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Beyond Traditional Hypogonadism: Distinctive Mechanisms and Clinical Implications in Subclinical Functional Hypogonadism (SFH) with Integrative Strategies for Hormonal Homeostasis

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Abstract

Subclinical Functional Hypogonadism (SFH) represents a novel and multifactorial condition that transcends traditional definitions of hypogonadism, characterized by normal or slightly altered testosterone levels but impaired hormonal activity at the tissue level. The physiological response to stress, essential for human survival, has evolved from acute and episodic mechanisms in the past to a chronic and prolonged nature typical of modern society. Studies on Peruvian mummies (Journal of Archaeological Science) show the presence of cortisol, suggesting that stress also existed in primitive humans (Mayer & Rosen, 1975). However, the stress experienced by modern humans is significantly different, arising from factors such as technological overload, work pressures, and disrupted circadian rhythms, further exacerbated by metabolic imbalances and environmental pollutants. These contemporary triggers lead to persistent activation of the HPA axis, resulting in elevated cortisol levels and altered SHBG dynamics, which suppress testosterone bioavailability and disrupt hormonal homeostasis.

Unlike classic hypogonadism, SFH often presents sub clinically, with mild or nonspecific symptoms such as reduced libido, fatigue, and increased body fat, alongside systemic impacts on metabolism, mood, and cognitive function. The article distinguishes SFH from stress-related hypogonadism and age-related hormonal decline (Late-Onset Hypogonadism - LOH), emphasizing its unique physiological mechanisms and clinical implications. It also explores integrative strategies, including hormonal therapies, bio-neurofeedback, and interventions targeting circadian rhythms, tailored to gender differences, to restore endocrine balance and mitigate the systemic consequences of SFH. This framework highlights the importance of early recognition, precise diagnostic criteria, and personalized approaches to improve hormonal health and overall psycho-physical well-being.

1. Introduction

Modern societies experience unprecedented levels of stress due to a combination of factors, including social pressure, excessive use of technological devices, and sedentary lifestyles (Woessner et al., 2021). Compared to primitive humans, today's sources of stress are chronic, moderate in intensity but persistent, and rarely accompanied by physical outlets that could regulate hormonal responses (Mayer & Rosen, 1975; [1]. This results in cortisol accumulation without the balancing effect of testosterone—a dynamic that once ensured effective adaptation to the environment but is now counterproductive, exposing individuals to the potential risk of developing what the author refers to as Subclinical Functional Hypogonadism (SFH) [2].

1.1 Difference Between Secondary Hypogonadism and Subclinical Functional Hypogonadism (SFH)

1.1.1 Secondary Hypogonadism

a) Caused by a central dysfunction at the level of the hypothalamus or pituitary gland, leading to insufficient secretion of gonadotropins (LH and FSH).

b) Often associated with structural or organic issues, such as pituitary tumors, trauma, infections, hyperprolactinemia, or systemic chronic diseases.

c) Hormonal levels: Both LH/FSH and testosterone are reduced.

d) Diagnosis relies on identifying the underlying cause through hormonal assays and imaging (e.g., MRI for pituitary abnormalities).

e) Treatment focuses on addressing the root cause and may include testosterone replacement therapy.

1.1.2 Subclinical Functional Hypogonadism (SFH)

a) A functional condition, primarily driven by factors like chronic stress, technological overload, circadian rhythm disturbances, obesity, or metabolic imbalances.

b) Hormonal levels: Testosterone levels may appear normal or slightly altered, but its action at the tissue level is impaired due to factors such as elevated cortisol or increased SHBG levels.

c) Diagnosis involves evaluating lifestyle, stress levels, metabolic markers, and testosterone bioavailability (e.g., free testosterone).

d) Treatment focuses on lifestyle modifications, stress management, and addressing metabolic imbalances, with hormonal therapy only in severe cases.

