMPs) and pattern recognition receptors (PRRs). PRRs are also activated by host nuclear, mitochondrial, and cytosolic proteins, known as damage-associated molecular patterns (DAMPs) that are released from cells during sepsis. Some well described members of the DAMP family are extracellular cold-inducible RNA-binding protein (eCIRP), high mobility group box 1 (HMGB1), histones, and adenosine triphosphate (ATP). DAMPs are released from the cell through inflammasome activation or passively following cell death. Similarly, neutrophil extracellular traps (NETs) are released from neutrophils during inflammation. NETs are webs of extracellular DNA decorated with histones, myeloperoxidase, and elastase. Although NETs contribute to pathogen clearance, excessive NET formation promotes inflammation and tissue damage in sepsis. Here, we review DAMPs and NETs and their crosstalk in sepsis with respect to their sources, activation, release, and function. A clear grasp of DAMPs, NETs and their interaction is crucial for the understanding of the pathophysiology of sepsis and for the development of novel sepsis therapeutics.

Epidemiology of intra-abdominal infection and sepsis in critically ill patients: "AbSeS", a multinational observational cohort study and ESICM Trials Group Project

suboptimal. This leads to both over- and underestimation of scores of four clinical prediction/diagnostic rules. The clinically most important effect could be a delay in diagnosis and treatment of (critically) ill patients.

<u>Biomarkers and clinical scores to identify patient</u> <u>populations at risk of delayed antibiotic administration</u> or intensive care admission.

Gonzalez Del Castillo J. et al Crit Care. 2019 Oct 29;23(1):335.

The performance of blood biomarkers (mid-regional proadrenomedullin (MR-proADM), procalcitonin (PCT), C-reactive protein (CRP), and lactate) and clinical scores (Sequential Organ Failure Assessment (SOFA), National Early Warning Score (NEWS), and quick SOFA) was compared to identify patient populations at risk of delayed treatment initiation and disease progression after presenting to the emergency department (ED) with a suspected infection. Patients with low severity signs of infection but high MR-proADM concentrations had an increased likelihood of subsequent disease progression, delayed antibiotic administration or ICU admission. Appropriate triage decisions and the rapid use of antibiotics in patients with high MR-proADM concentrations may constitute initial steps in escalating or intensifying early treatment strategies.

Neonatal, paediatric and maternal sepsis

<u>Sepsis: Precision-Based Medicine for Pregnancy and the Puerperium</u>

Greer, O et al

Int J Mol Sci. 2019 Oct 29;20(21). pii: E5388. Sepsis contributes significantly to global morbidity and mortality, particularly in vulnerable populations. Pregnant and recently pregnant women are particularly prone to rapid progression to sepsis and septic shock, with 11% of maternal deaths worldwide being attributed to sepsis. The impact on the neonate is considerable, with 1 million neonatal deaths annually attributed to maternal infection or sepsis. Pregnancy specific physiological and immunological adaptations are likely to contribute to a greater impact of infection, but current approaches to the management of sepsis are based on those developed for the non-pregnant population. Pregnancy-specific strategies are required to optimise recognition and management of these patients. We review current knowledge of the physiology and immunology of pregnancy and propose

Blot, S. et al

Intensive Care Med. 2019 Oct 29.

We describe the epidemiology of intra-abdominal infection in an international cohort of ICU patients according to a new system that classifies cases according to setting of infection acquisition (community-acquired, early onset hospital-acquired, and late-onset hospital-acquired), anatomical disruption (absent or present with localized or diffuse peritonitis), and severity of disease expression (infection, sepsis, and septic shock). This multinational, heterogeneous cohort of ICU patients with intraabdominal infection revealed that setting of infection acquisition, anatomical disruption, and severity of disease expression are disease-specific phenotypic characteristics associated with outcome, irrespective of the type of infection. Antimicrobial resistance is equally common in community-acquired as in hospitalacquired infection.

Comparison between the body mass index and the Controlling Nutritional status to determine the severity in patients with abdominal sepsis

Godinez-Vidal AR et al

Cir Cir. 2019;87(6):605-610.

The systemic response of the organism, in defense against the aggressor agent, generates acute catabolic response, which leads to deterioration of the nutritional status. We compare the usefulness of the body mass index (BMI) and the CONUT scale to determine the severity in abdominal sepsis. The level of malnutrition determined by CONUT is related to the severity determined by APACHE II, SOFA and mortality. BMI is not related to severity by APACHE II or mortality; although it does seem to relate to the severity evaluated by the SOFA scale.

<u>Process Mining of Incoming Patients with Sepsis.</u> Hendricks RM.

