

# INTERPRETATION AND ACTIONS FOLLOWING HORMONE PROFILE TESTING

Protocols and Methods of  
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## BACKGROUND

Two developments have occurred in recent years which have brought hormone testing and treatment into pain management:

- No. 1 The discovery of neurohormones which are produced in the central nervous system (CNS) to provide neuroprotection, neurogenesis, and analgesia.
- No. 2 The development of laboratory testing technology which rapidly provides practitioners with hormone profiles.

This protocol provides the author's guidelines and recommendations regarding the interpretation of hormone profiles and actions to take, including hormone supplementation. The common abnormalities observed in hormone profile testing of chronic pain patients are listed here.

### I. HIGH SERUM LEVEL OF CORTISOL OR ADRENOCORTICOTROPIN (ACTH)

#### RATIONALE

ACTH is the prime hormone that is released by the anterior pituitary to stimulate the release of cortisol in times of stress including excess pain.

#### INTERPRETATION

A high serum level of ACTH and/or cortisol should be interpreted to mean that pain is out-of-control and additional analgesia is needed. Besides ACTH and cortisol, high levels of other hormones such as pregnenolone and testosterone may also be observed with poor pain control.

#### ACTIONS

Increase systemic analgesia and retest serum ACTH and cortisol within 4 to 6 weeks to determine if enough analgesia has been given to normalize the hypothalamic-pituitary-adrenal axis (HPA).

### II. LOW SERUM LEVEL OF PREGNENOLONE OR DEHYDROEPIANDROSTERONE (DHEA)

#### RATIONALE

The first serum deficiency observed with chronic pain is usually pregnenolone or DHEA. Although DHEA is the most plentiful hormone in the human body and has numerous anabolic effects, pregnenolone appears to be more involved with pain control. It is a critical co-factor for gamma amino butyric acid (GABA) and neurotransmission. Patients deficient in pregnenolone usually complain of severe pain, anxiety, and poor response to opioids and neuropathic agents.

#### INTERPRETATION

Low pregnenolone and/or DHEA serum levels occur with chronic, uncontrolled pain, and they should be temporarily supplemented.

### ACTIONS

Assume that systemic analgesia is inadequate and increase it. Administer pregnenolone and/or DHEA with these dosages: start 50 to 100 mg a day and increase to 200 to 300 mg a day over a 4 week period.

Retest after 60 to 90 days. If serum levels have returned to normal, the hormone can be stopped to see if the patient can now produce enough hormone without supplementation. If the patient voices great relief with either or both hormones, continue to supplement them and monitor with repeat serum tests every 3 to 6 months.

### III. LOW SERUM LEVEL OF TESTOSTERONE

#### RATIONALE

Serum testosterone deficiencies may occur due to chronic, severe pain and/or opioid administration. Long-acting and intrathecal depress serum levels more than short-acting opioids. Testosterone in both sexes must be brought into normal range lest the patient suffer poor pain control, anergy, depression, fatigue, and loss of sexual activity. Anabolic metabolism necessary for neurogenic healing is greatly impaired with testosterone deficiency.

#### INTERPRETATION

If the patient is on long-acting or intrathecal opioids, assume that opioids are the cause of low serum levels. If not on opioids or low dosages of short-acting opioids, assume that the patient has had severe, disabling pain for a considerable time period and without adequate analgesia.

#### ACTIONS

Retest if you have a question as to whether the test is valid. Free testosterone and sex hormone binding globulin tests are optional.

Supplementation can be done by any number of commercially available products including topical gels, patches, oral cavity preparations, and injections. Use the commercial, administration instructions for males. The female dosage is about 1/4<sup>th</sup> that of the male.

Retest the patient within 30 to 60 days. If levels have returned to normal consider stopping testosterone administration. If the patient reports great benefit, continue testosterone indefinitely and retest every 3 to 6 months to avoid any complications. Keep the serum testosterone level within normal range by adjusting the dosage.

To save costs, I frequently use a testosterone topical compounded by my local pharmacy. Here are my starting dosages:

Male: Testosterone 5 to 10% concentration

Female: Testosterone 1 to 2% concentration

Issue a 60 gram container. Apply about 1 gram each day.

Retest serum every 90 to 120 days to keep testosterone in normal serum range.

#### IV. LOW SERUM LEVEL OF CORTISOL

##### RATIONALE

Serum cortisol may drop below normal range after an extended period of severe, uncontrolled pain. A low serum level, particularly on repeat testing, must be assumed to represent some diminished reserve of adrenal cortisol and possibly pituitary ACTH. In some, rare unfortunate patients it is probable that severe pain over an extended period lead to such severe adrenal depletion that death ensued. Cortisol is required for analgesia and multiple anabolic and neurogenic functions. Low serum levels are associated with uncontrolled pain, poor analgesia, depression, fatigue, lack of motivation, and muscle wasting.

