ORIGINAL ARTICLE

Transient Hypoadrenalism During Surgical Critical Illness

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Objective: To report the cortisol levels in 6 patients during and after severe inflammation.

Design: Patients with severe inflammatory disease had basal and stimulated (cosyntropin) serum cortisol levels determined at the time of severe and less severe inflammation.

Setting: Intensive care unit and wards of a tertiary care center.

Patients: Six patients with continued evidence of severe inflammation, despite aggressive management of the underlying inflammatory disease.

Interventions: Five of 6 patients received hydrocortisone at "physiologic" doses.

Main Outcome Measures: Basal and stimulated serum cortisol levels.

Results: The mean±SD cortisol data for these patients were as follows: baseline cortisol level during inflammation, 350±121 nmol/L (n=6); stimulated cortisol level during inflammation, 571±326 nmol/L (n=6); baseline cortisol level with less inflammation, 833±339 nmol/L (*P*=.03 vs baseline level during inflammation) (n=5); and stimulated cortisol level with less inflammation, 1090±295 nmol/L (*P*=.03 vs stimulated level during inflammation) (n=4). Manifestations of inflammation decreased with hydrocortisone administration.

Conclusions: Severe inflammation may result in lower-than-expected serum cortisol levels, which then increase significantly as the inflammation decreases. Transient hypoadrenalism may aggravate the adverse effects of severe inflammation. These effects may be ameliorated by administering physiologic rather than pharmacologic doses of hydrocortisone.

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SYSTEMIC inflammation is common in critical illness and is usually secondary to infection, direct tissue damage, and ischemia-reperfusion. Inflammation resulting from any of these causes may have effects that are both beneficial (eg, activation of host defenses and wound healing) and detrimental (eg, suppression of host defenses, organ malfunction). Severe, persistent systemic inflammation (systemic inflammatory response syndrome [SIRS]) is associated with the malfunction of many organs and an increased risk of death.[1]

Recent studies have investigated factors that both promote severe systemic inflammation (eg, hypoperfusion, tumor necrosis factor production, interleukin 1 production) and decrease it (eg, improved perfusion, antagonists that inhibit cytokine release or function). These studies increase the understanding of the pathophysiology of severe inflammation, and offer the potential of new therapeutic interventions.[2-6]

As part of the stress response, blood levels of the endogenous glucocorticoid cortisol are characteristically increased in critical illness and are usually greater than 828 nmol/L .[7-9] Cortisol exerts both metabolic and anti-inflammatory effects. Because absolute adrenal insufficiency decreases survival following acute insults, the effects of a physiological increase in cortisol concentration are presumably beneficial.[10,11]

Severe adrenal insufficiency during critical illness has been reported, usually associated with adrenal hemorrhage, infarction, or unrecognized adrenal suppression from prior steroid (glucocorticoid) administration.[8,12,13] However, during the past 20 years, several reports have suggested that lower-than-expected blood cortisol concentrations may be present during critical illness without anatomical disruption or previous suppressive therapy.[14-18] Ad-

Table 1. Clinical Parameters in Case Series

Case No./Age, y/Sex	Disease	Operation	Manifestations of Inflammation
1/63/M	Cholangiocarcinoma	Whipple	Fever, fluid sequestration, respiratory failure, hypotension, inotropic support
2/63/M	Pancreatitis, cholangitis, infected pancreatic necrosis	Débridement	Fever, respiratory failure
3/40/M	Severe pancreatitis	Drainage-infected pseudocyst	Fever, hypotension
4/30/M	Multiple trauma	Orthopedic, sigmoid colostomy	Hypotension, inotropic support, respiratory failure
5/27/M	Severe pancreatitis, infected necrosis	Débridement	Fever, fluid sequestration, respiratory failure
6/54/M	Perforated stomach, leiomyosarcoma	Gastrectomy	Hypotension, inotropic support

ministering cortisol to these patients using physiologic (eg, ≤300 mg/d of hydrocortisone [given as hydrocortisone sodium succinate]) rather than pharmacologic (eg, ≧300 mg/d of hydrocortisone, ≧50 mg/d of methylprednisolone [given as methylprednisolone sodium succinate]) doses appears to improve clinical status.[16,19,20]

Such reports suggest that critical illness and severe inflammation can sometimes be associated with low or "normal" rather than the expected increased blood cortisol concentrations. We report our series of 6 critically ill surgical patients (**Table 1**) who were treated at the Dartmouth-Hitchcock Medical Center, Lebanon, NH, and whose cortisol levels suggested inadequate adrenal response in the setting of critical illness. These patients demonstrated clinical improvement with the administration of hydrocortisone, and higher blood cortisol concentrations following amelioration of the severe inflammatory state.

