Disclosure

• Receive speaker bureau fees from Regenesis Biomedical and INSY Pharmaceutical and am an editor for Practical Pain Management.
Learning Objectives

• Discuss ways to enhance the hormone system to perform its natural functions of healing, neuroprotection, and pain control.
• Identify who needs hormone testing and what hormones should be tested.
• Interpret hormone test results.
• Implement hormone replacement and treatment in appropriate patients.

Self Assessment Questions

1. A Neurosteroid is:
   a) Hormone used by athletes
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   c) Hormones made and used within the CNS
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2. Chronic, severe pain causes the following effects on adrenal hormone serum levels:
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4. Hormone replacement in pain patients is:
   a) Total daily replacement
   b) Lifetime
   c) Substitute for analgesics
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5. A common side-effect of long-term excess cortisol is:
   a) Dementia
   b) Psoriasis
   c) Angina
   d) Osteoporosis

WHY A NEW FRONTIER?

- Pain relief depends on adequate hormone levels
- Pain causes profound hormone abnormalities
- Neurohormones are recognized as a therapeutic class
- Opioids suppress hormone production
- Hormone profiles are now available
- Clinical benefits of hormone administration are obvious
MAJOR PAIN CONTROL MECHANISMS OF HORMONES

- IMMUNE FACILITATION
- ANTI-INFLAMMATORY ACTION
- TISSUE REGENERATION
- GLUCOSE CONTROL
- CNS PAIN FUNCTIONS
  - Receptor Binding
  - Nerve Conduction
  - Neuroprotection
  - Neurogenesis
  - Maintenance Of Blood Brain Barrier

MAJOR HORMONES CRITICAL FOR PAIN CONTROL

- CORTISOL
- PREGNENOLONE
- DEHYDROEPIANDROSTERONE (DHEA)
- PROGESTERONE
- TESTOSTERONE
MAJOR HORMONES CRITICAL FOR PAIN CONTROL (Cont)

- ESTROGEN
- THYROID
- VITAMIN D
- HUMAN CHORIONIC GONADOTROPIN
- OXYTOCIN

CLINICAL BENEFITS OF HORMONE ADMINISTRATION

Minimize Opioids
HORMONE ADMINISTRATION

INCREASES
✓ Energy
✓ Physical activity
✓ Quality of Life
✓ Appetite
✓ Opioid Effectiveness
✓ Happiness
✓ Intellectual Functions
✓ Sleep
✓ Libido

HORMONE ADMINISTRATION

DECREASES
✓ Depression
✓ Hyperalgesia
✓ Hopelessness
✓ Allodynia
HORMONE ADMINISTRATION

POSITIVE EFFECTS ON PAIN

✓ Fewer Flares
✓ Decreased Baseline Pain
✓ Low Pain Days
✓ Longer Intervals Between Flares
✓ Pain Free Hours

HOW PAIN STIMULATES HORMONES
Uncontrolled pain can deplete pituitary, adrenal, and gonadal hormones.
NEUROHORMONES

“A HORMONE SECRETED BY A SPECIALIZED NEURON INTO THE BLOOD STREAM, THE CEREBROSPINAL FLUID, OR THE INTERCELLULAR SPACES OF THE NERVOUS SYSTEM.”

DORLAND’S ILLUSTRATED MEDICAL DICTIONARY-29th ED.

NEUROHORMONES CRITICAL FOR PAIN CARE

• PREGNENOLONE
• PROGESTERONE
• DEHYDROEPIANDROSTERONE (DHEA)
• ESTROGEN
• HUMAN CHORIONIC GONADOTROPIN
• OXYTOCIN

PATIENT EXAMPLE: “IT TOOK ME OVER”
NEUROHORMONE ADMINISTRATION MAY BE ESSENTIAL TO CONTROL AND MITIGATE SOME CENTRALIZED PAIN STATES

OPIOIDS SUPPRESS RELEASING HORMONES IN THE HYPOTHALAMUS

PREFERENTIAL

Gonadotropin Releasing Hormone (GRH)

SOMETIMES

Corticotropin Releasing Hormone (CRH)
MOST COMMON HORMONES SUPPRESSED BY OPIOIDS

• Testosterone

• Estrogen

Other hormones including cortisol, DHEA, pregnenolone, and thyroid can be suppressed

OPIOID HORMONE SUPPRESSION

• 80-85% with long-acting or intrathecal opioids

• Short-acting opioids have less suppression on hypothalamus
MAJOR CHARACTERISTICS OF OPIOID ENDOCRINOPATHY

• HISTORY OF GOOD OPIOID PAIN CONTROL WHICH LATER CEASES
• LOW TESTOSTERONE
• LOW ESTRADIOL
• AMENORRHEA/OLIGOMENORRHEA (Females)
• GYNECOMASTIA (Males)
• IMPOTENCE (Males)

COMMON CLINICAL MANIFESTATIONS OF TESTOSTERONE DEFICIENCY

• FATIGUE
• DECREASED LIBIDO AND PERFORMANCE
• DEPRESSION
• SLOW MENTATION
• POOR ANALGESIA CONTROL
• MUSCLE WEAKNESS
• GYNECOMASTIA
GYNECOMASTIA FROM HYPOTESTOSTERONEMIA

WHY TEST SERUM HORMONES?

