

## Q: When is perioperative ‘steroid coverage’ necessary?

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**A:** ALTHOUGH THE QUESTION is controversial, I still recommend perioperative steroid coverage for patients who are receiving more than 5 mg/day of prednisone or an equivalent and for patients who have recently stopped long-term steroid therapy. The stress dose should be proportionate to the severity of surgical stress and should be given for no longer than 1 to 3 days perioperatively.

See related editorial, pages 7–8.

Traditionally, patients on long-term corticosteroid therapy are given a brief dosage boost in situations that cause acute physiologic stress, such as surgery, trauma, infection, or severe illness. Although the need for such “steroid coverage” or “stress dosing” has recently been questioned, it seems prudent to continue it for the present.

Unfortunately, stress dosing in patients on long-term corticosteroid therapy has never been studied in large, randomized trials, and some observational studies and small trials suggest that it may be unnecessary. In this situation of uncertainty, clinicians should weigh the physiologic and clinical evidence about the normal hormonal response to surgery, the response in steroid-treated patients, and the risks of adrenal insufficiency.

### ■ THE CASE FOR STEROID COVERAGE

The physiologic rationale for steroid coverage is that long-term corticosteroid therapy for chronic autoimmune or inflammatory diseases (such as rheumatoid arthritis, ulcerative colitis, or asthma) suppresses the hypothalamic-pituitary-adrenal (HPA) axis. In normal patients, severe illness, trauma, stress, and surgery are

accompanied by activation of the HPA axis. Patients with HPA axis suppression from long-term corticosteroid therapy may be unable to produce this physiologic response to stress.

In normal subjects, daily cortisol production is estimated to be equivalent to 10 to 12 mg of oral hydrocortisone per day.<sup>1</sup> Endogenous cortisol levels rise rapidly in response to surgery: cortisol production rises to about 50 mg/day in response to minor surgery, and 75 to 150 mg/day in response to major surgery. This increased production is not uniform: the main increase takes place immediately after anesthesia is induced. Cortisol levels generally return to baseline within 24 to 48 hours after surgery. This short-term elevation of endogenous cortisol has a number of anti-inflammatory and other protective effects that prevent stress-induced hypotension and shock.

The current practice of giving preoperative steroid coverage started when two case reports published in the 1950s described young patients receiving long-term glucocorticoid therapy who died unexpectedly after routine orthopedic surgery.<sup>2,3</sup> Their deaths were attributed to adrenal insufficiency, although there was no biochemical confirmation of this.

### ■ THE CASE AGAINST STEROID COVERAGE

Recent studies have cast doubt upon this empiric standard of care by questioning not only the dosages but also the necessity of steroid coverage at all.<sup>4–6</sup> The question is complicated by poor correlation between biochemical data and clinical outcome.

#### Is adrenal insufficiency in patients on corticosteroids clinically important?

Many authors have challenged the need for steroid coverage, pointing out that adrenal insufficiency was confirmed biochemically in only a handful of the reported cases of periop-

**On balance, prudence supports giving moderate perioperative stress doses**

## Biochemical tests of adrenal reserve do not predict clinical effects

erative hypotension and death that were attributed to secondary adrenal insufficiency. They also point out that many patients on long-term glucocorticoid therapy have undergone major surgery without stress dosing—in some cases, without any steroid therapy at all—and most had uneventful courses.<sup>4-8</sup>

In 1991, Bromberg et al<sup>4</sup> prospectively studied 40 renal allograft recipients admitted to the hospital with significant physiologic stress from sepsis, metabolic abnormalities, or impending surgery. Although baseline prednisone doses were not changed (5–10 mg/day), none of the patients developed clinical adrenal insufficiency. Nevertheless, cosyntropin stimulation test results were abnormal in 25 patients (63%), indicating that biochemical test results do not correlate well with clinical events.

Friedman et al<sup>5</sup> prospectively studied 28 glucocorticoid-treated patients who received no dosage boost before a total of 35 major orthopedic operations. The patients had been taking 1 to 20 mg of prednisone for 6 months to 32 years. None of the patients had episodes of clinical adrenal insufficiency, and 18 of the 19 patients with complete data had appropriate biochemical responses to stress.

