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# SEPSIS BULLETIN

## 24 May 2019

### Neonatal, paediatric and maternal sepsis

[Neonatal sepsis due to glycopeptide resistant Enterococcus faecium from colonized maternal gut-rare case evidence](#)

Subramanya, S. H. et al.

**Antimicrobial Resistance & Infection Control**, 12/2019, Vol.8(1)

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.

[Severe Sepsis in Pediatric Liver Transplant Patients: The Emergence of Multidrug-Resistant Organisms.](#)

Alcamo AM, et al

**Pediatr Crit Care Med.** 2019 May 14

To describe characteristics of liver transplant patients with severe sepsis in the PICU. We report that

### Adult sepsis (cont.)

[Risk Factors for Myocardial Infarction and Stroke Among Sepsis Survivors: A Competing Risks Analysis.](#)

Hsieh YC, et al

**J Intensive Care Med.** 2019 May 12:885066619844936.

Predictors for post-sepsis myocardial infarction (MI) and stroke are yet to be identified due to the competing risk of death. Baseline comorbidities and sources of infection were associated with an increased risk of post-sepsis MI and stroke. The identified risk factors may help physicians select a group of patients with sepsis who may benefit from preventive measures, antiplatelet treatment, and other preventive measures for post-sepsis MI and stroke.

[Quantitative capillary refill time predicts sepsis in patients with suspected infection in the emergency department: an observational study.](#)

Yasufumi O, et al

**J Intensive Care.** 2019 May 6;7:29.

multidrug-resistant organisms are increasingly being identified as causative pathogens for sepsis in pediatric liver transplant recipients and are associated with significantly higher odds for mechanical ventilation and higher organ failure. The emergence of multidrug-resistant organism infections in pediatric liver transplant patients has implications for patient outcomes, antibiotic stewardship, and infection prevention strategies.

[Precision medicine in pediatric sepsis.](#)

Atreya MR, Wong HR.

**Curr Opin Pediatr.** 2019 Jun;31(3):322-327.

Precision medicine approaches may be used to subclassify, risk-stratify, and select pediatric patients with sepsis who may benefit from new therapies. Application of precision medicine will require robust basic and translational research, rigorous clinical trials, and infrastructure to collect and analyze big data.

[Predictors of early-onset neonatal sepsis or death among newborns born at <32 weeks of gestation.](#)

Palatnik A, et al

**J Perinatol.** 2019 May 14.

To develop a predictive model for early-onset neonatal sepsis or death among infants born at less than 32 weeks of gestation. Earlier gestational age at the time of delivery, intrapartum fever, meconium, and lower birth weight are independently associated with early-onset neonatal sepsis or death among deliveries occurring at <32 weeks of gestation; these factors can be used to create a model with fair predictive capability.

[Risk Factors for 30-Day Mortality in Neonatal Gram-Negative Bacilli Sepsis.](#)

Thatrimontrichai A et al

**Am J Perinatol.** 2019 May 14.

Multidrug-resistant gram-negative bacilli (MDR-GNB) have emerged globally as a serious threat and with a high case fatality rate (CFR). Neonates suspected of sepsis with septic shock need broad-spectrum empirical antimicrobial therapy until the second successive negative culture, especially in high MDR areas.

[Diagnostic value of neutrophil CD64 combined with CRP for neonatal sepsis: A meta-analysis.](#)

Song Y, et al

Outcomes in emergent patients with suspected infection depend on how quickly clinicians evaluate the patients and start treatment. This study was performed to compare the predictive ability of the quantitative capillary refill time (Q-CRT) as a new rapid index versus the quick sequential organ failure assessment (qSOFA) score and the systemic inflammatory response syndrome (SIRS) score for sepsis screening in the emergency department. In this study, Q-CRT/qSOFA combination had better sensitivity than the qSOFA score alone and better specificity than the SIRS score alone. There was no significant difference in accuracy between Q-CRT/qSOFA combination and the qSOFA score or lactate concentration. The ability of the Q-CRT to predict sepsis may be similar to that of the qSOFA score or serum lactate concentration; therefore, measurement of the Q-CRT may be an alternative for invasive measurement of the blood lactate concentration in evaluating patients with suspected sepsis.

