



Policy Statement—Postnatal Corticosteroids to Prevent or Treat Bronchopulmonary Dysplasia

abstract

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The purpose of this revised statement is to review current information on the use of postnatal glucocorticoids to prevent or treat bronchopulmonary dysplasia in the preterm infant and to make updated recommendations regarding their use. High-dose dexamethasone (0.5 mg/kg per day) does not seem to confer additional therapeutic benefit over lower doses and is not recommended. Evidence is insufficient to make a recommendation regarding other glucocorticoid doses and preparations. The clinician must use clinical judgment when attempting to balance the potential adverse effects of glucocorticoid treatment with those of bronchopulmonary dysplasia. *Pediatrics* 2010;126:800–808

INTRODUCTION

Chronic lung disease (CLD) after preterm birth, also known as bronchopulmonary dysplasia (BPD), a major morbidity of the very preterm infant, is remarkably resistant to therapeutic interventions and negatively affects neurodevelopmental outcomes.^{1–4} In 2002, the American Academy of Pediatrics (AAP), in a policy statement regarding the use of postnatal corticosteroids for prevention or treatment of CLD in preterm infants, concluded that routine dexamethasone therapy for the prevention or treatment of CLD could not be recommended.⁵ Instead, the AAP recommended that (1) use of dexamethasone for the prevention or treatment of CLD be limited to randomized, controlled trials (RCTs) with long-term follow-up, (2) alternative corticosteroids undergo further study, and (3) infants currently enrolled in RCTs of corticosteroids receive long-term neurodevelopmental follow-up. The statement added that outside the context of such trials, “the use of corticosteroids should be limited to exceptional clinical circumstances (eg, an infant on maximal ventilatory and oxygen support). In those circumstances, parents should be fully informed about the known short- and long-term risks and agree to treatment.”⁵

Postnatal use of dexamethasone for BPD has decreased since the publication of the AAP statement; however, the incidence of BPD has not decreased.⁶ Instead, several reports have suggested that the incidence or severity of BPD may have increased.^{4,7,8} Moreover, results of additional clinical trials, meta-analyses, and follow-up studies have been published, warranting a review of the new information and revision of the statement. The objectives of this revised statement are to review data published since the 2002 AAP statement and to reexamine previous recommendations for the use of glucocorticoid therapy in view of new information.

COMMITTEE ON FETUS AND NEWBORN

KEY WORDS

bronchopulmonary dysplasia, preterm infant, glucocorticoid, dexamethasone, chronic lung disease

ABBREVIATIONS

CLD—chronic lung disease

BPD—bronchopulmonary dysplasia

AAP—American Academy of Pediatrics

RCT—randomized, controlled trial

CP—cerebral palsy

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LITERATURE REVIEW

Dexamethasone

Reviews and meta-analyses cited in the previous AAP statement indicated that dexamethasone may decrease mortality rates, facilitate extubation, and generally decrease the incidence of BPD but that it carries a significant risk for short- and long-term adverse effects, especially impairment of growth and neurodevelopment.^{5,9–12} In recently updated systematic reviews, the Cochrane Collaboration continues to conclude that the benefits of dexamethasone therapy in the first week of life may not outweigh its many adverse effects.¹³ In contrast, it concludes that treatment after the first postnatal week may reduce mortality rates without increasing adverse long-term neurodevelopmental outcomes, although long-term follow-up data remain limited.¹⁴ Therefore, it has been suggested that “it appears prudent to reserve the

use of late corticosteroids to infants who cannot be weaned from mechanical ventilation and to minimize the dose and duration of any course of treatment.”¹⁴

Two other systematic reviews have added different perspectives on dexamethasone and BPD. In the first review, a risk-weighted meta-analysis, the authors emphasized the importance of the a priori risk of death or BPD in different study populations.¹⁵ In this analysis, the incidence of death or cerebral palsy (CP) was increased among dexamethasone-treated infants compared with placebo-treated infants in studies that enrolled patients at low risk (<35%) of BPD. In contrast, dexamethasone treatment decreased the risk of death or CP when infants at high risk of BPD ($\geq 65\%$) were studied.¹⁵ Thus, for infants at the highest risk of BPD, the beneficial effect of dexamethasone in reducing lung disease

seemed to outweigh its adverse effect of increasing the risk of CP. In the second meta-analysis, the authors compared outcomes for trials with different cumulative doses of dexamethasone and concluded that a higher cumulative dose improved rates of survival without BPD and did not increase adverse long-term effects.¹⁶ However, 3 small individual RCTs that directly compared high versus low dexamethasone doses, variably defined, have revealed no differences in efficacy (Table 1).^{17–19} These studies have generally been small and heterogeneous, which makes them difficult to compare.