REPORT OF CASES

CASE 1

This patient was a 63-year-old white man who had no significant medical history and who underwent a pancreaticoduodenectomy for cholangiocarcinoma. The procedure was complicated by considerable blood loss (8 L) and dusky bowel with suspected mesenteric venous occlusion. This prompted a second-look procedure, at which time the bowel was viable. Perioperatively, the patient was prescribed cefotetan, and subsequently vancomycin, gentamicin, and ketoconazole.

During the first 6 postoperative days, the patient's course was characterized by the following: sequestration of 6 to 12 L of fluid daily, increasing requirements for ventilator support (FIO_2 [fraction of inspired oxygen], 0.70; positive end-expiratory pressure [PEEP], 15 cm H_2O), elevated eosinophil count (0.045), fever and hemodynamic instability requiring dopamine (5 µg/kg per minute). Cultures were negative.

On postoperative day 5, a cosyntropin (corticotropin analog) stimulation test was performed, yielding a basal cortisol level of 359 nmol/L and a stimulated cortisol level of 276 nmol/L (30 minutes after cosyntropin administration). Normal basal values in this laboratory are as follows: morning, 193 to 690 nmol/L, and evening, 55 to 248 nmol/L. Common criteria for a normal cosyntropin test are to achieve both the following: a cortisol level that is double of baseline and that is at least 552 nmol/L 30 to 60 minutes after administration.[21]

On postoperative day 7, the patient received 50 mg of hydrocortisone every 8 hours. During the next 48 hours, the following clinical improvement occurred: hemodynamic stability allowed the dopamine to be tapered off, fluid balance shifted and resulted in a weight decrease of 9.1 kg, ventilator support decreased (FIO_2, 0.50; PEEP, 12 cm H_2O), and eosinophil count decreased to 0.006%.

After 1 week of hydrocortisone treatment and clinical improvement, the hydrocortisone regimen was decreased to 75 mg/d. The patient became hypotensive and required dopamine (3 µg/kg per minute), and his eosinophil count increased from 0.005 to 0.016. The hydrocortisone dosage was increased to 120 mg/d and the dopamine was tapered off. The eosinophil count decreased to 0.003.

One month postoperatively, the hydrocortisone was tapered off and repeated cosyntropin stimulation testing was performed. The patient had a basal cortisol level of 662 nmol/L and a stimulated cortisol level of 828 nmol/L. The test was obtained while the patient continued taking his course of ketoconazole (200 mg/d).

The patient's symptoms continued to improve and he was discharged home. He has required no further steroid supplementation.

CASE 2

This patient was a 63-year-old white man who developed pancreatitis and ascending cholangitis 10 weeks following cholecystectomy. Endoscopic retrograde cholangiopancreatography was performed with stone extraction and papillotomy, and the patient was admitted to the intensive care unit receiving broad-spectrum antibiotics (ie, ampicillin, gentamicin, clindamycin). Admission laboratory values included the following: white blood cell (WBC) count, 11.4×10^9/L; total bilirubin, 125 µmol/L (7.3 mg/dL); alkaline phosphatase, 205 U/L; γ glutamyl transpeptidase, 710 U/L; amylase, 2944 U/L; sodium, 136 mmol/L; and potassium, 4.4 mmol/L. He was initially afebrile.

The patient became febrile (temperature of 38.8°C) on hospital day 2. Peritoneal lavage, which is commonly used in our institution for severe pancreatitis, was begun for a diagnosis of severe pancreatitis, and the patient was intubated. By hospital day 6, the patient's liver test results and amylase level had normalized. Antibiotic therapy was discontinued on day 9.

For 21 days the patient showed no significant clinical improvement, remained ventilator dependent, and had a persistent unexplained fever (temperature, 39°C–40°C with negative cultures; WBC count, 12-14×10^9/L), but was hemodynamically stable.