[Secondary analysis of the WOMAN trial to explore the risk of sepsis after invasive treatments for postpartum hemorrhage.](#)

Cornelissen L, et al

**Int J Gynaecol Obstet.** 2019 May 13.

To examine the association between the use of invasive treatments for postpartum hemorrhage and the risk of sepsis and severe sepsis. In this secondary data analysis, certain invasive treatments for postpartum hemorrhage appear to increase the risk of sepsis. Further research is needed to confirm this finding and investigate the role of prophylactic antibiotics during these procedures. The harms and benefits of such interventions must be carefully weighed, both in treatment guidelines and during individual patient management.

[Informatics and interaction: Applying human factors principles to optimize the design of clinical decision support for sepsis.](#)

Schubel L, et al

**Health Informatics J.** 2019 May 13:1460458219839623.

In caring for patients with sepsis, the current structure of electronic health record systems allows clinical providers access to raw patient data without imputation of its significance. There are a wide range of sepsis alerts in clinical care that act as clinical decision support tools to assist in early recognition of sepsis; however, there are serious shortcomings in existing health information technology for alerting providers in a meaningful way. Little work has been done to evaluate and assess existing

**Am J Emerg Med.** 2019 May 3. pii: S0735-6757(19)30295-5.

Sepsis is the leading cause of morbidity and mortality in newborns. CD64 combined with c-reactive protein (CRP) could improve the sensitivity and specificity of neonatal sepsis diagnosis, but the results were still controversial. Therefore, this meta-analysis was conducted to clarify the importance of CD64 combined with CRP in the diagnosis of neonatal sepsis. The combined application of CD64 and CRP improved the accuracy of neonatal sepsis diagnosis.

#### [Minimum Duration of Antibiotic Treatment Based on Blood Culture in Rule Out Neonatal Sepsis.](#)

Ur Rehman Durrani N, et al

**Pediatr Infect Dis J.** 2019 May;38(5):528-532.

Neonatologists usually wait 48 hours for blood culture results before deciding to discontinue antibiotics. The objective of the study was to analyze time to positive blood culture in rule out sepsis and estimate the minimum duration of antibiotics. The probability of positive blood culture beyond 24 hours for a Gram-negative organism is small. Empiric antimicrobial treatment can be reduced after 24 hours to target only Gram-positive organisms in LOS and can be stopped in EOS unless clinical or laboratory parameters strongly suggest sepsis.

#### [Red cell distribution width and its association with mortality in neonatal sepsis.](#)

Martin SL, et al

**J Matern Fetal Neonatal Med.** 2019 Jun;32(12):1925-1930.

Neonatal sepsis is a major cause of mortality in the developing countries. However, with current severity scores and laboratory parameters, predicting outcomes of neonatal sepsis is a serious challenge. Red cell distribution width (RDW) is a readily available pragmatic means to predict outcomes of various comorbidities in adults and children, without causing any additional blood loss. However, its utility in neonates remains unexplored. Hence, the objective of the present study was to evaluate the association of RDW with neonatal sepsis and its role as a predictive marker for mortality. High RDW is associated with neonatal sepsis and is an independent outcome predictor for mortality associated with neonatal sepsis.

**Adult sepsis**

alerts using implementation and process outcomes associated with health information technology displays, specifically evaluating clinician preference and performance. We developed graphical model displays of two popular sepsis scoring systems, quick Sepsis Related Organ Failure Assessment and Predisposition, Infection, Response, Organ Failure, using human factors principles grounded in user-centered and interaction design. Models will be evaluated in a larger research effort to optimize alert design to improve the collective awareness of high-risk populations and develop a relevant point-of-care clinical decision support system for sepsis.

#### [Elevated CTRP1 Plasma Concentration Is Associated with Sepsis and Pre-Existing Type 2 Diabetes Mellitus in Critically Ill Patients.](#)

Yagmur E et al

**J Clin Med.** 2019 May 11;8(5). pii: E661.

The adipokine family of C1q/TNF-like proteins (CTRP) plays a critical role in regulating systemic energy homeostasis and insulin sensitivity. It is involved in pathophysiological processes including inflammation and insulin-resistant obesity. Sepsis is associated with metabolic alterations and dysregulated adipokines, but the role of CTRP1 in critical illness and sepsis is unclear. This study demonstrates significantly elevated levels of CTRP1 in critically ill patients, particularly with sepsis, and links circulating CTRP1 to inflammatory and metabolic disturbances.

