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 14 March 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.

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SEPSIS BULLETIN **28 February 2019**

Neonatal, paediatric and maternal sepsis

Neonatal sepsis due to glycopeptide resistant from colonized maternal gut-rare case evidence

Subramanya, S.H. et al

Antimicrobial resistance and infection control, 2019, Vol.8, pp.29

Vancomycin-resistant enterococcal infections in the neonatal ICU are growing global problems. We report a case of neonatal septicemia by multidrug-resistant vancomycin-resistant Enterococcus faecium (VRE), the source of infection being the mother's gut. Isolation of MDR-VRE from the blood culture of the baby and stool specimens of the mother and the baby with the same antibiogram profile and clonal similarities reveals that maternal gut colonization was responsible for neonatal sepsis. Optimal infection control measures and the development of guidelines for monitoring VRE colonization in pregnant women might be useful in reducing the occurrence of neonatal sepsis.

Evidence of Endotypes in Pediatric Acute Hypoxemic Respiratory Failure Caused by Sepsis

Yehya, N. et al

Adult sepsis (cont.)

The impact of dementia on hospital outcomes for elderly patients with sepsis: A population-based study Bouza, C. et al.

PloS One 2019, 14 (2): e0212196

Prior studies have suggested that dementia adversely influences clinical outcomes and increases resource utilization in patients hospitalized for acute diseases. However, there is limited population-data information on the impact of dementia among elderly hospitalized patients with sepsis. This nationwide population-based study shows that dementia is present in a substantial proportion of adults ≥65s hospitalized with sepsis, and while the condition does seem to come with a lower risk of organ dysfunction, it exerts a negative influence on in-hospital mortality and acts as an independent mortality predictor. Furthermore, it is significantly associated with shorter length of stay and lower hospital costs.

Platelet-to-lymphocyte ratio as a prognostic predictor of mortality for sepsis: interaction effect with disease severity-a retrospective study

Pediatric critical care medicine: a journal of the Society of Critical Care Medicine and the World **Federation of Pediatric Intensive and Critical Care Societies**, 1 February 2019, Vol.20(2), pp.110-112 Subclassification based on clinical or biologic commonalities (endotypes) is one approach to reduce heterogeneity in acute hypoxemic respiratory failure. In adults, biomarker-defined endotypes of respiratory failure have been described, with differential outcome profiles and response to therapy. To date, no studies have tested whether endotypes exist in pediatric acute hypoxemic respiratory failure, although messenger RNA expression-based endotypes have been described in pediatric sepsis. The aim of the present study was to test whether endotypes identified in pediatric sepsis are applicable to pediatric acute hypoxemic respiratory failure. Applying a previously reported endotyping strategy in children with septic shock identified endotypes of pediatric acute hypoxemic respiratory failure secondary to sepsis, with differential risk for poor outcomes. To our knowledge, this is the first demonstration of endotypes in pediatric respiratory failure. Our results support an investigation into using transcriptomics to identify messenger RNA-based endotypes in a dedicated, well-defined acute hypoxemic respiratory failure cohort.

Changing trend of microbiologic profile and antibiotic susceptibility of the microorganisms isolated in the neonatal nosocomial sepsis: a 14 years analysis Mutlu, M. et al.

The Journal of Maternal-Fetal & Neonatal Medicine, 12 February 2019, p.1-181

Neonatal sepsis , especially nosocomial sepsis (NS) is one of the main causes of mortality and morbidity in neonates. Our aim was to investigate microorganisms responsible of NS and antimicrobial susceptibility patterns and to compare them in the different period. Our result showed that multiresistant microorganisms, especially oxacillin-resistant staphylococci and gramnegative bacilli resistant to cephalosporin have an increasing rate. Every unit should be evaluated the causative agents and antimicrobial susceptibilities in order to select an appropriate regime for nosocomial sepsis. Periodic surveillance of organisms and their antibiotic resistance patterns in every unit might help physicians for proper selection of antibiotics for treatment of neonatal nosocomial sepsis.

Accuracy of presepsin in neonatal sepsis: systematic review and meta-analysis

Parri, N. et al.

Shen, Y. et al.

BMJ Open 2019 January 25, 9 (1): e022896 The role of platelet-to-lymphocyte ratio (PLR) as an indicator of inflammation has been the focus of research recently. We aimed to investigate the prognostic value of PLR for sepsis. High PLRs at admission were associated with an increased risk of mortality. In patients with vasopressor use, AKI or a SOFA score >10, this association was non-significant.