On hospital day 21, a cosyntropin stimulation test was performed. The patient had a basal cortisol level of 138 nmol/L and a 30-minute stimulated cortisol level of 497 nmol/L. Although the stimulated level was more than twice baseline, a stimulated concentration of less than 552 nmol/L was consistent with an insufficient response.[21] The patient was prescribed hydrocortisone (50 mg every 8 hours). Within 24 hours he defervesced and was able to tolerate a slow wean from the ventilator.

Beginning on hospital day 32, the patient underwent multiple operative débridements for infected pancreatic necrosis. During this time the patient's hydrocortisone dosage was increased to 100 mg every 8 hours. On hospital day 48, the patient's hydrocortisone dosage was decreased to 70 mg very 8 hours. The patient left the intensive care unit on day 50 and was discharged home on day 82, taking 20 mg prednisone daily. The patient's steroid requirement was tapered and discontinued altogether after 2 months. Repeated cortisol measurement at that time revealed a basal level of 1159 nmol/L. In the 2 years since this patient's illness, he has undergone 2 surgical procedures with no steroid replacement and without complication.

CASE 3

This patient was a 40-year-old white man who was admitted to our hospital with severe pancreatitis following abdominal trauma. Admission laboratory values were remarkable for a WBC count of 22×10^9/L (<0.01 eosinophils); lactate dehydrogenase, 635 U/L; glucose, 11.2 mmol/L (202 mg/dL); amylase, 1140 U/L; and lipase 21 300 U/L. On hospital day 2, peritoneal lavage was begun. On hospital day 4, the patient was febrile (temperature, 38.5°C-39.9°C) and intermittently mildly hypotensive, and remained so for the following 2 weeks. Cultures of sputum and maxillary sinus drainage were positive (*Staphylococcus aureus* and *Klebsiella*), but the patient's symptoms did not improve after he was given appropriate antibiotic therapy with a combination of ampicillin sodium and sulbactam sodium (Unasyn) and imipenem. A cosyntropin stimulation test performed on hospital day 8 demonstrated a basal cortisol level of 276 nmol/L and a 30-minute stimulated level of 1186 nmol/L. No steroids were given.

The patient remained in the hospital for 3 months with slow improvement, but he developed an infected pseudocyst that required surgical intervention. After clinical improvement, repeated cosyntropin stimulation testing was performed, yielding a basal cortisol level of 579 nmol/L and a stimulated cortisol level of 1186 nmol/L. The patient was discharged home on hospital day 90.

CASE 4

This patient was a 30-year-old white man who was admitted following multiple trauma (pelvic and lower-extremity fractures, rectal laceration, renal artery dissection). The patient underwent orthopedic procedures and sigmoid colostomy and was admitted to the intensive care unit with broad-spectrum antibiotics. On postoperative day 4, the patient was hypotensive and required dopamine (4 µg/kg per minute), and had a eosinophil count of 0.15. Cosyntropin stimulation testing yielded a basal cortisol level of 441 nmol/L and a stimulated value of 497 nmol/L. Hydrocortisone was administered (100 mg every 6 hours), the dopamine was tapered off, and the patient's requirements for ventilator support decreased.

The patient's hospital course was complicated by enterococcal bacteremia and pelvic wound infections, which were treated with imipenem and gentamicin. He underwent numerous débridements and a myocutaneous flap for coverage. Following clinical improvement and a steroid taper, repeated cortisol testing yielded a basal cortisol level of 1242 nmol/L and a stimulated value of 1462 nmol/L. The patient was discharged from the hospital on postoperative day 132. After spending 1 month in a rehabilitation facility, the patient was able to ambulate on crutches and was discharged home. At 1-year follow-up he required no further steroid treatment.

