

# Longitudinal Assessment of Adrenal Function in the Early and Prolonged Phases of Critical Illness in Septic Patients: Relations to Cytokine Levels and Outcome

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**Context:** Adrenal dysfunction remains a controversial issue in critical care. The long-stay intensive care unit (ICU) population may be at increased risk of adrenal insufficiency.

**Objective:** We aimed to determine whether adrenal dysfunction develops during the course of sepsis.

**Design:** This is a prospective observational longitudinal study.

**Setting:** The study was conducted in the ICU of a secondary/tertiary care hospital

**Patients:** We studied 51 consecutive mechanically ventilated patients with sepsis.

**Intervention:** We measured cortisol, ACTH, cortisol-binding globulin, cytokines, and cortisol 30 minutes after 1  $\mu\text{g}$  ACTH(1–24), upon sepsis diagnosis and every 3 to 4 days, until Day 30 or until recovery or death.

**Main Outcome Measures:** We looked for changes in baseline and stimulated cortisol levels and its relationship to ACTH levels, sepsis severity or survival.

**Results:** Baseline and stimulated cortisol levels did not vary significantly. Septic patients with shock had higher baseline ( $20 \pm 6$  vs  $17 \pm 5$   $\mu\text{g}/\text{dL}$ ,  $P = .03$ ) and stimulated cortisol levels ( $26 \pm 5$  vs  $23 \pm 6$   $\mu\text{g}/\text{dL}$ ,  $P = .04$ ), compared with those without shock. On Day 1, ACTH levels could not predict cortisol levels ( $R^2 = 0.06$ ,  $P = .08$ ). ACTH levels increased significantly after Day 10 and, at this time point, they related to cortisol levels ( $R^2 = 0.35$ ,  $P < .001$ ). Development of septic shock, or resolution from it, was not associated with changes in baseline, stimulated cortisol levels, or the cortisol increment. There was much inpatient variability in the diagnosis of adrenal dysfunction at different time points.

**Conclusions:** Total cortisol levels relate both to the severity and outcome of sepsis and remain fairly unchanged during the course of illness. Initially, cortisol levels are largely ACTH independent, whereas ACTH increases and correlates with cortisol levels later on. Adrenal dysfunction does not seem to be a major problem during the prolonged phase of sepsis. Although not significant, the variation in cortisol levels may be such that classification of patients varies, questioning the utility of arbitrary cut-offs to define adrenal dysfunction in septic patients. (*J Clin Endocrinol Metab* 99: 4471–4480, 2014)