Adherence to fluid resuscitation guidelines and outcomes in patients with septic shock: Reassessing the "one-size-fits-all" approach.

Truong, T-T.N. et al.

Journal of Critical Care February 5, 2019

The Surviving Sepsis Campaign and Centers for Medicare and Medicaid Services (CMS) Severe Sepsis and Septic Shock Management Bundle (SEP-1) recommend rapid crystalloid infusion (≥30 mL/kg) for patients with sepsis-induced hypoperfusion or septic shock. We aimed to assess compliance with this recommendation, factors associated with noncompliance, and how compliance relates to mortality.

Impact of Body Temperature Abnormalities on the Implementation of Sepsis Bundles and Outcomes in Patients With Severe Sepsis: A Retrospective Sub-Analysis of the Focused Outcome Research on Emergency Care for Acute Respiratory Distress Syndrome, Sepsis and Trauma Study.

Kushimoto, S. et al

Critical Care Medicine February 14, 2019

The study investigates the impact of body temperature on disease severity, implementation of sepsis bundles, and outcomes in severe sepsis patients. Hypothermia was associated with a significantly higher disease severity, mortality risk, and lower implementation of sepsis bundles.

<u>Does Obesity Protect Against Death in Sepsis? A</u>
<u>Retrospective Cohort Study of 55,038 Adult Patients.</u>
Pepper, D.J. et al.

Critical Care Medicine February 14, 2019

Observational studies suggest obesity is associated with sepsis survival, but these studies are small, fail to adjust for key confounders, measure body mass index at inconsistent time points, and/or use administrative data to define sepsis. To estimate the relationship between body mass index and sepsis mortality using detailed clinical data for case detection and risk adjustment. In adults with clinically defined sepsis, we demonstrate lower short-term mortality in patients with higher body mass indices compared with those

Expert review of anti-infective therapy, 18 February 2019

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 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.

Machine learning models for early sepsis recognition in the neonatal intensive care unit using readily available electronic health record data.

Masino AJ et al.

PLoS One. 2019 Feb 22;14(2):e0212665
Rapid antibiotic administration is known to improve sepsis outcomes, however early diagnosis remains challenging due to complex presentation. Our objective was to develop a model using readily available electronic health record (EHR) data capable of recognizing infant sepsis at least 4 hours prior to clinical recognition. Machine learning models can identify infants with sepsis in the NICU hours prior to clinical recognition. Learning curves indicate model improvement may be achieved with additional training examples. Additional input features may also improve performance. Further research is warranted to assess potential performance improvements and clinical efficacy in a prospective trial.

Maternal sepsis: new concepts, new practices.

Foeller, M.E. et al

Current Opinion in Obstetrics & Gynecology February 14, 2019

Sepsis is a leading cause of severe maternal morbidity and maternal death. As pregnancy-related sepsis can be difficult to recognize, clinicians should maintain a low threshold for early evaluation and treatment. Obstetricians have a heightened understanding of the physiologic changes in pregnancy and play a vital role in coordinating patient care and improving outcomes. The recent 2016 and 2017 revisions of definitions for maternal sepsis and treatment should be incorporated into clinical practice.

<u>Delivery-associated sepsis: trends in prevalence and mortality</u>

Kendle, A.M. et al.

American Journal of Obstetrics and Gynecology 2019 February 13

with normal body mass indices (both unadjusted and adjusted analyses) and higher short-term mortality in those with low body mass indices. Understanding how obesity improves survival in sepsis would inform prognostic and therapeutic strategies.

Analysis of a new best-practice advisory on time to initiation of antibiotics in surgical intensive care unit patients with septic shock

Chanas, T. et al.

Journal of the Intensive Care Society 2019, 20 (1): 34-39

Early administration of antibiotics in septic shock is associated with decreased mortality. Promptly identifying sepsis and eliciting a response are necessary to reduce time to antibiotic administration. A new best-practice advisory has been effective at eliciting a rapid response and reducing the time-to-antibiotics in surgical intensive care unit patients with septic shock. Team notification and pharmacist response are associated with decreased time-to-antibiotics.

Antibiotic use practice and predictors of hospital outcome among patients with systemic bacterial infection: Identifying targets for antibiotic and health care resource stewardship.

