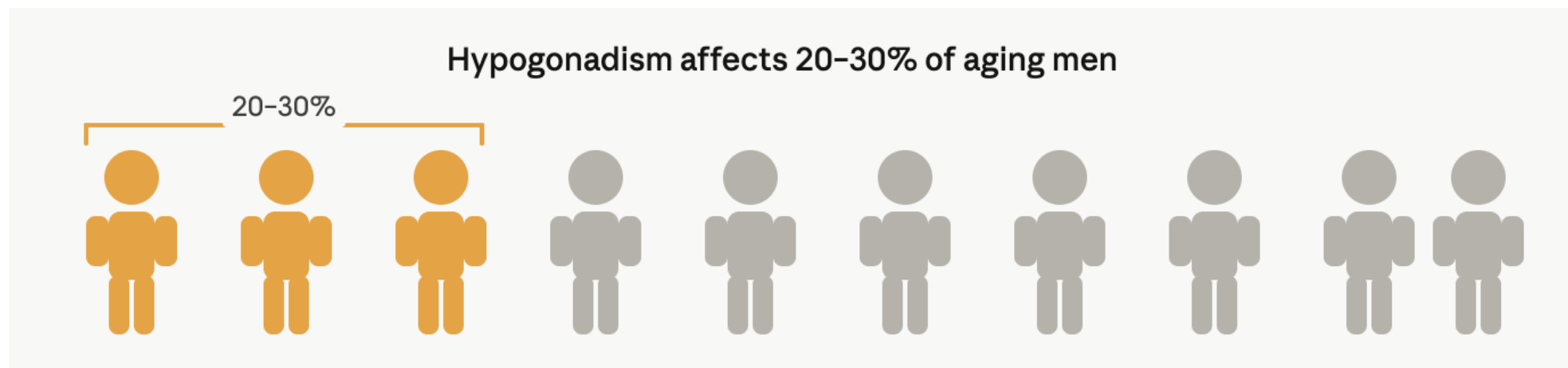


Testosterone Supplementation in Prostate Cancer Patients: Evidence, Safety, and Clinical Practice

Niki Parikh, MD, MBA, MSBA
Assistant Professor
UT Southwestern

Why Does This Matter?



- Prostate cancer is common in the same population

Why Does This Matter?



Risk Factors

- Obesity
- Diabetes
- Chronic illness
- Medications
- Testicular injury
- Normal aging



Symptoms

- Low libido
- Erectile dysfunction
- Depressed mood
- Fatigue
- Reduced muscle mass
- Increased body fat
- Hot flashes

Why is Testosterone Important?

Sexual function

Libido

Noticeable improvements in sexual desire and drive

Erectile function

Enhanced quality, frequency, and duration

Morning erections

Often an early sign that treatment is working

Energy & mood

Vitality & fatigue

Significant reductions in fatigue; increases in day-to-day energy

Mood stabilization

Relief from depression, irritability, and anxiety

Cognition

Faster mental processing, sharper focus, improved memory

Body composition

Muscle mass

Increased lean muscle bulk and overall strength

Fat loss

Reduction in body fat percentage and waist circumference

Bone density

Stimulates bone mineral density, reducing fracture risk

Clinical Problem: Can we safely give testosterone to men with prostate cancer?

Historical paradigm

-  Prostate cancer was viewed as **androgen-driven**
-  Androgen deprivation therapy (ADT) became a **cornerstone** of many treatments

Current clinical reality

-  Many men treated for PCa have **symptomatic hypogonadism**
-  Increasing number of **long-term survivors** with significant quality of life concerns

↔ tension between paradigm and reality



What data do we currently have?

Emerging evidence is beginning to challenge the historical contraindication — but how strong is it?

Background



Huggins & Hodges, 1941

Demonstrated that androgen deprivation leads to prostate cancer regression, establishing the foundation of androgen deprivation therapy (ADT).

→ Extrapolation from this work

Testosterone was assumed to directly stimulate prostate cancer growth

Higher testosterone levels were believed to increase tumor proliferation



Clinical implication (historical)

Testosterone became **contraindicated** in all men with prostate cancer.