The results of 3 RCTs that compared dexamethasone to placebo have been published since the previous AAP statement (Table 1); 1 was small and the other 2 were stopped early and are, therefore, underpowered.^{20–22} One trial compared an early, short course

TABLE 1 RCTs of Dexamethasone to Prevent or Treat BPD Reported Since 2001

Study, No. of Centers	<i>n</i>	Eligibility Criteria (All on Mechanical Ventilation)	Dexamethasone Dosing Regimen	Outcome
McEvoy et al, ¹⁷ 1 center	62	500–1500 g BW; ≤ 32 wk gestation; 7–21 postnatal days	5 mg/kg per d tapered over 7 d vs 0.2 mg/kg tapered over 7 d	Rate of survival without BPD ^a 76% vs 73% (NS); no benefit to higher dose
Odd et al, ¹⁸ 1 center	33	≤ 1250 g BW; 1–3 wk of age	0.5 mg/kg per d tapered over 42 d vs “individualized” (same dose, shorter course)	Rate of survival without BPD: 24% vs 30% (NS); no difference in 18-mo outcomes
Malloy et al, ¹⁹ 1 center	16 ^b	<1501 g BW; <34 wk gestation; <28 postnatal days	0.5 mg/kg per d tapered over 7 d vs 0.08 mg/kg per d for 7 d	Rate of survival without BPD: 11% vs 38% (NS); higher dose had more adverse effects, no apparent benefit
Walther et al, ²⁰ 1 center	36	≥ 600 g BW; 24–32 wk gestation; 7–14 d postnatal age	0.2 mg/kg per d tapered over 14 d vs placebo	Rate of survival without BPD: 65% vs 47% (NS); extubation: 76% vs 42% ($P < .05$)
Anttila et al, ²¹ 6 centers	109 ^b	500–999 g BW; ≤ 31 wk gestation; eligible at 4 h of age	0.25 mg/kg every 12 h \times 4 doses vs placebo	Rate of survival without BPD: 58% vs 52% (NS)
Doyle et al, ²² 11 centers	70 ^b	<1000 g BW; <28 wk gestation; >1 wk postnatal age	0.15 mg/kg per d tapered over 10 d vs placebo	Rate of survival without BPD: 14% vs 9% (NS); extubation: 60% vs 12% (odds ratio: 11.2 [95% confidence interval: 3.2–39.0])
Rozycki et al, ²³ 1 center	61	650–2000 g BW; ≥ 14 d postnatal age	0.5 mg/kg per d tapered over 42 d vs inhaled beclomethasone at 3 different doses for 7 d followed by above-listed dexamethasone course, if still mechanically ventilated	Rate of survival without BPD: 53% vs 46% (NS); extubation by 7 d: 7 of 15 vs 6 of 46 ($P < .01$)

BW indicates birth weight; NS, not significant.

^a BPD defined as receiving supplemental oxygen at 36 weeks postmenstrual age.

^b Patient enrollment terminated early.

of dexamethasone to placebo and revealed no significant difference in mortality or BPD rates.²¹ The other 2 trials evaluated the efficacy of a later, lower-dose course of dexamethasone for facilitating extubation, and the authors reported that significantly more dexamethasone-treated infants were successfully extubated during the treatment period.^{20,22} Similar results were reported from an additional study that compared systemic dexamethasone to inhaled beclomethasone for extubation: significantly more dexamethasone-treated infants were successfully extubated within 7 days (Table 1).²³ These extubation trials

were not powered to evaluate the effect of the treatment on rates of survival without BPD.