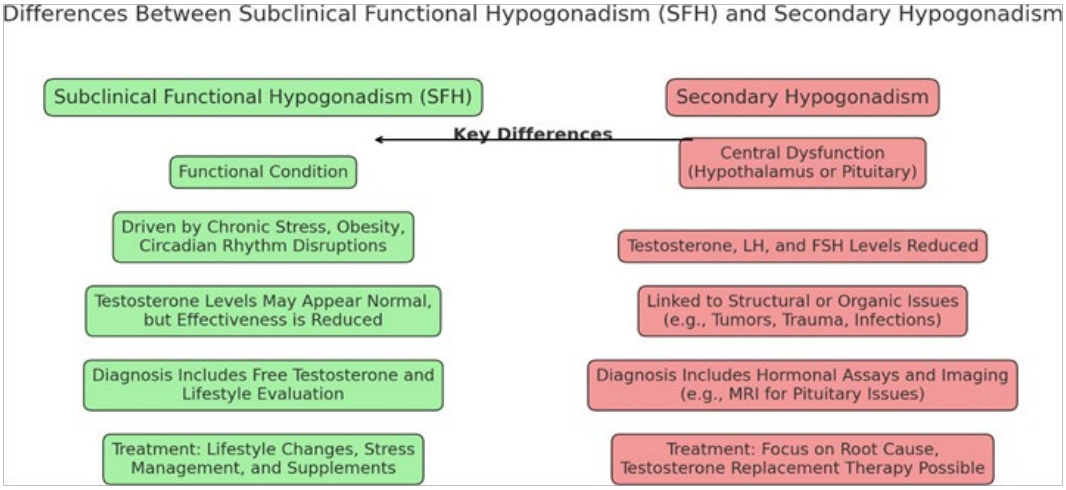

Figure 1: Differences Between Secondary Hypogonadism and SFH (Subclinical Functional Hypogonadism)

1.2 Distinction Between Subclinical Functional Hypogonadism and Stress-Related Hypogonadism: Specificity and Clinical Relevance

Subclinical Functional Hypogonadism (SFH) may appear as an extension of well-established concepts, such as hypogonadotropic hypogonadism or age-related hormonal decline (Late-Onset Hypogonadism - LOH), potentially overlapping with known conditions. However, SFH stands out for its functional and multifactorial origin, stemming from a combination of factors such as chronic stress, circadian rhythm disruptions, obesity, and exposure to pollutants, which lead to a complex interaction between cortisol and testosterone. This often results in normal or slightly reduced testosterone levels but impaired hormonal action at the tissue level. In contrast, stress- related hypogonadism has a specific origin, directly tied to chronic hyperactivation of the hypothalamic-pituitary-adrenal (HPA) axis, which suppresses GnRH secretion, reducing gonadotropin (LH and FSH) levels and consequently testosterone production. Clarifying these differences is crucial to avoid diagnostic overlap and to underscore the distinctiveness of SFH, which often presents subclinically with mild or nonspecific symptoms, unlike the more pronounced and clinically evident manifestations of stress-related hypogonadism. The use of distinctive diagnostic criteria, such as the assessment of free testosterone, SHBG levels, and metabolic markers, is therefore critical to ensuring the clinical significance of SFH is preserved and to guiding targeted interventions.

2. Chronic Stress and Hormonal Imbalance: A Receptor Competition

Testosterone and cortisol share intracellular receptors, creating functional competition. Under normal conditions, balanced testosterone levels can mitigate cortisol's negative effects, supporting neurogenesis and improving psychological well-being [3]. However, chronic stress elevates cortisol levels, reducing testosterone efficacy and favoring pathological conditions.

• Hyperactivating States (Anxiety): elevated cortisol levels are associated with increased neurophysiological arousal and vigilance, which, when prolonged, lead to chronic anxiety.

• Hypoactivating States (Depression): central nervous system exhaustion and suppressed neurogenesis, mediated by cortisol, contribute to depressive conditions [4].

2.1 Interaction Between Testosterone and Cortisol: a Complex Dynamic

2.1.1 Receptor Competition and Physiological Implications

a) Chronic Stress and Hyper-/Hypoactivation States

• Hyperactivation (Anxiety): Excess cortisol increases limbic system activity and reduces cortical inhibition, promoting persistent anxiety

• Hypoactivation (Depression): Cortisol-induced central nervous system exhaustion and suppressed neuroplasticity contribute to depressive states. Additionally, reduced testosterone amplifies these negative effects.

3. Subclinical Functional Hypogonadism (SFH)

SFH is a condition characterized by seemingly normal gonadal function with adequate testosterone production. However, an overproduction of cortisol can suppress testosterone's action at target tissues, compromising its physiological efficacy. This condition does not present obvious symptoms or manifests with mild signs but may be associated with factors such as chronic stress, obesity, or metabolic imbalances.

