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Core Urology
Endocrine–Andrology

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Disclosures

- None

Objectives

1. Develop an enhanced understanding of the male hypothalamic-pituitary-gonadal axis
2. Describe the evaluation of male hypogonadism
3. Describe normal testicular endocrine and exocrine function
4. Describe treatments and treatment monitoring for male hypogonadism

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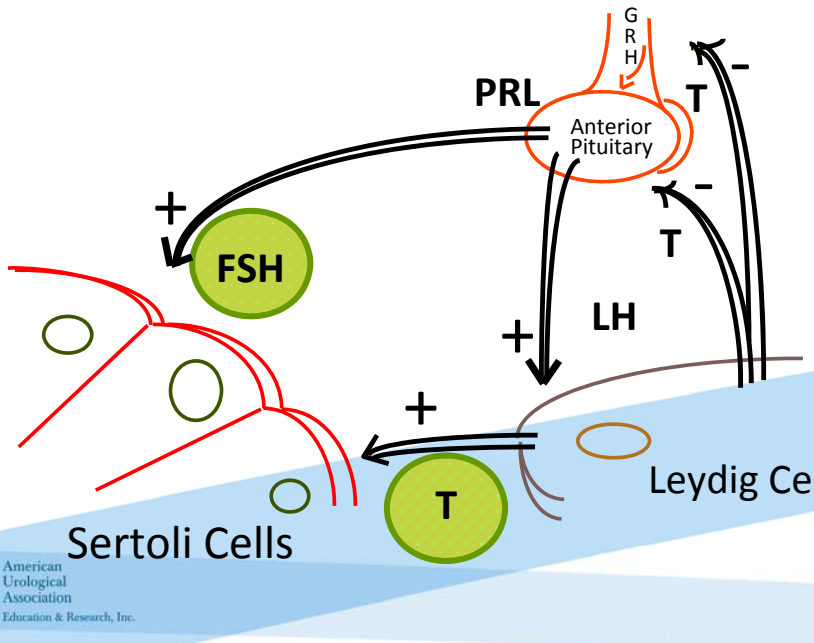
Hypothalamic–Pituitary–Gonadal Axis



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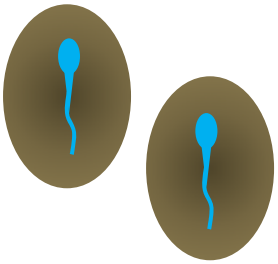
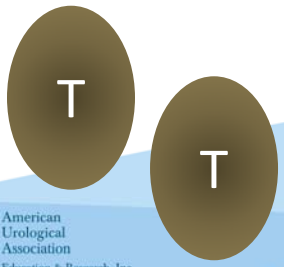
Testicular function

Endocrine

- Androgen production
- Primary feedback is LH
- Sequestered in the serum by SHBG and Albumin
- Key Concept: free and weekly bound Testosterone





Exocrine

- Sperm production
- Primary feedback is FSH
- Spermatogenesis is inhibited by exogenous Testosterone

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ARS Q1:

The following disease that manifests as primary hypogonadism is:

a) Chronic opioid abuse
b) Kallman Syndrome
c) Prolactinoma
d) Klinefelter's Syndrome

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Answer: D

D. Klinefelter's Syndrome

- Klinefelter's Syndrome results from the gonosomal karyotypic abnormality 47,XXY that results in testicular fibrosis and loss of both germ cell and Leydig cell elements of the testes
- It manifests as testicular failure, with signs and symptoms of hypogonadism with marked elevation of the gonadotropins (primary hypogonadism)
- All other diseases presented are example of secondary hypogonadism

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AUA Best Practice Statement: Optimal evaluation of the infertile male

Clinical Condition	FSH	LH	Testosterone	Prolactin
Normal spermatogenesis	Normal	Normal	Normal	Normal
Hypogonadotrophic hypogonadism (2º)	Low	Low	Low	Normal
Abnormal spermatogenesis	High/ Normal	Normal	Normal	Normal
Testicular failure (1º)	High	High	Normal/ Low	Normal
Prolactinoma	Normal/ Low	Normal/ Low	Low	High

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ARS Q2:

After starting gonadotropin replacement in a man with secondary hypogonadism and azoospermia, semen analysis should be performed after:

a) One week
b) One month
c) Three months
d) Six months

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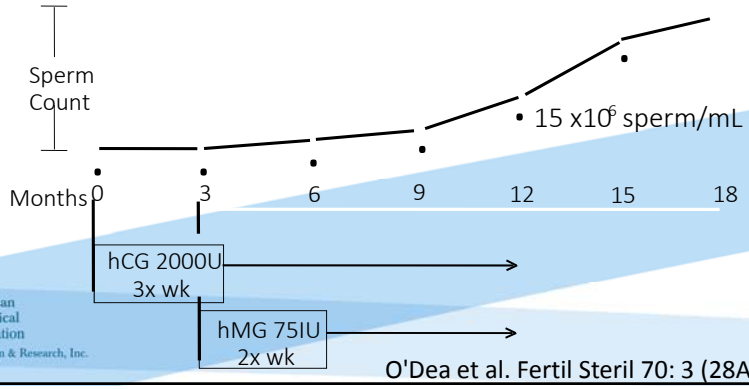
Answer: C