A randomized, double-blind, placebo-controlled study of 17 surgical patients with biochemical evidence of secondary adrenal insufficiency found that they did not develop signs of adrenal insufficiency when given only their daily dose of steroids.<sup>6</sup> The type of surgery ranged from bilateral orchiectomy under local anesthesia to splenectomy under general anesthesia. Unfortunately, the small number of patients was a major limitation of this study.

### Hypothalamic-pituitary-adrenal axis suppression is difficult to predict

Decreased adrenal reserve, as measured by a diminished response to exogenous adrenocorticotropic hormone (ACTH), does not directly translate into clinical adrenal insufficiency. Patients who have received very high doses of corticosteroids are more likely to have decreased response to exogenous ACTH than patients who have received extremely low doses. However, these biochemical test results are poorly correlated with clinically apparent adverse effects.

In addition, recent research shows that even this biochemical HPA suppression cannot be accurately predicted from the traditional risk factors: duration of corticosteroid therapy, highest dose of corticosteroid, and total cumulative dose. In a large study of patients receiving daily long-term therapy with 5 to 30 mg of prednisone or an equivalent, Schlaghecke et al<sup>9</sup> found that pituitary-adrenal function could not be reliably predicted by the dose or duration of glucocorticoid therapy. In another study of patients on doses of up to 10 mg/day, none of the patients receiving less than 5 mg had a suppressed HPA axis, and the remaining patients had widely varied responses.<sup>10</sup> Suppression could not be predicted by the total dose, the highest dose, or the duration of therapy.

Furthermore, the time to HPA axis recovery after stopping glucocorticoids may vary. It has been reported to be as little as 2 to 5 days and as long as 9 to 12 months.<sup>11</sup>

Thus, it is difficult to predict the presence of HPA axis suppression from the patient's history of corticosteroid use.

### WEIGHING RISKS AND BENEFITS

The arguments against steroid coverage are drawn from observational studies and small prospective studies, not from large, randomized trials, which would be much more compelling. In the absence of such studies, clinicians must weigh the known risks and benefits.

The benefit of steroid coverage is clear: it has the potential to prevent secondary adrenal insufficiency, which can be life-threatening. The risks are small: although high-dose steroids may have catabolic effects on wound healing<sup>12,13</sup> and may impair glucose metabolism, these adverse effects are small if the high dosage is limited to a very short period of time.

Thus, on balance, it seems prudent to boost glucocorticoid doses in the perioperative period for patients receiving long-term steroid therapy (> 5 mg/day of prednisone or an equivalent).

### Patients with a history of steroid use

Some patients previously treated with glucocorticoids should also receive steroid coverage. The literature suggests that, in some patients,

**TABLE 1****Recommended perioperative hydrocortisone dosage for patients on long-term steroid therapy**

SURGERY TYPE	STRESS DOSE	DURATION*
Minor (eg, inguinal herniorrhaphy)	25 mg/day	1 day
Moderate (eg, total joint replacement)	50–75 mg/day	1–2 days
Major (eg, cardiopulmonary bypass)	100–150 mg/day	2–3 days

\*In the absence of complications

BASED ON THE RECOMMENDATIONS OF SALEM M, TAINSH RE JR, BROMBERG J, LORIAUX DL, CHERNOW B. PERIOPERATIVE GLUCOCORTICOID COVERAGE: A REASSESSMENT 42 YEARS AFTER EMERGENCE OF A PROBLEM. ANN SURG 1994; 219:416–425.

the HPA axis may not recover for up to a year after glucocorticoid therapy is stopped, so it would be reasonable to prescribe supplements for patients who have stopped long-term glucocorticoid use within the past year.

On the other hand, stress doses are not required for patients who have recently received short bursts of corticosteroids (therapy lasting 1 week or less), because in these patients, HPA function recovers within 1 week.<sup>14,15</sup>

**Consensus recommendations on doses**

Traditionally, the dosage used for steroid coverage has been 100 mg of hydrocortisone every 8 hours, sometimes with a prolonged taper.

This dose is far higher than the physiologic cortisol increase, which peaks at 150 mg/day after major surgery and returns quickly to baseline.

A consensus paper<sup>16</sup> recommends giving much lower peak doses, and then quickly returning the dosage to baseline (TABLE 1). This strategy is designed to parallel the physiologic response of the normal adrenal gland to surgical stress. There is no evidence to suggest that steroid supplementation needs to be tapered over a prolonged period. A taper over 1 to 3 days is adequate in uncomplicated situations, and this helps to minimize any adverse effects of high-dose steroids.

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