Due to the (un)availability of new material and staff time, I shall be changing the frequency of the Sepsis Bulletin from fortnightly to monthly. This should improve the quality of the bulletin – as ever let me know if you would like to see specific topics covered in the bulletin.

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 September 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 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

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SEPSIS BULLETIN
August 2019

Neonatal, paediatric and maternal sepsis

Challenges and opportunities for antibiotic stewardship among preterm infants

Mukhopadhyay S, et al

Arch Dis Child Fetal Neonatal Ed. 2019 May;104(3):F327-F332.

Antibiotic stewardship programmes aim to optimise antimicrobial use to prevent the emergence of resistance species and protect patients from the side effects of unnecessary medication. The high incidence of systemic infection and associated mortality from these infections leads neonatal providers to frequently initiate antibiotic therapy and make empiric antibiotic courses one of the main contributors of antibiotic use in the neonatal units. Yet, premature infants are also at risk for acute life-threatening complications associated

Adult sepsis (cont.)

Association between state-mandated protocolized sepsis care and in-hospital mortality among adults with sepsis

Kahn JM, et al.

JAMA. doi:10.1001/jama.2019.9021

Beginning in 2013, New York State implemented regulations mandating that hospitals implement evidence-based protocols for sepsis management, as well as report data on protocol adherence and clinical outcomes to the state government. The association between these mandates and sepsis outcomes is unknown. The study evaluates the association between New York State sepsis regulations and the outcomes of patients hospitalized with sepsis. In New York State, mandated protocolized sepsis care was

with antibiotic use such as necrotising enterocolitis and for long-term morbidities such as asthma. In this review, we discuss specific aspects of antibiotic use in the very low birthweight preterm infants, with a focus on empiric use, that provide opportunities for stewardship practice. We discuss strategies to risk-stratify antibiotic initiation for the risk of early-onset sepsis, optimise empiric therapy duration and antibiotic choice in late-onset sepsis, and standardise decisions for stopping empiric therapy. Lastly, review the evolving role of biomarkers in antibiotic stewardship.

The combination of procalcitonin and C-reactive protein or presepsin alone improves the accuracy of diagnosis of neonatal sepsis: a meta-analysis and systematic review.
Ruan L, et al
Crit Care. 2018 Nov 21;22(1):316
Sepsis is an important cause of neonatal morbidity and mortality; therefore, the early diagnosis of neonatal sepsis is essential. ur aim was to compare the diagnostic accuracy of procalcitonin (PCT), C-reactive protein (CRP), procalcitonin combined with C-reactive protein (PCT + CRP) and presepsin in the diagnosis of neonatal sepsis. The combination of PCT and CRP or presepsin alone improves the accuracy of diagnosis of neonatal sepsis. However, further studies are required to confirm these findings.

Antimicrobial Stewardship in the Neonatal Intensive Care Unit: An Update
Gkentzi D, Dimitriou G.
Curr Pediatr Rev. 2019;15(1):47-52.
Neonates represent a vulnerable population for infections and neonatal sepsis is a major cause of mortality and morbidity worldwide. Therefore, antimicrobials are the most commonly prescribed drugs in the Neonatal Intensive Care Unit Setting but unfortunately are quite often used inappropriately with various short and long-term effects. The rational use of antimicrobials is of paramount importance in this population and structured antimicrobial stewardship interventions should be in place. These interventions are slightly different from those used in adults and older children due to the particularities of the neonatal medicine. The aim of this review is to provide an update in the field and identify areas for further consideration and future research.

Evaluating Newborns at Risk for Early-Onset Sepsis.

associated with a greater decrease in sepsis mortality compared with sepsis mortality in control states that did not implement sepsis regulations. Because baseline mortality rates differed between New York and comparison states, it is uncertain whether these findings are generalizable to other states.

Epidemiology and Changes in Mortality of Sepsis After the Implementation of Surviving Sepsis Campaign Guidelines
Herrán-Monge, R. et al
Journal of Intensive Care Medicine, September 2019, Vol.34(9), pp.740-750
We set out to determine the epidemiology and outcome of severe sepsis and septic shock after 9 years of the implementation of the Surviving Sepsis Campaign (SSC) and to build a mortality prediction model. Although the incidence of sepsis/septic shock remained unchanged during a 10-year period, the implementation of the SSC guidelines resulted in a marked decrease in the overall mortality. The lower severity of patients on ICU admission and the reduced early mortality suggest an improvement in early diagnosis, better initial management, and earlier antibiotic treatment.