Alemkere, G. et al

PloS One 2019

Malpractice and excess use of antimicrobials have been associated with multiple costs, including the development of resistant bacteria, which has become a threat to the human health. The aim of this study, therefore, was to assess the antibiotic use practice and to identify predictors of hospital outcome to uncover targets for stewardship. Generally, this observation entails an appropriate infection management and antimicrobial use policy. Any future policy should better start by addressing cases like pneumonia, and sepsis and drugs like cephalosporins.

Association between circulating mononuclear cell mitochondrial DNA copy number and in-hospital mortality in septic patients: A prospective observational study based on the Sepsis-3 definition Yang, Y. et al.

PloS One 2019, 14 (2): e0212808

To explore the association between circulating mononuclear cell mitochondrial DNA copy number and the prognosis of sepsis patients based on the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3 definition). Our data indicate first that circulating mononuclear cellular mtDNA copy

Sepsis is a leading cause of pregnancy-related mortality. Previous studies have reported an increased prevalence of sepsis during pregnancy. Despite national campaigns to increase sepsis awareness, there is a lack of pregnancy-specific guidelines. While rates of delivery-associated sepsis have increased, case fatality has decreased.

<u>Development of a novel bedside index for the early identification of severe maternal infection.</u>

O'Regan, C. et al.

European Journal of Obstetrics, Gynecology, and Reproductive Biology February 6, 2019

International consensus reports have recently recommended that the Systemic Inflammatory Response Syndrome (SIRS) criteria for the diagnosis of sepsis should cease and that new bedside criteria need to be developed to improve prevention, early diagnosis and treatment. The aim of this retrospective audit was to evaluate a suite of four bedside clinical criteria, called the Early Maternal Infection Prompts (EMIP), in helping to identify women with a suspected severe infection who were admitted to a High Dependency Unit (HDU) in a large tertiary referral stand-alone maternity hospital. The audit confirmed that this bedside index has potential in helping to identify maternal infection early before sepsis develops. Prospective studies are required to evaluate the index in different settings, for different infections and at the different stages of maternal infection.

Effect of a novel vital sign device on maternal mortality and morbidity in low-resource settings: a pragmatic, stepped-wedge, cluster-randomised controlled trial. Vousden, N. et al.

Lancet Glob Health. 2019 Mar;7(3):e347-e356 In 2015, an estimated 303 000 women died in pregnancy and childbirth. Obstetric haemorrhage, sepsis, and hypertensive disorders of pregnancy account for more than 50% of maternal deaths worldwide. There are effective treatments for these pregnancy complications, but they require early detection by measurement of vital signs and timely administration to save lives. The primary aim of this trial was to determine whether implementation of the CRADLE Vital Sign Alert and an education package into community and facility maternity care in low-resource settings could reduce a composite of all-cause maternal mortality or major morbidity (eclampsia and hysterectomy). There was an absolute 8% reduction in primary outcome during the trial, with no change in resources or staffing, but this reduction could not be directly attributed to the intervention due to variability. number might be helpful for outcome predictions in sepsis patients, and second that lower mtDNA copy number implied poor prognosis.

Management of sepsis in neutropenic cancer patients: 2018 guidelines from the Infectious Diseases Working Party (AGIHO) and Intensive Care Working Party (iCHOP) of the German Society of Hematology and Medical Oncology (DGHO).

Kochanek, M. et al

Annals of Hematology February 22, 2019
Sepsis and septic shock are major causes of mortality during chemotherapy-induced neutropenia for malignancies requiring urgent treatment. Thus, awareness of the presenting characteristics and prompt management is most important. Improved management of sepsis during neutropenia may reduce the mortality of cancer therapies. However, optimal management may differ between neutropenic and non-neutropenic patients. The aim of the current guideline is to give evidence-based recommendations for hematologists, oncologists, and intensive care physicians on how to manage adult patients with neutropenia and sepsis

The prognostic value of neurofilament levels in patients with sepsis-associated encephalopathy - A prospective, pilot observational study

Ehler, J. et al.

PLoS One , 14 (1) , Article e0211184. (2019) Sepsis-associated encephalopathy (SAE) contributes to mortality and neurocognitive impairment of sepsis patients. Neurofilament (Nf) light (NfL) and heavy (NfH) chain levels as biomarkers for neuroaxonal injury were not evaluated in cerebrospinal fluid (CSF) and plasma of patients with sepsis-associated encephalopathy (SAE) before. he present study showed for the first time that Nf levels provide complementary prognostic information in SAE patients indicating a higher chance of death and poorer functional/cognitive outcome in survivors.

