Hormone Treatment of Burnout Syndrome
Burnout: Multiple Hormone Deficiency Syndrome
Burnout Syndrome: Causes?
Acute severe trauma

Prolonged stress

Overproduction & Overconsumption of Hormones

Endocrine glands prematurely age

Multiple hormone depletions

Burnout
Burnout Syndrome: What?
I think you have a burnout!
### SYMPTOMS of BURNOUT

<table>
<thead>
<tr>
<th>Type</th>
<th>Physical</th>
<th>Emotional</th>
<th>Behavioral</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Difficulty sleeping</td>
<td>• Anxiety</td>
<td>• Aggression</td>
</tr>
<tr>
<td></td>
<td>• Fatigue &amp; exhaustion</td>
<td>• Depression</td>
<td>• Callousness</td>
</tr>
<tr>
<td></td>
<td>• Gastrointestinal problems</td>
<td>• Guilt</td>
<td>• Cynicism</td>
</tr>
<tr>
<td></td>
<td>• Headaches</td>
<td>• Irritability</td>
<td>• Defensiveness</td>
</tr>
<tr>
<td></td>
<td>• Increased vulnerability to illnesses, such as colds &amp; flu</td>
<td>• Sense of helplessness</td>
<td>• Pessimism</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Substance abuse</td>
</tr>
</tbody>
</table>

Typical of Hormone deficits
<table>
<thead>
<tr>
<th>Type</th>
<th>Symptoms of Burnout</th>
</tr>
</thead>
</table>
| Physical        | • Difficulty sleeping  
                  • Fatigue & exhaustion  
                  • Gastrointestinal problems  
                  • Headaches  
                  • Increased vulnerability to illnesses, such as colds & flu |
| Emotional       | • Anxiety  
                  • Depression  
                  • Guilt  
                  • Irritability  
                  • Sense of helplessness |
| Behavioral      | • Aggression  
                  • Callousness  
                  • Cynicism  
                  • Defensiveness  
                  • Pessimism  
                  • Substance abuse |

Typical of Growth hormone deficiency
Thyroid deficiency
Cortisol deficiency
Growth horm. deficiency
Testosterone deficiency
Oxytocin deficiency
<table>
<thead>
<tr>
<th>Type</th>
<th>SYMPTOMS of BURNOUT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Work-related</td>
<td>• Decreased or poor work performance</td>
</tr>
<tr>
<td></td>
<td>• Absenteeism</td>
</tr>
<tr>
<td></td>
<td>• Misuse of work breaks</td>
</tr>
<tr>
<td></td>
<td>• Tardiness, Attrition</td>
</tr>
<tr>
<td></td>
<td>• Thefts</td>
</tr>
<tr>
<td>Inter-personal</td>
<td>• Dehumanization of patients</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td></td>
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</tr>
</tbody>
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### SYMPTOMS of BURNOUT

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<td></td>
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</table>

**Typical of**
- Growth hormone deficiency
- Testosterone deficiency
- Oxytocin deficiency
Fig. 2. Scores of the 2 burnout groups for 7 subscales of 2 burnout questionnaires. TBS = Teacher Burnout Scale; job sat = job satisfaction; prcvd ad spprt = perceived administrative support; cpng strs = coping with job-related stress; att stdnts = attitudes toward students; MBI = Maslach Burnout Inventory; emot exhst = emotional exhaustion; dpers = depersonalization; red eff = reduced efficiency. All group differences => sign. with \( p < .05 \) (\( U \) test).

Jens C. Pruessner, PhD, Dirk H. Hellhammer, PhD and Clemens Kirschbaum, PhD. Burnout, Perceived Stress, and Cortisol Responses to Awakening. Psychosomatic Medicine 61:197-204 (1999)
More errors in Burnout syndrome

Jens C. Pruessner, PhD, Dirk H. Hellhammer, PhD and Clemens Kirschbaum, PhD  Burnout, Perceived Stress, and Cortisol Responses to Awakening Psychosomatic Medicine 61:197-204 (1999)
Burnout Syndrome: Its Hormone Deficiencies & treatments?
Overview

1. Growth hormone
2. Melatonin
3. Thyroid treatment
4. Progesterone
5. Estradiol
6. Cortisol treatment
7. DHEA
8. Fludrocortisone
9. Testosterone
Burnout: The critical deficiency: Cortisol ...
Healthy Cortisol
FLEA (Runs away)

FIGHT (Attacks)

Cortisol in all conditions

Stress (Danger)