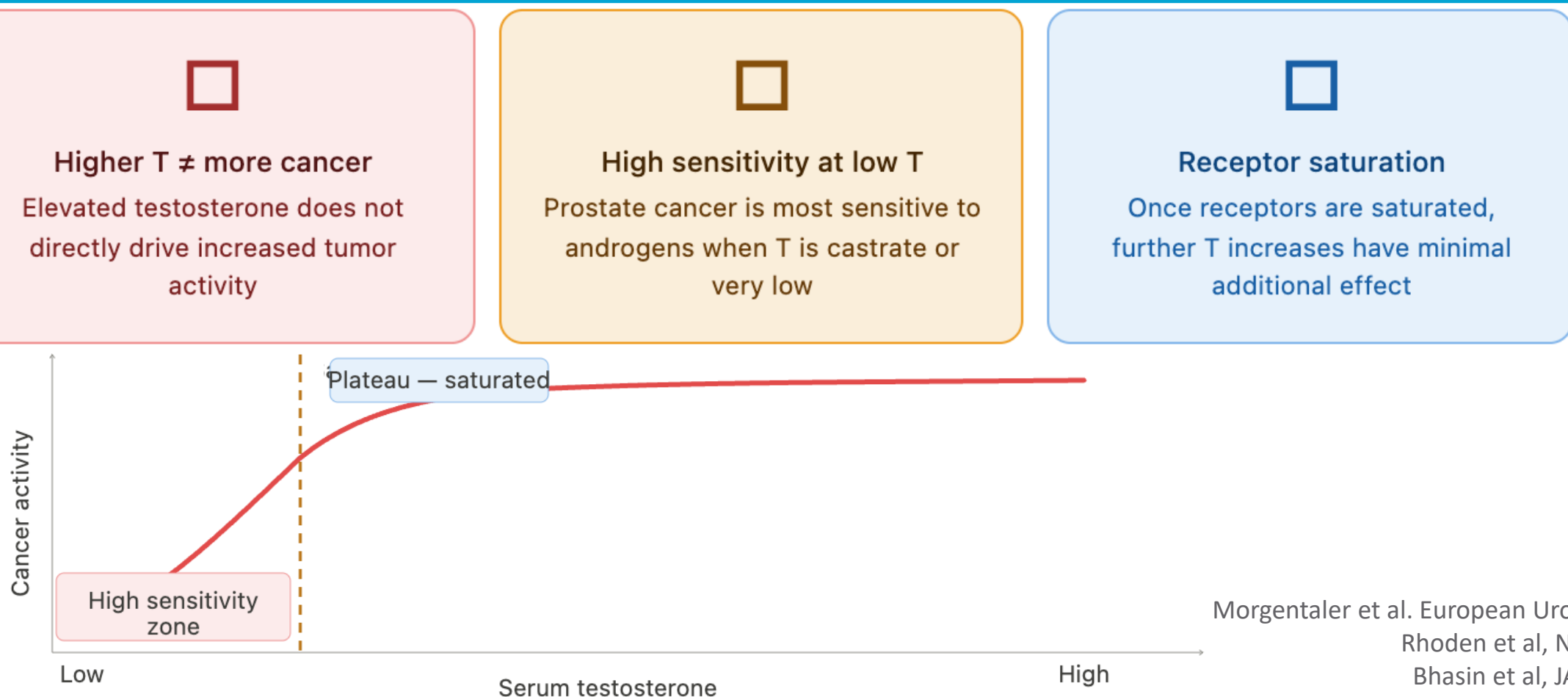
Huggins, C., Hodges, CV. Cancer Research, 1941

Traditional Teaching

TRT
CONTRAINDICATED
IN PROSTATE CANCER



Paradigm Shift: Androgen Saturation Model



Morgentaler et al. European Urology, 2009
Rhoden et al, NEJM, 2004
Bhasin et al, JAMA, 2026

Paradigm Shift: Androgen Saturation Model



Higher T $\neq$ more cancer



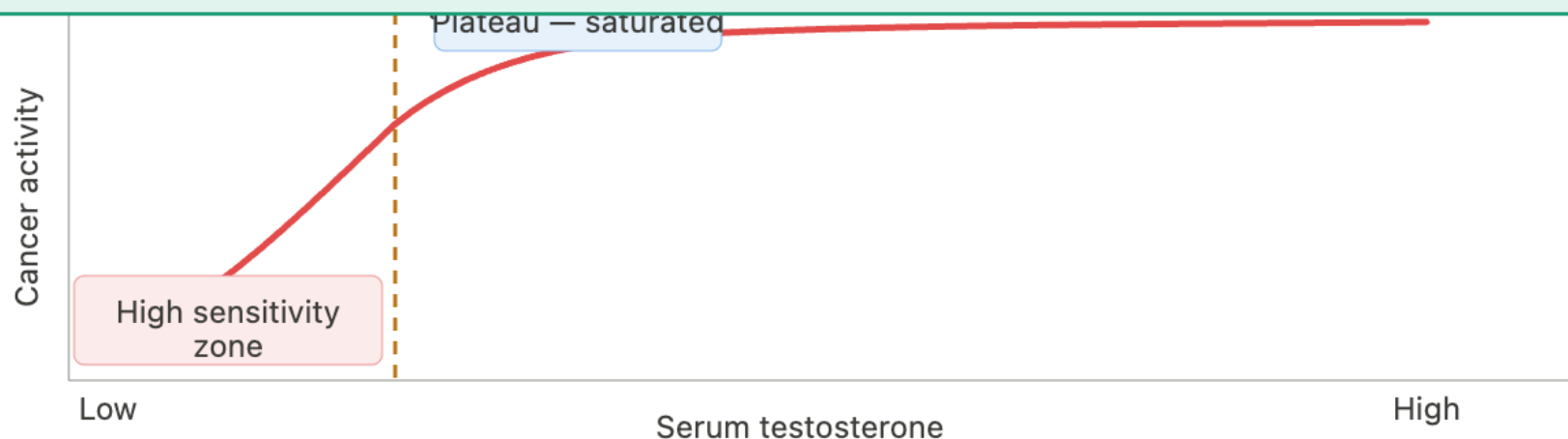
High sensitivity at low T



Receptor saturation



Key implication: Raising T from low to normal may not stimulate cancer growth — supporting TRT safety in carefully selected patients.