#### [Clinical and Demographic Parameters of Patients Treated Using a Sepsis Protocol.](#)

Ward HH, et al

**Clin Ther.** 2019 May 10. pii: S0149-2918(19)30166-3

The purpose of this study was to investigate potential differences by sex in the demographic and clinical characteristics of patients treated utilizing a sepsis electronic bundle order set. Risk factors for in-hospital mortality were also assessed. Women were more likely to have a genitourinary cause of sepsis and less likely to arrive by ambulance. Risk factors of in-hospital mortality were older age, arrival by ambulance, and an ESI level of 1 or 2, but not sex.

#### [Circulating microRNAs as biomarkers for Sepsis secondary to pneumonia diagnosed via Sepsis 3.0.](#)

Zhang W et al

**BMC Pulm Med.** 2019 May 14;19(1):93

Sepsis biomarkers have limited specificity and sensitivity. Few studies have investigated microRNA (miRNA)

[Shock index and modified shock index as triage screening tools for sepsis](#)

Althunayyan SM, et al.

**J Infect Public Health.** 2019 May 18. pii: S1876-0341(19)30169-8.

Fever is one of the common conditions encountered in the emergency department, which related to a spectrum of diseases severity. Identifying sepsis patients from uncomplicated febrile patients is challenging in the emergency triage areas and pre-hospital settings. Assess the triage shock index (SI) and modified shock index (MSI) in febrile patients as predictors for sepsis and sepsis-related outcomes. MSI and SI were found to be promising predictors in triaging febrile patients. However no single cut-off values of MSI or SI were found to have an optimal accuracy for prediction of sepsis and sepsis-related outcomes. Further studies are required to assess the incorporation of MSI in a multi-item scaling system for the prediction of sepsis and its related outcomes.

[MEDS score and vitamin D status are independent predictors of mortality in a cohort of Internal Medicine patients with microbiological identified sepsis.](#)

Mirijello A, et al

**Eur Rev Med Pharmacol Sci.** 2019 May;23(9):4033-4043.

Sepsis is a life-threatening disease resulting from the interaction between pathogen and host response; its dysregulation causes organ dysfunction, high morbidity, and mortality. Despite the increase of septic patients admitted to Internal Medicine wards, data about clinical predictors of mortality in this setting are still lacking. The aim of this study was to evaluate the role of MEDS score and vitamin D as predictors of mortality (28-day and 90-day) in septic patients admitted to the Internal Medicine department. MEDS score and vitamin D levels represent independent predictors of mortality in a cohort of Internal Medicine septic patients. Further studies on larger samples are needed to confirm our results and to clarify the pathophysiological mechanisms at the basis of vitamin D deficiency as a predictor of mortality in septic patients.

[Pure viral sepsis secondary to Community-Acquired Pneumonia in adults: risk and prognostic factors.](#)

Cillóniz C, et al

**J Infect Dis.** 2019 May 21. pii: jiz257.

biomarkers for sepsis secondary to pneumonia. This study aims to investigate the diagnostic and prognostic values of miRNAs in sepsis secondary to pneumonia. MiR-223-3p could be utilized to predict sepsis secondary to pneumonia.

[Trends and Outcomes in Sepsis Hospitalizations With and Without Atrial Fibrillation: A Nationwide Inpatient Analysis.](#)

Desai R, et al

**Crit Care Med.** 2019 May 13.

Atrial fibrillation is frequently seen in sepsis-related hospitalizations. However, large-scale contemporary data from the United States comparing outcomes among sepsis-related hospitalizations with versus without atrial fibrillation are limited. The aim of our study was to assess the frequency of atrial fibrillation and its impact on outcomes of sepsis-related hospitalizations. The presence of atrial fibrillation among sepsis-related hospitalizations is a marker of poor prognosis and increased mortality. Although we observed rising trends in sepsis and sepsis-atrial fibrillation-related hospitalizations during the study period, the rate and odds of mortality progressively decreased.