The hormonal dysregulation typical of SFH is particularly linked

to chronic stress, which stimulates cortisol secretion through the hypothalamic-pituitary-adrenal (HPA) axis. Recent studies highlight how elevated cortisol levels can antagonize testosterone's effects, leading to subclinical symptoms that impair quality of life and metabolic health (Rivier & Rivest, 1991) [5].

3.1 Key triggers for SFH

a) Cognitive Overload from Technological Devices

• Excessive use of technological devices, particularly in the evening, disrupts melatonin secretion and overstimulates the autonomic nervous system. This contributes to hormonal imbalances and increased stress levels (Cajochen et al., 2011).

b) Circadian Rhythm Disruption

• Exposure to artificial light and frequent use of electronic devices at night disturb circadian rhythms, impairing natural testosterone production and affecting overall endocrine health (Leproult & Van Cauter, 2011).

c) Environmental Pollutants

• Endocrine-disrupting chemicals, such as pesticides and bisphenol A (BPA), interfere with the endocrine system, reducing testosterone levels and contributing to a higher risk of hormonal dysfunction (Gore et al., 2015).

c) Low sunlight exposure

• Reduced sunlight exposure leads to vitamin D deficiency, which is strongly associated with lower testosterone levels and dysregulation of the hypothalamic-pituitary-gonadal (HPG) axis [6].

d) Chronic Stress

• Persistent stress activates the hypothalamic-pituitary-adrenal (HPA) axis, increasing cortisol secretion. Elevated cortisol suppresses testosterone production and disrupts the balance of the HPG axis [5].

e) Obesity

• Excess body fat increases aromatase activity, an enzyme that converts testosterone into estrogen. This exacerbates hormonal imbalances and amplifies the feedback cycle of testosterone reduction [7].

f) Metabolic Imbalances

• Conditions such as insulin resistance and metabolic syndrome impair the production of sex hormones. These metabolic disruptions are closely linked to the development of SFH (Laaksonen et al., 2004).

g) Sleep Disorders

• Poor sleep quality, including insufficient deep sleep and sleep apnea, reduces testosterone production and elevates cortisol levels, worsening hormonal dysfunction (Leproult & Van Cauter, 2011; Wang et al., 2019).

h) Pre-Existing Medical Conditions

• Chronic illnesses such as diabetes, cardiovascular diseases, and autoimmune diseases are associated with reduced testosterone levels and impaired HPG axis function (Stanworth & Jones, 2008).

i) Psychological Distress

• Anxiety, depression, and emotional stress contribute to SFH by altering cortisol dynamics and impairing neuroendocrine regulation. This perpetuates a negative cycle of declining mental and hormonal health (Zarrouf et al., 2009).

j) Occupational and Relationship Stress

• Work-related stress and interpersonal conflicts elevate cortisol levels, negatively affecting the endocrine system. Chronic relational or professional pressures exacerbate imbalances within the HPG axis [7].

3.2 Primary Symptoms

Even in the absence of clinically evident manifestations, SFH may be associated with the following symptoms:

a) Reduced Libido: linked to decreased receptor sensitivity to testosterone (Morgan et al., 2000).
b) Chronic Fatigue: related to persistent HPA axis imbalance.
c) Loss of Muscle Mass: a consequence of reduced anabolic activity of testosterone (Maggio et al., 2005).
d) Increased Body Fat: particularly in the abdominal area, due to cortisol's catabolic effect (Francis, 2011).
e) Reduced bone density: potential risk of long-term osteoporosis.
f) Mood Disorders: Irritability and depression are common in cases of hypogonadism (Zarrouf et al., 2009).
g) Cognitive Performance Decline: attributed to the neurotoxicity of elevated cortisol.

Diagnosis and management of SFH require a multidisciplinary approach, including endocrinological evaluations, stress management, and lifestyle modifications. Further studies are needed to better understand the molecular mechanisms underlying this condition and to develop targeted therapeutic strategies (Rosen et al., 2022).

3.3 Diagnostic Criteria

According to the Endocrine Society and the European Male Aging Study (EMAS):

a) Presence of symptoms or signs consistent with androgen deficiency.
b) Total testosterone levels in the lower normal range, with further evaluation of free testosterone.
c) Exclusion of other causes (e.g., thyroid disorders, hyperprolactinemia).