Many short-term adverse effects of dexamethasone therapy have been described; however, the main reason for the decline in its use is an adverse effect on neurodevelopment, particularly higher rates of CP. Since publication of the previous AAP statement, additional follow-up data on the adverse effects of dexamethasone have become available from RCTs (Table 2).^{17,24–32} The heterogeneity of these reports makes it problematic to combine them meaningfully. Some studies re-

vealed no adverse effects on neurodevelopmental outcomes at various ages, whereas others did. Most of the studies were small, which reduced their ability to either prove or disprove causation. Two RCTs that used low doses of dexamethasone revealed no significant increase in CP or other neurodevelopmental impairments when compared with placebo. Because only a total of 96 dexamethasone-treated infants were evaluated in these studies, the results must be interpreted with caution.^{25,26}

Cohort studies of dexamethasone have revealed an association of its use with

TABLE 2 Neurodevelopmental Follow-up of Dexamethasone RCTs Reported After 2001

Study, Planned Age at Follow-up	Follow-up, % (No. of Infants Seen)	Treatment Start Time	Dexamethasone Dosing Regimen	Primary Neurodevelopmental Findings
McEvoy et al, ¹⁷ 1 y	66 (39)	At 7–21 d	High vs low dose: 7-d taper from 0.5 mg/kg per d vs 0.2 mg/kg per d	MDI < 70: 24% (high) vs 17% (low) (NS); CP: 10% vs 11% (NS)
Armstrong et al, ²⁴ 18 mo chronological age	96 (64)	On day 7	42-d taper vs 3-d pulse	No difference in 18-mo outcomes No disability: 34% vs 31% (NS)
Doyle et al, ²⁵ 2 y corrected age	98 (58)	After 7 d	0.15 mg/kg per d tapered over 10 d	Death or major disability: 46% vs 43% (NS); death or CP: 23% vs 37% (NS); CP: 14% vs 22% (NS); major disability 41% vs 31% (NS)
Stark et al, ²⁶ 18–22 mo corrected age	74 (123)	On day 1	0.15 mg/kg per d tapered over 7 d	MDI < 70: 51% vs 43% (NS); PDI < 70: 30% vs 35% (NS); abnormal neurologic exam: 25% each group
Romagnoli et al, ²⁷ 3 y	100 (30)	On day 4	0.5 mg/kg per d tapered over 1 wk	No differences in any parameter; CP: 9% vs 14% (NS)
Wilson et al, ²⁸ 7 y	84 (127)	Before 3 d	4 groups: 0.5 mg/kg per d tapered over 12 d vs late (15 d) selective, vs inhaled early or late selective	No difference in cognitive, behavioral, CP, or combined outcomes
Yeh et al, ²⁹ school age (mean: 8 y)	92 (146)	On day 1	0.5 mg/kg per d for 1 wk, then tapered for a total of 28 d	Treated children were shorter ($P = .03$), had smaller head circumference ($P = .04$), lower IQ scores ($P = .008$), and more significant disabilities (CP, IQ < 5th percentile, vision or hearing impairment): 39% vs 22% ($P = .04$)
O'Shea et al, ³⁰ 4–11 y	89 (84)	On day 15–25	0.5 mg/kg per d tapered over 42 d vs placebo	Death or major NDI ^a : 47% vs 41% (NS); major NDI alone: 36% vs 14% ($P = .01$)
Gross et al, ³¹ 15 y	100 (22)	On day 14	0.5 mg/kg per d tapered over 42 d vs 18-d taper vs placebo	Intact survival (IQ > 70, normal neurologic exam, regular classroom): 69% vs 25% (18-d course) vs 18% (placebo) ($P < .05$)
Jones and the Collaborative Dexamethasone Trial Follow-up Group, ³² 13–17 y	95 (150)	At 2–12 wk	0.5 mg/kg per d for 7 d	No difference in moderate/severe disability (defined as IQ > 2 SDs < mean, CP, hearing or vision loss); CP: 24% vs 15% (relative risk: 1.58 [95% confidence interval: 0.81–3.07])

MDI indicates Bayley Mental Developmental Index; NS, not significant. PDI, Bayley Psychomotor Development Index; NDI, neurodevelopmental impairment.

^a Major neurodevelopmental impairment included CP and/or an IQ score of <70.

impaired neurodevelopmental outcomes^{3,4,35}; however, such an association cannot be construed as definitive evidence of harm. A clinician's decision to use a therapy incorporates numerous undocumented factors and varies from one clinician to the next, which may seriously confound the interpretation of such studies. Patients who receive dexamethasone for BPD are likely to be perceived as having more severe respiratory disease than infants who are not treated; such infants may have worse overall outcomes regardless of dexamethasone therapy. Authors of small series have also reported that infants treated with dexamethasone have more abnormalities on MRI than those not treated; again, causation cannot be attributed in the absence of an RCT.^{34,35} Two previously reported RCTs revealed more cranial ultrasound abnormalities in dexamethasone-treated infants compared with those treated with placebo, but the patient numbers were quite small.^{36,37}

In summary, high daily doses of dexamethasone have been linked frequently to adverse neurodevelopmental outcomes, and this therapy is discouraged. Because an increase in adverse neurodevelopmental outcomes in treatment studies that used low doses of dexamethasone has not

been reported, further studies of low-dose dexamethasone to facilitate extubation are warranted.