- BIOMARKERS OF UNCONTROLLED PAIN
- NEED TO REPLACE HORMONES
- MONITOR TREATMENT SUCCESS
- SUSPECT COMPLICATIONS OF HORMONE DEFICIENCY OR EXCESS
HORMONE PANELS

BASIC

• Adrenocorticotropin (ACTH)
• Cortisol
• Pregnenolone
• Testosterone
• DHEA
• Progesterone

HORMONE PANELS

OPTIONS

• Thyroid
• Vitamin D
• Prolactin
• Epidural Growth Factor
• Insulin Growth Factor
• Estradiol
WHO SHOULD BE SCREENED FOR HORMONE ABNORMALITIES

- ANY PATIENT WHO REQUIRES DAILY OPIOIDS

- PATIENTS WHO COMPLAIN THAT THEIR CURRENT TREATMENT REGIMEN IS NOT EFFECTIVE

- PATIENTS WITH CENTRALIZED PAIN INCLUDING TBI

BEST TIMES TO TEST AND REPLACE

- BEFORE STARTING OPIOIDS

- BEFORE STARTING A LONG-ACTING OPIOID

- PATIENTS WHO ARE FAILING STANDARD TREATMENT
SITUATION #1
SHOULD OPIOIDS BE STARTED?

• 34 y/o female with fibromyalgia. On duloxetine (Cymbalta®) and celoxecib (Celebrex®). Had low pregnenolone and DHEA. Replacements avoided opioids.

SITUATION #2
SHOULD A LONG-ACTING OPIOID BE ADDED?

• 44 y/o male with lumbar spine degeneration. On hydrocodone (Vicodin®) and gabapentin (Neurontin®). Had low testosterone and pregnenolone. Replacements avoided a LA opioid.
HORMONE REPLACEMENT IN PAIN PATIENTS

• USUALLY TEMPORARY

• NOT A SUBSTITUTE FOR ANALGESICS

• MAY MINIMIZE OPIOIDS

HORMONE REPLACEMENT SAFETY

➤ IN PAIN PATIENTS THE PITUITARY, ADRENALS, AND GONADS ARE USUALLY NORMAL, SO TOTAL REPLACEMENT ISN’T USUALLY NECESSARY OR PERMANENT

➤ HORMONE SERUM LEVELS IN THEIR NORMAL RANGE AREN’T KNOWN TO CAUSE PITUITARY SUPPRESSION OR CANCER
SUB-REPLACEMENT

- SUB-REPLACEMENT IS USED IN PAIN MANAGEMENT-NOT TOTAL

Example: Adrenals make 20 to 30 mg of hydrocortisone-equivalence a day. Pain patients usually require less.

- USE BIO-IDENTICAL HORMONES AND NOT POTENT SYNTHETICS

Example: Use hydrocortisone or cortisol and not methylprednisolone, dexamethasone, or prednisone.

COMMON REPLACEMENTS

<table>
<thead>
<tr>
<th>HORMONE</th>
<th>START DAILY DOSAGES*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone</td>
<td>5 to 15 mg</td>
</tr>
<tr>
<td>Pregnenolone</td>
<td>100 to 300 mg</td>
</tr>
<tr>
<td>Testosterone Male:</td>
<td>10 – 100 mg</td>
</tr>
<tr>
<td>Testosterone Female:</td>
<td>2.5 – 25 mg</td>
</tr>
<tr>
<td>Dehydroepiandrosterone(DHEA)</td>
<td>100 to 300 mg</td>
</tr>
<tr>
<td>Progesterone</td>
<td>50 to 100 mg</td>
</tr>
</tbody>
</table>

*Start low and titrate upward.
MAJOR HORMONE COMPLICATIONS

• Pituitary-adrenal Failure
• Osteopenia-Osteoporosis

LABORATORY FINDINGS

• CORTISOL LESS THAN—1.0 mcg/dl
• ACTH LESS THAN — 5 pg/ml
• TESTOSTERONE LESS THAN — 3 ng/ml
ADRENAL FAILURE

- Physical Collapse/Immobile
- Nausea
- Hypotension
- Tachycardia
- Pain Flares
- Skin Pigmentation
- Muscle Wasting—Especially Fingers
- Bronze Coloring of Skin
OSTEOPOROSIS-OSTEOPENIA

• CERVICAL “BUFFALO” HUMPING
• KNEE-HIP-SPINE ARTHRALGIAS
• VERTEBRAL COLLAPSE

CERVICAL HUMPING OF HYPERCORTISOLEMIA
CERVICAL HUMPING OF HYPERCORTISOLEMIA

“BUFFALO HUMP”
CENTRALIZED PAIN WITH LOW TESTOSTERONE, HIGH CORTISOL, AND SEVERE OSTEOPOROSIS

THEORY OF BUILDING HORMONE RESERVE

ANY EXERCISE THAT TEMPORARILY RAISES HORMONE SERUM LEVELS WILL CAUSE THE GLAND TO PRODUCE AND STORE MORE HORMONE.
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References


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