Normal

Stress (Pleasure)
Healthy cortisol serum levels & stress response

- **High Morning Peak**
- **Low Night Nadir**
- **Gradual decline during the day**
- **Short peaks secreted in stressful situations**

Graph showing cortisol concentration over time during the day, highlighting key points of interest.
Unhealthy Cortisol
Higher cortisol in the morning in high stress perception

Jens C. Pruessner, PhD, Dirk H. Hellhammer, PhD and Clemens Kirschbaum, PhD. Burnout, Perceived Stress, and Cortisol Responses to Awakening. Psychosomatic Medicine 61:197-204 (1999)
Women + high level of hardship

Unhealthy serum cortisol & stress response

Higher Morning Peak

Short peaks secreted in stressful situations

Gradual decline during the day

Lower Night Nadir

Too high levels

Women + high level of hardship
The feeling of Burnout:

The lack of combativity
The confusion & despair
in stress conditions

Cortisol deficiency!
Teachers + burnout => ↓ overall cortisol

SUBJECTS: 66 teachers (42 W & 24 M, mean age 42 years)

=> On each day, cortisol levels at awakening & 15, 30, & 60’ after

RESULTS: Perceived stress correlated w/ ↑ of cortisol levels during the first hour after awakening after dexamethasone pretreatment.

Teachers scoring ↑ on burnout =>

• ↓ overall cortisol secretion on all sampling days
• ↑ suppression of cortisol secretion after DXM administration

Teachers + ↑ levels of perceived stress + ↑ burnout =>

• ↓ overall cortisol secretion on the first 2 days
• + stronger ↑ during the 1st h after awakening after DXM suppression
• the lowest self-esteem, the highest external locus of control
• the highest number of somatic complaints

Center for Psychobiological and Psychosomatic Research, University of Trier, Germany.
Women with high level of hardship experience unhealthy serum cortisol & stress response.

- Higher Morning Peak
- Short peaks secreted in stressful situations during the day
- Gradual decline during the day
- Too low levels

Graph shows cortisol concentration over time, with red line indicating higher morning peak and green line showing gradual decline during the day.
Fig. 3. Mean salivary cortisol levels (± SE) for 2 groups of teachers with low & high burnout (BO) on 3 days at 0, 15, 30, & 60’ after awakening. On day 3, an overnight DXM suppression test (0.5 mg) was performed.

Jens C. Pruessner, PhD, Dirk H. Hellhammer, PhD and Clemens Kirschbaum, PhD Burnout, Perceived Stress, and Cortisol Responses to Awakening Psychosomatic Medicine 61:197-204 (1999)
Women + burnout => ↓↓ urinary free cortisol

SUBJECTS: 16 female patients + burnout;
16 control subjects

RESULTS: patients + burnout (vs controls)
the reduction of urine free-cortisol excretion = the most striking finding

- Sign. ↓ initial urinary free cortisol:
  mean +/- SEM = 47.2 +/- 11.0 vs 79.0 +/- 6.8 nmol/L (p = 0.02)
- No sign. changes in the other hormonal & biochemical data.

CCL: functional hypocortisolism in burnout

Department of Pharmacy and Pharmacology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg
Burnout => ↓ serum cortisol in morning, & smaller ↑ cortisol awakening response

SUBJECTS: 42 clinically burned-out patients

RESULTS: More severe burnout symptoms => consistently assoc. w/
• ↓ level & smaller ↑ cortisol awakening response
• ↑ DHEAS levels
• ↓ cortisol/DHEAS ratios
• stronger suppression after DST

CCL: severity of burnout symptoms is assoc. w/ HPA-axis functioning

Sonnenschein M, Mommersteeg PM, Houtveen JH, Sorbi MJ, Schaufeli WB, van Doornen LJ. Exhaustion and endocrine functioning in clinical burnout: an in-depth study using the experience sampling method. Biol Psychol. 2007 May;75(2):176-84. Utrecht University, Faculty of Social Sciences, Department of Clinical and Health Psychology, P.O. Box 80140, 3508 TC Utrecht, The Netherlands
Women with a high level of hardship experience unhealthy serum cortisol and stress response.

- **Excessive Morning Peak**
- **Blunted Morning Peak**
- **Low Night Nadir**

During the day, there is a gradual decline in cortisol concentration.
Men + positive family history of hypertension

=> ↓ morning cortisol during periods of highest strain

SUBJECTS: men + positive family history of hypertension

• the increase in systolic blood pressure at work was particularly pronounced

• ↓ than expected level of morning cortisol was found measured during the period + highest level of strain

Burnout => not much diff. with no burnout

SUBJECTS: 29 burned-out, 33 work-engaged, & 26 healthy ref. managers

RESULTS:

• The burned-out, work-engaged, & reference groups did not differ in the cortisol & DHEAS levels, the slope of the cortisol awakening response, & the cortisol : DHEAS ratio.