##### INTERPRETATION

Low serum levels indicate that there has been poor pain control over an extended time period. Serum levels below 1.0 ug/dl should be considered an urgency that requires immediate corticoid administration

##### ACTIONS

If you have questions about test results, repeat the cortisol serum test. The proper action is supplementation with a corticoid for a period of 60 to 90 days. Normal adrenal glands secrete 30 to 40 mg of cortisol daily. Sub-replacement or supplementation is a corticoid dosage equivalent to about 15 to 20 mg. If serum cortisol levels have returned to normal, corticoid supplementation can be stopped to determine if adrenal reserve and output have normalized.

##### Starting Supplementation Dosages

- a. Hydrocortisone 5 mg, given 2 to 3 times a day
- b. Compounded pure cortisol, 5 to 7 mg twice a day
- c. Prednisone 5 to 10 mg a day

#### V. LOW SERUM LEVEL OF PROGESTERONE OR ESTRADIOL

##### RATIONALE

Progesterone and estradiol are members of the neurohormone class as they are made within the CNS as well as adrenals and gonads. They are neuroprotective and neurogenic. To date serum testing has been primarily in females and normal ranges have been assigned based on age and menstrual status. Due to their critical importance in pain management and other neurologic conditions, commercial laboratories are currently developing and adopting precise serum ranges for men and women. Due to this very recent development, we do not have as much clinical experience with estradiol and progesterone in pain patients as we do with testosterone, pregnenolone, DHEA, and

cortisol. Clinical experience to date, however, is that some chronic pain patients voice great relief and benefit when progesterone or estradiol are administered.

#### INTERPRETATION

Low serum levels in males should be considered to represent depletion caused by long-standing, chronic pain. The same consideration should apply to females, but age and menstrual status may confound interpretation.

#### ACTIONS

At this time, I recommend a supplementation trial of 30 days. Only if the patient reports considerable benefit after this time, do I continue. If supplementation is continued, I do a repeat serum testing at 90 days. Dosage is reduced if serum levels are above normal range. Here are my starting supplementation dosages:

##### Estradiol

Males, .5 mg a day

Females, 2 mg a day

##### Progesterone

Males, 50 mg a day or 100 mg every other day

Females, 100 mg a day

#### VI. LOW SERUM LEVEL OF ACTH

##### RATIONALE

ACTH secretion from the anterior pituitary is initially elevated by severe pain. If the pain is not controlled, ACTH levels may drop below normal range. Opioid administration and organic disease may also cause low ACTH serum levels.

Besides increasing serum cortisol levels, ACTH has some direct analgesic action in the CNS. Low serum levels are, therefore, almost always associated with uncontrolled pain that has been present for an extended time period.

##### INTERPRETATION

Evaluate for 3 possible causations: (1) severe, chronic, uncontrolled pain; (2) opioid suppression; (3) organic disease. Opioid suppression should only be suspected in most cases if the patient is on long-acting or intrathecal opioids. The most common organic cause of low ACTH seen in pain management is traumatic brain injury (TBI).

##### ACTIONS

Provide additional analgesia if the patient complains of uncontrolled pain. Supplement any hormone deficiency. Retest in 30 to 60 days and inquire as to whether the patient has achieved better pain control.

If on repeat testing a low ACTH is still present along with low levels of 2 or more other hormones (i.e. cortisol, pregnenolone, testosterone, etc.) refer to an endocrinologist. TBI cases usually require on-going, indefinite hormone replacement of some hormones.

## VII. NORMAL SERUM HORMONE PROFILE

### RATIONALE

A normal hormone profile means that pain has not been severe enough or been present long enough to cause significant HPA axis disturbances.

### INTERPRETATION

No hormone replacement is required.

### ACTIONS

Treat the patient systemically with the practitioner's analgesic regimen of choice. If opioids are administered as part of the treatment regimen, retest in 90-120 days to determine if any hormone suppression has occurred. Do a hormone profile at any time the patient complains that their treatment regimen is inadequate or that you believe opioid hyperalgesia may be present. If, on retesting, one or more hormone deficiencies are detected, supplement the hormone until serum levels return to normal.

## VIII. SUMMARY

The protocol and methods presented here are those of one practitioner. No claims are made that they are optimal. In fact, they are presented in hopes that improvements will occur in the future and that other practitioners will contribute to this improvement.

