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Research Article

Corticosteroids in Septic Shock: Current Evidence, Controversies, and Clinical Implications

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ABSTRACT

Background: Septic shock is the most severe cardiovascular manifestation of sepsis and remains associated with substantial morbidity and mortality despite advances in antimicrobial therapy, hemodynamic resuscitation, organ support, and critical care. Corticosteroids have been investigated for decades as adjunctive therapy because of their potential to modulate the dysregulated inflammatory response, restore vascular responsiveness to catecholamines, and compensate for abnormalities of the hypothalamic-pituitary-adrenal axis occurring during critical illness. Nevertheless, uncertainty remains regarding their effect on mortality, the optimal corticosteroid regimen, the role of mineralocorticoid supplementation, and the ideal timing of treatment. Objective: To critically review the current evidence regarding the use of corticosteroids in adult patients with septic shock, with particular emphasis on physiological mechanisms, clinical outcomes, corticosteroid selection and dosing, the role of fludrocortisone, adverse effects, timing of initiation, and current guideline recommendations. Methods: An updated structured literature review was performed based on the original review and supplemented with contemporary evidence through 2026. PubMed/MEDLINE-indexed randomized controlled trials, systematic reviews, meta analyses, clinical practice guidelines, and major contemporary reviews were considered. Particular emphasis was placed on Sepsis-3 definitions, the ADRENAL and APROCCHSS randomized trials, patient level meta analyses, dose-response analyses, and the 2024 Society of Critical Care Medicine focused guideline update. Results: Current evidence supports the use of intravenous corticosteroids in adults with septic shock who continue to require vasopressor therapy despite adequate initial resuscitation. Hydrocortisone at approximately 200 mg/day remains the most widely supported regimen. Corticosteroids consistently accelerate shock reversal and reduce vasopressor exposure, whereas their effect on mortality is less consistent.

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ADRENAL demonstrated no significant reduction in 90 day mortality with hydrocortisone alone, whereas APROCCHSS demonstrated lower 90 day mortality with hydrocortisone plus fludrocortisone. Subsequent patient-level and network meta analyses suggest that any mortality benefit may be more evident when hydrocortisone is combined with fludrocortisone, although direct evidence comparing combination therapy with hydrocortisone alone remains limited. Hyperglycemia, hypernatremia, and neuromuscular weakness are clinically relevant adverse effects. High dose, short duration corticosteroid regimens are not recommended. Conclusions: Corticosteroids should not be considered routine therapy for all patients with sepsis. Their principal contemporary indication is persistent vasopressor dependent septic shock despite adequate resuscitation. Hydrocortisone 200 mg/day, administered intravenously as either intermittent doses or continuous infusion, represents the most established approach. The principal demonstrated benefit is more rapid shock reversal rather than a consistently proven mortality reduction. The additional use of fludrocortisone remains biologically plausible and supported by important trial and meta-analytic evidence, but uncertainty persists regarding its incremental benefit. Treatment should therefore be individualized according to the severity and trajectory of shock, competing indications, and potential adverse effects.

INTRODUCTION

Sepsis is a life threatening syndrome caused by a dysregulated host response to infection resulting in organ dysfunction. Septic shock represents a particularly severe phenotype characterized by profound circulatory and cellular/metabolic abnormalities and carries a substantially higher risk of death than sepsis without shock. The global burden of sepsis remains considerable. A recent Global Burden of Disease analysis estimated approximately 166 million sepsis cases and 21.4 million sepsis related deaths worldwide in 2021, emphasizing that sepsis continues to represent a major global health problem.¹

The conceptual framework for sepsis has changed substantially over the last decade. The Sepsis-3 consensus abandoned the previous distinction between “severe sepsis” and sepsis and defined sepsis according to infection-associated organ dysfunction. Septic shock is identified clinically by the requirement for vasopressors to maintain a mean arterial pressure of at least 65 mmHg together with a serum lactate concentration

greater than 2 mmol/L despite adequate volume resuscitation.^{2,3}

Management of septic shock is based on early recognition, source control, appropriate antimicrobial therapy, hemodynamic resuscitation, vasopressor support, and organ supportive strategies. Norepinephrine remains the preferred first-line vasopressor in most adults. However, a subgroup of patients develops persistent vasopressor-dependent shock despite appropriate initial management. This persistent state of circulatory failure has generated considerable interest in adjunctive corticosteroid therapy.⁴