Does Early Follow-Up Improve the Outcomes of Sepsis Survivors Discharged to Home Health Care?
Deb, P. et al.
Medical care, August 2019, Vol.57(8), pp.633-640
There is little evidence to guide the care of over a million sepsis survivors following hospital discharge despite high rates of hospital readmission. We examined whether early home health nursing (first visit within 2 days of hospital discharge and at least 1 additional visit in the first posthospital week) and early physician follow-up (an outpatient visit in the first posthospital week) reduce 30-day readmissions among Medicare sepsis survivors. Our findings suggest that, together, early postdischarge care by home health and medical providers can reduce hospital readmissions for sepsis survivors.

Non-utility of sepsis scores for identifying infection in surgical intensive care unit patients
Krebs, E.D. et al
American journal of surgery, August 2019, Vol.218(2), pp.243-247
The Sequential Organ Failure Assessment (SOFA) and quick SOFA (qSOFA) have replaced the Systemic

Good PI, Hooven TA.
Pediatr Clin North Am. 2019 Apr;66(2):321-331
Early-onset sepsis (EOS) is an important cause of neonatal morbidity. Despite extensive study, identifying at-risk newborns remains challenging, especially if they are initially well appearing. Existing official EOS recommendations suggest a conservative approach that likely results in overtreatment of a low-risk population. Recent studies indicate that more precise risk assessment and alternative management strategies could decrease the number of infants exposed to blood draws and antibiotics during evaluations for EOS. This article reviews existing guidelines and provides an overview of the Bayesian sepsis calculator and serial observation as an alternative to laboratory studies and empirical antibiotics.

Unusual presentation of late-onset disseminated staphylococcal sepsis in a preterm infant.
Khattak SG, Dady I, Mukherjee D.
BMJ Case Rep. 2019 Mar 15;12(3).
An ex-30-week gestation, preterm male baby was admitted to a tertiary neonatal unit and noted to have increased ventilator requirements and diagnosed with sepsis. The baby also developed an abscess over the left elbow and over the xiphisternum along with a decrease in movement of the left hand and the right leg. Panton-Valentine leukocidin (PVL)-producing Staphylococcus aureus (SA) was isolated from the blood culture. A whole body MRI showed disseminated abscess with multiple foci in the lung, left elbow and over the xiphisternum. Disseminated sepsis with multiple septic foci has not been previously reported in neonates. We would like to highlight the fact that sepsis due to PVL toxin-producing SA can cause significant morbidity and mortality in neonates. Proper screening should be done to rule out septic foci in neonates. MRI is a good non-invasive investigation to document septic foci in a neonate and rule out multiorgan involvement.

Accuracy of presepsin in neonatal sepsis: systematic review and meta-analysis
Parri, N. et al.
Expert Review Of Anti-Infective Therapy. Volume 17:Issue 4 (2019); pp 223-232
Neonatal sepsis represents a major cause of morbidity and mortality in neonates. No diagnostic test has been demonstrated to be sufficiently accurate to confirm or

Inflammatory Response System (SIRS) criteria for sepsis, however are not well investigated in surgical populations or for identifying infections, as they are often used in practice. In this study, neither daily SOFA, qSOFA, nor SIRS criteria correlated with new infection in a population of critically ill surgical patients. Scores were globally elevated in non-infected patients, potentially related to high levels of existing inflammation in this population.

Sepsis-related Organ Failure Assessment Score is a strong predictor of survival in acute-on-chronic liver failure
Cold, F. et al
Danish medical journal, August 2019, Vol.66(8)
The mortality of patients with an exacer-bation of decompensated liver cirrhosis is high even if treated in the intensive care unit (ICU), and the criteria for referral to ICU are not well defined. The objective of this study was to identify variables associated with mortality. The mortality was high in these severely ill patients, even when they received optimum supportive therapy in the ICU. The finding that the SOFA score and age best predicted mortality shows that the increased mortality was caused mainly by insufficiency of organs other than the liver.

Clinical trial design for unmet clinical needs: a spotlight on sepsis
Vincent, Jean-Louis ; Sakr, Yasser
Expert review of clinical pharmacology, 22 July 2019, pp.1-8
Despite considerable advances in our understanding of how sepsis develops and multiple clinical trials of potential therapies, no new pharmacologic agent has been consistently shown to improve survival. We reviewed relevant publications identified through PubMed and from the authors' knowledge of this field. We discuss the main reasons why clinical trials on new therapeutic interventions have failed in the past, including heterogeneity of study populations and choice of outcome measures. We discuss how changes in study design and in patient selection could help improve identification of effective agents in the future. The search for new sepsis therapies must continue but lessons must be learned from previous clinical trials so that the same mistakes are not repeated. Rather than grouping all patients with sepsis together, we should study only those most likely to benefit from the intervention. Better characterization of patients will be

exclude neonatal sepsis. This study aimed to evaluate the diagnostic accuracy of presepsin (P-SEP) for neonatal sepsis. Diagnostic accuracy of P-SEP resulted high in detecting neonatal sepsis. Even though it cannot be recommended as a single diagnostic test, P-SEP could be a helpful and valuable biomarker in neonates with suspected sepsis.