C. Three months

- Secondary hypogonadism resulting in infertility with suppressed sperm production can be treated with FSH and LH analogues
- Sperm production is a ~ 70-80 day process



O'Dea et al. Fertil Steril 70: 3 (28A), 1998

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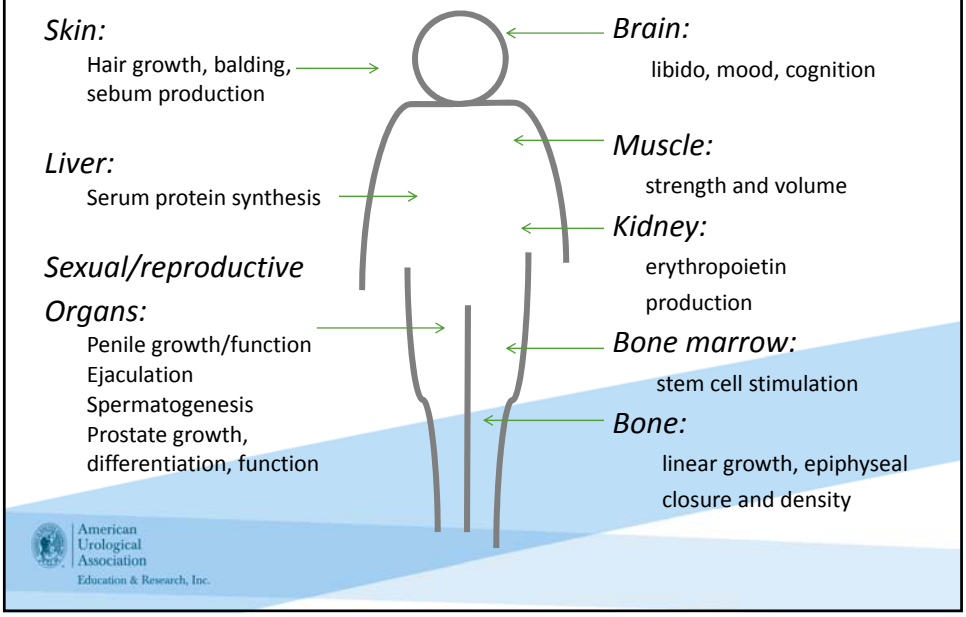
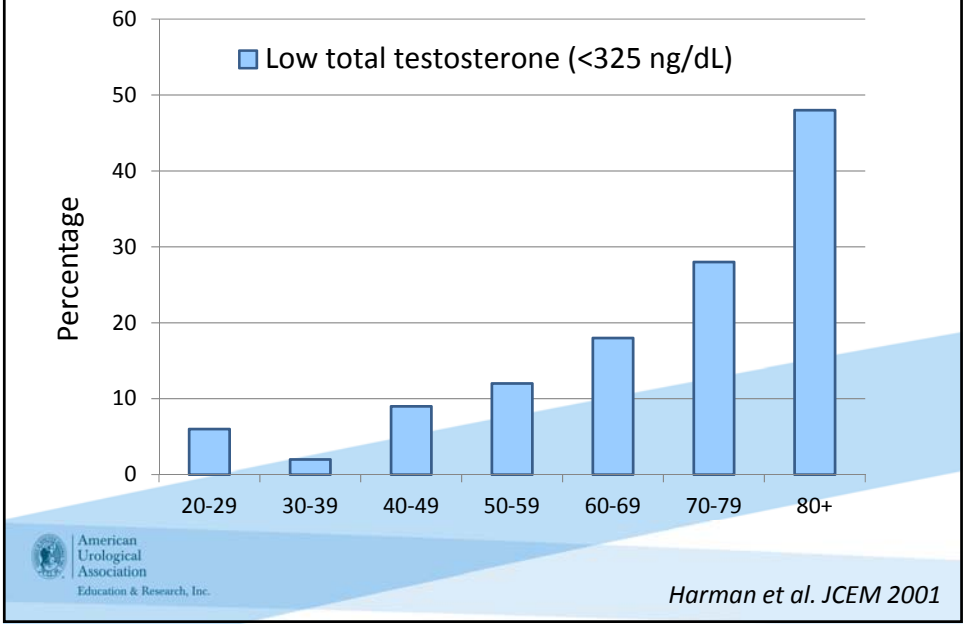
Endocrine: The Effects of Androgens