Protocols for Point-of-Care-Ultrasound (POCUS) in a Patient with Sepsis; An Algorithmic Approach Alonso, J.V.

Bulletin of Emergency & Trauma, 2019, Vol.7(1), p.67-71

Point-of-care ultrasound (POCUS) has become a standard tool for the emergency physician in a variety of presentations in the emergency department. Several protocols are currently established including extended focused assessment with sonography in trauma (eFAST) for trauma, Bedside Lung Ultrasound

We encountered unanticipated methodological challenges with this trial design, which can provide valuable learning for future research and inform the trial design of future international stepped-wedge trials.

Adult sepsis

The value of delta neutrophil index in neonatal sepsis diagnosis, follow-up and mortality prediction Celik, I.H. et al.

Early Human Development, April 2019, Vol.131, pp.6-9 The complete blood cell count (CBC) and peripheral blood smear were the most commonly ordered tests for the diagnosis of neonatal sepsis. Delta neutrophil index (DNI) shows leucocyte differentiation and calculated while CBC is performed. We aimed to evaluate the value of DNI in neonatal sepsis. DNI was found to be useful in the diagnoses, follow-up and mortality prediction of neonatal sepsis without extra blood to CBC.

<u>Sepsis: mechanisms of bacterial injury to the patient</u> Minasyan, Hayk

Scandinavian journal of trauma, resuscitation and emergency medicine, 14 February 2019, Vol.27(1), p.19 In bacteremia the majority of bacterial species are killed by oxidation on the surface of erythrocytes and digested by local phagocytes in the liver and the spleen. Sepsis-causing bacteria overcome this mechanism of human innate immunity by versatile respiration, production of antioxidant enzymes, hemolysins, exoand endotoxins, exopolymers and other factors that suppress host defense and provide bacterial survival. Entering the bloodstream in different forms (planktonic, encapsulated, L-form, biofilm fragments), they cause different types of sepsis (fulminant, acute, subacute, chronic, etc.). Sepsis treatment includes antibacterial therapy, support of host vital functions and restore of homeostasis. A bacterium killing is only one of numerous aspects of antibacterial therapy. The latter should inhibit the production of bacterial antioxidant enzymes and hemolysins, neutralize bacterial toxins, modulate bacterial respiration, increase host tolerance to bacterial products, facilitate host bactericidal mechanism and disperse bacterial capsule and biofilm.

Impact of a hospital-wide sepsis pathway on improved quality of care and clinical outcomes in surgical patients at a comprehensive cancer centre

Hiong, A. et al.

in Emergency (BLUE) and Rapid Assessment of Dyspnea with Ultrasound (RADiUS) for dyspnoea, Rapid Ultrasound in Shock (RUSH) for shock and Focused Echocardiography in Emergency Life support (FEEL) for cardiac arrest. POCUS is a very useful imaging technique for the emergency medicine physician widely used in the European countries and part of the program of emergency medicine residency programs in the United States and Canada. There is no current protocol for POCUS in sepsis. The potential benefits of POCUS for sepsis include infection control, haemodynamic monitoring and treatment guidance. In this case, we will demonstrate how POCUS can assist in clinical decision making in patients with sepsis.

Sepsis Surveillance Using Adult Sepsis Events
Simplified eSOFA Criteria Versus Sepsis-3 Sequential
Organ Failure Assessment Criteria

Rhee, C. et al

Critical care medicine, March 2019, Vol.47(3), pp.307-314

Sepsis-3 defines organ dysfunction as an increase in the Sequential Organ Failure Assessment score by greater than or equal to 2 points. However, some Sequential Organ Failure Assessment score components are not routinely recorded in all hospitals' electronic health record systems, limiting its utility for wide-scale sepsis surveillance. The Centers for Disease Control and Prevention recently released the Adult Sepsis Event surveillance definition that includes simplified organ dysfunction criteria optimized for electronic health records (eSOFA). We compared eSOFA versus Sequential Organ Failure Assessment with regard to sepsis prevalence, overlap, and outcomes. The Adult Sepsis Event's eSOFA organ dysfunction criteria identify a smaller, more severely ill sepsis cohort compared with the Sequential Organ Failure Assessment score, but with good overlap and similar clinical characteristics. Adult Sepsis Events may facilitate wide-scale automated sepsis surveillance that tracks closely with the more complex Sepsis-3 criteria.