3.3.1 Differential Diagnosis

Conditions with overlapping symptoms to exclude:

a) Chronic Fatigue Syndrome
b) Depression
c) Metabolic Syndrome
d) Obstructive Sleep Apnea

3.3.2 Contextual Diagnosis

Subclinical hypogonadism may be context-specific, such as:
a) Stress-induced HPG axis suppression.
b) Age-related testosterone decline (late-onset hypogonadism).
c) Impact of chronic illnesses (e.g., diabetes, obesity).

3.4 Laboratory Test and Diagnostic for SFH

a. Morning Total Testosterone

• **Timing:** total testosterone should be measured between 7:00 and 10:00 a.m., while fasting, due to diurnal variations with peaks in the early morning [8].
• **Clinical significance:** total testosterone levels near the lower normal limit (300–350 ng/dL) may indicate subclinical hypogonadism, even in the absence of evident symptoms (Wang et al., 2009).

b) Free Testosterone

• **Importance:** free testosterone, which represents the bioactive fraction of the hormone, provides a more precise indication of hormonal availability, especially in conditions that alter SHBG levels [9].
• **Clinical relevance:** low free testosterone levels, even with normal total testosterone, often indicate subclinical hypogonadism [10].

c) SHBG (Sex Hormone-Binding Globulin)

• **Role:** SHBG regulates testosterone bioavailability. Altered SHBG levels, often observed in metabolic conditions such as obesity and diabetes, can mask or amplify testosterone deficiencies [11].
• **Clinical Implications:** low SHBG levels may increase bioavailable testosterone but can also produce falsely normal results in total testosterone measurements, making free testosterone evaluation essential (Travison et al., 2006).

d) LH and FSH (Luteinizing Hormone and Follicle-Stimulating Hormone)

• **Differential diagnosis:** Low or normal levels suggest central hypogonadism (secondary), indicative of hypothalamic or pituitary dysfunction [10].

Elevated levels indicate primary hypogonadism, signaling testicular dysfunction [12].

e) Estradiol and Prolactin

• **Secondary causes:** elevated prolactin (e.g., due to prolactinomas) or increased estradiol from excessive aromatase activity can mimic hypogonadism [13].
• **Screening Value:** Measuring these hormones is essential to exclude secondary endocrine disorders contributing to reduced testosterone (Ramasamy et al., 2014).

3.4.1 Imaging and Specialized Tests (if Indicated)

a) Pituitary MRI

• **Purpose:** recommended in cases of central hypogonadism with low gonadotropin levels to identify structural abnormalities such as adenomas or pituitary lesions [14].

b) DEXA Scan (Dual-Energy X-ray Absorptiometry)

• **Utility:** evaluates bone mineral density in patients with osteopenia or osteoporosis, complications often associated with prolonged testosterone deficiency (Ebeling, 2008).

c) Adrenal and Thyroid Functional Tests

• **Objective:** to exclude adrenal insufficiency or thyroid dysfunction, both of which can mimic or exacerbate hypogonadism symptoms (Bhasin et al., 2018).

d) Stimulation Tests (if Necessary) HCG Stimulation Test

• **Application:** assesses Leydig cell function by measuring testosterone response to hCG stimulation. Useful for distinguishing functional versus structural testicular defects (Paduch et al., 2009).

e) GnRH Stimulation Test

• **Purpose:** differentiates hypothalamic from pituitary dysfunction by evaluating LH and FSH responses to GnRH administration in cases of suspected central hypogonadism (Dwyer & Quinton, 2014).

3.5 SFH in Men and Women

SFH is characterized by hormonal disruptions affecting the hypothalamic-pituitary-gonadal (HPG) axis, with no evident clinical symptoms or mild manifestations. It affects both men and women differently due to gender-specific endocrine functions. In men, it primarily involves reduced testosterone levels, while in women, dysfunctions include estrogen and progesterone. Chronic stress, obesity, metabolic alterations, and circadian rhythm disorders play central roles. Identifying and managing this condition is critical to prevent long-term complications such as osteoporosis, sexual dysfunction, and metabolic syndrome.

