FP Essentials
Call for Authors – May 2022

Hormone Therapy

We are seeking an author or author group to write an edition of FP Essentials that will update family physicians about Hormone Therapy. This edition will cover four topics:

1. Testosterone replacement therapy
2. Menopausal hormone therapy
3. Antiaging hormone replacement and supplementation
4. Hormone therapy for transgender patients

The main text of the manuscript should be approximately 10,000 words in length, divided into four sections of approximately 2,500 words each, plus an abstract of approximately 200 words for each section. In addition, there should be key practice recommendations, a maximum of 15 tables/figures total, suggested readings, and up to 200 references to provide support for all recommendations and factual statements in the manuscript.

This edition should focus on what is new in each topic and should answer the key questions listed for each section. Each section should begin with an illustrative case, similar to the examples provided, with modifications to emphasize key points; each case should have a conclusion that demonstrates resolution of the clinical situation. The references provided here include information that should be considered in preparation of this edition of FP Essentials. However, these should be used only as a starting point in identifying the most current guidelines and references to include in the edition.

Needs Assessment: Marketing of hormone therapy for Food and Drug Administration (FDA)-approved and non-FDA-approved indications has skyrocketed in recent years, leading to numerous inquiries from patients and patient use of over-the-counter and integrative medicine therapies to supplement and boost hormone levels. Despite this, current education about endocrinology and hormone therapy often is inadequate in medical school and residency training for physicians to feel confident in the diagnosis and management of deficiency states and supplementation. In recent decades, substantial literature has described benefits and risks of hormone therapy, often with conflicting outcomes. Prescribers need to be knowledgeable of current guidelines and recommendations for initiating hormone therapy in men and women, as well as in transgender patients who plan to transition. In addition, it is important to know the effect of hormonal therapy on other conditions and cancer risk. The aim for this FP Essentials is to narrow knowledge gaps, to build clinician confidence regarding the unique challenges in providing safe hormone therapy and appropriate monitoring, and to reduce potential barriers to health care.
Section 1: Testosterone Replacement Therapy

Example case: AS is a 57-year-old man with a history of coronary artery disease with two drug-eluting stents, poorly controlled type 2 insulin-requiring diabetes, hypertension, hyperlipidemia, severely obesity, and cardiometabolic syndrome. Within the past year he developed erectile dysfunction, decreased libido, and decreased exercise stamina. He has tried over-the-counter “male enhancement” therapies without significant symptomatic improvement. He has read about the benefits of testosterone replacement therapy, but has some concerns about potential risks.

Key questions to consider:

- What is the prevalence of testosterone deficiency (TD) in men? What are considered to be normal, normal declining, and decreased testosterone levels?

- What are the most accurate tests for assessing testosterone hormone levels, and at what time of day? What is the role of salivary hormone testing and when should it be performed?

- What are the common symptoms of TD in men? Should any of those symptoms prompt testing testosterone levels?

- What is the differential diagnosis in men with suspected TD?

- What common comorbid conditions exist in men with TD?

- What are the current evidence-based guidelines for the evaluation and treatment of men with TD? When should testosterone replacement therapy (TRT) be considered, and when is it contraindicated?

- What formulations of TRT exist? What are the common adverse effects of each formulation? What is the recommended monitoring of patients taking TRT? How do hormone levels after treatment influence dose adjustment?

- What is the role of bioidentical hormone replacement therapy in men with TD?

- What are the proven benefits of TRT? What effects does TRT have on diabetes, abdominal obesity, hypertension, heart failure, and other cardiometabolic parameters?

- What are the proven risks of TRT? What concerns exist regarding the studies that have posited significant cardiovascular and cerebrovascular risks of TRT?

- Is TRT effective in the treatment of erectile dysfunction?

- What is the relationship between TRT and the development of prostate cancer? Benign prostatic hyperplasia (BPH)? Lower urinary tract symptoms (LUTS)?

- Can TRT be used safely in men with prostate cancer undergoing surveillance, or in those who have undergone prostatectomy?

- What over-the-counter and natural supplements, dietary factors, and exercise recommendations have proven efficacy in increasing testosterone levels? What common ingredients and additives in these supplements have proven harm?

Initial references to consider:

Section 2: Menopausal Hormone Therapy

Example case: KF is a 52-year-old woman with a history of major depressive disorder and moderate obesity; she has a family history of breast cancer in a paternal aunt. She comes to your office to discuss whether she needs to take hormones now that she has undergone menopause. She continues to experience hot flushes, episodic night sweats, and occasional irritability. She mentions that when her mother completed menopause, she took estrogen replacement therapy. She adds that she has heard that she may be a candidate.