• The work-engaged group showed a stronger cortisolsuppression in response to the dexamethasone suppression test than the other two groups, the finding suggesting higher feedback sensitivity among work-engaged managers.

CCL: Burned-out & work-engaged managers only differ marginally in HPA-axis functioning.

Men + severe amnesia => no morning ↑ serum cortisol after awakening, circadian cortisol ↓↓

SUBJECTS: 6 men + severe amnesia due to hypoxia, herpes simplex encephalitis or closed head injury; healthy controls

RESULTS: amnesic patients:

• absent morning cortisol ↑ (typically observed in healthy subjects & also observed in the control group).
• a normal circadian day profile in the amnesic patients
• pronounced circadian cortisol ↓↓

Post-traumatic stress disorder
Post-traumatic stress disorder in doctors

Doctors have an increased risk of developing posttraumatic stress disorder. Raj Persuad considers the reasons why and describes the treatments available.

Post-traumatic stress disorder (PTSD) is often elicited when a person has experienced, witnessed, or been confronted with an event which entailed actual or threatened death or injury or a threat to the physical integrity of themselves or others.

By the very nature of their profession, doctors, like firefighters & police officers, are much more likely to encounter traumatic events and experiences than most other professionals. While some doctors, such as those in the armed forces, accident & emergency medicine, or acute specialties, are even more likely to witness trauma, no branch of medicine will escape an encounter sooner or later with incidents of an emotional or shocking nature beyond the norm.
Holocaust Survivors
Holocaust survivors with PTSD => ↓ 24h urinary cortisol

SUBJECTS: Holocaust survivors with PTSD => 24 h urine samples

RESULTS: Holocaust survivors with PTSD
- Sign. ↓ mean 24h urinary cortisol excretion than the 2 groups of subjects without PTSD.
- Sign. assoc. between urinary cortisol & severity of PTSD due to a substantial assoc. w/ scores on the avoidance subscale.

CCL:
↓ Urinary cortisol => associated with PTSD symptoms of a clinically sign. nature, rather than occurring as a result of exposure to trauma per se, &
↓ urinary cortisol => may persist for decades following exposure to trauma among individuals w/ chronic PTSD

War veterans

For some vets the war never ended...
Heavy combat exposure =>
morning serum cortisol in current PTSD

STUDY: Vietnam "theater" (n = 2,490) & "era" veterans (n = 1,972) without service in Vietnam

RESULTS: Theater veterans + current PTSD
• ↓ morning serum cortisol (vs era or theater veterans + lifetime PTSD)

Among theater veterans:
• Cortisol => inversely rel. to combat exposure
  => Veterans exposed to heavy combat
  => lowest serum cortisol

Treatment: Elevate Cortisol levels
Psychotherapy to elevate cortisol levels
Burnout => Sign. ↓ cortisol level after awakening, improved by psychotherapy

SUBJECTS: 22 participants + clinical burnout; 21 healthy controls.

RESULTS: the burnout group (vs control group)

• Sign. ↓ cortisol level after awakening after 14 sessions of psychotherapeutic intervention =>
  • Sign. ↓ complaints
  • ↑ of the initially lowered morning cortisol levels
  • No consistent correlations between the changes in subjective complaints & the change in cortisol parameters

No effect of stress management ⇒↓↓ urinary free cortisol of women + burnout

SUBJECTS: 16 female patients + burnout. 16 + untreated control subjects

RESULTS: patients + burnout (vs controls)

the reduction of urine free-cortisol excretion = the most striking finding

• Sign. ↓ initial urinary free cortisol (mean +/- SEM = 47.2 +/- 11.0 vs 79.0 +/- 6.8 nmol/L, p = 0.02)

• Remained sign. ↓ at 4 mo despite stress management intervention (mean +/- SEM = 44.0 +/- 6.1 vs 91.1 +/- 8.8 nmol/L, p = 0.0001)

• No sign. changes in the other hormonal & biochemical data.

CCL: functional hypocortisolism in burnout ⇒ not immediately restored on stress management intervention despite clinical and psychological improvement.