3.5.1 SFH in Men

a) Hormonal Mechanism:

• Excess cortisol suppresses testosterone production or inhibits its receptor-level action.
• Testosterone is essential for sexual function, muscle mass, bone density, and mental well- being.

b) Main Symptoms:

• **Reduced libido and erectile dysfunction:** low or ineffective testosterone directly impacts sexual function.
• **Loss of muscle mass and increased body fat:** typically redistributed to the abdominal area.
• **Chronic fatigue and reduced physical performance.**
• **Decreased bone density:** increased risk of osteoporosis over time.
• **Mood disorders:** irritability, depression, anxiety, and cognitive difficulties.

c) Specific Implications:

• In men, testosterone decline directly affects reproductive health and fertility, reducing sperm production.

3.5.2 SFH in Women

1. Hormonal Mechanism:

• Cortisol can interfere with estrogen and progesterone secretion, disrupting ovarian function and the hypothalamic-pituitary-gonadal (HPG) axis.

• Estrogen and progesterone are vital for the menstrual cycle, reproductive health, bone density, and emotional stability.

2. Main Symptoms:

• **Irregular menstrual cycle or amenorrhea:** reduced ovulation and cycle alterations.

• **Reduced libido:** often associated with vaginal dryness.

• **Chronic fatigue and decreased energy levels.**

• **Increased body fat and muscle mass loss.**

• **Mood disorders:** anxiety, depression, irritability, and concentration difficulties.

• **Reduced bone density:** Increased risk of early osteoporosis.

3. Specific Implications:

• In women, SFH can lead to fertility issues and increase the risk of metabolic syndrome, as the imbalance between cortisol and estrogen/progesterone disrupts fat and carbohydrate metabolism.

3.6 SFH Therapy in Men and Women

SFH therapy employs a multidimensional approach combining hormonal, nutritional, and lifestyle interventions.

• **In Men:** focuses on restoring testosterone levels through targeted treatments like replacement therapy or specific supplements.

• **In Women:** centers on regulating estrogen and progesterone, often with personalized hormonal therapies.

Both genders benefit from complementary strategies, including stress reduction, circadian rhythm improvements, and correction of metabolic imbalances. Medical supervision is essential to ensure effectiveness and safety.

3.6.1 SFH Therapy in Men

3.6.1.1 Cortisol Reduction

a) Stress Management

• Techniques like bioneurofeedback, meditation, or cognitive-behavioral therapy

• effectively reduce cortisol levels and improve stress response [15].

b) Nutritional Supplements

• **Ashwagandha:** clinical studies demonstrate its ability to significantly reduce cortisol levels [16].

• **Magnesium and Vitamin B6:** support stress reduction and improve sleep quality [17]

c) Moderate Exercise

• Moderate physical activity reduces cortisol, while excessive exercise may elevate it [18].

3.6.1.2 Testosterone Support

a) Non-pharmacological Interventions

• **Zinc and vitamin D:** essential for testosterone production [6].

• **Sleep Quality:** Deep sleep enhances testosterone production (Leproult & Van Cauter, 2011).

b) Testosterone Replacement Therapy (TRT)

• Used only in persistent cases of functional hypogonadism under strict medical supervision [12].

c) Modulating Medications

• **Clomiphene:** stimulates endogenous testosterone production [19].

3.6.2 SFH Therapy in Women

3.6.2.1 Cortisol Reduction

a) Similar Strategies to Men

• Bioneurofeedback, mindfulness, magnesium, and ashwagandha have comparable effects in women (Verma et al., 2021).

b) Circadian Rhythm Regulation

• Improve natural light exposure and reduce the use of electronic devices, especially in the evening [20].

3.6.2.2 Support for Estrogens and Progesterone

a) Targeted Nutrition

• **Soy Isoflavones:** support hormonal regulation [21].

b) Hormone Replacement Therapy (HRT)

• **Bioidentical estrogens and progesterone:** recommended for severe imbalances [22].

c) DHEA Supplementation:

• Useful for supporting endogenous estrogen production in women [23].

d) Fertility Restoration (if Necessary)

• **Ovulation-Inducing Medications:** Such as clomiphene or gonadotropins [24].

