

## Induced hypothermia does not improve outcomes for patients with severe bacterial meningitis

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In a study of adults with severe bacterial meningitis, therapeutic hypothermia (reduction of body temperature) did not improve outcomes, and it may even have been harmful, according to a study appearing in the November 27 issue of *JAMA*.

Among adults with bacterial meningitis, the case fatality rate and frequency of neurologic complications are high, especially among <u>patients</u> with pneumococcal meningitis. In animal models of meningitis, moderate <u>hypothermia</u> has shown favorable effects, according to background information in the article.

Bruno Mourvillier, M.D., of the Universite Paris Diderot, Sorbonne Paris Cite, Paris, and colleagues examined the effect of induced hypothermia on outcomes in patients with severe bacterial meningitis. The study, conducted at 49 intensive care units in France, randomized 98 comatose adults to hypothermia (n = 49), comprising a loading dose of  $4^{\circ}$ C cold saline and cooling to  $32^{\circ}$ C to  $34^{\circ}$ C for 48 hours; or standard care (n = 49). The primary outcome measure was the score at 3 months on the Glasgow Outcome Scale, an assessment of physical function following cerebral injuries.

The trial was stopped early at the request of the data and safety monitoring board because of concerns over excess mortality in the hypothermia group (25 of 49 patients [51 percent]) vs. the control group



(15 of 49 patients [31 percent]). Pneumococcal meningitis was diagnosed in 77 percent of patients. At 3 months, 86 percent in the hypothermia group compared with 74 percent of controls had an unfavorable outcome.

After adjustment for factors that might explain the findings, mortality remained higher, although the increase was no longer statistically significant, in the hypothermia group. Subgroup analysis on patients with pneumococcal meningitis showed similar results. "Although there was a trend toward higher mortality and rate of unfavorable outcome in the hypothermia group, early stopping of clinical trials is known to exaggerate treatment effects, precluding firm conclusions about harm of <u>therapeutic hypothermia</u> in bacterial meningitis," the authors write.

"In conclusion, our trial does not support the use of hypothermia in adults with severe <u>meningitis</u>. Moderate hypothermia did not improve outcome in patients with severe <u>bacterial meningitis</u> and may even be harmful. Our results may have important implications for future trials on hypothermia in patients presenting with septic shock or stroke. Careful evaluation of safety issues in these future and ongoing trials are needed."

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