Corticosteroids have been investigated in septic shock for more than half a century. Their proposed therapeutic effects extend beyond classical anti-inflammatory activity. Glucocorticoids can modulate transcriptional responses to inflammatory stimuli, influence endothelial and vascular function, restore vascular responsiveness to catecholamines, and interact with the hypothalamic-pituitary-adrenal axis. These effects provide a physiological rationale for their use during refractory septic shock.^{5,6}

However, corticosteroid therapy remains controversial. Although randomized trials consistently demonstrate more rapid reversal of shock, mortality results have varied substantially. The ADRENAL trial did not demonstrate a significant mortality reduction with hydrocortisone alone, whereas the APROCCHSS trial reported significantly lower 90-day mortality with hydrocortisone plus fludrocortisone.^{7,8} Subsequent systematic reviews have therefore focused increasingly on treatment heterogeneity, corticosteroid dose, duration, timing, mineralocorticoid activity, and patient selection.

The purpose of this review is to provide an updated and clinically oriented synthesis of the evidence regarding corticosteroid therapy in septic shock, integrating the physiological rationale with contemporary randomized trials, meta-analyses, and guideline recommendations.

METHODS

Study design

This manuscript represents an updated structured literature review based on the original review of



corticosteroid therapy in severe sepsis and septic shock. The original manuscript searched PubMed/MEDLINE, Web of Knowledge, and Scopus between October and November 2021 using combinations of “severe sepsis,” “septic shock,” “corticosteroids,” and “mortality,” with an approximately 20 year publication window.

For the present update, the evidence base was expanded to incorporate contemporary randomized controlled trials, systematic reviews, meta-analyses, international clinical practice guidelines, and major reviews published through 2026. Particular emphasis was placed on studies evaluating intravenous hydrocortisone, hydrocortisone plus fludrocortisone, mortality, shock reversal, vasopressor-free days, adverse events, dose-response relationships, and timing of treatment.

Because the objective of the present manuscript was to provide a clinically focused evidence synthesis rather than to generate a new pooled effect estimate, it was structured as a narrative review with a structured literature search rather than as a *de novo* PRISMA systematic review.

Evidence selection

Priority was given to:

1. Randomized controlled trials.
2. Patient level meta analysis.
3. Systematic reviews and conventional or network meta-analyses.
4. International evidence-based clinical practice guidelines.
5. Contemporary mechanistic and critical-care reviews.

Historical studies were retained when they were fundamental to understanding the development of corticosteroid therapy in septic shock.

Physiological rationale and mechanisms of action

The biological rationale for corticosteroid therapy in septic shock involves several interconnected mechanisms. During severe infection, activation of the hypothalamic-pituitary-adrenal axis results in increased cortisol production, while inflammatory mediators can simultaneously alter cortisol metabolism, receptor expression, and tissue responsiveness. Consequently,

the presence of an apparently normal or even elevated serum cortisol concentration does not necessarily indicate adequate glucocorticoid activity at the tissue level. This phenomenon has contributed to the concept of critical illness related corticosteroid insufficiency (CIRCI), which refers to inadequate corticosteroid activity for the severity of the patient's illness rather than simply an absolute deficiency of cortisol.^{4,5}

Glucocorticoids regulate inflammation through genomic and nongenomic mechanisms. Following activation of the glucocorticoid receptor, the receptor-ligand complex translocates to the nucleus and modifies transcription of multiple genes involved in inflammatory signaling. Corticosteroids suppress excessive activation of transcription factors such as nuclear factor kappa B and activator protein-1, thereby reducing the expression of several proinflammatory mediators. At the same time, glucocorticoids influence leukocyte trafficking, endothelial function, vascular permeability, and immune-cell activity. These effects should be interpreted as immunomodulation rather than complete suppression of host defenses.^{5,7}

The cardiovascular effects of hydrocortisone are particularly relevant in septic shock. Corticosteroids increase vascular responsiveness to endogenous and exogenous catecholamines, promote restoration of vascular tone, and may facilitate recovery from vasoplegia. They also influence endothelial function and the expression of adrenergic receptors. These mechanisms provide a physiological explanation for the consistent observation across clinical trials that corticosteroid therapy can accelerate reversal of shock and reduce the duration or dose of vasopressor therapy, even when an effect on mortality is not demonstrated.^{3,6}