Key questions to consider:

- What are the common symptoms of menopause, and which ones commonly persist for years after menopause?
- Is a hormonal evaluation for the woman with suspected menopause necessary? How do hormone level abnormalities correlate to symptoms and guide potential replacement? How do hormone levels after treatment influence dose adjustment? What is the role of salivary hormone testing and when should it be performed?
- What are the current evidence-based indications and strategies for menopausal hormone therapy (MHT)? Should MHT be started at the beginning of menopause or when/if symptoms arise? How long should MHT continue?
- What are the evidence-based benefits of MHT? What are the concerning risks? Are there differences in outcomes relative to starting MHT at the beginning of menopause or when symptoms arise?
- What were the findings of the Women’s Health Initiative (WHI) study, and how has clinical practice evolved in the past 2 decades since that study?
- What effect does MHT have on chronic health conditions, including cardiovascular disease, diabetes, cognitive decline, migraine headaches, sexual health, urogenital symptoms, and mood?
- What strategies exist to calculate the potential risk and benefits of MHT? How should women taking MHT be monitored?
- What is the relationship between MHT and venous thromboembolic disease?
- What is the relationship between MHT and cancer risk? When should MHT be avoided?
- What formulations of MHT exist? Which ones are preferred and at what dose? What are the common adverse effects of each formulation? What is the recommended monitoring of the patient taking MHT?
- What is the interaction between MHT and thyroid hormones?
- What is the role of bioidentical hormones in the treatment of the postmenopausal women? Do these hormones have the same risks of cancer as conventional hormone replacement therapy?
- When is testosterone therapy recommended for MHT?
• What over-the-counter and natural supplements, dietary factors, and exercise recommendations have proven efficacy in relieving menopausal symptoms? What common ingredients and additives in these supplements have proven harm?

Initial references to consider:


• Chester RC, Kling JM, Manson JE. What the Women’s Health Initiative has taught us about menopausal hormone therapy. Clin Cardiol. 2018;41(2):247-252.


Section 3: Antiaging Hormone Replacement and Supplementation

Example case: JJ is a 60-year-old man and previous competitive athlete who comes to your office to discuss his concerns about aging. In the past year few years, he has become frustrated that he is not as fast or as strong as he was decades ago. Although he maintains a healthy lifestyle without substance use, exercises regularly, and eats a sensible diet, he wants to feel and function like he did when he was in his 20s. He has read about the potential benefits of human growth hormone (hGH) but wants to discuss the potential risks and benefits with you.

Key questions to consider:

NOTE TO AUTHOR: Testosterone replacement/supplementation is discussed in Section 2, and should not be reviewed in this section.

- What hormone levels commonly decline in men and women during aging? When, if at all, should these be measured? How are these hormone levels best measured?
- With regard to human growth hormone (hGH), dehydroepiandrosterone (DHEA), dehydroepiandrosterone-sulfate (DHEA-S) and melatonin:
  - What are the common symptoms of deficiency? What is the recommended evaluation for patients with suspected deficiency?
  - What are the potential benefits of replacement/supplementation?
  - What are the common adverse effects and potential risks?
  - What are the Food and Drug Administration (FDA)-approved indications for use?
  - What are the recommended guidelines for replacement/supplementation?
  - What monitoring is recommended for patients who take these therapies?
  - How effective are they with regard to antiaging and managing various symptoms?
  - What additional steroids and supplements are commonly used in conjunction with these therapies relative to any antiaging effects?
  - What are the effects, if any, on male and woman fertility?
  - What over-the-counter supplements have been shown to naturally augment these hormone levels?

Initial references to consider:

Section 4: Hormone Therapy for Transgender Patients

Example case: CB is a 16-year-old healthy transgender girl (they/them) who wishes to begin medical transition. They are specifically interested in starting female hormone therapy to grow breasts, and minimize and eliminate secondary hair, and are considering eventual sex reassignment surgery.

Key questions to consider:

- What is the prevalence of Americans who identify as transgender? How does this statistic compare with rates in other countries? Why is the rate of transgender identity increasing?
- What strategies exist to create a comfortable and welcoming environment for transgender patients in the health care setting?
- At what age can transgender patients receive hormone therapy with or without parental consent?
- What are the current guidelines/criteria for feminizing and masculinizing hormone therapy for transgender patients? What are the medical indications and contraindications to hormone therapy in this population?
- What monitoring should occur in patients who receive hormone therapy and how often? Is any special training needed for family physicians or other primary care clinicians to prescribe hormone therapy for transgender patients? How can patients and physicians best identify subspecialists with expertise in this area?
- What are the metabolic effects of hormone therapy in transgender patients, specifically related to diabetes, bone health, and cardiovascular health?
- What are the potential short- and long-term health risks associated with hormone therapy in transgender patients?
- What is the relationship between hormone therapy in transgender patients and pelvic, testicular, and scrotal pain?
- What are the risks of mood disorder and suicide in transgender children and adolescents before and after pubertal suppression? What are the risks in adults before and after hormone therapy?
- What are the current recommendations for cancer screening in transgender patients who receive hormone therapy?
- What is the current status of insurance coverage for sex-affirming hormone therapy?
- Are there any laws/regulation that govern or prohibit administration of these therapies?

Initial references to consider:

• UCSF Transgender Care. Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People. 2nd ed. Deutsch MB, ed. June 2016. transcare.ucsf.edu/guidelines