Online J Public Health Inform. 2019 Sep 19;11(2):e14. Data mining is a technique for analyzing large amounts of data, in various formats, often called Big Data, in order to gain knowledge about it. The healthcare industry is the next Big Data area of interest as its large variability in patients, their health status and their records which can include image scans, graphical test results, and hand-written physician notes, has been untapped for analysis. In addition to data mining, there is a newer analysis method called process mining. Process mining is similar to data mining in that

areas of research, which may advance the development of pregnancy-specific diagnostic and therapeutic approaches to optimise the care of pregnant women and their babies.

<u>Development of the FAST-M maternal sepsis care</u> <u>bundle for use in low resource settings: a modified</u> <u>Delphi process</u>

Lissauer D. et al BJOG. 2019 Nov 2.

We develop a sepsis care bundle for the initial management of maternal sepsis in low resource settings. A clinically relevant maternal sepsis care bundle for low resource settings has been developed by international consensus. Consensus was reached after three consultation rounds, with the same items deemed most important and feasible by both the healthcare practitioners and expert panel. Final bundle items selected were: i) Fluids, ii) Antibiotics, iii) Source identification and control, iv) Transfer (to appropriate higher-level care) and v) Monitoring (of both mother and neonate as appropriate). The bundle was given the acronym "FAST-M".

<u>Serum Biomarkers for the Early Detection of the Early-Onset Neonatal Sepsis: A Single-Center Prospective Study.</u>

Ahmed AM et al

Adv Neonatal Care. 2019 Oct;19(5):E26-E32
Reducing the hazards of the early-onset neonatal sepsis (EONS) is a priority justifying the further investigation for potential biomarkers for its early diagnosis.
Presepsin was the most accurate biomarker followed by procalcitonin, IL-8, and IL-6 regarding the early diagnosis and management of EONS. The combination between these biomarkers is highly recommended.
Further studies are needed to investigate the diagnostic ability of the combination of these biomarkers.

Early recognition of pediatric sepsis simulation checklist - An exploratory study.

Diaz DA et al

J Pediatr Nurs. 2019 Oct 29;50:25-30.

We aim to report on the modification and exploration of a 21-item Early Detection of Pediatric Sepsis Assessment Checklist aimed at improving nursing students' recognition of key factors that contribute to early detection of sepsis in pediatric patients through clinical simulation. Two factors emerged from the

large data files are reviewed and analyzed, but in this case, event logs specific to a particular process or series of processes, are analyzed. Process mining allows one to understand the initial baseline, determine any bottlenecks or resource constraints, and evaluate a recently implemented change. Process mining was conducted on a hospital event log of patients entering the emergency room with sepsis, to better understand this newer analysis method, to highlight the information discovered, and to determine its role with data mining. Not only did the analysis of the event logs provide process mapping and process analysis, but it also highlighted areas in the clinical operations in need of further investigation, including a possible relationship with patient re-admission and their release method. In addition, the data mining method of creating a histogram, of the process data, was applied, allowing data mining and process mining to be utilized complimentary.

Influencing outcomes with automated time zero for sepsis through statistical validation and process improvement

Colorafi KJ et al

Mhealth. 2019 Sep 17;5:36.

Sepsis is a life threating complication of infection acquired by more than 1.5 million people in the United State annually. Each year, sepsis claims the lives of at least 250,000 people. Real-time, automated surveillance for sepsis among hospitalized patients is of critical importance, given that one in three people who die in hospitals have sepsis. The early identification and treatment of sepsis is associated with reduced mortality and costly intensive care bed days. The objective of this analysis was to improve the performance of an electronic medical record based sepsis algorithm (early identification) and improve evidence based bundle compliance (early intervention) with the addition of a real-time, automated time zero calculation. The addition of a real-time, automated sepsis time zero calculation improved the performance and timeliness of a predictive sepsis alert provided through a system developed mobile application for clinicians and administrators.

<u>Sepsis induced cardiomyopathy: Pathophysiology and use of mechanical circulatory support for refractory shock</u>

Nabzdyk CS et al

J Crit Care. 2019 Sep 12;54:228-234.

analysis which is key to improving the early detection of pediatric sepsis. Assessment, factor one, accounted for the nursing students' central skills of recognizing baseline vital signs and timely medication administration. Deterioration, factor two, contained items reflecting the recognition of changes from baseline that require action. Conceptually, these factors reflect the most central points in the early detection of signs in pediatric patients at risk for sepsis. This checklist forms a valuable tool to assess the knowledge of pre-licensure students and may possibly be extended as a tool to assess the clinical readiness and performance of new graduates through the safety and supervision allotted by simulation.

<u>Late-Onset Sepsis as a Risk Factor for</u>
<u>Bronchopulmonary Dysplasia in Extremely Low Birth</u>
<u>Weight Infants: A Nationwide Cohort Study</u>
Jung, E. et al

Sci Rep. 2019 Oct 29;9(1):15448.

