Basics of Male Libido: Dysfunction & Treatment

Ripu Hundal MD FACE
First State Endocrinology
Newark, DE
Sexual Hormones

• **Steroid hormones**
  – Commonly referred to as “male sex hormones” and “female sex hormones,” although both sexes produce both types of hormones.
  – **Testosterone**: the major androgen, or male sex hormone
    • Produced in the testes (men), adrenal glands (men and women), & ovaries (women).
    • Men typically produce 20-40X more testosterone than women.
  – **Estrogen**: the major female sex hormones
    • produced by ovaries & testes.
    • Testes produce much smaller quantities of estrogens than ovaries.

• **Neuropeptide hormones**
  – **Oxytocin**: “love hormone;” is made in hypothalamus, influence erotic and emotional attraction.
Hormones in Male sexual behavior

- **Testosterone** influence male sexual desire.
  - Men with low testosterone level may be fully capable of erection and orgasm but might have little interest in sex. Testosterone replacement helps to improve libido.
  - Castrated males show significant reduction in sexual desire and activity.
  - Androgen-blocking drugs (antiandrogens)
    - Have been used to treat sex offenders to reduce sexual desire
Oxytocin in sexual behavior

• **Oxytocin**: a neuropeptide produced in the hypothalamus in both sexes.

• Stimulates release of milk during breast-feeding; thought to facilitate mother-child bonding

• Released during physical intimacy
  – Increases skin sensitivity to touch
  – High levels are associated with orgasm and levels remain high after orgasm; promoting emotional and erotic bonding of partners

• oxytocin is important for facilitating social attachments and development of feelings of love.

• Stress lowers oxytocin secretion.
Anatomical regions of the brain involved in sexual arousal & response

**Cerebral cortex:** thinking center of the brain

**Limbic system:** associated w/emotion & motivation; also includes the “pleasure center”

Sexual arousal can occur without any sensory stimulation, through thoughts and fantasy alone.
**Limbic system**

- Associated with emotion, motivation, and memory
- Includes several brain structures
  - Hypothalamus, hippocampus, amygdala, cingulate gyrus
- 1950s study: rats implanted with electrodes in regions of limbic system that could be activated by a lever.
  - Rats pressed lever over and over, in preference to eating or drinking, eventually dying of exhaustion.
- Limbic stimulation in people: patients reported intense sexual pleasure.
- Damage to certain parts of the hypothalamus seems to dramatically reduce sexual behavior of both males and females in several species.
Neurotransmitters and sexual arousal

- **Dopamine**
  - Released in the “pleasure center” of the limbic system.
  - Facilitates sexual arousal and response.
  - Testosterone stimulates dopamine release in both males and females.

- **Oxytocin**

- **Serotonin**
  - Inhibits sexual activity
  - Inhibits release of dopamine.
  - Antidepressants called SSRIs increase serotonin levels in the brain--side effects often include decreased libido and diminished sexual response.
Sexual arousal: the role of the senses

• **Touch** is the dominant "sexual sense”
  
  – **Primary erogenous zones**: areas of the body that contain dense concentrations of nerve endings.
    
    • Includes genitals, buttocks, anus, perineum, breasts, inner thighs, armpits, navel, neck, ear lobes, mouth.
    
    • Varies from one person to another.
  
  – **Secondary erogenous zones**: areas of the body that may become erotically sensitive through learning and experience.
    
    • Virtually any other region of the body--depends on personal erotic experiences.
Sexual arousal: the role of the senses

- **Vision:** usually next important sense in arousal.
  - males are more aroused by visual stimuli than females.

- **Smell:** highly influenced by a person’s sexual history and social conditioning.
  - In some cultures, the smell of genital secretions are considered a sexual stimulant.
  - U.S.: near obsession with masking any natural body odor makes it difficult to study effect of natural odors on sexual desire.
  - Even so, many report being aroused by the smell of their partner, or by people to whom they are attracted.
Sexual arousal: the role of the senses

• **Taste**: seems to play a minor role in arousal.

• **Hearing**: highly variable.
  – Some people find words, erotic conversation, moans, etc. to be very arousing
  – Others prefer more silent sex.
Models of sexual response: Masters & Johnson four-phase model

1. excitement
2. plateau
3. orgasm
4. resolution
Changes in sexual response cycle with Age

- Longer time to develop an erection
  - i.e. several minutes of stimulation vs. 8-10 seconds

- Erection may be less firm.
  - Complete penile erection is often not obtained until late in the plateau phase, just before orgasm.
  - However older men are often more able to sustain the plateau phase longer, enhancing pleasure for both partners.