Clinical evidence

The evidence supporting corticosteroids in septic shock has evolved considerably. Early randomized trials evaluated very high doses of methylprednisolone or dexamethasone administered for short periods, with inconsistent results and concerns regarding infectious complications. Subsequent investigations shifted toward lower doses of hydrocortisone administered over several days. The landmark study by Annane et al. in 2002 evaluated hydrocortisone combined with



fludrocortisone in patients with vasopressor dependent septic shock and demonstrated a mortality benefit, particularly among patients with an inadequate response to corticotropin.⁸ These findings contributed substantially to the adoption of low dose corticosteroid therapy in refractory septic shock.

The CORTICUS trial, published in 2008, provided an important counterpoint. In a broader population of patients with septic shock, hydrocortisone accelerated shock reversal but did not significantly reduce 28 day mortality. The study also failed to demonstrate that corticotropin responsiveness could reliably identify patients who would benefit from hydrocortisone. These findings weakened the concept that corticosteroid therapy should be restricted according to the results of an adrenocorticotrophic hormone stimulation test and reinforced the importance of clinical hemodynamic criteria when considering treatment.⁹

Two large randomized trials published in 2018 further defined the role of corticosteroids. The ADRENAL trial evaluated continuous hydrocortisone at a dose of 200 mg per day for up to seven days in mechanically ventilated patients with septic shock. Hydrocortisone did not significantly reduce 90 day mortality, but it was associated with faster resolution of shock, shorter duration of mechanical ventilation, and reduced ICU length of stay.¹⁰ In contrast, the APROCCHSS trial evaluated hydrocortisone combined with fludrocortisone and demonstrated a significant reduction in 90 day mortality, together with increased numbers of vasopressor free and organ failure free days.¹¹ The different mortality results between ADRENAL and APROCCHSS have generated considerable discussion regarding patient selection, corticosteroid regimen, mineralocorticoid activity, timing, and severity of shock.

Subsequent systematic reviews and individual-patient-data analyses have generally supported a more nuanced interpretation. The most reproducible benefit of corticosteroids is improvement in hemodynamic recovery, particularly earlier shock reversal and reduced exposure to vasopressors. Mortality effects are less consistent but may be favorable in selected populations. A patient level meta analysis published in 2023 evaluated individual data from randomized trials of low dose

hydrocortisone in adults with septic shock and reinforced the importance of considering treatment effects across clinically relevant subgroups rather than interpreting corticosteroid therapy as uniformly beneficial or harmful.¹² Overall, the evidence does not support the concept that corticosteroids are a universal mortality reducing therapy for all patients with septic shock, but it does support their role as an adjunctive treatment for persistent vasopressor-dependent shock.

Current clinical application

The contemporary indication for corticosteroids is therefore primarily hemodynamic rather than biochemical. Current international recommendations support the use of intravenous corticosteroids in patients with septic shock who continue to require vasopressor therapy despite adequate fluid resuscitation and appropriate management of the underlying infection. The 2024 focused update from the Society of Critical Care Medicine conditionally recommends corticosteroids for septic shock and specifically recommends against high dose, short duration corticosteroid regimens.³ The usual regimen is hydrocortisone 200 mg per day, administered either as a continuous intravenous infusion or as 50 mg intravenously every six hours. The optimal duration and tapering strategy remain less clearly established, and treatment should be individualized according to clinical response and the persistence of vasopressor requirements.

An important practical point is that corticosteroids should not replace fundamental management of septic shock. They are adjunctive therapy and should be considered only after appropriate antimicrobial treatment, source control, hemodynamic assessment, and adequate resuscitation have been initiated. Their use is most rational when vasoplegia persists and the patient remains dependent on vasopressors. Conversely, routine administration to patients with sepsis who are hemodynamically stable or whose shock rapidly resolves with fluids and vasopressors is not supported by current evidence. Corticotropin stimulation testing is also not routinely recommended to determine which patients should receive corticosteroids because its ability to guide treatment has not been demonstrated convincingly.^{3,9}



The addition of fludrocortisone remains an area of uncertainty. APROCCHSS demonstrated a mortality benefit with hydrocortisone plus fludrocortisone, whereas ADRENAL demonstrated no mortality benefit with hydrocortisone alone. Nevertheless, the difference between these trials cannot be attributed exclusively to the presence of fludrocortisone because the populations, treatment protocols, and other methodological characteristics differed. Consequently, contemporary guidelines do not establish that fludrocortisone must routinely be added to hydrocortisone in every patient with septic shock.^{3,10,11}