Prevalence of Men with Low Testosterone



Male Hypogonadism Diagnosis

- Manifestation of androgen deficiency AND consistently low T level
  - Symptoms and signs
  - Low T x 2, in AM
- Symptoms alone OR low T level alone DO NOT EQUAL hypogonadism
  - Results in misclassification and over-diagnosis

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Bhasin S, et al, J Clin Endocrinol Metab 95: 2536-2559, 2010

Hypogonadism Symptoms and Signs

Sexual	Physical	Psychological
• Poor sexual development • Decreased libido • Decreased sexual activity • ED • Infertility	• Gynecomastia • Decreased male hair • Decreased muscle mass and physical activity • Decreased BMD • Abdominal adiposity	• Decreased energy and vitality • Depressed mood • Decreased concentration and memory • Sleep disturbance • Irritability

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Bhasin S, et al, J Clin Endocrinol Metab 95: 2536-2559, 2010

Other Causes…

- Symptoms and signs not caused by low T level
  - Depression
  - Medications (opioids)
  - Co-morbid illness
- Low T level not caused by hypogonadism
  - Transient T suppression: illness/surgery, medications
  - Biologic variability (30% normal on retest)
  - Low SHBG

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Matsumoto AM, Endocrinol Metab Clin N Am 42:271-286, 2013

ARS Q3:

To avoid over-diagnosis of hypogonadism, patients most likely to benefit from the measurement of both total and *FREE* testosterone are:

a) Patients taking thiazide diuretics long term
b) Obese patients
c) Patients with primarily sexual symptoms
d) Patients taking anticonvulsants long term

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Answer: B

B. Obese patients

Alterations SHBG are common

- Obesity: ↓ SHBG and total T → over-diagnosis
- ~60% of men with low total T → normal free T
- Anticonvulsant: ↑ SHBG and total T → under-diagnosis

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Testosterone Treatment: Risks and Benefits

- The FDA has issued a statement concerning the safety of testosterone in light of data on T use and cardiovascular disease outcomes
- Contemporary data are mixed, and to date there is no consensus on T safety
- Data regarding T and prostate cancer remains limited
- The T trials have demonstrated benefit to T treatment in men 65+ with hypogonadism

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ARS Q4:

Baseline assessment of a man with hypogonadism prior to initiating testosterone therapy should include:

a) Bone density scan
b) Complete blood count
c) PSA for men 35 years and older
d) Electrocardiogram (ECG)

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Answer: B

B. Complete blood count

- The Endocrine Society recommends:
  - Baseline assessment of CBC given role of T in erythropoiesis
  - Baseline PSA in men aged 40 and older
  - DRE for patient with PSA >0.6ng/dL
  - T levels, CBC, and PSA should be monitored initially at 3 to 6 month intervals after T initiation
  - Bone density should be checked 1-2 years after T initiation

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Testosterone Treatment Options

1. 50-200 mg T enanthate or cypionate IM every 7-14 days
2. 750 mg T undecanoate IM (gluteal) every 10 weeks
3. 2-6 mg T patches applied nightly to back, thigh, or upper arm
4. 5–10 g of a 1% T gel applied daily over a covered area of nongenital skin (wash hands after application)
   - Also 1.62% gel and 2% gel formulations
5. 30 mg buccal T tablet applied to buccal mucosa every 12 h
6. 11mg nasal T gel in each nostril every 8 hours
7. 6-12 T pellets (75mg/pellet) implanted SC (buttock/flank) in office every 3-4 months
8. Oral T undecanoate (not available in U.S.)

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www.auanet.org/guidelines/testosterone-deficiency-(2018)

Alternative Therapies

1. Clomiphene citrate 25-50 mg every 1-2 days
2. Tamoxifen 20 mg daily
3. Anastrozole 0.5-1.0 mg every 1-3 days

None of above are FDA-approved for use in males

4. hCG 500-4000 units SQ/IM 2-3 times per week
   - hCG is FDA-approved for use in males with hypogonadotropic hypogonadism and pediatric patients with cryptorchidism

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www.auanet.org/guidelines/testosterone-deficiency-(2018)

ARS Q5:

Testosterone therapy should be discontinued immediately if:

a) Hematocrit level is 54% or above
b) PSA level rises greater than 10% over baseline
c) Patient experiences chest pain
d) Testosterone level is 800 ng/dL

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Answer: A

A. Hematocrit level is 54% or above

- T stimulates erythropoiesis
- In studies of T replacement, older men can develop polycythemia (Hct >52)
- Patches/gels associated with less polycythemia than injectable T
- If hematocrit is above 54%, stop therapy until hematocrit decreases to a safe level, evaluate the patient for hypoxia and sleep apnea, and reinitiate therapy at a reduced dose (Endocrine Society)

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