Morgentaler et al. European Urology, 2009
Rhoden et al, NEJM, 2004
Bhasin et al, JAMA, 2026

Impacts of Low Testosterone



Higher Gleason grade

Low T is associated with more poorly differentiated tumors at biopsy



More advanced stage

Men with low T more frequently present at diagnosis with locally advanced or metastatic disease

Botto et al, Journal of Urology, 2011
Park et al., BJU International, 2016

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Greater tumor burden

Higher volume disease and more positive biopsy cores observed in hypogonadal men



Worse oncologic outcomes

Some studies report poorer biochemical recurrence-free and overall survival in low-T men

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Clinical implication: Low testosterone should not be assumed to be protective. It may signal more aggressive disease biology and warrants careful oncologic evaluation before initiating TRT.

Botto et al, Journal of Urology, 2011
Park et al., BJU International, 2016

Current Evidence

TRT and Prostate Cancer Incidence

No clear association in current evidence

TRAVERSE

- Prostate cancer in 12/2596 (0.46%) on testosterone
- Prostate cancer in 11/2602 (0.42%) on placebo
- No difference in high-grade prostate cancer incidence

Bhasin et al, NEJM, 2025

Baik et al, Journal of Clinical Endocrinology and Metabolism, 2025

Siltari et al, Acta Oncologia, 2023

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Baik et al.

- 546,964 propensity-matched Medicare beneficiaries
- TRT associated with 16% reduction in prostate cancer hazard

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Baik et al.

- 546,964 propensity-matched Medicare beneficiaries
- TRT associated with 16% reduction in prostate cancer hazard

Siltari et al.

- 78,615 Finnish men, 18 year follow-up
- No increased prostate cancer incidence
- Lower prostate cancer-specific mortality

Bhasin et al, NEJM, 2025

Baik et al, Journal of Clinical Endocrinology and Metabolism, 2025

Siltari et al, Acta Oncologia, 2023

TRT and Active Surveillance- Low Risk Disease



**Progression rates similar
between groups**
(rates 0–32%)

No patients have been upgraded

**No adverse progression events
identified**



Society for Endocrinology
(2022) review:

Rates of 15.4%–57.1%
cited: quality of
evidence low

Santucci et al. BJUI, 2025

Ory et al. Urology, 2016

Kaplan et al. European Urology, 2016

Society for Endocrinology, 2022

TRT after Radical Prostatectomy- Low Risk Disease

SPIRIT Trial

- Organ-confined, low-grade prostate cancer, undetectable PSA
- TC 100 mg IM weekly vs placebo for 12 weeks
- Results:
 - No participant in either group experienced biochemical recurrence
 - TRT improved sexual activity, desire, body composition, loaded stair-climbing power, and VO_2 peak. No changes in ED

Other studies:

- Flores et al.-no differences in biochemical recurrence
- TRT group had lower BCR and TRT independently predicted recurrence-free survival

Bhasin et al, JAMA, 2025
Flores et al, Journal of Urology, 2025
Ahlering et al, BJUI, 2020

TRT after Radiation Therapy- Low Risk Disease

Reported outcomes

 Improved **fatigue, mood, and sexual symptoms** in treated patients

 **42.9%** of anemic patients had corrected anemia following TRT

 Biochemical recurrence rates post-RT ranged from **0-6%**

Patient criteria

 **Undetectable or stable PSA**

✓ **Favorable pathology:** negative margins, negative seminal vesicles, negative lymph nodes

 **≥2 years post-treatment**

 **Symptomatic hypogonadism**

Chandra et al. Endocrine Practice, 2026

Santucci et al. BJUI, 2025

Ory et al, Urology, 2016

High Risk Disease (Grade Group 4-5, 4+3 or higher)

Largest study had 26 patients

- No increased recurrence compared to controls
- Significant PSA increase was observed