[Hypertonic Saline in Human Sepsis: A Systematic Review of Randomized Controlled Trials.](#)

Orbegozo D. et al

**Anesth Analg.** 2019 Jun;128(6):1175-1184.

The role of hypertonic saline in sepsis remains unclear because clinical data are limited and the balance between beneficial and adverse effects is not well defined. In our meta-analysis of studies in patients with sepsis, hypertonic saline reduced the volume of fluid needed to achieve the same hemodynamic targets but did not affect survival.

[Time course of fluid responsiveness in sepsis: the fluid challenge revisiting \(FCREV\) study.](#)

Roger C, et al

**Crit Care.** 2019 May 16;23(1):179.

Fluid challenge (FC) is one of the most common practices in Intensive Care Unit (ICU). The present study aimed to evaluate whether echocardiographic assessment of the response to FC at the end of the infusion or 20 min later could affect the results of the FC. This study shows that 51.3% of initial responders have a persistent response to fluid 30 min after the beginning of fluid infusion and only 41.3% have a transient response highlighting that fluid responsiveness is time dependent.

We investigated the risk and prognostic factors of pure viral sepsis in adult patients with community-acquired pneumonia (CAP), using the Sepsis-3 definition. Pure viral sepsis was found in 3% of all patients admitted to the emergency department with a diagnosis of CAP (138 out of 4,028), 19% of all CAP patients admitted to the intensive care unit (ICU) (138 out of 722) and 61% of all patients with a diagnosis of viral CAP (138 out of 225). Our data indicate that males and patients aged  $\geq 65$  years are at increased risk of viral sepsis

[European Society of Emergency Medicine position paper on the 1-hour sepsis bundle of the Surviving Sepsis Campaign: expression of concern.](#)

Freund Y, et al

**Eur J Emerg Med.** 2019 May 20.

In 2018 the Surviving Sepsis Campaign issued new guidance with a revised version of their sepsis bundle. Instead of the 2016 3-hour sepsis bundle, the Surviving Sepsis Campaign now recommends that blood cultures, lactate measurement, broad-spectrum antibiotic therapy and 30 ml/kg crystalloid fluid administration should be initiated within 1 hour after triage. The European Society of Emergency Medicine wishes to express its concerns regarding the low level of evidence that underlies this guidance, and the potential implications from an emergency physician point of view.

[Prognostic accuracy of the sequential organ failure assessment \(SOFA\) and quick SOFA for mortality in cancer patients with sepsis defined by systemic inflammatory response syndrome \(SIRS\).](#)

Chae BR, et al

**Support Care Cancer.** 2019 May 22.

We aimed to assess the prognostic accuracy of SOFA and qSOFA scores in cancer patients with sepsis, and also to determine if the addition of hyperlactatemia to qSOFA increases the accuracy in predicting the 30-day mortality. In cancer patients with sepsis, qSOFA was inferior to SOFA in predicting mortality. However, adding lactate to qSOFA resulted in greater prognostic accuracy for short-term mortality, comparable with SOFA.

[Comparison of the source and prognostic utility of cfDNA in trauma and sepsis.](#)

Jackson Chornenki NL et al

**Intensive Care Med Exp.** 2019 May 22;7(1):29.

[Association between increased arterial stiffness and clinical outcomes in patients with early sepsis: a prospective observational cohort study.](#)

Kazune S, et al

**Intensive Care Med Exp.** 2019 May 16;7(1):26.

Conduit arteries, especially the aorta, play a major role in ensuring efficient cardiac function and optimal microvascular flow due to their viscoelastic properties. Studies in animals and on isolated arteries show that acute systemic inflammation can cause aortic stiffening which affects hemodynamic efficiency. Carotid-femoral pulse wave velocity, a measure of aortic stiffness, may be useful as a bedside investigational method in patients with early sepsis admitted to intensive care, as circulatory changes can lead to multiple organ failure and increased mortality. This study aims to investigate arterial stiffness in early sepsis and its association with clinical outcomes. Patients with severe sepsis and septic shock admitted to intensive care have higher arterial stiffness than in the general population. No convincing association was found between pulse wave velocity at admission and the progression of multiple organ or cardiovascular failure, although the group with pulse wave velocity  $> 24.7$  m/s had shorter survival time.