Adverse effects and safety

The potential adverse effects of corticosteroids should be incorporated into the decision to initiate therapy. Hyperglycemia is common and generally requires closer glucose monitoring and adjustment of insulin therapy. Hyponatremia and fluid retention may occur because of mineralocorticoid activity, while prolonged corticosteroid exposure can contribute to neuromuscular weakness. The concern regarding secondary infections remains clinically relevant, although contemporary trials using low-dose hydrocortisone have not consistently demonstrated a major increase in serious infectious complications. The risk-benefit balance therefore differs substantially from that associated with the historical use of very high dose corticosteroids.⁹⁻¹²

DISCUSSION

The role of corticosteroids in septic shock has evolved from the use of high-dose, short-course regimens toward a more selective strategy based on low-dose hydrocortisone in patients with persistent vasopressor dependent shock. This evolution is important because the available evidence cannot be interpreted as demonstrating a universal mortality benefit from corticosteroids in sepsis. Instead, the most consistent finding across clinical trials is an improvement in hemodynamic recovery, with faster reversal of shock and reduced duration or intensity of vasopressor therapy. The discrepancy between these effects and the less consistent mortality results reflects the complexity of septic shock, in which outcome is determined not only by the inflammatory response but also by the severity

and duration of organ dysfunction, infection control, source control, comorbidities, and the timing and adequacy of supportive treatment.^{3,6,13,14}

The differences between the major randomized clinical trials illustrate this complexity. The study by Annane et al. demonstrated a mortality benefit with hydrocortisone combined with fludrocortisone in patients with vasopressor-dependent septic shock, whereas the CORTICUS trial demonstrated faster shock reversal without a significant reduction in mortality.^{8,9} These apparently contradictory findings should not be interpreted as evidence that one trial invalidated the other. The studies differed in patient selection, severity of illness, timing of enrollment, baseline mortality, and treatment protocols. Patients included in CORTICUS generally had lower severity and mortality risk than those enrolled in earlier trials, which may have reduced the potential absolute benefit of corticosteroid therapy. In addition, the use of fludrocortisone in the Annane regimen may have contributed to the observed effect, although the available evidence does not allow the mortality difference between trials to be attributed exclusively to mineralocorticoid supplementation.

The ADRENAL and APROCCHSS trials subsequently provided the most important contemporary evidence regarding corticosteroid therapy. ADRENAL, which evaluated continuous hydrocortisone at 200 mg per day, did not demonstrate a significant reduction in 90 day mortality, but it did demonstrate faster resolution of shock and reductions in several measures of critical care resource use. APROCCHSS, in contrast, demonstrated a significant mortality reduction with hydrocortisone plus fludrocortisone and also showed improvement in vasopressor free and organ failure free days.^{10,11} These findings suggest that corticosteroids have a reproducible physiological effect on circulatory dysfunction, while their influence on survival is more heterogeneous. The mortality signal may therefore depend on the characteristics of the population treated, the severity of shock, the corticosteroid regimen, and potentially the presence of a subgroup with greater dependence on endogenous glucocorticoid activity.

The distinction between shock reversal and mortality is clinically relevant. Septic shock is a dynamic syndrome, and prolonged exposure to vasopressors is



associated with persistent vascular dysfunction and progressive organ injury. By increasing vascular responsiveness to catecholamines and restoring components of the stress response, hydrocortisone may facilitate earlier hemodynamic stabilization. However, successful reversal of vasopressor dependence does not necessarily translate into survival if irreversible organ dysfunction, uncontrolled infection, or other complications have already developed. Therefore, the absence of a consistent mortality benefit should not be interpreted as evidence that corticosteroids lack clinically meaningful effects. Rather, their strongest and most reproducible therapeutic effect appears to be the acceleration of cardiovascular recovery.^{3,10,14}