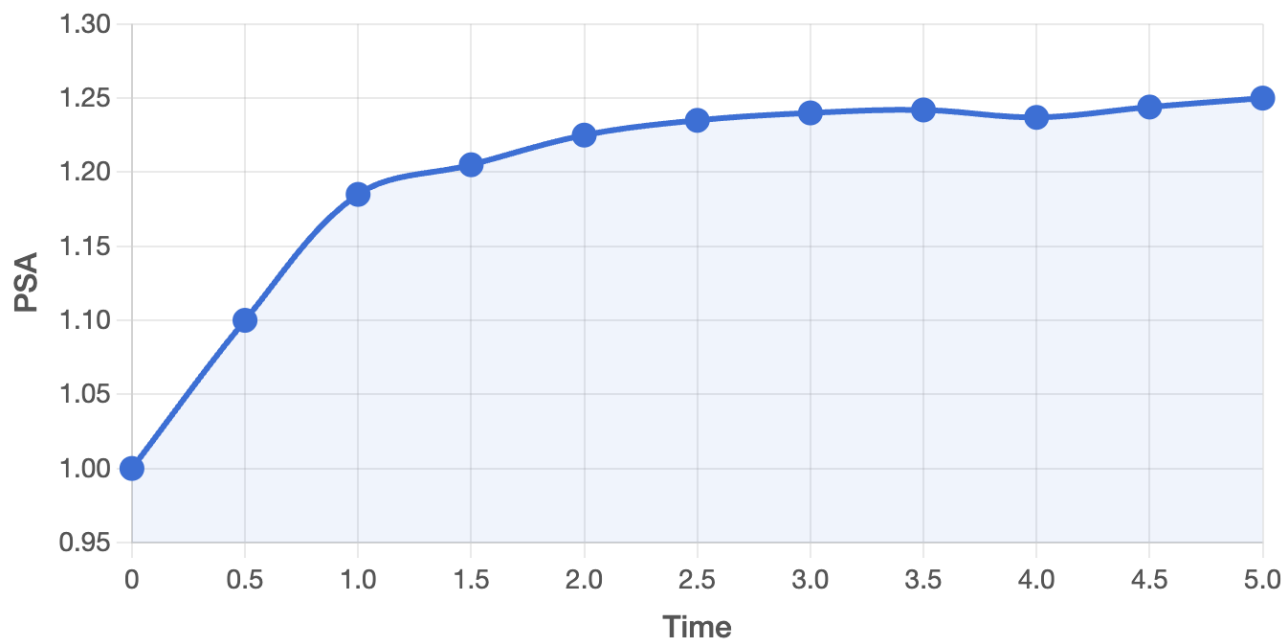
ASCO 2024 Abstract

- 21 men with locoregional prostate cancer treated with TRT after prior ADT + RT
- No prostate recurrence seen

Pastuszak et al. Urology, 2013
ASCO, Clinical Oncology, 2021

PSA Effects with TRT

PSA Response After TRT



Observed changes: small, early PSA increase within first 3-6 months

Restoration of androgen activity in prostate tissue NOT necessarily cancer recurrence

Tends to plateau after initial rise, remain stable with therapy

Guideline Recommendations



Endocrine Society

Recommends **against** TRT in men with prostate cancer.



American Urological Association (AUA)

Inadequate evidence to quantify the risk-benefit ratio; no definitive recommendation for or against.



TRT in locally advanced or metastatic disease should ideally be performed under **research settings** only.



NCCN Survivorship Guidelines

Initiation of TRT is **controversial** and should be coordinated with the treating oncology team.



Important caveat: Men actively undergoing ADT should **not** receive TRT.

What Do We Do In Practice?

Recommended Populations

Active surveillance

Low- or intermediate-risk prostate cancer with two stable PSA values

After radical prostatectomy or radiation

Low- or intermediate-risk, biochemically disease-free

- ≥ 2 consecutive undetectable PSAs after prostatectomy
- Stable nadir PSA following radiation

High-risk — post-treatment

Following prostatectomy or radiation, disease-free for **≥ 18 months**

Short-term ADT (≤ 6 months)

Disease-free for **≥ 18 months**



AND — required for all above: two testosterone levels < 350 ng/dL

Not Recommended

Metastatic prostate cancer

Any evidence of metastatic disease

Longer-term ADT (>6 months)

Men who have received prolonged androgen deprivation therapy

Rising PSA or recurrence

Any rising PSA or clinical evidence of disease recurrence

Timing of Initiation

- ☐ **For all options:** Avoid long-acting formulations (e.g. testosterone pellets) to allow rapid discontinuation if needed. Target testosterone **400–700 ng/dL**; dosing based on patient symptomatology.

Timing of Initiation

- ❑ New prostate cancer diagnosis on TRT
 - **Low/intermediate-risk:** shared decision-making; continuation acceptable
 - **High-risk:** shared decision-making; counsel on limited evidence; continuation may be considered
 - **Metastatic or recurrent:** strongly consider discontinuation

Timing of Initiation

☐ New prostate cancer diagnosis on TRT

- **Low/intermediate-risk:** shared decision-making; continuation acceptable
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- **Metastatic or recurrent:** strongly consider discontinuation

☐ Active surveillance

- Require ≥ 2 negative/stable PSA readings prior to initiation
- A modest PSA increase may occur after initiation — this should stabilize and plateau

Timing of Initiation

Post-surgery (RARP)

If naïve to TRT or TRT was discontinued prior to surgery

- **Low-risk:** delay until ≥ 2 undetectable PSA readings
- **Unfavorable intermediate or high-risk:** strongly consider delaying ≥ 18 months post-surgery with stable PSA

Timing of Initiation

Post-surgery (RARP)

If naïve to TRT or TRT was discontinued prior to surgery

- **Low-risk:** delay until ≥ 2 undetectable PSA readings
- **Unfavorable intermediate or high-risk:** strongly consider delaying ≥ 18 months post-surgery with stable PSA

Post-radiation therapy

- **Low/intermediate-risk:** wait for PSA nadir before initiating TRT
- **High-risk:** wait ≥ 18 months with stable PSA before starting

Monitoring Protocol

Baseline labs

Testosterone Free testosterone Estradiol
PSA Hematocrit LFTs HbA1c Lipid panel
Vitamin D Vitamin B12 Consider PSMA PET

Monitoring Protocol

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PSA Hematocrit LFTs HbA1c Lipid panel
Vitamin D Vitamin B12 Consider PSMA PET