[Immune function testing in sepsis patients receiving sodium selenite.](#)

Guo A, et al

**J Crit Care.** 2019 May 4;52:208-212

We examined in a longitudinal study the role of sodium selenite in sepsis patients in strengthening the immune performance in whole blood samples using immune functional assays. Selenium has long been an adjuvant therapy in treating sepsis. Recently, it was proven to not have beneficial effects on the mortality outcome. Using data from our center in this sub-cohort study, we identified no relative improvement in cytokine release of stimulated blood immune cells ex vivo from patients with selenium therapy over a three-week period. This offers a potential explanation for the lack of beneficial effects of selenium in sepsis patients.

[Influence of systemic hemodynamics on microcirculation during sepsis.](#)

Collet M, et al

**J Crit Care.** 2019 May 6;52:213-218.

During sepsis, improvement of hemodynamic may not be related to improvement of microcirculation. The aim of this study was to investigate influence of systemic

Circulating cell-free DNA (cfDNA) may contribute to the pathophysiology of post-injury inflammation and coagulation in trauma. However, the source and mechanism of release of cfDNA in trauma is not well understood. One potential source of cfDNA is from Neutrophil Extracellular Traps (NETs), released by activated neutrophils during the process of NETosis. The primary objective of our study was to determine if cfDNA has prognostic utility in trauma. The secondary objective of this study was to determine the source of cfDNA in trauma compared to sepsis. Our studies suggest that the source and mechanism of release of cfDNA differ between trauma and sepsis patients. In sepsis, cfDNA is likely primarily released by activated neutrophils via the process of NETosis. In contrast, cfDNA in trauma appears to originate mainly from injured or necrotic cells. Although cfDNA is elevated in trauma and sepsis patients compared to healthy controls, cfDNA does not appear to have prognostic utility in trauma patients.

[Interleukin 28 is a potential therapeutic target for sepsis.](#)

Luo Q, et al.

**Clin Immunol.** 2019 May 20. pii: S1521-6616(19)30209-8

Identification of new therapeutic targets for the treatment of sepsis is imperative. We report here that cytokine IL-28 (IFN- $\lambda$ ) levels were elevated in clinical and experimental sepsis. Neutralization of IL-28 protected mice from lethal sepsis induced by cecal ligation and puncture (CLP), which was associated with improved bacterial clearance and enhanced neutrophil infiltration. Conversely, administration of recombinant IL-28 aggravated mortality, facilitated bacterial dissemination and limited neutrophil recruitment, in the model of sepsis induced by CLP. This study defines IL-28 as a detrimental mediator during sepsis and identifies a potential therapeutic target for the immune therapy in sepsis.

[The clinical efficacy of intravenous IgM-enriched immunoglobulin \(pentaglobin\) in sepsis or septic shock: a meta-analysis with trial sequential analysis](#)

Cui, J. et al

**Annals of Intensive Care**, 12/2019, Vol.9(1)

Sepsis is characterized by a complex immune response. This meta-analysis evaluated the clinical effectiveness of intravenous IgM-enriched immunoglobulin (IVIgM) in patients with sepsis and septic shock.

circulation on microcirculation in septic ICU patients. DAP was the only independent determinant of resStO<sub>2</sub> in septic patients. Fluid challenges may improve microcirculation. CVP did not influence resStO<sub>2</sub>.

[Impact of a qSOFA-based triage procedure on antibiotic timing in ED patients with sepsis: A prospective interventional study.](#)

Petit J, et al

**Am J Emerg Med.** 2019 May 10. pii: S0735-6757(19)30333-X.

It has not been investigated whether the quick sepsis-related organ failure assessment score (qSOFA), a new bedside tool for early sepsis detection, may help accelerating antibiotic initiation in ED patients with sepsis. A qSOFA-based triage procedure does not improve antibiotic timing and outcomes in patients with sepsis admitted to a high-volume ED. The qSOFA value at triage was poorly sensitive for early sepsis detection.

[Derivation, Validation, and Potential Treatment Implications of Novel Clinical Phenotypes for Sepsis.](#)

Seymour CW, et al

**JAMA.** 2019 May 19.

Sepsis is a heterogeneous syndrome. Identification of distinct clinical phenotypes may allow more precise therapy and improve care. In this retrospective analysis of data sets from patients with sepsis, 4 clinical phenotypes were identified that correlated with host-response patterns and clinical outcomes, and simulations suggested these phenotypes may help in understanding heterogeneity of treatment effects. Further research is needed to determine the utility of these phenotypes in clinical care and for informing trial design and interpretation.