4. Critical Age: After 30 years

a) With age, testosterone levels naturally decline, with an estimated annual reduction of 1– 2% after 30 years [11].

b) This phenomenon, combined with factors such as a sedentary lifestyle, circadian rhythm disruptions, and obesity, leaves the endocrine system vulnerable to cortisol dominance.

c) Testosterone production naturally decreases after 30–35 years, a phenomenon exacerbated by inactivity and poor diet [25].

d) Physical inactivity further worsens the situation, reducing testosterone production and increasing insulin resistance (Zucker et al., 1972).

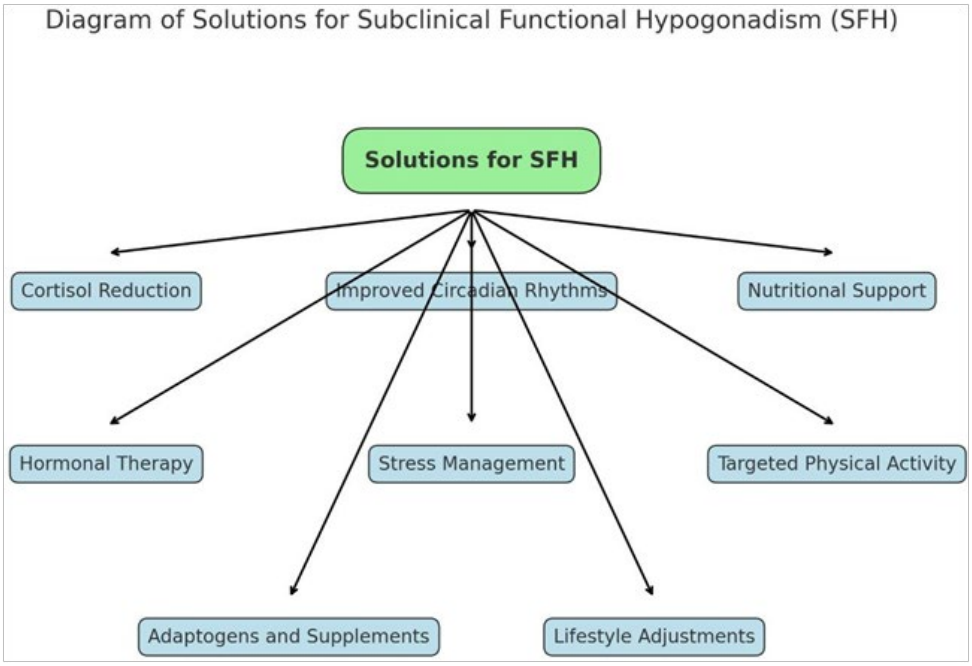

Figure 2: Solution to Address SFH

5. Clinical Consequences for SFH

a) Anxiety and Depression

a) Cortisol dominance and reduced testosterone activity amplify anxiety and depression by impairing neurogenesis and neurotransmitter regulation (dopamine, serotonin) [3].

b) Chronic SFH is linked to HPA axis hyperactivation, which increases cortisol secretion, exacerbating anxiety and mood instability [5].

c) In long-term cases, HPA axis hypoactivation can result in attenuated cortisol responses, leading to low energy, anhedonia, and depressive symptoms [26].

d) Low testosterone directly impacts activity in brain regions regulating mood, such as the amygdala and prefrontal cortex (Zarrouf et al., 2009).

b) Metabolic Syndrome

a) SFH is associated with increased risks of insulin resistance, visceral fat accumulation, and cardiovascular complications [11].

b) Visceral obesity, driven by low testosterone and elevated cortisol, plays a central role in metabolic dysregulation. Elevated aromatase activity in adipose tissue further reduces bioavailable testosterone, perpetuating a vicious cycle [7].

c) Longitudinal studies suggest that testosterone deficiency is an independent predictor of type 2 diabetes and systemic inflammation, both key components of metabolic syndrome [27].

c) Cognitive Decline and Brain Health

a) Testosterone has a neuroprotective role, supporting synaptic plasticity, neurogenesis, and mitochondrial function in the brain. Its deficiency, combined with high cortisol levels, has been linked to cognitive disorders, including memory deficits and reduced executive function [28].

b) Dysregulation of the HPA axis results in chronic glucocorticoid exposure, exacerbating hippocampal atrophy and impairing cognitive resilience [29].

d) Cardiovascular Complications

a) Testosterone deficiency is associated with increased arterial stiffness, endothelial dysfunction, and atherosclerosis. Elevated cortisol contributes to hypertension and vascular inflammation, worsening cardiovascular risks (Maggio et al., 2005).

