

HOW TO REPLACE CORTISOL

CHAPTER 8
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BRINGING A NEW DIMENSION TO PAIN CARE

Information presented here is a public service for health practitioners. It is provided by the Tennant Foundation.

Contact Information:

Tennant Foundation
334 S. Glendora Ave.
West Covina, CA 91740-3043
Ph: 626-919-7476
Fax: 626-919-7497
E-mail: veractinc@msn.com



**Information
Network**

Precis: Low serum cortisol levels almost always return to normal range by low dose administration of hydrocortisone.

INDICATION FOR REPLACEMENT

Any chronic pain patient with a low serum cortisol level.

<u>PROTOCOL</u>
➤ Begin with 5 mg of hydrocortisone 1 to 2 times a day.
➤ Do not use prednisone, methylprednisolone, dexamethasone, or triamcinolone.
➤ Retest within 2 to 4 weeks to determine if the serum level has increased. Raise hydrocortisone by no more than 5 mg a week.
➤ Continue raising the hydrocortisone dosage until the serum cortisol is in normal range.
➤ Once good pain control is achieved, the hydrocortisone dosage can be reduced and even stopped if the patient maintains a normal serum cortisol level.
➤ Some patients keep their pain better controlled and use fewer opioids if they maintain on a low, sub-replacement dosage of 5 to 15 mg a day.

DON'T FEAR COMPLICATIONS

Most practitioners fear corticoid prescribing because they are aware that adrenal suppression and/or Cushing's Syndrome may result.^{1,2} Be it clearly known that the average adult produces about 30 mg of hydrocortisone equivalent a day.¹ When administered, the liver rapidly converts hydrocortisone to cortisol.¹ Therefore, a dosage below 30 mg is actually sub-replacement. Pituitary and adrenal suppression only occurs with supra-physiologic dosages of hydrocortisone or its analogues are chronically administered. The synthetic corticoids, prednisone, methylprednisolone, dexamethasone, and triamcinolone, can easily exceed physiologic replacement equivalents and cause pituitary-adrenal

suppression, osteoporosis, and other complications typical of Cushing's Syndrome.^{1,2} Stick with plain sub-replacement dosage of hydrocortisone.

BE PREPARED FOR FIRST WEEK REACTOINS

Some pain patients biologically adjust to low serum levels of cortisol and they may have endured this state for a considerable time period. Consequently, the administration of even a low dosage of hydrocortisone may be a "jolt" to the system. Fundamentally, the administration of hydrocortisone may awaken and stimulate a number of dormant biologic systems. Warn the patient that the "awakening" can cause these temporary, unpleasant symptoms:

HEADACHE, EDEMA, NAUSEA, DIZZINESS, INSOMNIA, MENSTRUAL BLEEDING

These nuisance symptoms fade within a few days, but you may have to temporarily lower the initiating dose of hydrocortisone to 2.5 to 5 mg a day before raising it to sufficient levels to achieve a normal serum range..

SIMULTANEOUS ADMINISTRATION OF MEDICATION

You can simultaneously initiate hydrocortisone and other medications, including antidepressants, anti-inflammatories, neuropathic agents, and opioids. If possible, our recommendation is to hold off on opioids until you see how much pain relief you can obtain with hydrocortisone and raising the serum cortisol levels. Practitioners are starting to report that they often don't have to start opioids or elevate opioid dosages if normal serum cortisol levels are attained.

OPIOID SUPPRESSION OF CORTISOL

Although less well known and infrequent than testosterone suppression, opioids may suppress serum cortisol.³⁻⁵ Long-acting and intrathecal as opposed to short-acting opioids commonly cause hormone suppression.^{6,7} Short-acting opioids let the hormone system function normally during periods when little or no opioid is in the serum.