Hydrocortisone

Results of 4 RCTs designed to evaluate the ability of early hydrocortisone therapy to improve rates of survival without BPD have been published (Table 3).^{38–41} These studies were based on the premise that extremely preterm infants may have immature adrenal gland function, predisposing them to a relative adrenal insufficiency and inadequate anti-inflammatory capability during the first several weeks of life.^{42–46} In contrast to the heterogeneous nature of previous dexamethasone trials, these studies were similar in design, time of initiation, duration, and dose. The direction of effect favored the hydrocortisone-treated infants in all 4 studies, and a significant increase in rate of survival without BPD in the hydrocortisone-treated infants was reported for 2 of the studies. The largest trial ($n = 360$) did not reveal a significant benefit of hydrocortisone treatment in the overall study group; however, for infants exposed to prenatal inflammation ($n = 149$), identified before the trial as a specific group for analysis, hydrocortisone treatment resulted in a significant decrease in mortality rate and an in-

crease in rate of survival without BPD.³⁹

Patient enrollment was halted early in 3 of these 4 studies because of a significant increase in spontaneous gastrointestinal perforation discovered in the largest trial,³⁹ a complication also observed with early dexamethasone.^{47,48} The perforations may have resulted from an interaction between high endogenous cortisol concentrations and indomethacin therapy in the first 48 hours; however, because administration of indomethacin was not randomized, this hypothesis remains to be tested.

Neurodevelopmental outcomes at 18 to 22 months' corrected age have been published for 3 of these trials, and no adverse effects of hydrocortisone treatment were found.^{49,50} In the largest multicenter trial, the incidence of death or major neurodevelopmental impairment (52% [hydrocortisone-treated] vs 56% [placebo]), major neurodevelopmental impairment alone (39% vs 44%), and CP (16% vs 18%) were similar.⁴⁹ The only significant findings favored the hydrocortisone-treated group and included a decreased incidence of a Bayley Scales of Infant Development (2nd ed) Mental Developmental Index (MDI) 2 SDs below the mean (MDI < 70, 27% vs 37%;

TABLE 3 RCTs of Early Hydrocortisone to Prevent BPD

Study, No. of Centers	<i>n</i>	Population: Mechanically Ventilated Infants	Hydrocortisone Dosing Regimen	Rate of Survival Without BPD ^a HC vs Placebo, %
Watterberg et al, ³⁸ 2 centers	40	500–999 g BW; <48 h postnatal age	0.5 mg/kg every 12 h for 9 d 0.25 mg/kg every 12 h for 3 d	60 vs 35 ($P = .04$)
Watterberg et al, ³⁹ 9 centers	360 ^b	500–999 g BW; <48 h postnatal age	0.5 mg/kg every 12 h for 12 d 0.25 mg/kg every 12 h for 3 d	35 vs 34 (aOR ^c : 1.20 [95% CI: 0.72–1.99])
Peltoniemi et al, ⁴⁰ 3 centers	51 ^b	501–1250 g BW; <36 h postnatal age	2.0 mg/kg per d tapered to 0.75 mg/kg per d over 10 d	64 vs 46 (OR: 1.48 [95% CI: 0.49–4.48])
Bonsante et al, ⁴¹ 2 centers	50 ^b	500–1249 g BW; <48 h postnatal age	0.5 mg/kg every 12 h for 9 d; 0.25 mg/kg every 12 h for 3 d	64 vs 32 ($P < .05$)
Total	601	—	—	—

BW indicates birth weight; aOR, adjusted odds ratio; OR, odds ratio; CI, confidence interval.

^a BPD was defined as receiving supplemental oxygen at 36 weeks' postmenstrual age.

^b Study enrollment was terminated early because of concern for spontaneous gastrointestinal perforation.

^c Adjusted for center, birth weight, risk factors (gender, "outborn" [infants who were born at an outlying institution and transported into the study center], white race, vaginal delivery, no prenatal steroids, hydrocortisone, and/or vasopressor support at study entry).

odds ratio: 0.47 [95% confidence interval: 0.25–0.87]) and a higher incidence of awareness of object permanence (an early test of working memory and prefrontal executive function) (89% vs 79%; odds ratio: 2.19 [95% confidence interval: 1.06–4.52]).