<u>Perianal sepsis: surgical perspective and practical MRI</u> <u>reporting for radiologists</u>

Ho, E. et al

Abdominal radiology (New York), 15 February 2019 This article describes the development of a structured MRI reporting template and diagrammatic worksheet for perianal sepsis through collaboration between radiologists and colorectal surgeons at our institution, and the rationale behind each component of the worksheet. Benefits of this reporting worksheet

European journal of cancer care, 13 February 2019, pp.e13018

Sepsis is a significant complication following cancer surgery. Although standardised care bundles improve sepsis outcomes in other populations, the benefits in cancer patients are unclear. The objectives of this study were to describe the epidemiology of sepsis in cancer patients post-surgery, and to evaluate the impact of a clinical sepsis pathway on management and clinical outcomes. A dedicated hospital-wide sepsis pathway had significant impact on the quality of care and clinical outcomes of sepsis in cancer surgery patients. Costbenefit analysis of sepsis pathways for cancer patients is required.

<u>Cerebral Autoregulation-Guided Optimal Blood</u>
<u>Pressure in Sepsis-Associated Encephalopathy: A Case</u>
Series

Rosenblatt, K. et al.

Journal of intensive care medicine, 13 February 2019, pp.885066619828293

Impaired cerebral autoregulation and cerebral hypoperfusion may play a critical role in the high morbidity and mortality in patients with sepsisassociated encephalopathy (SAE). Bedside assessment of cerebral autoregulation may help individualize hemodynamic targets that optimize brain perfusion. We hypothesize that near-infrared spectroscopy (NIRS)derived cerebral oximetry can identify blood pressure ranges that enhance autoregulation in patients with SAE and that disturbances in autoregulation are associated with severity of encephalopathy. In this high-fidelity group of patients with SAE, continuous, NIRS-based monitoring can identify blood pressure ranges that improve autoregulation. This is important given the association between cerebral autoregulatory function and severity of encephalopathy. Individualizing blood pressure goals using bedside autoregulation monitoring may better preserve cerebral perfusion in SAE than current practice.

<u>Troponin Testing for Assessing Sepsis-Induced</u>
<u>Myocardial Dysfunction in Patients with Septic Shock</u>
Kim, J-S. et al.

Journal of clinical medicine, 12 February 2019, Vol.8(2) Background: Myocardial dysfunction in patients with sepsis is not an uncommon phenomenon, yet reported results are conflicting and there is no objective definition. Measurement of troponin may reflect the state of the heart and may correlate with echocardiographically derived data. This study aimed to evaluate the role of admission and peak troponin-I testing for the identification of sepsis-induced

include optimizing communication of key imaging findings that have a real impact on patient management, less time spent on reporting the study, and easier comparison between studies. We illustrate the utility of the report template with case studies. We summarize the current surgical approaches to perianal sepsis to help radiologists focus on reporting the findings relevant to surgical planning.

Cardiac Autophagy in Sepsis

Sun, Y. et al

Cells, 10 February 2019, Vol.8(2)

Sepsis is a leading cause of death in intensive care units, and cardiac dysfunction is an identified serious component of the multi-organ failure associated with this critical condition. This review summarized the current discoveries and hypothesizes of how autophagy changes in the heart during sepsis and the underlying mechanisms. Recent investigations suggest that specific activation of autophagy initiation factor Beclin-1 has a potential to protect cardiac mitochondria, attenuate inflammation, and improve cardiac function in sepsis. Accordingly, pharmacological interventions targeting this pathway have a potential to become an effective approach to control sepsis outcomes. The role of autophagy during sepsis pathogenesis has been under intensive investigation in recent years. It is expected that developing therapeutic approaches with specificities targeting at autophagy regulatory factors may provide new opportunities to alleviate organ dysfunction caused by maladaptive autophagy during sepsis.

<u>Peripheral Blood Mononuclear Cells Demonstrate</u> <u>Mitochondrial Damage Clearance During Sepsis</u> Kraft, B.D. et al.