Moch SL, Panz VR, Joffe BI, Havlik I, Moch JD. Longitudinal changes in pituitary-adrenal hormones in South African women with burnout. Endocrine. 2003 Aug;21(3):267-72. Department of Pharmacy and Pharmacology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg
Cortisol Supplementation to elevate cortisol levels
In which Burnout patients will Cortisol help?
↑ Serum Prolactin in burnout
⇒ Cortisol = beneficial

STUDY: double-blind within-subject study ⇒ 9 female burnout subjects & 9 controls + 35 mg cortisol & placebo orally

RESULTS: The burnout subjects
⇒ extreme distribution of basal prolactin levels vs controls.

• ↓ prolactin burnouts ⇒ profoundly low attachment scores & tended to low oxytocin levels

• ↑ prolactin burnouts ⇒ cortisol ⇒ ↑ fatigue, & ↓ vigor

CCL: burnout subjects are either characterized by
- ↓ serotonergic function ⇒ no impt efficacy of cortisol
- ↓ dopaminergic function =+ the latter group benefits from cortisol replacement

Tops M, Boksem MA, Wijers AA, van Duinen H, Den Boer JA, Meijman TF, Korf J. The psychobiology of burnout: are there two different syndromes? Neuropsychobiology. 2007;55(3-4):143-50 Department of Experimental and Work Psychology, University of Groningen, Groningen, The Netherlands. mtops@fsw.leidenuniv.nl
BRAIN DOPAMINE RECEPTORS & GLUCOCORTICOCIOIDS

**brain dopamine D₂ - receptor**
- CONTROL
- ADX + DXM - 23%

**brain dopamine D₂ - receptor**
- CONTROL
- ADX + DXM - 8%

**brain dopamine D₁ - receptor**
- CONTROL
- ADX + DXM - 38%

**figure**: 28 days after adrenalectomy, dopamine D₂ receptors decrease in the anterior & middle striatum, dopamine D₁ receptors decrease in the substantia nigra. This suggests that glucocorticoids play a role in the dopamine system and may explain part of the excitatory effects of glucocorticoids (↑ euphoria, motor activity & aggressive behaviors). (Birn D et al, Neuroendocrinology, 1992, 55 : 468-476)
Doses?
5-10 mg/day?
CHRONIC FATIGUE SYNDROME & HYDROCORTISONE THERAPY

fatigue score

Hydrocortisone

PLACEBO

5 or 10 mg / day (1 month)

↓ - 7.2

1 month

figure: 1 month of low dose hydrocortisone therapy improves significantly the fatigue of CFS patients (n = 32). In 28 % (9 patients) the score became similar to the one of normal subjects. No adrenal suppression occurred in those low-dosed patients (at the insulin tolerance test). (Cleare AJ, Heap E, Malhi GS, Wessely S, O'Keane V, Miell J. Low-dose hydrocortisone in chronic fatigue syndrome: a randomised crossover trial. Lancet. 1999 Feb 6;353(9151):455-8.)
15-40 mg/day!
HYDROCORTISONE TREATMENT in WOMEN

<table>
<thead>
<tr>
<th>DEFICIENCY</th>
<th>HYDROCORTISONE</th>
</tr>
</thead>
<tbody>
<tr>
<td>MILD</td>
<td>10 mg - 5 to 10 mg - 0 - 0</td>
</tr>
<tr>
<td>MODERATE</td>
<td>15 mg - 10 mg - (5) - 0</td>
</tr>
<tr>
<td>SEVERE</td>
<td>20 mg - 10 mg - (5) - 0</td>
</tr>
<tr>
<td>DEFICIENCY</td>
<td>Dosage</td>
</tr>
<tr>
<td>---------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>MILD</td>
<td>20 mg (15) - 10</td>
</tr>
<tr>
<td>MODERATE</td>
<td>25 mg (20) - 10 mg</td>
</tr>
<tr>
<td>SEVERE</td>
<td>30 mg (30) - 10</td>
</tr>
</tbody>
</table>

Note: 25 mg Cortisone = 20 mg Hydrocortisone
Balance

Androgens (esp. DHEA)
Estrogens
GH
Melatonin

Cortisol
improvement in self-rating wellness score (worst = 0; optimal = 10)

**Figure**: Hydrocortisone-treated patients had a greater improvement in mean wellness score, a greater % recording an improvement of 5 or more points in wellness score and a higher average improvement in wellness score in more days than did placebo recipients. (hydrocortisone 16 mg/m² = 20-30 mg at 8AM, 5 mg at 2PM during 12 weeks ⇒ 30 % net increase in daily cortisol exposure) (McKenzie R et al, JAMA, 1998, 280: 1061-1066)
Burnout: The feeling of fainting: Aldosterone deficiency ...
Feeling like fainting
Overtraining $\Rightarrow$ ↓ aldosterone, cortisol

SUBJECTS: 7 runners $\Rightarrow$ overtraining syndrome.