- Some men report reduced intensity of orgasm
  - Reduced number of contractions, force of ejaculation is reduced, less semen produced.

- More rapid resolution

- Refractory period between orgasm and next excitement phase gradually lengthens (could be hours to days)
Normal Male Reproductive Axis

Hypothalamus

Pituitary

Testes

Seminiferous Tubule

Leydig Cell

GnRH

FSH    LH

Sperm Inhibin

T  E

Aromatase

5 α reductase

Estradiol

DHT
Testosterone: Target Organs

Brain
Libido, aggression, cognition

Skin
Male pattern body and facial hair, balding, sebum production

Muscle
Increase in strength and volume

Liver
Synthesis of serum proteins

Fat
Decrease fat mass

Bone Marrow
Stimulation of stem cells

Bone
Accelerated linear growth, closure of epiphyses, maintains BMD

Kidney
Stimulation of erythropoietin production

Male sexual organs
Penile growth, spermatogenesis, prostate growth and function
Erectile Dysfunction (ED)

- **Definition:** the consistent or recurrent inability of a man to attain and/or maintain an erection sufficient for sexual performance lasting for 3 months or longer.

*First International Consultation on Erectile Dysfunction, WHO, 1999*
Prevalence of ED

• Prevalence increases from 5% to 15% as age increases from 40 to 70 yrs.

• In another study at age 40, approximately 40% of men are affected, rate increases to nearly 70% in men aged 70 yrs.

• 50% of males with diabetes have ED problems, approximately 3.5 times more than controls
Classification of Erectile Dysfunction

• Psychogenic- anxiety, depression, stress,
• Neurogenic
• Vascular
• Mixed (psychogenic and organic)
• Iatrogenic- medications and surgical trauma
Physical or organic causes of ED - 90% of cases

- CAD-Men with ED have 65-85% increased risk of CAD
- Diabetes
- Pelvic surgery or injury to spinal cord, radiation, or trauma
- Parkinson’s disease, multiple sclerosis
- Hypertension
- Hypercholesterolemia
- Recreational or prescribed medication use- smoking, alcoholism, cocaine
- Obesity and metabolic syndrome, OSA
- Endocrine disorders- thyroid dysfunction, hyperprolactinemia, testosterone deficiency.
- Structural or anatomical disorders of penis
- Prostate disease and its treatments
Conditions with a High Prevalence of Low Testosterone (Screening Suggested)

- Sellar mass, radiation to sella, other sellar disease
- On meds that affect T production or metabolism
  - Glucocorticoids, ketoconazole, opioids
- HIV-associated weight loss
- ESRD and maintainence hemodialysis
- Moderate to severe COPD
- Osteoporosis or low trauma fracture (esp if young)
- Type 2 diabetes mellitus
- Infertility
Meds causing ED

• Antihypertensive – methydopa, reserpine, Thiazide diuretics, spironolactone, beta blockers
• TCAs, SSRIs
• Statins, fibrates.
• Inhibit Testosterone Production – ketoconazole, cimetidine, Cyproterone, PPIs, Testosterone and anabolic steroids, opioids
• Inhibit GnRH – progesterone, estrogen, GnRH agonist elevated Prolactin, TCAs, Reserpine, cocaine/opioids, steroids
• Some chemotherapeutics
Physical Exam

• Amount of body hair
• Breast exam for enlargement/tenderness
• Size and consistency of testicles
• Size of the penis
• Signs of severe & prolonged Androgen Deficiency
  – Loss of body hair
  – Reduced muscle bulk and strength
  – Osteoporosis
  – Smaller testicles
Testicle volume measured in mL

- Childhood
- Early Puberty
- Mid Puberty
- Late Puberty
- Adulthood

1 inch
Symptoms/Signs of AD in Men

- Incomplete sexual development, eunuchoidism
- ↓ Sexual desire & activity
- ↓ Spontaneous erections
- Breast discomfort, gynecomastia
- ↓ Body hair (axillary & pubic), ↓ shaving
- Very small or shrinking testes (esp < 5 ml)
- Inability to father children, low/zero sperm counts
- ↓ Height, low-trauma fracture, low BMD
- ↓ Muscle bulk & strength
- Hot flashes, sweats
Less Specific Symptoms/Signs of AD