Immunologic biomarkers for diagnostic of early-onset neonatal sepsis
Memar, M.Y. et al.
The Journal Of Maternal-Fetal & Neonatal Medicine. Volume 32:Number 1 (2019); pp 143-153
Accurate identification of early onset neonatal sepsis (EOS) is challenging. Blood culture has been considered as a gold standard method but the identification of EOS is intricate by a high false-negative results. This review provides an overview of biomarkers as indicators for the diagnosis of EOS. There is an affluence of studies appraising diagnostic indicators in the identification of EOS. Acute-phase reactants, cytokines, and cell surface antigens have been investigated as indicators for EOS, but none of them are presently in routine clinical setting. Despite the promising data for some immunologic biomarkers, present evidence shows that none of them can constantly diagnose 100% of infections. IL-6 is the most potent marker for evaluation of EOS prognosis. Procalciton (PCT) and C-reactive protein (CRP) are appropriate indicators for the detection and monitoring of antibiotics therapy. A panel of sepsis biomarkers along with presently routine tests will make easy earlier identification, appropriate management, and improved outcome may be more efficient than single indicator.

Efficacy and safety of applying a neonatal early-onset sepsis risk calculator in China
He, Yi ; et al
Journal of paediatrics and child health, 22 July 2019
Aim was to evaluate and compare the performance of the early-onset sepsis (EOS) risk calculator with procalcitonin (PCT), complete blood count (CBC) and C-reactive protein (CRP) for predicting neonatal EOS. In this pilot study, applying the EOS calculator in China, the EOS risk calculator and PCT showed good predictive value compared to CBC and CRP. Risk scores from the EOS risk calculator strongly correlated with EOS, and the EOS risk calculator offered increased predictive value when used in combination with blood biomarkers.

facilitated using modern 'omics technology and analysis of the increasingly large quantities of clinical data available, enabling more personalized patient selection for trial inclusion. New clinical trial design and inclusion of other endpoints in addition to mortality will also aid our search for the elusive positive clinical trial and effective interventions for sepsis.

Neutrophil activation in septic acute kidney injury: A post-hoc analysis of the FINNAKI study
Törnblom, S. et al
Acta anaesthesiologica Scandinavica, 20 July 2019
Inflammation, reflected by high plasma interleukin-6 concentration, is associated with acute kidney injury (AKI) in septic patients. Neutrophil activation has pathophysiological significance in experimental septic AKI. We hypothesized that neutrophil activation is associated with AKI in critically ill sepsis patients. Interleukin-8 in plasma and urine was associated with septic AKI. Elevated plasma activin A indicates intravascular neutrophil activation in septic AKI. Concomitant plasma and urine myeloperoxidase measurements suggest neutrophil accumulation into injured kidneys.

Non-antibiotic therapies for sepsis: an update
Vincent, Jean-Louis; Mongkolpun, Wasineenart
Expert Review Of Anti-Infective Therapy. Volume 17:Issue 3 (2019); pp 169-175
Sepsis, defined as infection plus some degree of organ dysfunction, is still associated with high mortality and morbidity rates. Management focuses on three key areas: infection control, hemodynamic stabilization and organ support, and modulation of the sepsis response. Hemodynamic stabilization essentially involves the use of adequate fluid resuscitation and vasopressors. Fluid and vasopressor choices and targets are discussed, and the need to adapt these to the individual patient is stressed. No drugs are currently available that modulate the sepsis response, with the possible exception of corticosteroids in the most severe cases. The place of vasopressin is not well defined. Some of the immunomodulatory agents currently in development are briefly discussed. Management of the patient with sepsis remains a challenge and needs to be personalized. The search for new immunomodulatory drugs continues and will be facilitated by better characterization of patients using modern 'omics' technology and complex analysis of

Strategic Trials to Define the Best Available Treatment for Neonatal and Pediatric Sepsis Caused by Carbapenem-resistant Organisms
Donà, D. et al
The Pediatric infectious disease journal, August 2019, Vol.38(8), pp.825-827
The optimal standard of care for carbapenem-resistant bloodstream infections in children is currently unknown. This systematic review, aiming to define the best available treatments to be compared with new antibiotics in clinical trials, clearly points out the paucity of available data. The simplification and a wider harmonization of study design are a global priority to inform the best strategies to treat these life-threatening infections in children.