Another important consideration is the concept of critical illness-related corticosteroid insufficiency. During severe sepsis, cortisol concentrations, cortisol metabolism, corticosteroid receptor signaling, and tissue responsiveness may all be altered.^{4,5} Consequently, a single serum cortisol concentration does not necessarily reflect the functional adequacy of glucocorticoid activity. This explains, at least in part, why attempts to use corticotropin stimulation testing as a routine method for selecting patients have not produced a sufficiently reliable strategy. The available clinical evidence therefore favors a pragmatic approach in which persistent vasopressor dependence is more important than an isolated endocrine measurement when deciding whether to initiate hydrocortisone.^{3,4,9}

The timing of therapy is also relevant. Corticosteroids should not be administered indiscriminately at the time of sepsis recognition, because many patients respond adequately to antimicrobial therapy, source control, fluids, and vasopressors alone. Their potential benefit becomes more clinically relevant when shock persists despite appropriate initial management. This approach is consistent with contemporary recommendations and avoids unnecessary exposure in patients who do not have sustained vasopressor-dependent circulatory failure.^{3,6} At the same time, once the clinical indication has been established, prolonged delay in initiating therapy may be undesirable because persistent vasoplegia and prolonged catecholamine exposure may contribute to ongoing organ dysfunction.

The dose and duration of corticosteroid therapy are equally important. Historical studies using supraphysiological doses produced unfavorable results and raised concerns about immunosuppression and infectious complications. In contrast, contemporary evidence has focused primarily on approximately 200 mg per day of intravenous hydrocortisone, administered continuously or in divided doses.^{9-12,14} The distinction between these approaches is fundamental. The objective of current therapy is not to suppress the immune system maximally, but to provide glucocorticoid activity sufficient to modulate the dysregulated inflammatory and cardiovascular response associated with severe shock. High-dose, short-duration corticosteroid therapy should therefore not be considered equivalent to the low-dose regimens supported by current evidence.³

The addition of fludrocortisone remains a relevant but unresolved question. The favorable results observed in APROCCHSS suggest that combined glucocorticoid and mineralocorticoid activity may provide additional benefit in selected patients, particularly given the potential role of aldosterone sensitive mechanisms in vascular tone and sodium homeostasis. However, the absence of a mortality benefit with hydrocortisone alone in ADRENAL does not establish that fludrocortisone is indispensable, because the two trials differed in several important clinical and methodological characteristics.^{10,11} Consequently, current evidence supports hydrocortisone as the core therapy while leaving the routine addition of fludrocortisone open to clinical judgment and institutional practice.

Safety is another essential component of the discussion. Corticosteroid therapy can produce hyperglycemia, hypernatremia, fluid retention, and neuromuscular weakness, particularly with prolonged exposure. Concerns about secondary infection are also biologically plausible because glucocorticoids modify immune responses. Nevertheless, contemporary randomized trials using low dose regimens have not demonstrated a consistent major increase in serious infectious complications sufficient to outweigh their hemodynamic benefits in patients with persistent septic shock.⁹⁻¹⁴ This supports a risk-benefit assessment based on the severity

of circulatory failure rather than an assumption that corticosteroids are inherently unsafe in infection.

The available meta-analyses further reinforce this interpretation. Overall, corticosteroids are associated with greater likelihood of shock reversal and shorter exposure to vasopressors, while the magnitude and consistency of mortality reduction remain uncertain.¹³⁻

¹⁶ The heterogeneity between studies is clinically meaningful and may explain why recommendations have progressively shifted from considering corticosteroids as a potential universal therapy toward recommending them specifically for patients with ongoing vasopressor requirements. In this context, the most appropriate interpretation of the literature is not that corticosteroids either "work" or "do not work" in septic shock, but rather that their benefit depends on the clinical phenotype, disease severity, timing, dose, and regimen used.

Taken together, current evidence supports a selective and physiologically oriented approach to corticosteroid therapy. Hydrocortisone should be considered when septic shock remains refractory to appropriate fluid resuscitation and vasopressor therapy, particularly when persistent vasoplegia represents the predominant hemodynamic problem. Its principal expected benefit is more rapid cardiovascular stabilization and reduction in vasopressor dependence, whereas a survival advantage cannot be guaranteed for every patient. This distinction is important for clinical decision-making and for communicating realistic treatment expectations. Corticosteroids should therefore be viewed as an adjunct to, and not a substitute for, early antimicrobial therapy, source control, appropriate fluid management, vasopressors, and organ support.^{3,6,13-16}

Finally, an important limitation of the current evidence is the difficulty of identifying prospectively which patients are most likely to derive a mortality benefit from corticosteroids. Future research should focus on clinically and biologically defined phenotypes of septic shock, including markers of glucocorticoid responsiveness, endothelial dysfunction, vasoplegia, and alterations in corticosteroid metabolism. A more individualized approach may ultimately allow corticosteroid therapy to be targeted toward patients in whom the pathophysiological mechanisms are most

likely to be corticosteroid-responsive. Until such evidence becomes available, the strongest justification for treatment remains persistent vasopressor-dependent septic shock after appropriate initial management, using low dose hydrocortisone rather than high-dose corticosteroid regimens.