Follow-up schedule

STANDARD (PSA + TESTOSTERONE)

3 mo 6 mo 12 mo q6-12 mo

HIGHER-RISK / POST-ADT / POST-RADIATION (PSA)

q3 mo × year 1 q4 mo × year 2 q6 mo

Monitoring Protocol

Action thresholds — urologic evaluation warranted

Active surveillance

- PSA rise >1.0 ng/mL in 12 months
 - PSA density >0.1
 - Consistent upward trend
- *consider discontinuation*

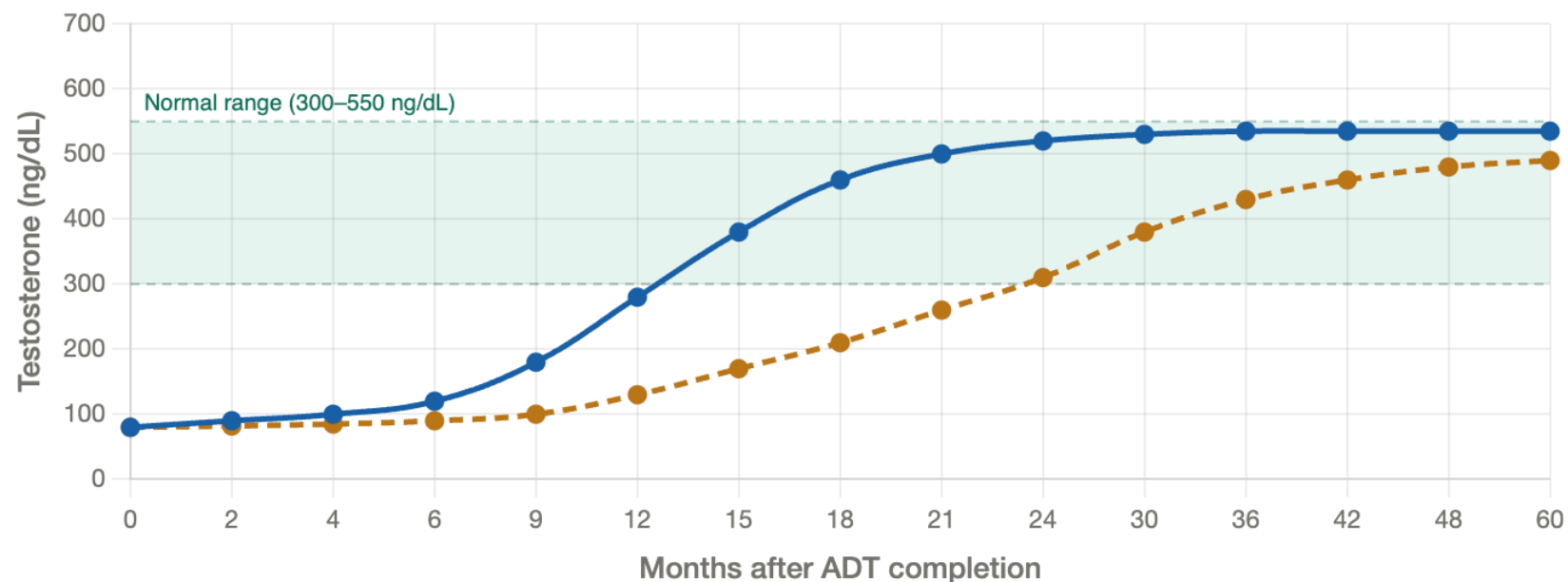
After radical prostatectomy

Two confirmatory PSA values
 ≥ 0.1 ng/mL
→ *urologic evaluation*

After radiation therapy

PSA rise of
 ≥ 2.0 ng/mL above
post-treatment nadir
→ *urologic evaluation*

Testosterone Recovery After ADT



— Short-term ADT (≤6 months)

Median recovery **12–18 months**

Most men recover to eugonadal range

- - Long-term ADT (≥18–36 months)

Median recovery **18–36 months**; some men need **3–5 years**

Recovery may remain **incomplete**

Post-ADT Recovery

↘ Predictors of delayed/incomplete recovery

- Older age
- Longer ADT duration
- Lower baseline testosterone

PMIDs: 31080102, 18710743, 40693904, 39304428, 38552845

✓ TRT initiation post-ADT

Connell et al. demonstrated safe TRT initiation a median of **17 months after ADT**, with no recurrences.

PMID: 40114830

Our Current Policy



Routine TRT not recommended

Testosterone therapy is **not recommended** in men currently on androgen deprivation therapy.



May be considered — short-term ADT (≤ 6 months)

Consideration may be given for men previously on short-term ADT who meet **both** criteria:



Disease-free interval

Stable and disease-free for **≥ 18 months**



Documented response

Cell death response at 18 months — **biopsy warranted before initiation**



Contraindicated — long-term or continuous ADT

Testosterone therapy is **contraindicated** outside of a clinical trial in men on long-term or continuous ADT.

Metastatic Disease



Absolute contraindication

Testosterone therapy is **contraindicated in all men** with a history of metastatic prostate cancer or concern for recurrence.