Strategies for preventing early-onset sepsis and for managing neonates at-risk: wide variability across six Western countries
Berardi, A. et al.
The journal of maternal-fetal & neonatal medicine
September 2019, Vol.32(18), pp.3102-3108
Group B streptococcus (GBS) early-onset sepsis (EOS) has declined after widespread intrapartum antibiotic prophylaxis. However, strategies for preventing EOS may differ across countries. The analysis of their strategies allows to compare the effectiveness of prevention in different countries and suggests opportunities for improvement. Wide variations exists in preventing EOS. They depend on national epidemiology of GBS infections, compliance, cost, and feasibility of the strategy. The extreme variability of approaches for managing neonates at risk for EOS reflects the even greater uncertainty regarding this issue, and may explain the persisting, great use of resources to prevent a disease that has become very rare nowadays.

Adult sepsis
The Comparative Epidemiology of Pediatric Severe Sepsis
Hartman, M.E. et al
Journal Of Intensive Care Medicine. Volume 34:Number 6 (2019); pp 472-479
To determine whether the coding strategies used to identify severe sepsis in administrative data sets could identify cases with comparable case mix, hospitalization characteristics, and outcomes as a the large quantities of clinical data increasingly available.

Point of care technologies for sepsis diagnosis and treatment
Oeschger, T. et al
Lab On A Chip. Volume 19:Issue 5 (2019); pp 728-737
Sepsis is a rapidly progressing, life threatening immune response triggered by infection that affects millions worldwide each year. Current clinical diagnosis relies on broad physiological parameters and time consuming lab-based cell culture. If proper treatment is not provided, cases of sepsis can drastically increase in severity over the course of a few hours. Development of new point of care tools for sepsis has the potential to improve diagnostic speed and accuracy, leading to prompt administration of appropriate therapeutics, thereby reducing healthcare costs and improving patient outcomes. In this review we examine developing and commercially available technologies to assess the feasibility of rapid, accurate sepsis diagnosis, with emphasis on point of care.

Sepsis in 2018: a review
Wentowski, C. et al
Anaesthesia And Intensive Care Medicine. Volume 20:Issue 1 (2019); pp 6-13
Sepsis is responsible for tremendous morbidity, mortality and healthcare expenditure worldwide. Recently, the conceptualization of sepsis has shifted away from one based upon the inflammatory response to infection to one based upon a dysregulated immune response and resulting organ dysfunction. Revised definitions of sepsis and septic shock have been proposed in order to improve the specificity of the diagnostic criteria and to provide tools to facilitate accurate and timely (i.e. early) diagnoses at the bedside. The crux of sepsis management remains early identification and diagnostic testing, early antimicrobial therapy, and early haemodynamic resuscitation. The most recent guidelines recommend that first steps in this process should take place within 1 hour from when sepsis is suspected. Additional important new elements in the most recent sepsis management guidelines include the use of dynamic parameters to assess fluid responsiveness, a conservative fluid strategy following initial resuscitation (with ‘de-resuscitation’ when possible), serial re-assessments of haemodynamic status, and adaptable treatment plans. This article provides a

cohort of children diagnosed with severe sepsis using strict clinical criteria. The ICD-9-CM codes for "severe sepsis" and "septic shock" identify smaller but higher acuity cohorts of patients that more closely resemble the children enrolled in the largest clinical trial of pediatric severe sepsis to date.

Death due to sepsis in patients diagnosed with prostate cancer
Alanee, S. et al
The Prostate. Volume 79:Issue 3 (2019); pp 295-301
To examine the prevalence and determinants of death due to sepsis in patients diagnosed with prostate cancer (Pca), we performed a retrospective analysis of 910 986 patients diagnosed with Pca between 1992 and 2010 identified from the Surveillance, Epidemiology, and End Results (SEER) database.. Patients diagnosed with Pca are at increased risk of dying from sepsis, and the sepsis-related IBMR in these patients is increasing over time. There are significant disparities in the outcome of sepsis among Pca patients that require further research.

summary of the most recent clinical evidence and professional guidelines for the diagnosis and treatment of the sepsis in the critical care setting.

Antimicrobial resistance local data in sepsis
Ginting, F.; et al
International Journal Of Infectious Diseases Volume 79 (2019) Supplement 1; pp 53-
Antimicrobial resistance (AMR) is one of the life-threatening world problems which should be noticed and controlled seriously. One of the major causes of the increasing AMR is the inappropriate use of antimicrobial where antimicrobial choices should be based on local data pattern to select the proper antibiotic. Sepsis causes high mortality and needs appropriate antibiotic while antimicrobial treatment should be started as soon as sepsis is suspected to prevent the development of further complications and progression. The aim of the study is to find the AMR prevalence, the causal bacteria in sepsis adult can be used as antibiotic guidelines for sepsis. AMR in sepsis patients is very high in Indonesia. It needs local data as guidelines for empirical treatment that can reduce the inappropriate use of antibiotic in an effort to control the AMR from spreading and increasing.