CASE 5

This patient was a 27-year-old white man who was transferred to our institution for treatment of severe alcoholic pancreatitis. Three months prior to transfer the patient had recurrent pancreatitis associated with ethanol intake and a deep vein thrombosis requiring anticoagulation. Upon transfer, the patient was intubated with bilateral flank ecchymose and had the following laboratory data: amylase, 230 U/L; lipase, 2719 U/L; lactate dehydrogenase, 3491 U/L; calcium, 1.7 mmol/L (6.8 mg/dL), and WBC count, 5.1×10^9/L (0.014 eosinophils). Peritoneal lavage was begun. The following day the patient underwent an exploratory laparotomy with débridement of infected pancreatic necrosis, loop ileostomy, and feeding jejunostomy. During the subsequent 5 days the patient required increased ventilatory support (to F_{IO_2}, 1.00; PEEP, 12 cm H_2O; and paralysis), his WBC count ranged from 9.9×10^9/L to 16.5×10^9/L (0.004-0.026 eosinophils), and he required 1 to 4 L of fluid daily. The patient was also treated for alcohol withdrawal and required large amounts of medication (ie, diazepam, 40 mg hourly; haloperidol, 5 mg hourly; and fentanyl citrate, 540 mL hourly).

On postoperative day 6, results of a cosyntropin stimulation test revealed a basal cortisol level of 441 nmol/L and a stimulated level of 607 nmol/L. A course of hydrocortisone was begun at 50 mg every 8 hours. By postoperative day 12, the patient's ventilator requirements decreased (F_{IO_2}, 0.40; PEEP, 7.5 cm H_2O). He stopped sequestering fluid but did not begin significant diuresis at that time. His WBC count did not change significantly.

The patient's symptoms continued to improve slowly. His hospital course for the next month was significant for persistent fevers with abdominal abscesses and ventilator dependence. The patient's hydrocortisone dosage was decreased to 25 mg every 8 hours on postoperative day 28, and he was weaned completely on day 42. A

repeated cosyntropin stimulation test yielded a basal cortisol level of 524 nmol/L and a stimulated cortisol level of 883 nmol/L.

On postoperative day 54, the patient's ventilator support was discontinued. He was discharged to a rehabilitation facility on postoperative day 97. He returned to our institution 3 months later for an ileostomy takedown. This procedure was performed without steroid supplementation and without complication.

CASE 6

This patient was a 54-year-old white man who was transferred to our hospital with a perforated stomach secondary to a leiomyosarcoma. The patient underwent a total gastrectomy with Roux-en-Y esophagojejunostomy and splenectomy. At this time he was afebrile; his WBC count was 23.2×10^9/L with 0.01 eosinophils.

Following surgery, the patient was afebrile and hypotensive. He was prescribed fluconazole, piperacillin, gentamicin, and metronidazole hydrochloride. Dopamine treatment was started on postoperative day 2. By postoperative day 6, the patient was receiving 15 µg/kg per minute of dopamine and had an eosinophil count of 0.05. Cultures taken subsequent to surgery were negative.

On postoperative day 8, a cosyntropin stimulation test was performed. The patient had a basal cortisol level of 441 nmol/L and a 30-minute stimulated cortisol level of 359 nmol/L. Hydrocortisone therapy was begun at 100 mg every 8 hours. Hemodynamics improved and the patient was weaned off dopamine. On postoperative day 15, the patient's antibiotics were discontinued. Two days later, the hydrocortisone dose was halved. The remainder of the patient's hospital course was significant for an *Enterobacter* pneumonia. He was extubated on postoperative day 25 and discharged home on postoperative day 32, taking prednisone (5 mg/d). Three weeks after discharge he stopped taking prednisone. He had no further steroid requirement and died ultimately of his malignancy.

DATA SUMMARY

Inflammatory State

Evidence of severe systemic inflammation at the time of the first-measured cortisol levels was compared with such evidence later in the hospital course. Data were collected based on the definitions of SIRS and severe inflammation; SIRS requires the presence of 2 or more of the following: temperature greater than 38°C or less than 36°C; heart rate greater than 90/minute; respiratory rate greater than 20 breaths per minute or $PaCO_2$ less than <32 mm Hg; and WBC count greater than 12×10^9/L, less than 4×10^9/L, or greater than 10% immature forms. Severe inflammation is present when hypotension (systolic blood pressure <90 mm Hg or a reduction of >40 mm Hg from baseline), and/or hypoperfusion, and/or organ malfunction (ie, oliguria, change in mental status, respiratory failure) are present.[22]

Fluid sequestration and weight increase are characteristic manifestations of severe inflammation, which abate when inflammation decreases. In this retrospective analysis, data consistently available for measurement showed the trends listed in **Table 2**. The mean value for each parameter was closer to normal at the time of the second cortisol measurements, but statistical significance was achieved only for the difference in body weight.