- ↓ energy, motivation, initiative, aggressiveness, self-confidence
- Feeling sad or blue, depressed mood, dysthymia
- Poor concentration and memory
- Sleep disturbance, increased sleepiness
- Mild anemia
  - Normochromic, normocytic, in the female range
- Increased body fat, BMI
- Diminished physical or work performance
Guidelines on Screening

• Initial screen = morning total testosterone
  – Levels are highest in the morning
  – Normal T is generally 300-1000 ng/dl

• Confirmation = repeat morning total T
  – Free or bioavailable T in some

• Do not screen during acute or subacute illness
  – Illness, malnutrition, and certain medications may temporarily lower testosterone
Testosterone Deficiency: Laboratory Diagnosis

- About 1%-2% of testosterone is free (unbound)
- About 30% to 50% is bound to albumin with low affinity
- Only free and albumin-bound T is bioavailable
- About 40% to 50% is bound to sex hormone binding globulin (SHBG)

T = testosterone
Hx + PE

Morning Total T

Low T (< 300 ng/dL)

Exclude reversible illness, drugs, nutritional deficiency
Repeat T (use free or bio T, if suspect altered SHBG)

LH + FSH

Confirmed low T

Low T, Low or normal FSH + LH

Secondary hypogonadism

Normal T, FSH + LH

Low T, High FSH + LH

Primary hypogonadism

Normal T

Follow up
Treatment of ED

• Identify and Treat Organic Comorbidities and other risk factors
• Counsel and Educate the Patient and Partner
• Identify and Treat any Psychosexual Dysfunctions
• Medications and Devices
• Surgery
Non-surgical management of ED

• Lifestyle Modification
  Regular exercise
  Healthy diet
  Smoking cessation
  Alcohol Avoidance
  Bicycling ED 2x as frequent in long distance bikers
Non-surgical Rx of ED

• 1st Line therapy: PDE5 inhibitor
• Inhibits breakdown of cGMP. PDE5 isoenzyme is enriched in the penis
• Effective in organic, psychogenic and mixed ED
• Effective in 70-80% of patients
Drug Therapies

- Phosphodiesterase Type 5 (PDE-5) Inhibitors
  - Sildenafil (Viagra)- onset 30-60 min, Duration 4-8 hrs
  - Tadalafil (Cialis)- onset 45 min, Duration 24-36 hrs
  - Vardenafil (Levitra)- onset 25-40 min, Duration 6 hrs
  - Avanafil (Standa)- onset 15-30 min, Duration 4-6 hrs
- Yohimbine- alpha adrenoceptor antagonist
- Intracavernosal and intraurethral prostaglandins
Side Effects of PDEi

- Headache
- Indigestion
- Flushing
- Nasal congestion
- Blue hue to vision
Contraindications

- Not to use with nitrates
- Not to use if severe CV disease
- Cautious use of vardenafil if has prolonged QT
- With alpha blocking agents – may cause significant hypotension
Goals of Testosterone Therapy

• Improve/maintain secondary sexual characteristics
• Improve libido and erections
• Increase energy and well-being
• Improve muscle mass and strength
• Improve bone mineral density
Contraindications to Testosterone Therapy

- Breast or prostate cancer
- Lump/hardness on prostate exam by DRE
- PSA >3 ng/ml
- Severe untreated BPH
- Erythrocytosis (hematocrit >50%)
- Hyperviscosity
- Untreated obstructive sleep apnea
- Severe heart failure
Testosterone Enanthate or Cypionate Injections (IM)

- T levels are supraphysiologic, then gradually drop to hypogonadal range
  - Peaks and valleys
  - Fluctuation of mood or libido
- Relatively inexpensive if self-administered
- Start at 75-100 mg IM weekly
  - Or 150-200 mg IM every other week
- Pain at injection site
- Excessive erythrocytosis (esp in older pts)
Other Preparations

• Nasal gel - used three times a day
• Submucosal tabs- keep by side of mouth
Safety Monitoring

• Baseline
  – Testosterone level
  – DRE
  – PSA
  – Hematocrit

• Follow-up ~3 months then annually
  – Assess improvement/side effects
  – Testosterone level
  – DRE
  – PSA
    • age- and race-appropriate interval
  – Hematocrit

• If osteoporosis - DXA at 1-2 years
Thanks

Q&A