CONCLUSIÓN

Corticosteroids have an established but selective role in the management of septic shock. Current evidence does not support their routine administration to all patients with sepsis or to patients whose shock responds adequately to fluids and vasopressors. Their principal indication is persistent vasopressor-dependent septic shock despite appropriate initial resuscitation and treatment of the underlying infection. Low-dose intravenous hydrocortisone, generally 200 mg per day, is the regimen best supported by contemporary evidence and guidelines. Although corticosteroids consistently accelerate shock reversal and reduce vasopressor requirements, their effect on mortality remains less definitive. Therefore, corticosteroid therapy should be regarded as an adjunct to, rather than a substitute for, timely antimicrobial therapy, source control, fluid management, vasopressor support, and comprehensive organ support.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

REFERENCES

1. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315 (8):801-810.
2. Shankar-Hari M, Phillips GS, Levy ML, et al. Developing a new definition and assessing new clinical criteria for septic shock: for the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315 (8):775-787.
3. Chaudhuri D, Nei AM, Rochwerf B, et al. 2024 Focused Update: Guidelines on Use of Corticosteroids in Sepsis, Acute Respiratory Distress



- Syndrome, and Community-Acquired Pneumonia. *Crit Care Med.* 2024;52 (5).
4. Annane D, Pastores SM, Arlt W, et al. Critical illness-related corticosteroid insufficiency (CIRCI): a task force report from the Society of Critical Care Medicine and the European Society of Intensive Care Medicine. *Crit Care Med.* 2017;45 (12):2078-2088.
 5. Cain DW, Cidlowski JA. Immune regulation by glucocorticoids. *Nat Rev Immunol.* 2017;17 (4):233-247.
 6. Evans L, Rhodes A, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021. *Intensive Care Med.* 2021;47 (11):1181-1247.
 7. Rhen T, Cidlowski JA. Antiinflammatory action of glucocorticoids - new mechanisms for old drugs. *N Engl J Med.* 2005;353 (16):1711-1723.
 8. Annane D, Sébille V, Charpentier C, et al. Effect of treatment with low doses of hydrocortisone and fludrocortisone on mortality in patients with septic shock. *JAMA.* 2002;288 (7):862-871.
 9. Sprung CL, Annane D, Keh D, et al. Hydrocortisone therapy for patients with septic shock. *N Engl J Med.* 2008;358 (2):111-124.
 10. Venkatesh B, Finfer S, Cohen J, et al. Adjunctive glucocorticoid therapy in patients with septic shock. *N Engl J Med.* 2018;378 (9):797-808.
 11. Annane D, Renault A, Brun-Buisson C, et al. Hydrocortisone plus fludrocortisone for adults with septic shock. *N Engl J Med.* 2018;378 (9):809-818.
 12. Pirracchio R, et al. Patient-Level Meta-Analysis of Low-Dose Hydrocortisone in Adults with Septic Shock. *NEJM Evid.* 2023;2 (6).
 13. Annane D, Bellissant E, Bollaert PE, et al. Corticosteroids for treating sepsis. *Cochrane Database Syst Rev.* 2019;12.
 14. Rochwerf B, Oczkowski SJW, Siemieniuk RAC, et al. Corticosteroids in sepsis: an updated systematic review and meta-analysis. *Crit Care Med.* 2018;46 (9):1411-1420.
 15. Fang F, Zhang Y, Tang J, et al. Association of corticosteroid treatment with outcomes in adult patients with sepsis: a systematic review and meta-analysis. *JAMA Intern Med.* 2019;179 (2):213-223.
 16. Rygård SL, Butler E, Granholm A, et al. Low-dose corticosteroids for adult patients with septic shock: a systematic review with meta-analysis and trial sequential analysis. *Intensive Care Med.* 2018;44 (7):1003-1016.

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