Table 2. Indicators of Inflammation and Organ Malfunction*

Variable	Mean±SD Value		*P*
	Low Cortisol	Clinical Improvement	
Temperature, °C	38.4±1.1	37.1±0.3	.06
Heart rate, beats/min	116±9	99±23	.10
WBC count, $\times10^9$/L	15.0±4.2	13.8±3.5	.50
Creatinine, µmol/L (mg/dL)	168±168 (1.9±1.9)	88±35 (1.0±0.4)	.18
Po_2/Fio_2, mm Hg	173±70	260±71	.06
Body weight, kg	112±25	87±16	.01

**WBC indicates white blood cell; Fio_2, fraction of inspired oxygen.*

Cortisol Data

The mean±SD cortisol data for these patients are summarized as follows: baseline cortisol level during severe inflammation, 350±121 nmol/L(n=6); stimulated cortisol level during severe inflammation, 571±326 nmol/L (n=6); baseline cortisol level at the time of less severe inflammation, 833±339 nmol/L(*P*=.03 vs baseline level during inflammation) (n=5); and stimulated cortisol level at the time of less severe inflammation, 1090±295 nmol/L (*P*=.03 vs stimulated level during severe inflammation) (n=4).

COMMENT

The concept of depressed adrenal function associated with the clinical picture of shock and systemic inflammation is not new. In 1933, Swingle described the similarity between adrenalectomized dogs and those in shock.[10] Other early work examined the adrenal glands of animals subjected to shock and found small areas of focal necrosis.[10] Severe infection from meningococcus and hemorrhage during anticoagulation can result in anatomical adrenal disruption.[8,13]

Despite evidence of the potential loss of physiological function of the adrenal glands in severe shock and infection, most investigations from the 1960s through the 1980s assessed the effects of administering high doses (ie, pharmacologic, ≧300 mg/d of hydrocortisone, ≧50 mg/d of methylprednisolone) rather than physiologic doses (≤300 mg/d of hydrocortisone) of steroids in animals and humans suffering from the adverse effects of severe infection or endotoxin exposure. Pretreatment in experimental studies demonstrated improved cell-membrane function, decreased capillary permeability, and improved survival.[23,24] Early studies in humans also suggested a benefit, but prospective randomized studies found no demonstrable improvement in outcome with the use of high doses of steroids.[25-30]

Table 3. Possible Causes of Adrenocortical Suppression/Decreased Blood Levels*

Suppression of ACTH synthesis and/or release
Hypoperfusion
Cytokine or other mediator inhibition
Drugs
Suppression of adrenal cortical synthesis/release
Hypoperfusion
Cytokine or other mediator inhibition
Drugs
Plasma protein dilution
Rapid metabolism

*Adapted from references 29 and 38 through 44.

A syndrome of relative rather than absolute adrenal insufficiency during critical illness has been suggested by several authors.[16-19,31-36] As in the present series, data from other studies are often difficult to interpret. Usual cortisol blood levels in critical illness are not well documented, particularly as a time-dependent variable. For instance, because critically ill patients are stressed 24 hours a day, circadian alterations in cortisol levels are not expected, but this has not been well studied. Most authors agree, however, that blood cortisol concentrations that are not elevated above the normal range or do not increase in response to corticotropin are consistent with suppression of adrenocortical function during severe illness.[15,16,18,29,37] These authors also describe a possible benefit of administering nonpharmacologic doses of hydrocortisone.

If such adrenocortical suppression is present in critical illness, the mechanism underlying this dysfunction is unknown (**Table 3**).[38-44] The administration of ketoconazole has been linked to adrenal insufficiency. Most often these patients received higher doses (600-800 mg/d) than did the patients in the present series (200 mg/d).[38] In the present series, one patient did not receive ketoconazole and one was still receiving the drug when the higher cortisol levels were measured.

All 6 patients in the present series suffered from severe inflammation and associated organ malfunction when blood cortisol levels were first measured. Three criteria for the definition of SIRS (ie, temperature, heart rate, WBC count) were present at that time. Although fluid sequestration and weight gain are not included in the SIRS definition, the association of these clinical phenomena with severe inflammation is common and has been linked to mortality risk.[45]

Later in the hospital course, the indicators of inflammation and organ malfunction improved in this series. Only the change in body weight was statistically different. This may reflect both the small sample size and a state of illness that improved but had not resolved completely. In fact, baseline cortisol levels were elevated at the time when the patients no longer required intensive care management, suggesting that the acute illness had not resolved completely.