- ↑ training volume (ITV) $\Rightarrow$ mean training volume of 85.9 km/week ↑ within 3 weeks to 176.6 km/week - and 96-98% of training volume was performed as long-distance runs at mean(s.d.) 67(8)% of maximum capacity $\Rightarrow$ plateau in endurance performance and decrease in maximum performance occurred during ITV, probably due to overtraining $\Rightarrow$ months of performance incompetence

- 47-53% ↓ ↓ Nocturnal catecholamine excretion (contrary to exercise-related plasma catecholamine responses, which increased).

- ↓ Resting & exercise-related cortisol & aldosterone levels

- ↑ training intensity (1 year later) $\Rightarrow$ ↑ Speed endurance, high-speed & interval runs averaging 9 km/week within 3 weeks to 22.7 km during ITI, & total volume ↑ from 61.6 to 84.7 km. $\Rightarrow$ Improvement in endurance and maximum performance occurred during ITI indicating a failure to cause an overtraining syndrome in ITI

  - clearly -9-26% ↓ nocturnal catecholamine excretion & exercise-related catecholamine responses showed a significant decrease,
  - cortisol & aldosterone levels remained almost constant
  - exercise-related prolactin levels decreased slightly.

CCL: The ↓ nocturnal catecholamine excretion during ITV might indicate a ↓ intrinsic sympathetic activity in exhausted sportsmen.

Fatigue in Hormone Deficiencies

↓ Cortisol

AT STRESS

+ in THE EVENING

↓ Aldosterone

IN VERTICAL POSITION
Fludrocortisone => increases BP

Figure: Treatment increased upright BP by limiting the decrease in cardiac output. The period during which the patients were able to remain in the standing position without orthostatic complaints increased minimally from 3 to 10 minutes.

Treatment: Elevate Aldosterone levels
Fludrocortisone or Aldosterone Supplementation to elevate aldosterone action
**ALDOSTERONE THERAPY**

→ How to prescribe?

| LOW ALDOSTERONE in U 24 h w/ low to moderate salt intake + | TREATMENT  
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>slightly low blood pressure (110 mg Hg)</td>
<td>9-α-fluorohydrocortisone</td>
</tr>
<tr>
<td>low blood pressure (low BP: 96-109 mg Hg) in stress + upright position)</td>
<td>50-75 µg/day in the morning</td>
</tr>
<tr>
<td>very low blood pressure (80-95 mg Hg)</td>
<td>100 µg/day in the morning (starting dose)</td>
</tr>
<tr>
<td></td>
<td>125-150 µg/day in the morning</td>
</tr>
</tbody>
</table>

+ 25-50 µg/day increase if a lot standing activities!!
Burnout:
The slow thinking, slow moving:
Thyroid deficiency ...
The Thyroid

Triiodothyronine
Tired

Slow to move

Slow to think
Overtraining (interval training) => T3 ↓, rT3 ↑

SUBJECTS: 15 highly trained males

Interval training => 12 h after exercise:
- Sign. T3 ↓
- Sign. rT3 ↑

CCL: Interval exercise => suppressed peripheral conversion of T₄ to T₃ implying that a longer recovery period is necessary for hormonal levels to return to normal following interval exercise compared to slow endurance exercise.

Treatment: Elevate Thyroid levels
Thyroid Treatment

Slow, very progressive increase to optimal dose

- T3/T4 (Thyrolar®, Euthyral, Novethyral®)
  \( \frac{1}{2} \) to 1 ½ tablets

- T4 (Thyroxine, levethyrox): 50 to 150 µg/day

- Armour Thyroid: 30 mg to 120 mg/day

+ 15-30 mg Armour tHyroid or 5-20 µg T3 if intellectual challenge!!!
Burnout: The poor resistance to noise: DHEA deficiency...
DHEA DEFICIENCY

MENTAL:

Lower quality of life

- Fatigue
- Depression
- Anxiety
- Moderately poor resistance to stress
- Poor resistance to noise
- Arthralgias
Treatment: Elevate DHEA levels
## Oral DHEA Treatment

<table>
<thead>
<tr>
<th>Deficiency</th>
<th>DHEA</th>
<th>WHEN?</th>
<th>ROUTE</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MILD</strong></td>
<td></td>
<td>morning (&amp; before bedtime) before breakfast or at meals</td>
<td><strong>oral</strong> (or sublingual)</td>
<td>- normal forms: too short action?</td>
</tr>
<tr>
<td><strong>MODERATE</strong></td>
<td></td>
<td></td>
<td></td>
<td>- slow released forms: poor absorption?</td>
</tr>
<tr>
<td><strong>SEVERE</strong></td>
<td></td>
<td></td>
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### Normal Forms
- Too short action?