Critical care medicine, 05 February 2019
Metabolic derangements in sepsis stem from mitochondrial injury and contribute significantly to organ failure and mortality; however, little is known about mitochondrial recovery in human sepsis. We sought to test markers of mitochondrial injury and recovery (mitochondrial biogenesis) noninvasively in peripheral blood mononuclear cells from patients with sepsis and correlate serial measurements with clinical outcomes. Our findings support data that sepsis-induced mitochondrial damage is reversed by activation of mitochondrial biogenesis and that gene transcripts measured noninvasively in peripheral blood mononuclear cells can serve as novel biomarkers of sepsis recovery

myocardial dysfunction (SIMD) by transthoracic echocardiography (TTE). About two-thirds of patients with an elevated hs-TnI level have various cardiac dysfunctions in terms of TTE. Rather than the initial level, the peak hs-TnI and ST-T change may be considered as a risk factor of SIMD.

<u>Systemic inflammatory response syndrome in Sepsis-3: a retrospective study</u>

Zhang, W. et al.

BMC infectious diseases, 11 February 2019, Vol.19(1), pp.139

In the new Sepsis-3 definition, sepsis is defined as "life-threatening organ dysfunction due to a dysregulated host response to infection." We tested the predictive validity of the systematic inflammatory response syndrome (SIRS) criteria in patients in the Sepsis-3 cohort. In this cohort study of the new Sepsis-3 definition, we found that the SIRS criteria are weaker than the SOFA criteria with respect to their predictive efficacy for in-hospital death.

<u>Emergency department door-to-antibiotic time and long-term mortality in sepsis</u>

Peltan, I.D. et al Chest Feb 2019

The impact of antibiotic timing on sepsis outcomes remains controversial due to conflicting results in prior studies. This study investigated the association of doorto-antibiotic time with long-term mortality in emergency department (ED) patients with sepsis. Delays in ED antibiotic initiation time are associated with clinically important increases in long-term risk-adjusted sepsis mortality.

<u>Ureteral stent-associated infection and sepsis:</u> <u>pathogenesis and prevention: a review</u>

Scotland, K.B. et al.

Biofouling, 08 February 2019, p.1-11

Ureteral stents are commonly used devices in hospital settings. However, their usage is often complicated by associated urinary tract infections as a result of bacterial adhesion onto the indwelling implant surfaces, followed by the formation of layers of biofilm. Once formed, the biofilm is exceedingly difficult to remove, potentially leading to further morbidity and even urosepsis. Urosepsis, where pathogens from the urinary tract enter the bloodstream, has a mortality rate of up to 50% of severely infected patients. Hence, it is important to understand its pathogenesis. In this review, ureteral stent-associated urinary tract infection and urosepsis will be addressed. In particular, the bacterial mechanisms involved, as well as the

<u>Cardiovascular Events and Hospital Deaths Among</u>
<u>Patients With Severe Sepsis</u>

Patel, N. et al

The American Journal of Cardiology Feb 2019
The burden of cardiovascular events among patients hospitalized with severe sepsis and the association of these events with in-hospital mortality is not well known. We examined the incidence of cardiovascular events and their association with in-hospital mortality among patients with severe sepsis. In conclusion, among patients with severe sepsis, incident cardiovascular events occur frequently. Further research is required to improve recognition and treatment of new-onset cardiovascular events in patients with severe sepsis.

Immune Checkpoint Inhibition in Sepsis: A Phase 1b Randomized, Placebo-Controlled, Single Ascending Dose Study of Antiprogrammed Cell Death-Ligand 1 (BMS-936559)

Hotchkiss, R.S. et al

Critical Care Medicine, 2019, p.1

To assess for the first time the safety and pharmacokinetics of an antiprogrammed cell deathligand 1 immune checkpoint inhibitor (BMS-936559, Bristol-Myers Squibb, Princeton, NJ) and its effect on immune biomarkers in participants with sepsisassociated immunosuppression. In this first clinical evaluation of programmed cell death protein-1/programmed cell death-ligand 1 pathway inhibition in sepsis, BMS-936559 was well tolerated, with no evidence of drug-induced hypercytokinemia or cytokine storm, and at higher doses, some indication of restored immune status over 28 days. Further randomized trials on programmed cell death protein-1/programmed cell death-ligand 1 pathway inhibition are needed to evaluate its clinical safety and efficacy in patients with sepsis.

