



**Dr. Techy says,
Intrathecal and long-acting
opioids wreck hormone
production!**

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HORMONE REPLACEMENT FOLLOWING OPIOID SUPPRESSION

Just about everyone who receives this Bulletin is aware that opioids suppress hormone levels. After all, we've known about opioid suppression for over 30 years.¹⁻⁶ Given this fact, the big question is—however—why isn't every practitioner who prescribes opioids testing for and treating with hormones?

We propose 2 main reasons:

- 1. Not sure how to go about it.**
- 2. Rotten attitude—lets ignore the issue and maybe it will go away.**



Here are some **BOLD-FACE** facts about opioids and hormones—as unpleasant as they may be.

1. Hormone deficiencies in a pain patient worsen and prolong the pain. You can't heal without hormones!⁷⁻¹²
2. Opioids don't work well and provide much relief without normal hormone levels.⁷⁻¹⁰
3. Low hormone levels in opioid-maintained patients may cause all sorts of problems: depression, anergy, mental impairments, amenorrhea, loss of libido, erectile dysfunction, hyperalgesia, weakness, weight loss, osteoporosis.¹³⁻²²

WHICH OPIOIDS ARE THE WORST OFFENDERS?

Intrathecal and long-acting opioids including transdermal fentanyl are the worst offenders.¹⁸⁻²⁶ Intrathecal opioids cause the hypothalamus to be constantly bathed in opioids. Long-acting opioid administered orally or by patch produce a constant blood level which not only coats the hormone producing centers in the brain, but also the adrenals, and gonads.

One thing is clear. Intrathecal and long-acting opioids due to their almost universal proclivity to suppress hormones (about 85% of the time), should only be used as a last resort when short-acting opioids fail to control pain.^{15,16}

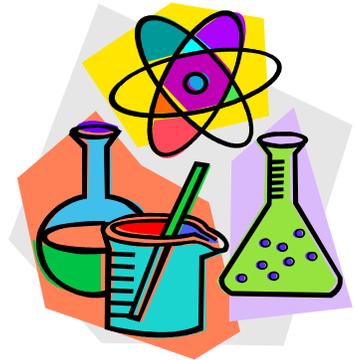
WHICH HORMONES ARE SUPPRESSED BY OPIOIDS?

Testosterone has gotten the most press, but pregnenolone, DHEA, and estrogen are commonly suppressed.^{15,16} Cortisol, progesterone, and oxytocin may even be lowered by opioids.¹⁶ Estrogen suppression results in amenorrhea in females.^{10,12} Opioids like to preferentially suppress gonadal releasing hormone in the hypothalamus but they may also directly affect hormone production in the pituitary, adrenals, and gonads.

WHAT HORMONES SHOULD BE TESTED AND TREATED?

Due to today's easy access to commercial laboratories, we recommend a hormone profile in pain patients consisting of:

- 1. Cortisol**
- 2. Pregnenolone**
- 3. Testosterone**
- 4. Dehydroepiandrosterone (DHEA)**
- 5. Progesterone**
- 6. Corticotropin (ACTH)**

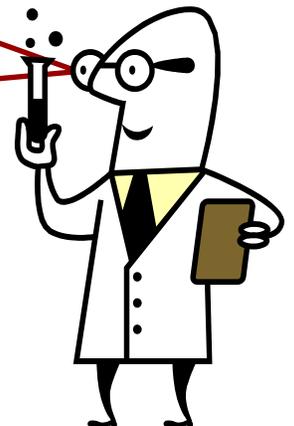


In a pain patient maintained on intrathecal or long-acting opioids, hormone testing should be done at least twice a year and whenever any of the complications (fatigue, hyperalgesia, etc.) occur. Replacement of deficient hormones should be done and the patient followed with repeat tests.²⁷

MAIN MESSAGE: Isn't it time that hormone testing and replacement in patients on intrathecal and long-acting opioids be standard care? Given the serious complications of hormonal deficiencies, there is no longer any good excuse to avoid this clinical issue. Put another way, if you feel you are qualified and willing to prescribe intrathecal and other long-acting opioids, shouldn't you be prepared to deal with their complications?

Dr. Hormone says,

Isn't it time that hormone testing and replacement be standard of care in patients on intrathecal and long-acting opioids?