The present case series thus supports the concept that the pathophysiology of severe inflammation can include physiologic rather than anatomical interference with adrenocortical function. Most supportive is the evidence that blood concentrations of cortisol at baseline and in response to corticotropin increased when the severity of inflammation had decreased. In addition, these patients frequently underwent additional procedures at times of little inflammation and did not require steroid supplementation. This transient association of lower baseline and stimulated cortisol levels during the most severe phase of illness, when cortisol would be expected to be most elevated, supports this first concept.

The second concept related to the possibility of inadequate adrenal cortisol secretion during severe inflammation is that "physiologic" rather than "pharmacologic" doses of hydrocortisone might diminish the detrimental effects of severe inflammation in patients with lower-than-expected endogenous blood cortisol concentrations. After the administration of nonpharmacologic doses of hydrocortisone to 5 patients in our series, each experienced a rapid decrease in fever, fluid sequestration, and hemodynamic and ventilatory support. For 2 patients, symptoms worsened when the hydrocortisone was tapered, but improved with cortisone reinstitution. Therefore, in patients with lower-than-expected blood levels of cortisol, some improvement in organ function may follow the administration of nonpharmacologic doses of hydrocortisone, suggesting that physiologic doses of steroids are helpful in balancing the beneficial and detrimental effects of severe inflammation. However, patient 4 demonstrated that a good outcome is possible without the administration of hydrocortisone.

Following tissue injury from any cause, inflammation can cause effects that are both beneficial (eg, increased host defenses and wound healing) and detrimental (eg, decreased host defenses, organ malfunction). The preservation of organ function and life may depend on a delicate balance between the beneficial and detrimental effects of inflammation.[11] Circumstances that allow inflammation to progress unabated (eg, hemorrhagic infarction of the adrenals during meningococcal infection), or that severely suppress inflammation (eg, high-dose steroid administration) may result in a poor outcome. A better understanding of disease and treatment may help maintain a balance in favor of the beneficial effects of inflammation.[20]

The prevalence of this type of a transient hypoadrenal state in critical illness is unknown. Our clinical experience leads us to believe that the estimates of a prevalence of less than 1% reflect inadequate clinical suspicion or diagnosis,[15] and that the incidence may actually be closer to the 24% rate reported recently.[29] Routine surveillance of adrenal function in critically ill patients is not indicated. However, cosyntropin stimulation testing should be considered for any patient who exhibits ongoing inflammation and such clinical difficulties as refractory hypotension, fever of obscure origin, prolonged failure to wean from ventilatory support, or prolonged fluid sequestration.[21] An elevated eosinophil count may coexist with adrenal insufficiency and can also serve as a prompt cortisol level measurement.[22] Moreover, since eosinopenia usually accompanies cortisol elevation and is also characteristic of critical illness, even a "normal" eosinophil count in a patient exhibiting inflammation can be considered an indication for testing.

Further study is necessary to define diagnostic thresholds, but basal cortisol levels of less than 552 nmol/L, or stimulated values that do not double or that remain less than 552 nmol/L should prompt the physician to consider steroid administration. Treatment with hydrocortisone (50-100 mg every 8 hours, or a continuous drip of 150-300 mg/d) may help support these patients through the inflammatory phase of illness.

Although clinical improvement was noted in the present series, a prospective, randomized study will be required to define the incidence of transient hypoadrenalism and any potential benefit of hydrocortisone administration. Even if hydrocortisone administration does not clearly diminish mortality, the inhibition of severe inflammation may result in the decreased use of a hospital's scarce and expensive resources, namely, critical care facilities and personnel. An inexpensive therapy, such as low-dose hydrocortisone administration, may provide significant cost-benefit advantages if it can decrease the days of ventilator use, inotropic support, and aggressive fluid management. Further study should examine these end points as well as mortality.