6. Therapeutic and Lifestyle Interventions for Hormonal Imbalances

a) Testosterone Gel Supplementation

a) Testosterone gel application improves hormonal balance and alleviates symptoms such as depression and anxiety in men with hypogonadism [2].

b) In women, DHEA supplementation is considered a safe alternative to support hormonal balance, given the physiological differences from men [7].

c) Regular medical monitoring is crucial to prevent side effects and ensure treatment efficacy.

b) Biofeedback and Neurofeedback

a) These techniques aim to reduce cortisol levels and improve autonomic nervous system regulation, contributing to better hormonal balance [1].

b) Biofeedback, in particular, has been shown to modulate HPA axis activity, which is often hyperactive in chronic stress conditions.

c) These methods enhance HPA axis control, lowering cortisol levels and promoting testosterone activity [1].

c) Circadian Rhythms and Vitamin D

• Synchronizing circadian rhythms through sunlight exposure and proper sleep hygiene promotes testosterone production [6].

• Vitamin D, synthesized in the skin under sunlight, plays a crucial role in regulating the HPA axis and testosterone levels [4].
• Interventions such as managing exposure to artificial light and adopting regular sleep schedules are essential for maintaining hormonal balance.

d) Body Fat Reduction

• Body fat accumulation increases aromatase enzyme activity, converting testosterone into estrogens and reducing available testosterone levels [25].
• Longitudinal studies show that obesity is correlated with a significant decline in androgen levels in men, further aggravating hormonal imbalance [4].
• A regular exercise program combined with a balanced diet is essential to reduce aromatization and improve hormonal levels.

e) Nutrition Rich in Essential Nutrients

• A diet rich in proteins, healthy fats, and micronutrients such as zinc, magnesium, and omega-3 supports optimal hormonal production [30].
• Omega-3 fatty acids particularly improve insulin sensitivity and reduce cortisol levels [30].
• Consuming antioxidant-rich foods, such as fruits and vegetables, helps combat oxidative stress associated with hormonal imbalances.

f) Stress Management Techniques

• Practices such as meditation, yoga, and cognitive-behavioral therapy can lower cortisol levels and promote better hormonal balance [15].
• Diaphragmatic breathing has a calming effect on the HPA axis, promoting deep relaxation and reduced cortisol levels.

g) Natural Adaptogen Supplementation

• The use of adaptogens like ashwagandha and Siberian ginseng can help reduce chronic stress and improve HPA axis function [16].
• These supplements should be used under the supervision of a healthcare professional to ensure safety and efficacy.

h) Personalized Physical Exercise

• Moderate resistance exercise can improve testosterone levels, while excessively intense or prolonged training may increase cortisol and worsen hormonal imbalances [18].
• Incorporating relaxation exercises, such as tai chi, can further enhance the balance of the autonomic nervous system.

i) Specific Pharmacological Support

• In severe hormonal imbalances, medications like mifepristone or ketoconazole may be used to reduce cortisol production [31].
• Clomiphene, when indicated, can stimulate endogenous testosterone production in men [19].
• In women, a personalized combination of bioidentical estrogens and progesterone can help restore hormonal balance [22].

7. Conclusions

This article emphasizes the importance of recognizing SFH as a multifactorial condition requiring personalized and multidisciplinary treatment. The masked androgen deficiency (SFH) is a form of secondary hypogonadism caused by factors such as stress, significant weight loss, intense physical exercise, or eating disorders, which lead to a reduction in gonadotropin secretion and, consequently, a decrease in testosterone production. This condition is reversible with the removal of the triggering factor. SFH is characterized by its subclinical nature, often lacking evident symptoms but associated with mild manifestations and progressive systemic damage, such as metabolic syndrome, increased cardiovascular risk, and cognitive decline. Early diagnosis and personalized management are essential to prevent long-term complications. While the hormonal mechanisms underlying this condition are complex, appropriate stress management combined with targeted interventions can restore endocrine balance and significantly improve patients' quality of life. Finally, further research is needed to refine existing therapies and develop new strategies to address this growing challenge in contemporary health.

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