### Slow Released Forms
- Poor absorption?
However

- Severe burnout symptoms are associated with a lower level or smaller increase of the cortisol awakening response (CAR), higher dehydroepiandrosterone-sulphate (DHEAS) levels, lower cortisol/DHEAS ratios and stronger suppression as measured by the dexamethasone suppression test (DST).

Burnout: The permanent fatigue: Sex hormone deficiency ...
Treatment: Elevate Female Hormone levels
Disturbance of ovarian homeostasis => a mechanism of accelerated follicle loss in mice


“Ovarian follicle burnout”
<table>
<thead>
<tr>
<th>DEFICIENCIES</th>
<th>$E_2$</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>100 mg 18/26 day of the cycle</td>
</tr>
<tr>
<td>- MILD</td>
<td>2.50 g</td>
<td>5/25</td>
</tr>
<tr>
<td>- MODERATE</td>
<td>3.75 g</td>
<td>5/25</td>
</tr>
<tr>
<td>- SEVERE</td>
<td>5.00 g</td>
<td>5/25</td>
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of a 0.6 mg/g transdermal gel

+ 1-2 grams if strong increase in physical activities
Burnout: The sports fatigue: Testosterone deficiency ...
Fatigue in Hormone Deficiencies

↓ Estrogens/DHEA

PERMANENT

↓ Androgens

PERMANENT + AT PHYSICAL EFFORT
Low free testosterone/cortisol ratio = marker of overtraining.

Reliability of the criterion of FTCR decrease of 30% or more to indicate temporary incomplete recovery from intensive training and residual weariness and, consequently, of reduced effectiveness for competitive purposes.

Overtraining => \(\downarrow\) testosterone & cortisol; **Multivitamin** => \(\uparrow\) recovery

**Subjects:** 240 young men (male Chinese field artillery personnel with physical overtraining)

**RESULTS:** Overtraining =>
- Sign. \(\uparrow\) thyroid function, somatization, anger & tension
- **Sign. \(\downarrow\) testosterone**, adrenal cortex & immunological function + **multivitamin/multimineral** (compared to placebo)
  - => sign. \(\uparrow\) functional recovery of the pituitary -adrenal axis, -gonadal axis, -thyroid axis
  - sign. \(\uparrow\) recovery of immune system & psychological parameters.

- Department of Endocrinology, Chinese PLA General Hospital, Beijing.
Overtraining => ↑ SHBG; no ↑ in basal testosterone/cortisol ratio with training

SUBJECTS: 57 men = an 8-week Finnish military basic training period

OVERTRAINED SUBJECTS had to fulfill 3 of 5 criteria: ↓ aerobic physical fitness (VO2max), ↑ rating of perceived exertion (RPE) in 45-minute submaximal test at 70% of VO2max or sick absence from these tests, ↑ somatic or emotional symptoms of OR, & ↑ incidence of sick absence from daily service. VO2max improved during the first 4 weeks of BT. During the second half of basal training:

- A stagnation of increase in VO2 max
- ↑ basal serum sex hormone-binding globulin (SHBG)
- ↓ insulin-like growth factor-1
- ↓ cortisol; ↓ submaximal exercise-induced increases in cortisol
- ↓ maximum heart rate, and ↓ post-exercise increase in blood lactate

=> 33% = overtrained => ↑ basal SHBG before & after 4 & 7 weeks of training & higher basal serum cortisol at the end of BT than no OR subjects. In addition, in contrast to no OR, OR subjects exhibited no ↑ in basal testosterone/cortisol ratio but a ↓ in maximal La (lactate) /RPE (perceived exertion) ratio during basal training

Treatment: Elevate Testosterone levels
## TRANSDERMAL TESTOSTERONE TREATMENT: Liposomal GEL

<table>
<thead>
<tr>
<th>Tubes</th>
<th>100 g of 100 mg/g liposomal gel (10%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily dose</td>
<td>0.5 to 4 grams of 100 mg/g gel in 1 or 2 x / day</td>
</tr>
</tbody>
</table>

### Advantage
- Avoids liver passage
- More natural, physiologic
- Less suppression of endogenous LH & testosterone production

### Disadvantage
- after 3 to 12 months: more DHT produced (skin 5α-reductase)

### Indication
- most androgen – deficiencies in men

### Contra-indication
- women with hirsutism
Transdermal TESTOSTERONE: doses

DEFICIENCY                      TESTOSTERONE
                                 liposomal gel  100 mg/g

- Mild                        0.5-1 g/day  (0.5 – 1)
- Moderate                    2            (1 – 2.5)
- Severe                      3-4 g/day   (2.5 - 4)
Burnout: The agitated sleep: Melatonin deficiency ...
Treatment:
Elevate
Melatonin levels
# MELATONIN THERAPY: Oral or sublingual?