[Monocyte Distribution Width: A Novel Indicator of Sepsis-2 and Sepsis-3 in High-Risk Emergency Department Patients.](#)

Crouser ED, et al

**Crit Care Med.** 2019 May 17

Most septic patients are initially encountered in the emergency department where sepsis recognition is often delayed, in part due to the lack of effective biomarkers. This study evaluated the diagnostic accuracy of peripheral blood monocyte distribution width alone and in combination with WBC count for early sepsis detection in the emergency department. An monocyte distribution width value of greater than 20.0 U is effective for sepsis detection, based on either Sepsis-2 criteria or Sepsis-3

Administration of IVIgGM to adult septic patients may be associated with reduced mortality. Treatment effects tended to be smaller or less consistent when including only those studies deemed adequate for each indicator. The available evidence is not clearly sufficient to support the widespread use of IVIgGM in the treatment of sepsis.

[The glycocalyx: a novel diagnostic and therapeutic target in sepsis](#)

Uchimido, R. et al

**Critical Care**, 12/2019, Vol.23(1)

The glycocalyx is a gel-like layer covering the luminal surface of vascular endothelial cells. It is comprised of membrane-attached proteoglycans, glycosaminoglycan chains, glycoproteins, and adherent plasma proteins. The glycocalyx maintains homeostasis of the vasculature, including controlling vascular permeability and microvascular tone, preventing microvascular thrombosis, and regulating leukocyte adhesion. In this review, we first analyze the underlying mechanisms of glycocalyx degradation in sepsis. Second, we demonstrate how the blood and urine levels of glycocalyx components are associated with patient outcomes. Third, we show beneficial and harmful effects of fluid therapy on the glycocalyx status during sepsis. Finally, we address the concept of glycocalyx degradation as a therapeutic target.

[Safety of vitamin C in sepsis: a neglected topic.](#)

Khoshnam-Rad N, Khalili H.

**Curr Opin Crit Care**. 2019 May 16

Although vitamin C is essentially a nontoxic vitamin; however, it is important to be aware regarding the safety of high doses before the wide clinical use. Minor side effects of vitamin C have been reported, many being reported in earlier studies. High doses of vitamin C (up to 1.5 g/kg three times a week as intravenously) were safe in cancer patients with normal renal function and perfect glucose-6-phosphate dehydrogenase activity. As the dose and duration of administration of vitamin C in sepsis are lower and shorter than those used in cancer patients, it seems that it is relatively safe for this population. In ongoing trials, safety of high doses of vitamin C is considered. Data regarding the safety of high doses of vitamin C are scant. Until more data become available, caution should be applied in the use of high doses of vitamin C in patients with hemochromatosis, glucose-6-

criteria, during the initial emergency department encounter. In tandem with WBC, monocyte distribution width is further predicted to enhance medical decision making during early sepsis management in the emergency department.

[Renal protection in sepsis: Is hypertonic sodium \(lactate\) the solution?](#)

Honore, P.M. et al

**Annals of Intensive Care**, 12/2019, Vol.9(1)

Hypertonic sodium solutions are useful for minimizing secondary brain injury from cerebral edema but also attractive for “small-volume” resuscitation in severe hypovolemia and shock because they rapidly mobilize endogenous water from the intracellular reservoir, thereby reducing endothelial cell volume and restoring microcirculation.

[An overview of positive cultures and clinical outcomes in septic patients: a sub-analysis of the Prehospital Antibiotics Against Sepsis \(PHANTASi\) trial](#)

Nannan Panday RS, et al

**Crit Care**. 2019 May 21;23(1):182.

Sepsis remains one of the most important causes of morbidity and mortality worldwide. In approximately 30-50% of cases of suspected sepsis, no pathogen is isolated, disabling the clinician to treat the patient with targeted antimicrobial therapy. Studies investigating the differences in the patient outcomes between culture-positive and culture-negative sepsis patients have only been conducted in subgroups of sepsis patients and results are ambiguous.

phosphate dehydrogenase deficiency, renal dysfunction, kidney stone, oxaluria, and pediatrics.

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