Clinical update no. 509
7March 2018

New studies on sepsis have not necessarily made things any clearer. Recognition is still problematic. Previous lack of clarity about the role of steroids has not really been made any clearer – the recomendation to consider steroids if not responsing to fluids and vasopressors essentially remains, though now based on 2 more large trials giving conflicting results. And the fluid debate goes on. Saline v balanced crystalloids has been studied in 2 trials shoiwng little outcome difference, though there were biochemical differences.

REVIEW ARTICLE

Review article: Sepsis in the emergency department – Part 1: Definitions and outcomes

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SEPSIS DEFINITION

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.

Defined as Organ dysfunction, not abnormal vital signs

Sepsis recognition in the ED

Sepsis is a clinical syndrome with no tissue diagnostic or reliable serological test. Sepsis often presents insidiously, and the clinical features can be heterogeneous and non-specific.

The question of how to optimally identify sepsis in the ED remains unresolved.

qSOFA (Quick SOFA) Score for Sepsis

Use to predict mortality, NOT to diagnose sepsis.

Altered mental status GCS <15	No	Yes
Respiratory rate ≥22	No	Yes
Systolic BP ≤100	No	Yes

2 points qSOFA Score — 2 of 3 –> 10% mortality

High Risk

SIRS and qSOFA are not validated for sepsis evaluation in ED

Evaluating sepsis

	Sensitivity	Specifity
qSOFA	0.51	0.83
SIRS	0.86	0.29

No biomarker to date has been sufficiently validated as a single test to rule-in or rule-out sepsis

Adjunctive Glucocorticoid Therapy in Patients with Septic Shock

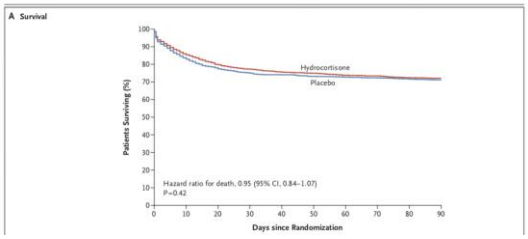
for the ADRENAL Trial Investigators and the Australian–New Zealand Intensive Care Society Clinical Trials Group*

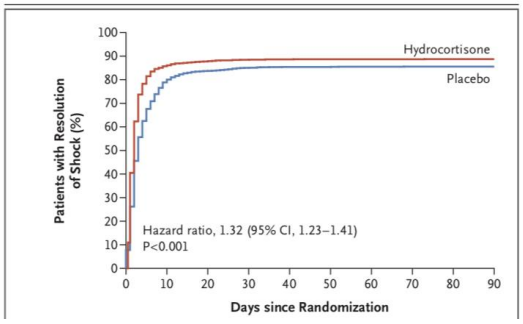
SEPSIS, WHICH HAS BEEN IDENTIFIED BY the World Health Organization as a global health priority, has no proven pharmacologic treatment, other than the appropriate antibiotic agents, fluids, and vasopressors as needed;

Current clinical practice guidelines recommend the use of hydrocortisone in patients with septic shock if adequate fluid resuscitation and treatment with vasopressors have not restored hemodynamic stability; however, the guidelines classify the recommendation as weak, on the basis of the low quality of available evidence.[15]

Hydrocortisone 200mg/day given by infusion was evaluated in septic shock. There was no mortality benefit, but there was some benefit measured by resolution of shock, weaning off ventilation and time in ICU.

Available at http://www.heti.nsw.gov.au/programs/emergency-medicine-training/emergency-medicine-training-test/educational-resources/em-clinical-updates/





The difference in resolution is fairly marginal.

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ORIGINAL ARTICLE

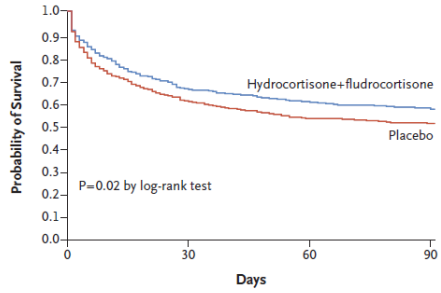
Hydrocortisone plus Fludrocortisone for Adults with Septic Shock

for the CRICS-TRIGGERSEP Network*

N ENGL J MED 378;9 NEJM.ORG MARCH 1, 2018

CONCLUSIONS

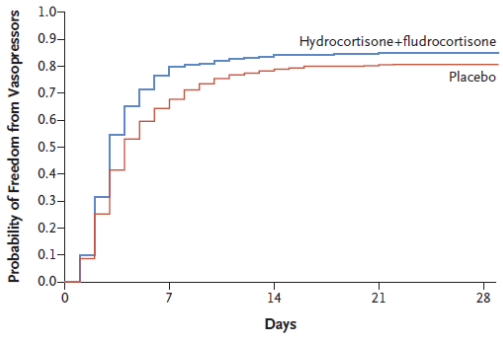
In this trial involving patients with septic shock, 90-day all-cause mortality was lower among those who received hydrocortisone plus fludrocortisone than among those who received placebo. (Funded by Programme Hospitalier de Recherche Clinique 2007 of the French Ministry of Social Affairs and Health; APROCCHSS ClinicalTrials.gov number, NCT00625209.)



No. at Risk				
Hydrocortisone+ fludrocortisone	614	405	372	353
Placebo	627	381	333	319

Figure 1. 90-Day Survival Distributions.

Time to Weaning from Vasopressors



In conclusion, 7-day treatment with a 50-mg intravenous bolus of hydrocortisone every 6 hours and a daily dose of 50 μg of oral fludrocortisone resulted in lower mortality at day 90 and at ICU and hospital discharge than placebo among adults with septic shock.

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EDITORIALS

A Role for Hydrocortisone Therapy in Septic Shock?

Studies on the role of steroids in sepsis have given conflicting results, and their role is unclear. The ADRENAL and APROCCHSS trials are landmark studies, and by far the largest ever done. Entry criteria for both studies were vasopressor-dependent shock and need for mechanical ventilation, using APACHE and SOFA scores respectively.

Outcomes of the 2 trials differed, with about 28% mortality in ADRENAL (no difference between groups) and 43 v 49% for the 2 groups in the APROCCHSS trial which showed improved outcomes with hydrocortisone + fludrocortisone. Both trials showed improved resolution of shock and more rapid cessation of mechanical ventilation. Rates of serious adverse events, beyond hyperglycemia with bolus glucocorticoid doses, were low.

Better data will not be forthcoming any time soon. Hydrocortisone may improve outcomes in the more seriously ill, but identifying those who might benefit is difficult and prognosis is difficult to predict early on.

It would be reasonable to use hydrocortisone for patients not improving with other optimised intervention - i.e. vasopressors, appropriate antibiotics, volume resuscitation and source control.

Not a lot different from earlier Guidelines.

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

H. CORTICOSTEROIDS

1. We suggest against using IV hydrocortisone to treat septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability. If this is not achievable, we suggest IV hydrocortisone at a dose of 200 mg per day (weak recommendation, low quality of evidence).

Available at http://www.heti.nsw.gov.au/programs/emergency-medicine-training/emergency-medicine-training-test/educational-resources/em-clinical-updates/