## MELATONIN

<table>
<thead>
<tr>
<th>Deficiencies</th>
<th>Efficient absorption (Sublingual)</th>
<th>Average</th>
<th>Poor absorption (Oral)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Mild</td>
<td>0.05 mg</td>
<td>0.2 mg</td>
<td>0.3 mg</td>
</tr>
<tr>
<td>- Moderate</td>
<td>0.15-0.5 mg</td>
<td>1 mg</td>
<td>1.5 mg</td>
</tr>
<tr>
<td>- Severe</td>
<td>0.5-1 mg</td>
<td>2 mg</td>
<td>10 mg</td>
</tr>
</tbody>
</table>
Burnout: The exhaustion: GH deficiency ...
Overtraining => horses: ↓ peak GH secretion, irregular GH pulsatility

SUBJECTS: 10 young (1.5 yr) horses => trained on a treadmill for 32 => 4 phases (4, 18, 6, and 4 wk, resp): 1) habituation to high-speed treadmill trotting, 2) normal training, in which speed and duration of training sessions => ↑ gradually 3) in this phase, 2 groups of horses: control (C) & intensified trained (IT) group. In intensified trained, training intensity, duration, and frequency were further increased, whereas in control these remained unaltered, & 4) reduced training (RT).

RESULTS: Intensified training => overtraining (performance decreased by 19% vs C), => assoc. w/ an ↑ concentration peaks number (3.6 vs. 2.0, resp.), a smaller peak secretion pattern w/ prolonged half-life (15.2 vs. 7.3 min, resp.), & an ↑ approximate entropy (0.89 vs. 0.49, resp.) Reduced training did not lead to full recovery for the overtrained horses.

CCL: overtraining => ↑ irregularity of nocturnal GH pulsatility pattern = a loss of coordinated control of GH regulation. Longer phases of somatostatin withdrawal = the underlying mechanism for the observed changes in GH pulsatility pattern??

Overtraining => ↓ IG-1

SUBJECTS: 57 men = an 8-week Finnish military basic training period

OVERTRAINED SUBJECTS had to fulfill 3 of 5 criteria: ↓ aerobic physical fitness (VO2max), ↑ rating of perceived exertion (RPE) in 45-minute submaximal test at 70% of VO2max or sick absence from these tests, ↑ somatic or emotional symptoms of OR, & ↑ incidence of sick absence from daily service. VO2max improved during the first 4 weeks of BT. During the second half of BT:

• a stagnation of increase in VO2max was observed,
• ↑ basal serum sex hormone-binding globulin (SHBG)
• ↓ insulin-like growth factor-1
• ↓ cortisol; ↓ submaximal exercise-induced increases in cortisol
• ↓ maximum heart rate, and ↓ post-exercise increase in blood lactate

=> of 57 subjects, 33% were classified as OR => ↑ basal SHBG before & after 4 & 7 weeks of training & higher basal serum cortisol at the end of BT than no OR subjects. In addition, in contrast to no OR, OR subjects exhibited no ↑ in basal testosterone/cortisol ratio but a ↓ in maximal La (lactate) /RPE (perceived exertion) ratio during basal training

Treatment: Elevate GH levels
<table>
<thead>
<tr>
<th>BODY SIZE</th>
<th>SMALL</th>
<th>MEDIUM</th>
<th>BIG</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEFICIENCY</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- MILD</td>
<td></td>
<td>Doses for MENTAL improvement</td>
<td></td>
</tr>
<tr>
<td>- MODERATE</td>
<td>- 25 to 50 %</td>
<td>0.10 – 0.20 mg/d to 0.25 – 0.5 IU/d</td>
<td>+ 25% to +50%</td>
</tr>
<tr>
<td>- SEVERE</td>
<td></td>
<td>0.12 – 0.42 mg/d to 0.35 – 1.25 IU/d</td>
<td></td>
</tr>
</tbody>
</table>

PHYSICAL improvement: often 2 x dose
GH THERAPY ➔ How to administer?