Two other RCTs have evaluated administration of hydrocortisone to preterm infants during the first week of life with the objective of reducing respiratory morbidity. The first, published in 1974, had the objective of decreasing the severity of respiratory distress syndrome.⁵¹ The investigators used a much higher dose (25 mg/kg per day on the first day of postnatal life), which showed no effect on respiratory distress syndrome. The second, published in 2003, was based on the hypothesis that extremely preterm infants have immature sodium channels and, therefore, cannot clear their lung liquid after birth.⁵² Triiodothyronine (T_3) was given together with hydrocortisone to stimulate maturation of the sodium channels. The medications were started within 5 hours of birth and given as a constant infusion for 7 days. The investigators enrolled 253 infants and found no difference in their primary outcome variables of death or ventilator dependence at 7 days and at 14 days. At 36 weeks' postmenstrual age, 47% of the treated survivors and 51% of the placebo group remained on oxygen.

Reports of hydrocortisone therapy given to facilitate extubation have been limited to cohort studies. In the first reported study, 25 infants treated with hydrocortisone at 1 hospital (5 mg/kg per day, tapered over 3 weeks) were compared with 25 untreated infants at the same hospital and additionally with a cohort of 23 infants treated with dexamethasone (0.5 mg/kg per day, tapered over 3 weeks) at a separate hospital.⁵³ The investigators found that hydrocortisone was as effective as

dexamethasone in weaning infants from the ventilator and in decreasing supplemental oxygen therapy, with fewer short-term adverse effects. Follow-up of these children at school age revealed no differences in neurodevelopmental outcomes between hydrocortisone-treated infants and their comparison group, whereas dexamethasone-treated infants more often had an abnormal neurologic examination and less favorable school performance than their comparison cohort.^{53,54} Subsequently, several large cohort studies from the same institution reported that, although hydrocortisone-treated children were younger, smaller, and sicker than their untreated comparison groups, there were no adverse effects of hydrocortisone treatment on IQ, visual motor integration, memory testing, CP, or findings on MRI.^{55–57} Investigators from this institution have also reported that neonatal dexamethasone but not hydrocortisone therapy resulted in long-lasting changes in hypothalamic-pituitary-adrenal axis and T-cell function.⁵⁸

Other Glucocorticoids (Systemic or Inhaled)

Since the previous AAP statement, no RCTs of other systemic glucocorticoids, such as prednisone or methylprednisolone, to treat or prevent BPD have been published. No additional evidence has been published to support the efficacy of inhaled glucocorticoids to prevent or decrease the severity of BPD.^{59,60}

DISCUSSION: DIFFERENCES BETWEEN DEXAMETHASONE AND HYDROCORTISONE

As described previously, many RCTs have shown adverse neurodevelopmental outcomes after postnatal dexamethasone treatment for BPD, but neither multicenter RCTs nor cohort studies have revealed adverse effects

on functional or structural neurologic outcomes after neonatal hydrocortisone therapy. One possible explanation for the observed differences between dexamethasone and hydrocortisone is the difference in effective glucocorticoid dose. Neonatal animal studies have consistently revealed adverse effects on brain growth after high doses of glucocorticoid,^{61,62} and results of evaluation of 22 patients who received high-dose hydrocortisone in a study from the early 1970s were suggestive of harm.^{63,64} High-dose dexamethasone (0.5 mg/kg per day) is equivalent to at least 15 to 20 mg/kg per day of hydrocortisone,⁶⁵ far higher than the doses of hydrocortisone given in the recent studies described previously. Low-dose dexamethasone (0.1–0.15 mg/kg per day) may be equivalent to 3 to 6 mg/kg per day of hydrocortisone; however, because of its much longer biological half-life, it could have a much higher relative potency.⁶⁶ Lowering the dose of dexamethasone may, therefore, decrease its adverse effects, as is suggested by the 2 studies of outcome after lower-dose dexamethasone therapy.^{25,26}