History of metastatic disease

Any prior diagnosis of metastatic prostate cancer, regardless of current disease status



Concern for recurrence

Rising PSA, biochemical recurrence, or any clinical evidence suggesting disease activity

Patient Consent Prior to TRT Initiation

 All patients must sign a consent form acknowledging the following before initiating TRT.

Patient Consent Prior to TRT Initiation



All patients must sign a consent form acknowledging the following before initiating TRT.



Potential risks

Possibility of biochemical recurrence or disease progression following initiation of testosterone therapy.

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Lifelong monitoring commitment

Ongoing PSA and testosterone monitoring will be required indefinitely for the duration of TRT.

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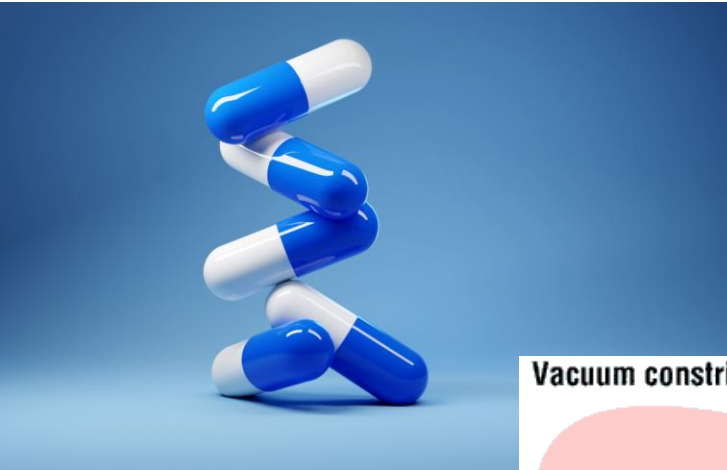
Evolving evidence base

The current evidence supporting TRT in this setting is limited and continues to evolve; long-term outcomes remain under investigation.

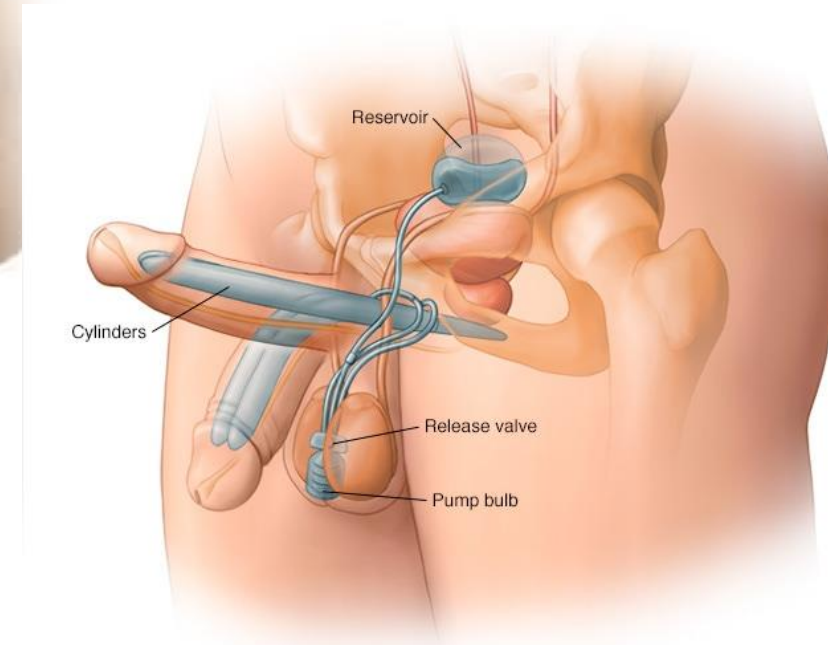
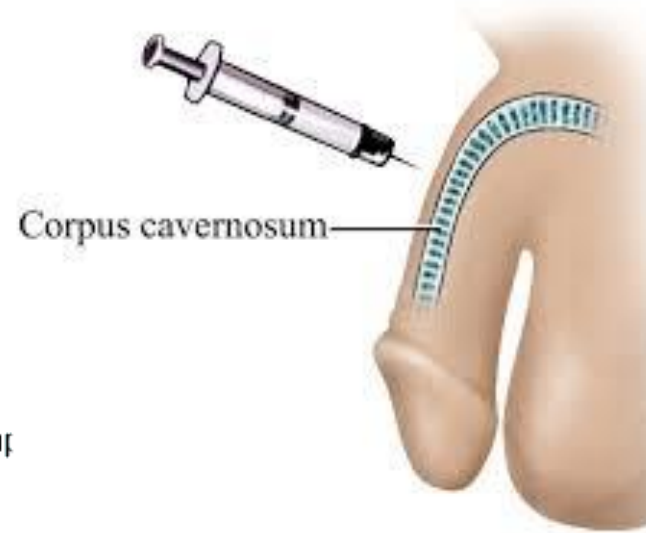
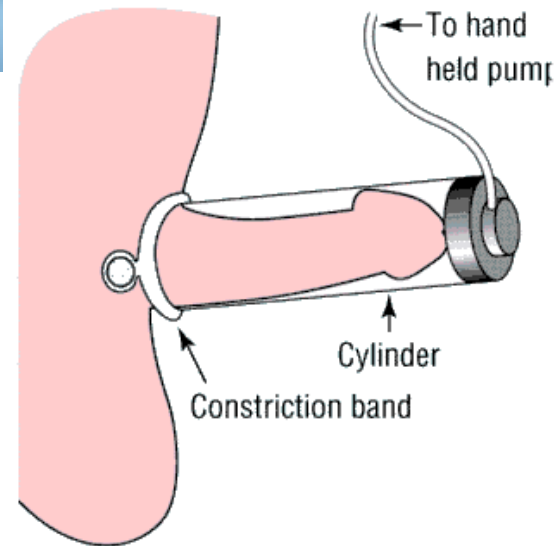
My Practice

Erectile Dysfunction

What Can Urologists Do?