**DELAY OPIOIDS UNTIL
HYDROCORTISONE
HAS TIME TO RAISE
SERUM CORTISOL**

**CHECK SERUM
CORTISOL IF OPIOIDS
LOSE EFFECTIVENESS
OR "HYPERALGESIA"
IS PRESENT**

Practitioners commonly express concern about opioid "hyperalgesia" which has become a "catch-all" term whenever opioids lose effectiveness. Before rotating or reducing an opioid, first check the serum cortisol. A low serum cortisol may render opioids ineffectual as adrenal corticoids are necessary for opioid receptor binding, maintenance of the blood brain barrier, and physiologic nerve conduction.⁸⁻¹²

URGENCY REPLACEMENT

Life is not sustainable without a minimal level of serum cortisol. Little is known, however, as to what the minimal, sustainable level must be. Patients who have died from adrenal failure (Addison's Disease) have characteristically exhibited an illness over a 1 to 2 year period of increasing fatigue, depression, weight loss, apathy, reclusiveness, hypotension, and a bed or house bound state.^{13,14} Two of the 11 cases of death described by Dr. Addison in 1855 were patients with chronic pain.¹⁴ Cortisol serum testing was not invented until about 1960, and we cannot find any literary references on death-related levels. In lieu of this lack of published information, we recommend that serum levels under 1.0 mcg/dl be considered an urgency. In this situation hydrocortisone replacement should be urgently initiated and maintained until pain is well controlled and cortisol serum levels elevate to normal.

**CONSIDER A CORTISOL LEVEL UNDER 1.0 mcg/dl
AN URGENT MATTER**

References

1. Krasner AS. Glucocorticoid-induced adrenal insufficiency. JAMA 1999;282:671-676.
2. Henzen C, Suter A, Lerch E, et al. Suppression and recovery of adrenal response after short-term, high dose glucocorticoid treatment. Lancet 2000;355:542-545.
3. Rhodin A, Stridsberg M, Torsten G. Opioid endocrinology: a clinical problem in patients with chronic and long-term oral opioid treatment. Clin J Pain 2010;26:374-380.
4. Vuong C, Van Urim SHM, O'Dell L, et al. The effects of opioids and opioid analogs in animal and human endocrine systems. Endocrin Rev 2010;31:98-132.
5. Elliott JA, Horton E, Fibuch EE. The endocrine effects of long-term oral opioid therapy: a case report and review of the literature. J Opioid Manag 2011;7:145-154.
6. Rubinstein AL, Carpenter DM, Minkoff J. Hypogonadism in men using daily opioid therapy for non-cancer pain is associated with duration of action of opioid. Presented at Amer Acad Pain Med Palm Springs, Feb 2012.
7. Abs R, Verhelst J, Maeyaert J, et al. Endocrine consequences of long term intrathecal administration of opioids. J Clin Endocrinol Metab 2000;85(6):2215-2222.
8. Mensah-Nyagan A.G., Meyer L., Schaeffer V., et al. Evidence for a key role of steroids in the modulation of pain. Psychoneuroendocrinology, Volume 34, Issue SUPPL. 1, 2009, S169-S177.
9. McEwen BS, de Kloet ER, Rostene W. Adrenal steroid receptors and action in the central nervous system. Physio Rev 1986;66:1121-1188.
10. Svec F. Glucocorticoid receptor regulation. Life Sci 1985;36:2359-2366.
11. Holaday JW, Law PY, Loli HH, et al. Adrenal steroids indirectly modulate morphine and betaendorphin effects. J Pharmacol Exp Ther 1979;208:176-83.
12. Long JB, Holaday JW, Blood -brain barrier: Endogenous modulation by adrenal-cortical function. Science 1985;227: 1580-1583.
13. Ten S, New M, Maclaren N. Clinical Review130: Addison's Disease 2001; J Clin Endocrinol Metab 2001;86:2909-2922.

14. Addison T. On The Constitutional And Local Effects Of Disease Of The Supra-Renal Capsules. Samuel Highley, 32 Fleet St, London, 1855.