Second, the observed differences in neurodevelopmental outcomes may result from the different effects of these agents on the hippocampus, an area of the brain critical to learning, memory, and spatial processing.^{67,68} The hippocampus contains a high density of both mineralocorticoid and glucocorticoid receptors.^{69,70} Hydrocortisone, which is identical to native cortisol, can bind to both classes of receptors. In contrast, dexamethasone binds only to glucocorticoid receptors, which, in animal models, has been shown to result in degeneration and necrosis of hippocampal neurons.^{71,72} This effect of dexamethasone is blocked by simultaneous administration of corticosterone (the cortisol equivalent in the rat).⁷¹ In humans,

neonatal treatment with dexamethasone, but not hydrocortisone, has been shown to alter hippocampal synaptic plasticity and associative memory formation in later life.⁷³ Dexamethasone exposure has also been linked to decreased hippocampal volume in 1 cohort study,⁷⁴ but cohort studies of infants treated with hydrocortisone have revealed no decrease in hippocampal volume,⁵⁵ no adverse effect on hippocampal metabolism, and no adverse effect on memory at school age⁵⁷ when compared with a larger, more mature group of nontreated infants.

Whatever the underlying explanation(s) for the observed differences in short- and long-term outcomes may be, further RCTs are needed to answer the many remaining questions, including whether lower doses of dexamethasone can avoid previously observed adverse effects, whether hydrocortisone is efficacious for extubation, whether specific groups of infants may derive particular benefit from hydrocortisone therapy, and whether the incidence of spontaneous gastrointestinal perforation during early glucocorticoid administration can be decreased by avoiding concomitant indomethacin or ibuprofen therapy and/or by monitoring cortisol concentrations.

SUMMARY AND RECOMMENDATIONS

- BPD remains a major morbidity of the extremely preterm infant and is consistently associated with adverse effects on long-term outcomes, including neurodevelopment. Additional RCTs of postnatal glucocorticoids are warranted to optimize therapy and improve outcomes for these infants. Those who design such trials in the future should attempt to minimize the use of open-label glucocorticoid, which

has confounded analysis of most previous trials, and should include assessment of long-term pulmonary and neurodevelopmental outcomes.

- High daily doses of dexamethasone (approximately 0.5 mg/kg per day) have been shown to reduce the incidence of BPD but have been associated with numerous short- and long-term adverse outcomes, including neurodevelopmental impairment, and at present there is no basis for postulating that high daily doses confer additional therapeutic benefit over lower-dose therapy. **Recommendation: in the absence of randomized trial results showing improved short- and long-term outcomes, therapy with high-dose dexamethasone cannot be recommended.**
- Low-dose dexamethasone therapy (<0.2 mg/kg per day) may facilitate extubation and may decrease the incidence of short- and long-term adverse effects observed with higher doses of dexamethasone. Additional RCTs sufficiently powered to evaluate the effects of low-dose dexamethasone therapy on rates of survival without BPD, as well as on other short- and long-term outcomes, are warranted. **Recommendation: there is insufficient evidence to make a recommendation regarding treatment with low-dose dexamethasone.**
- Low-dose hydrocortisone therapy (1 mg/kg per day) given for the first 2 weeks of life may increase rates of survival without BPD, particularly for infants delivered in a setting of prenatal inflammation, without adversely affecting neurodevelopmental outcomes. Clinicians should be aware of a possible increased risk of isolated intestinal perforation associated with early concomitant treatment with inhibitors of prosta-

glandin synthesis. Further RCTs powered to detect effects on neurodevelopmental outcomes, aimed at targeting patients who may derive most benefit and developing treatment strategies to reduce the incidence of isolated intestinal perforation, are warranted. **Recommendation: early hydrocortisone treatment may be beneficial in a specific population of patients; however, there is insufficient evidence to recommend its use for all infants at risk of BPD.**

- Higher doses of hydrocortisone (3–6 mg/kg per day) instituted after the first week of postnatal age have not been shown to improve rates of survival without BPD in any RCT. RCTs powered to assess the effect of this therapy on short- and long-term outcomes are needed. **Recommendation: existing data are insufficient to make a recommendation regarding treatment with high-dose hydrocortisone.**

IMPLICATIONS FOR PRACTICE

Because available data are conflicting and inconclusive, clinicians must use their own clinical judgment to balance the adverse effects of BPD with the potential adverse effects of treatments for each individual patient. Very low birth weight infants who remain on mechanical ventilation after 1 to 2 weeks of age are at very high risk of developing BPD.¹⁴ When considering corticosteroid therapy for such an infant, clinicians might conclude that the risks of a short course of glucocorticoid therapy to mitigate BPD is warranted.¹⁵ This individualized decision should be made in conjunction with the infant's parents.

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