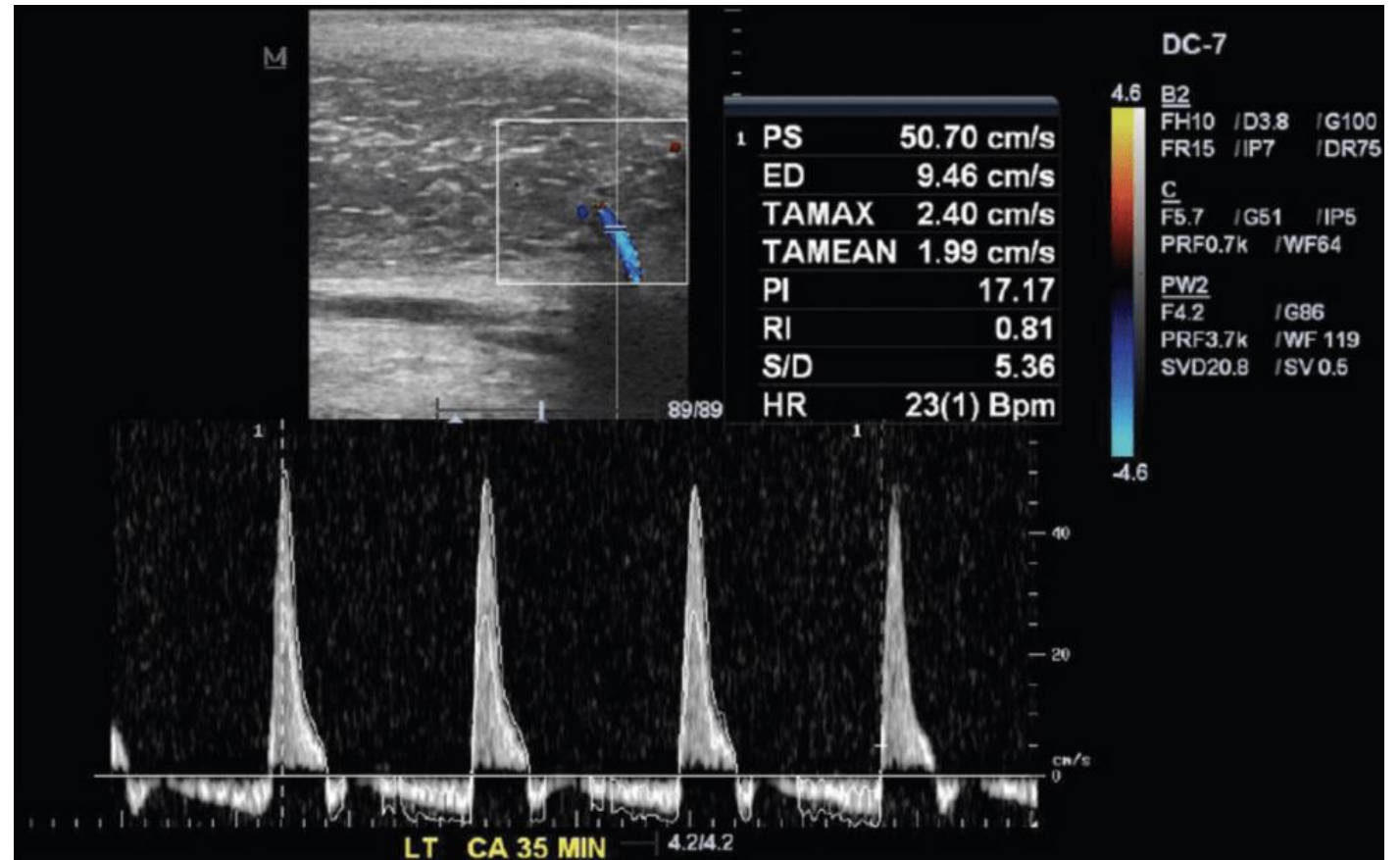


Vacuum constriction device



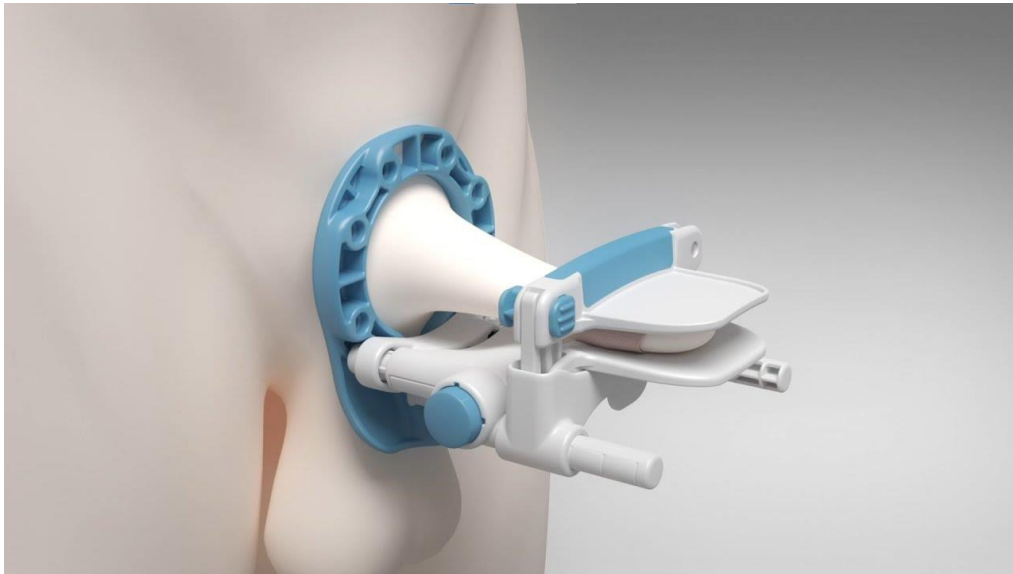
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Penile Duplex Ultrasound



Peyronie's Disease

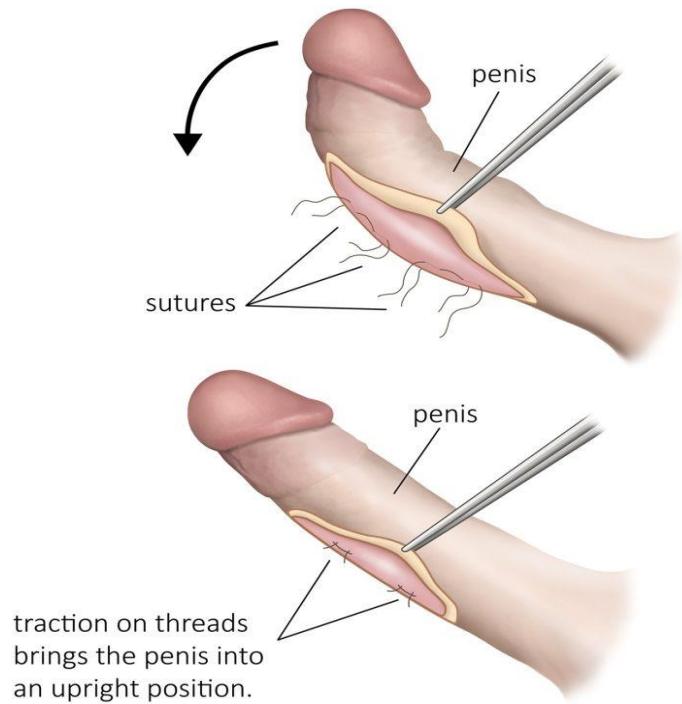
Conservative Options



