

# Review: adjuvant corticosteroid therapy reduces death, hearing loss, and neurological sequelae in bacterial meningitis

van de Beek D, de Gans J, McIntyre P, *et al*. Corticosteroids in acute bacterial meningitis. *Cochrane Database Syst Rev* 2003;(3):CD004305.

Clinical impact ratings IM/Ambulatory care ★★★★★☆☆ Internal medicine ★★★★★☆☆ Neurology ★★★★★☆☆ Infectious disease ★★★★★☆☆

**Q** In children and adults with acute bacterial meningitis (ABM), is adjuvant corticosteroid therapy more effective than placebo for reducing mortality, hearing loss, and neurological sequelae?

## METHODS

**Data sources** studies were identified by searching the Cochrane Central Register of Controlled Trials (2003), Medline (1966 to January 2003), EMBASE/Excerpta Medica (1974 to April 2002), and Healthline (1988 to April 2002); reviewing current trials published before April 2002; scanning reference lists; hand searching abstracts of congresses; and contacting researchers and experts.

**Study selection and assessment** studies in any language were selected if they were randomised controlled trials that compared any type of corticosteroid therapy adjuvant to antibiotics with placebo in patients with ABM and recorded case fatality rates. 2 reviewers independently assessed the quality of studies using the Jadad scale.

**Outcomes** mortality, severe hearing loss (bilateral hearing loss > 60 dB or requiring bilateral hearing aids), and short term (discharge to 6 wk) or long term (6 to 12 mo after discharge) neurological sequelae.

Abstract and commentary also appear in *ACP Journal Club*.

## Commentary

ABM remains one of the most catastrophic of infectious diseases. Victory against ABM requires the same strategies used against other life threatening infectious diseases: prevention (with vaccination and effective public health measures), killing of invading organisms, and suppressing the host's deleterious immune response. Although recent vaccine developments against ABM have shifted the proportion of infections to adults in developed countries, ABM continues to threaten both children and adults in developing countries.

Failed treatment of ABM is rarely a bug and drug problem despite recent concerns about drug resistant pneumococci and meningococci. The fact that a host's immune response causes the bulk of neurological morbidity in ABM (which can be attenuated by adjunctive corticosteroids before administering antibiotics) has been supported by extensive animal research. Vancomycin does not cross the rabbit blood brain barrier effectively when meningeal inflammation is reduced, raising the concern that corticosteroids might reduce the effectiveness of vancomycin in humans. However, in children with ABM caused by cephalosporin resistant pneumococci, cerebrospinal fluid penetration of vancomycin seems unaffected by adjunctive use of corticosteroids.<sup>1</sup>

van de Beek *et al* should be commended on a sound review of the effect of corticosteroids on ABM in children and adults. A similar meta-analysis done with fewer eligible studies reached similar conclusions for childhood ABM and remained cautious regarding the use of corticosteroids in adults with ABM.<sup>2</sup> More importantly, a recent randomised controlled trial by de Gans *et al* showed that corticosteroids were beneficial in ABM, especially in pneumococcal meningitis (which has the gravest prognosis).<sup>3</sup> Corticosteroids should be given as early as possible in all cases of ABM, using the published dose of dexamethasone, 10 mg every 6 hours in adults, or 0.4 to 0.6 mg/kg per day divided in 4 daily doses for children for 4 days. Ideally, dexamethasone should be administered before the antibiotics.

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1 Klugman KP, Friedland IR, Bradley JS. *Antimicrob Agents Chemother* 1995;**39**:1988-92.

2 McIntyre PB, Berkey CS, King SM, *et al*. *JAMA* 1997;**278**:925-31.

3 de Gans J, van de Beek D. *N Engl J Med* 2002;**347**:1549-56.

## MAIN RESULTS

18 studies (1853 patients) met the selection criteria. Overall, fewer patients who received corticosteroids died than did those who received placebo (table); groups did not differ for mortality in 14 studies with children only (relative risk [RR] 0.95, 95% CI 0.65 to 1.37). Fewer patients in the corticosteroid than in the placebo group had severe hearing loss (table). Children with ABM from pathogens other than *Haemophilus influenzae* who received corticosteroids also had a reduced risk of hearing loss (RR 0.42, CI 0.20 to 0.89). Although the groups did not differ in 7 studies for short term neurological sequelae (RR 0.72, CI 0.48 to 1.06), the corticosteroid group had a reduction in risk of long term neurological sequelae (table). Groups did not differ for adverse events.

## CONCLUSION

In children and adults with acute bacterial meningitis, adjuvant corticosteroid therapy reduces mortality, hearing loss, and long term neurological sequelae.

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### Corticosteroids v placebo for acute bacterial meningitis at up to 12 months\*

Outcomes	Patients	Number of studies	Weighted event rates			
			Corticosteroids	Placebo	RRR (95% CI)	NNT (CI)
Mortality	All	18	8.6%	11.6%	24% (3 to 41)	34 (20 to ∞)
	Adults	3	8%	21%	62% (22 to 82)	8 (5 to 25)
Severe hearing loss	All	13	2.4%	7.4%	63% (38 to 78)	20 (15 to 50)
	Children	12	2.8%	9.8%	69% (46 to 82)	15 (10 to 25)
Long term neurological sequelae	All	10	6%	9%	55% (0 to 55)	34 (17 to ∞)

\*Abbreviations defined in glossary; weighted events, RRR, NNT, and CI calculated from data in article using a fixed effects model.