1: Crit Care Med. 1994 Jun;22(6):914-21.

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Induction of the heat shock response reduces mortality rate and organ damage in a sepsis-induced acute lung injury model.

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OBJECTIVE: To test the hypothesis that induction of heat shock proteins before the onset of sepsis could prevent or reduce organ injury and death in a rat model of intra-abdominal sepsis and sepsis-induced acute lung injury produced by cecal ligation and perforation. DESIGN: Prospective, blind, randomized, controlled trial. SETTING: University research laboratory. SUBJECTS: One-hundred forty-two adult Sprague-Dawley rats (weight range 200 to 300 g). INTERVENTIONS: Production of intra-abdominal sepsis and exposure to heat stress. Animals were randomly divided into four groups: heated and septic, heated and sham-septic, unheated and septic, and unheated and sham-septic. MEASUREMENTS AND MAIN RESULTS: We evaluated the mortality rate and pathologic changes in lung, heart, and liver at 18 hrs after cecal perforation, at 24 hrs after removal of the cecum, and at 7 days after perforation. Heated animals exhibited a maximum increase in heat shock protein of 72 kilodalton molecular weight protein concentrations in the lungs and heart 6 to 24 hrs after the hyperthermic stress. By 18 hrs after perforation, 25% of the septic, unheated animals had died whereas none of the septic heated animals had died ($p < .005$). Septic, heated animals showed a marked decrease in 7-day mortality rate (21%) compared with septic unheated animals (69%) ($p < .01$). Furthermore, septic heated animals showed less histologic evidence of lung and liver damage than septic unheated animals. CONCLUSIONS: These data suggest that thermal pretreatment, associated with the synthesis of heat shock proteins, reduces organ damage and enhances animal survival in experimental sepsis-induced acute lung injury. Although the mechanisms by which heat shock proteins exert a protective effect are not well understood, these data raise interesting questions regarding the importance of fever in the protection of the whole organism during bacterial infection.

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