PATIENT WITH weak ADRENALS
(low cortisol levels/therapy)
+ whose other hormone deficiencies aren’y being corrected
+ weak financial situation

START 0.05 mg 0.15 I.U. a day (1 click/0.015 ml on SC inject.pen) the 1st 2 weeks
then 0.10 mg 0.3 I.U. a day (2 clicks / 0.03 ml)

[ [ [ .........................................................the 2nd 2 weeks
then 0.15 mg 0.45 I.U. a day (3 clicks /0.045 ml) ] ] ]

........................................... until the next consultation
then see the patient for evaluation the 3th month
The complete Burnout:
No strong reactions anymore

Adrenaline deficiency
Overtraining => -50% ↓ nighttime catecholamine excretion

SUBJECTS: 7 runners => overtraining syndrome.

• ↑ training volume (ITV) => mean training volume of 85.9 km/week ↑ within 3 weeks to 176.6 km/week- and 96-98% of training volume was performed as long-distance runs at mean(s.d.) 67(8)% of maximum capacity => plateau in endurance performance and decrease in maximum performance occurred during ITV, probably due to overtraining => months of performance incompetence - 47-53% ↓ ↓ Nocturnal catecholamine excretion (contrary to exercise-related plasma catecholamine responses, which increased).

• ↓ Resting & exercise-related cortisol & aldosterone levels

• ↑ training intensity (1 year later) => ↑ Speed endurance, high-speed & interval runs averaging 9 km/week within 3 weeks to 22.7 km during ITI, & total volume ↑ from 61.6 to 84.7 km. => Improvement in endurance and maximum performance occurred during ITI indicating a failure to cause an overtraining syndrome in ITI
  – clearly -9-26% ↓ nocturnal catecholamine excretion & exercise-related catecholamine responses showed a significant decrease,
  – cortisol & aldosterone levels remained almost constant
  – exercise-related prolactin levels decreased slightly.

CCL: The ↓ nocturnal catecholamine excretion during ↑ training volume might indicate a ↓ intrinsic sympathetic activity in exhausted sportsmen.

Adrenaline Treatment

Check for thyroid & estrogen deficiencies, If present:
- Thyroid treatment
- Estradiol & progesterone treatment (women)

They increase catecholamines
Conclusion: Hormone Treatment of Burnout
Fatigue in Hormone Deficiencies

↓ Thyroid hormones
IN THE MORNING (esp. waking up) + AT REST

↓ Cortisol
AT STRESS + IN THE EVENING

↓ Estrogens/DHEA
PERMANENT

↓ Aldosterone
IN VERTICAL POSITION

↓ Androgens
PERMANENT + AT PHYSICAL EFFORT

↓ GH
PERMANENT AFTER MIDNIGHT + POOR RECOVERY
Basic Principles
Basic Principle nr 1

Improve the diet:

• Take out sweets, chocolate, soft drinks,
• Take out milk products
• & often bread, pastas, muesli
• Avoid high t° cooked food

As they lower the levels of essential hormones!!!!

• Increase (animal) protein intake, but cooked at low t°
• Increase fresh food: vegetables & fruits

As they increase hormones & ATP-NADPH production
Basic Principle nr 2

Improve the sleep

• Dark bedroom
• Increases morning (day)light
• No electric furniture near the bed
• Ear plugs

• Take if deficiency, hormone treatments that improve sleep:
  • Melatonin
  • Growth hormone
  • Sex hormones, esp. Progesterone
  • Oxytocin
Basic Principle nr 3

Treat the adrenal deficiency

Cortisol

DHEA

& often aldosterone/fludrocortisone
Basic Principle nr 4

Treat the other hormone deficiencies

GH
Thyroid
Estradiol-progesterone
Testosterone
Basic Principle nr 5

Treat the nutritional deficiencies

- Iron
- Magnesium
- Folic acid
- Vit. B12
- Vit. E
- Others
Hormone treatments of burnout

- Growth hormone
- Melatonin => OK at small doses (0.1 mg/day sublingual)
- Thyroid treatment
- Estradiol + progesterone in women
- Cortisol treatment => hydrocortisone
- DHEA
- Fludrocortisone
- Testosterone => avoid, if not essential

=> slight increases in stress, additional efforts required, etc.
THE HORMONE HANDBOOK

The keys to safe hormone therapies:
How to do it and how to solve therapy problems

The Worldwide Bestseller: 2nd edition

NEW: 6 major hormones: IGF-1, VP, MSH, OXY, PTH, INS
MORE: + 30% practical information & updated references
NEW: Crucial data on cancer-protective hormones & lab test anomalies

Thierry Hertoghe, MD
International Medical Books - Publications
Thank you for your attention