

# Pain Medication/ Sexual Frustration



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**H**ypogonadism, secondary to opioid use, is an under recognized and undertreated phenomenon. The association between opioid use and low levels of testosterone and estrogen was first established in the 1970s in heroin and methadone users and has since been confirmed in both intrathecal and oral opioid users.<sup>1-2</sup>

## How do opioids cause hypogonadism?

It is well known that both endogenous and exogenous opioids have physiologic effects in the hypothalamus. Excess endogenous opioids can decrease the frequency of gonadotropin releasing hormone (GnRH) pulses, resulting in impaired secretion of luteinizing hormone (LH) and follicular stimulating hormone (FSH) and thus, in hypothalamic hypogonadism.<sup>3</sup> Further, opioid antagonists, such as naloxone have been shown to increase LH release.<sup>4</sup> As in Jack's case, laboratory tests in opioid-induced hypogonadism usually show low or inappropriately normal levels of LH and/or FSH, together with decreased testosterone (or estradiol) levels. This supports a central cause of the hypogonadism.

## Jack's Situation

- Jack, 48, is a patient of the chronic pain clinic who is referred to endocrinology for decreased testosterone levels.
- His history is significant for hypertension and complex regional pain syndrome secondary to carpal tunnel release surgery. He has been on morphine, 100 mg, three times daily, for 10 years.
- Other medications include:
  - Atenolol
  - Hydrochlorothiazide
  - Amitriptyline
- Jack's symptoms include:
  - Decreased libido
  - Decreased energy
  - Loss of morning erection
  - Erectile dysfunction

For more on Jack, go to page 79.

## FAQ

### Who is affected by opioid-induced hypogonadism?

Premenstrual and postmenopausal men and women are all affected. However, postmenopausal women are usually asymptomatic.

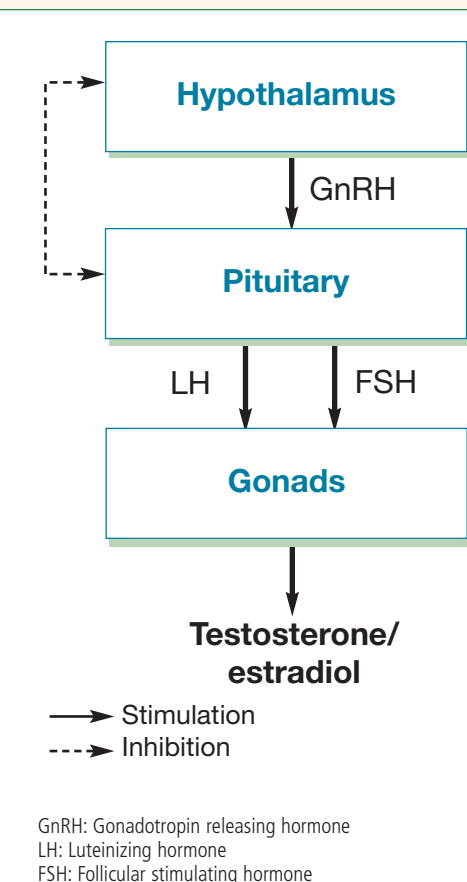
**Table 1**

## Signs and symptoms of hypogonadism

- Decreased libido
- Depression
- Anxiety
- Impotence
- Infertility
- Amenorrhea/menstrual irregularities in women
- Fatigue
- Decreased muscle mass
- Osteoporosis and fractures

**Figure 1**

## Hypothalamus-pituitary-gonadal axis



## More on Jack

- Jack's laboratory tests show:
  - decreased levels of testosterone (6 nmol/L, normal is 10 nmol/L to 28 nmol/L),
  - luteinizing hormone (LH) (<1 IU/L, normal is 2 IU/L to 12 IU/L),
  - his follicular stimulating hormone (FSH) and prolactin levels are in the normal range at 2 IU/L and 14 µg/L, respectively
- Jack's hypogonadism is secondary to his opioid use.
- He is started on regular testosterone injections and his symptoms resolve.

## Are there other endocrine abnormalities caused by chronic opioid use?

Hypogonadism is the most well established endocrine abnormality caused by chronic opioid use. It may result in decreased sexual function and osteoporosis. Multiple other hormonal disturbances have been noted in some patients in various studies, but these disturbances are less frequent. These abnormalities include:

- Increase of prolactin
- Decrease of cortisol and growth hormone
- Abnormal thyroid function<sup>5</sup>



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**Table 2**

## Diagnosis of opioid-induced hypogonadism

Chronic opioid or methadone use

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Signs and symptoms of hypogonadism

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Low testosterone/estradiol and normal/low LH-FSH

### FAQ

#### What are the side-effects of testosterone therapy?

Polycythemia (check hemoglobin and hematocrit) and worsening of sleep apnea may occur. Monitoring for prostate cancer and benign prostatic hyperplasia is indicated, particularly in elderly men.

### Take-home message

1. Hypogonadism is a common complication of chronic opioid drug use.
2. Opioid use must be considered in the differential diagnosis of hypogonadism.
3. Opioid users should be screened for signs and symptoms of hypogonadism.
4. Opioid users are at risk for the complications of hypogonadism including:
  - depression,
  - sexual dysfunction,
  - fatigue,
  - osteoporosis and
  - decreased muscle mass.

### How can opioid induced hypogonadism be treated?

There is some evidence that the suppression of sex steroids by opioids is dose-dependent.<sup>2</sup> Therefore, decreasing the opioid dose, or replacing it with a non-opioid analgesic when possible, is the first step. Another option, is the new analgesic drug buprenorphine (a partial mu-opioid receptor agonist) which does not cause hypogonadism.<sup>6</sup> If the opioid can not be discontinued, hormonal replacement therapy (testosterone in men, estrogens/oral contraceptive pills in premenopausal women) should be considered. Increased quality of life and resolution of hypogonadal symptoms in chronic opioid patients on replacement therapy have been reported.<sup>7</sup>

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