This study aimed to determine the effect of late-onset sepsis (LOS) on the development of bronchopulmonary dysplasia (BPD) in extremely low birth weight (ELBW) infants. The impact of multiple episodes of LOS on BPD was prominent in infants who received mechanical ventilation for two weeks or less. The estimated odds ratios for BPD and severe BPD were greater with fungal LOS than with bacterial LOS. In conclusion, LOS, particularly complicated by multiple episodes and/or fungi, was a risk factor for BPD in ELBW infants.

<u>Cumulative evidence for association of sepsis and</u> retinopathy of prematurity

Huang J et al

Medicine (Baltimore). 2019 Oct;98(42):e17512. Retinopathy of prematurity (ROP) is a retinal vasoproliferative disease affected by multiple factors such as infection and preterm birth. The role of sepsis in the development of ROP remains controversial. This systematic review and meta-analysis aimed to identify the impact of sepsis on ROP. Sepsis increased the risk of any stage ROP, especially for the severe ROP. Further high-quality clinical studies are needed to eliminate heterogeneity and publication bias to validate these findings.

Thromboelastography Variables, Immune Markers, and Endothelial Factors Associated With Shock and NPMODS in Children With Severe Sepsis

Saini A et al

Sepsis remains a major cause of morbidity and mortality, and sepsis-induced cardiomyopathy (SCM) has been recognized as a relevant complication. In this article, the pathophysiology of SCM and the literature regarding the clinical care with a focus on the use of mechanical circulatory support for the rescue of patients with severe SCM are reviewed. Lastly, a pragmatic approach to the care of this complex patient population is provided using a representative case example.

Presepsin versus other biomarkers to predict sepsis and septic shock in patients with infection defined by Sepsis-3 criteria: the PREDI study of diagnostic accuracy

Contenti J et al

Emergencias. 2019 Oct;31(5):311-317.

An accurate diagnosis of sepsis in the emergency department must be made before appropriate treatment can be started. Many biomarkers that are potentially useful have been studied. The main aim of this study was to compare the diagnostic accuracy of blood levels of presepsin, lactate, C-reactive protein (CRP), and procalcitonin (PCT) for predicting sepsis as defined by the Sepsis-3 criteria. The secondary aim was to evaluate the diagnostic accuracy of these biomarkers for predicting bacteremia whether or not sepsis or septic shock was present. Presepsin and PCT seem to be the best predictors of a diagnosis of sepsis or septic shock in emergency department patients.

Clinical characteristics, risk factors, immune status and prognosis of secondary infection of sepsis: a retrospective observational study

Chen Y et al

BMC Anesthesiol. 2019 Oct 18;19(1):185.

Secondary infection has a higher incidence in septic patients and affects clinical outcomes. This study aims to investigate the clinical characteristics, risk factors, immune status and prognosis of secondary infection of sepsis. Urinary and deep venous catheterization increased the risk of secondary infection, in which underlying immunosuppression might also play a role. Secondary infection affected the prognosis of septic patients and prolonged in-hospital length of stay.

Front Pediatr. 2019 Oct 18;7:422.

Evaluate hemostatic dysfunction in pediatric severe sepsis by thromboelastography (TEG) and determine if TEG parameters are associated with new or progressive multiple organ dysfunction syndrome (NPMODS) or shock, defined as a lactate ≥2mmol/L. We explored the relationship between TEG variables, selective cytokines, and endothelial factors. This exploratory analysis of hemostasis dysfunction on TEG in pediatric severe sepsis suggests that while hypercoagulability is more common, a hypocoagulable state is associated with shock and NPMODS. In addition, TEG abnormalities are also associated with immune and endothelial factors. A larger cohort study is needed to validate these findings.

Antibiotic Treatment of Suspected and Confirmed Neonatal Sepsis Within 28 Days of Birth: A Retrospective Analysis

Wagstaff JS et al

Front Pharmacol. 2019 Oct 15;10:1191.

Neonatal sepsis causes significant mortality and morbidity worldwide. Diagnosis is usually confirmed via blood culture results. Blood culture sepsis confirmation can take days and suffer from contamination and false negatives. Empiric therapy with antibiotics is common. This study aims to retrospectively describe and compare treatments of blood culture-confirmed and unconfirmed, but suspected, sepsis within the University of Utah Hospital system. The results may not be generalized to all hospitals and the use of cefotaxime may be a surrogate for other factors. Given the low rate of blood culture positive diagnosis and the high exposure rate of empiric antibiotics, this patient population might benefit from improved diagnostics with reevaluation of antibiotic use guidelines.

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