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References

1. Lafiscu S, Bolelli G, Franceschetti F, et al. Hormone levels in methadone-treated drug addicts. Drug Alcohol Depend 1998;8:229-234.
2. Cicero TJ, Bell RD, Wiest WG, et al. Function of the male sex organs in heroin and methadone users. N Engl J Med 1975;292:882-887.
3. Ragni G, DeLauretis L, Bestetti O, et al. Gonadal function in male heroin and methadone addicts. Int J Androl 1988;11:93-100.
4. Woody G, McLellan AT, O'Brien C, et al. Hormone secretion in methadone-dependent and abstinent patients. NIDA Res Monogr 1988;81:216-223.
5. Cushman PJ, Kreek MJ. Methadone-maintained patients: Effect of methadone on plasma testosterone, FSH, LH, and prolactin. NY State J Med 1974;74:1970-1973.
6. Hanbury R, Cohen M, Stimmel B. Adequacy of sexual performance in men maintained on methadone. Am J Drug Alcohol Abuse 1977;4:13-20.
7. Pednekar J, Mulgaonker VK. Role of testosterone on pain threshold in rats. Indian J Physiol Pharmacol. 1995;39:423-4.
8. Fischer L, Clemente JT, Tambeli CH. The protective role of testosterone in the development of temporomandibular joint pain. J Pain. 2007;8:437-42.
9. Forman IJ, Tingle V, Estilow S, Caler J. The response to analgesia testing is affected by gonadal steroids in the rat. Life Sci. 1989;45:447-54.
10. Mensah-Nyagan AG, Meyer L, Schaeffer V, Kibaly C, Patte-Mensah C. Evidence for a key role of steroids in the modulation of pain. Psychoneuroendocrinology. 2009;34(Suppl. 1):S169-77.
11. Aloisi AM, Ceccarelli I, Fiorenzani P, et al. Testosterone affects pain-related responses differently in male and female rats. Neurosci Lett. 2004;361:262-4.
12. Aloisi AM, Bonifazi M. Sex hormones, central nervous system and pain. Horm Behav 2006;50:1-7.
13. Daniel HW. Hypogonadism in men consuming sustained-action oral opioids. J Pain 2002;3:377-84.
14. Daniell HW. Opioid endocrinopathy in women consuming prescribed sustained-action opioids for control of nonmalignant pain. J Pain 2008;9:28-36.
15. Vuong C, Van Uum SH, O'Dell LE, Lutfy K, Friedman TC. The effects of opioids and opioid analogs in animal and human endocrine systems. Endocr Rev 2010;31:98-132.
16. 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;7:145-54.
17. Aloisi AM, Buonocore M, Merlo L, et al. Chronic pain therapy and hypothalamic-pituitary-adrenal axis impairment. Psychoneuroendocrinology 2011;36:1032-9.
18. Finch PM, Roberts LJ, Price L, et al. Hypogonadism in patients treated with intrathecal morphine. Clin J Pain 2000;16:251-4.
19. Roberts LJ, Finch PM, Pullan PT, et al. Sex hormone suppression by intrathecal opioids: a prospective study. Clin J Pain 2002;18:144-8.
20. 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. Poster presentation at the 2012 Annual Meeting of the American Academy of Pain Medicine, February 23-26, 2012; Palm Springs, CA, USA; Abstract #229.
21. Abs R, Verhelst J, Maeyaert J, et al. Endocrine consequences of long term intrathecal administration of opioids. J Clin Endocrinol Metab 2000;85:2215-22.

22. Brennan MJ. The effect of opioid therapy on endocrine function. *Am J Med* 2013;126:Suppl 1:12-18)
23. Daniell HW. DHEAS deficiency during consumption of sustained-action prescribed opioids: evidence for opioid-induced inhibition of adrenal androgen production. *J Pain* 2006;7(12):901-907.
24. Daniell HW. Opioid endocrinopathy in women consuming prescribed sustained-action opioids for control of nonmalignant pain. *J Pain* 2008;9:28-36.
25. Duarte RV, Raphael JH, Southall JL, Labib MH, Whallett AJ, Ashford RL. Hypogonadism and low bone mineral density in patients on long-term intrathecal opioid delivery therapy. *BMJ Open* 2013 Jun 20;3(6).
26. Roberts LJ, Finch PM, Pullan PT, et al. Sex hormone suppression by intrathecal opioids: a prospective study. *Clin J Pain* 2002;18:144-148.
27. Daniell HW, Lentz R, Mazer NA. Open label pilot study of testosterone patch therapy in men with opioid-induced androgen deficiency. *J Pain* 2006;7:200-210.