Emergency department sepsis huddles: Achieving excellence for sepsis benchmarks in New York State Walsh, D. et al

American Journal of Emergency Medicine Feb 2019
The sepsis order set at our institution was created with the intent to facilitate the prompt initiation of appropriate sepsis care. Once clinical features meeting criteria for systemic inflammatory response syndrome (SIRS) are identified and an infectious source is considered, a "sepsis huddle" is concomitantly initiated. The sepsis huddle was implemented in March of 2016 in order to increase compliance with the sepsis bundles. Utilizing and adhering to the guidelines of this methodology in the management of

prevention and treatment of these infections will be discussed.

Central Venous Access Capability and Critical Care
Telemedicine Decreases Inter-Hospital Transfer Among
Severe Sepsis Patients: A Mixed Methods Design
Ilko, S.A. et al.

Critical care medicine, 05 February 2019
Severe sepsis is a complex, resource intensive, and potentially lethal condition and rural patients have worse outcomes than urban patients. Early identification and treatment are important to improving outcomes. The objective of this study was to identify hospital-specific factors associated with interhospital transfer. The insertion of central venous catheters and access to a critical care physician during sepsis treatment are important capabilities in hospitals that transfer fewer sepsis patients. In the future, hospital-specific capabilities may be used to identify institutions as regional sepsis centers.

Clinical Value of Presepsin in Comparison to hsCRP as a Monitoring and Early Prognostic Marker for Sepsis in Critically III Patients

Hassan, E.A

Medicina (Kaunas, Lithuania), 2 February 2019, Vol.55(2)

Sepsis carries a poor prognosis for critically ill patients, even withintensive management. We aimed to determined early predictors of sepsis-related inhospital mortality and to monitor levels of presepsin and high sensitivity C reactive protein (hsCRP) during admission relative to the applied treatment and the development of complications. Overall, in comparison with hsCRP, presepsin was an early predictor of sepsis-related in-hospital mortality in ICU patients. Changes in presepsin concentrations over time may be useful for sepsis monitoring, which in turn could be useful for stratifying high-risk patients on ICU admission that benefit from intensive treatment.

<u>Prevalence, Underlying Causes, and Preventability of Sepsis-Associated Mortality in US Acute Care Hospitals</u> Rhee, C. et al.

JAMA network open, 01 February 2019, Vol.2(2), pp.e187571

Sepsis is present in many hospitalizations that culminate in death. The contribution of sepsis to these deaths, and the extent to which they are preventable, is unknown. Our objective was to estimate the prevalence, underlying causes, and preventability of sepsis-associated mortality in acute care hospitals. We found that in this cohort from 6 US hospitals, sepsis

these patients has enabled our hospital to improve benchmarking compliance from previously underperforming at the 31st and 49th percentiles in 2015, prior to initiation of the huddle, to a peak compliance at the 81st and 91st percentiles in 2016 and 65th and 83rd percentiles in 2017 for the 3-hour and 6-hour bundles respectively.

<u>Sepsis and septic shock: current approaches to management</u>

Thompson, K. et al

Internal medicine journal, February 2019, Vol.49(2), pp.160-170

Sepsis, defined as life-threatening organ dysfunction due to a dysregulated host response to infection, is recognised by the World Health Organization as a global health priority. Each year, 5000 of the 18 000 adults with sepsis treated in Australian intensive care units die, with survivors suffering long-term physical, cognitive and psychological dysfunction, which is poorly recognised and frequently untreated. There are currently no effective pharmacological treatments for sepsis, making early recognition, resuscitation and immediate treatment with appropriate antibiotics the key to reducing the burden of resulting disease. In this narrative review, we provide a summary of current knowledge on epidemiology of sepsis and septic shock and recommendations on the optimum approach to the management of these conditions in adults.

Non-antibiotic therapies for sepsis: an update Vincent, J-L. et al

Expert Review of Anti-infective Therapy, 04 March 2019

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. Areas covered: This review will not cover infection control. Hemodynamic stabilization essentially involves 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. Expert opinion: Management of the patient with sepsis remains a challenge and needs to be personalized. The search for new immunomodulatory drugs continues

was the most common immediate cause of death. However, most underlying causes of death were related to severe chronic comorbidities and most sepsis-associated deaths were unlikely to be preventable through better hospital-based care. Further innovations in the prevention and care of underlying conditions may be necessary before a major reduction in sepsis-associated deaths can be achieved.

and will be facilitated by better characterization of patients using modern "omics" technology and complex analysis of the large quantities of clinical data increasingly available.

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