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obviously would be present to some extent. You are correct that we do not realize the cost savings until the actual reduction occurs, but the practical benefit for us in an ICU, where we tend to be gridlocked and have trouble getting patients in, was that we actually created more vacant space and the availability to admit patients more easily because we freed up the space by reducing the length of stay.

Third, what is the role of the admitting surgeons? I should say that in our critical care units we looked here at 16 beds. We have another 16 beds that are used primarily by cardiothoracic, vascular, and general surgery, and we have a variety of management methods depending on the surgeon preference. For many of the subspecialty surgeons, they prefer to put the patient in the unit and have them managed totally by the intensive care team. For the trauma surgeons and the general surgeons, management is by a joint procedure in which the primary service and the ICU service both round on the patients, collaborate actively in determining management, and finally in the vascular service and the cardiothoracic service, they prefer to manage the ventilator entirely on their own and involve the intensive care team only by consultation. So, those patients were not included in this. The admitting surgeons are very actively involved, and this is done with their full participation and consent.

Dr Moore, you asked how one gets the individual surgeons to participate. To a great extent, the group is the same. The trauma service consisting of 6 surgeons primarily is also the critical care service for the most part. When those surgeons are taking call in the critical care unit, they round exclusively there for 1 or 2 weeks at a time. Those same surgeons take call on the trauma service. So, it is not really a different group of surgeons; it is only a primary responsibility for the week they are on call. There is great collaborative interaction among them and, in essence, the people making the calls in the ICU are the same ones who are participating in another week when they are not primarily on ICU call but are taking trauma call. So, we are not really talking about different groups of people; all of these people are critical care certified in doing the trauma care and there is a tendency to have a great deal of mutual respect for decision making.

In addition, participation of enrollment of patients in the study was voluntary by the participating surgeons. The number who chose not to participate was very tiny because by and large, it was the same people involved.

Dr Wolfe, we thank you for your comments.

Dr Hartford, you asked about the Hawthorne effect. That may have some role here, but, in fact, this has been a very sustained effect and the data you saw for the first months of 1997 indicate that improvement is continuing. I do not know if it is due to the Hawthorne effect or something else, but whatever it is, we will take it because it seems to improve resource allocation and has not had adverse effects that we can see. Why were cardiac patients excluded? The answer is that they are in a separate ICU and the cardiac surgeons manage their own ventilatory status; they were on their own fast-track weaning protocol, which was slightly different from this, but has resulted also in significant shortening using protocol weaning. How many individual surgeons were involved? Again, the 6 trauma surgeons are the principal ICU rounders. There are another 12 or 13 general surgeons who participate, but do not make rounds in the ICU, and then there are a number of subspecialty surgeons (orthopedics, urology, and so forth) whose patients come into the unit sporadically. All of them participated.

Dr Schiller, the starting point of the weaning protocol was defined. It is the general stability of the patient and fraction of inspired oxygen of less than 50%, positive end-expiratory pressure of less than 5, minute ventilation of less than 10 liters per minute, and overall stability or improvement of the patient. That is probably defined better in the manuscript than Mattie had time to review in the presentation. What variations were present in practice before? We did not really document those because the individual people making rounds in the ICU or the individual primary surgeons tended to have their own different patterns and there is no uniformity in defining the end points at which weaning would begin. I think that is common in many places. All we did was institute a common end point of saying when these are present, we should undertake the effort at weaning. Time of the day for weaning as a result of the effect? I do not think that had a big effect. In general, we never wean and extubate the patient on the 11 to 7 shift. That was true before and after; however, most of the other shifts are pretty fair game and it is true that the therapist is there 24 hours a day, but I do not think that is the primary cause of the effect.

Dr Wilson, regarding the role of tracheostomy, I do not think it had a role here. In general, we perform tracheostomies fairly late, typically after about 2 weeks, if we see the patient is not likely to be extubatable in the immediate future. Most of these patients were extubated by that time, and you saw the mean period of ventilation was originally 6 to 7 days and decreased to about 4 days.

Correction

Error in Text. In the article titled "Transient Hypoadrenalism During Surgical Critical Illness," published in the February issue of the ARCHIVES (1998;133:199-204), the pharmacologic doses of hydrocortisone and methylprednisolone in line 4 on page 200 were incorrectly stated. The correct values should read ⩾300 mg/d of hydrocortisone and ⩾50 mg/d of methylprednisolone.