Ziegelmann et al. Journal of Urology, 2019.
Joseph et al. Journal of Sexual Medicine, 2020.

Surgical Treatment- Stable Phase

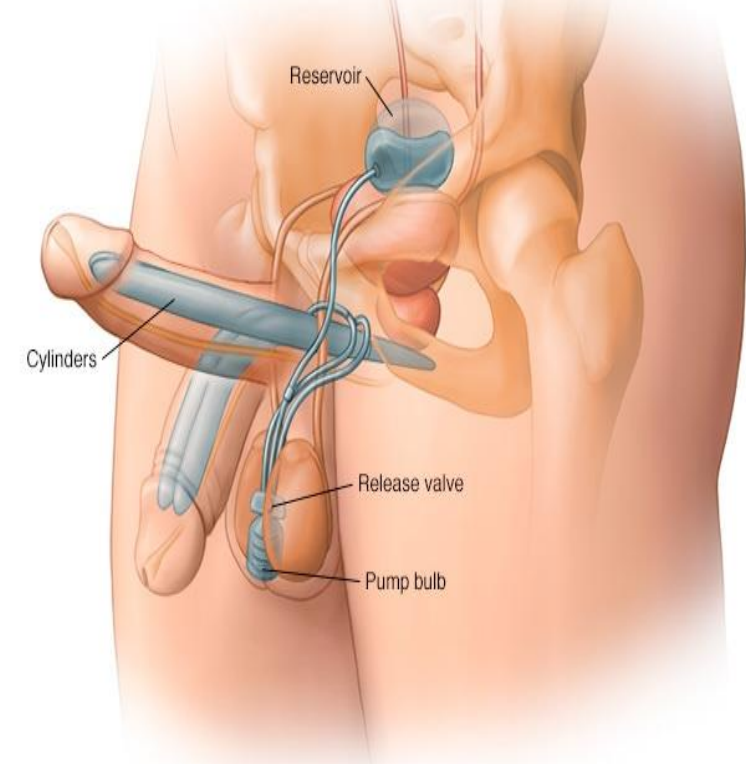
Penile Plication



Incision/Excision and Grafting



Inflatable Penile Prosthesis



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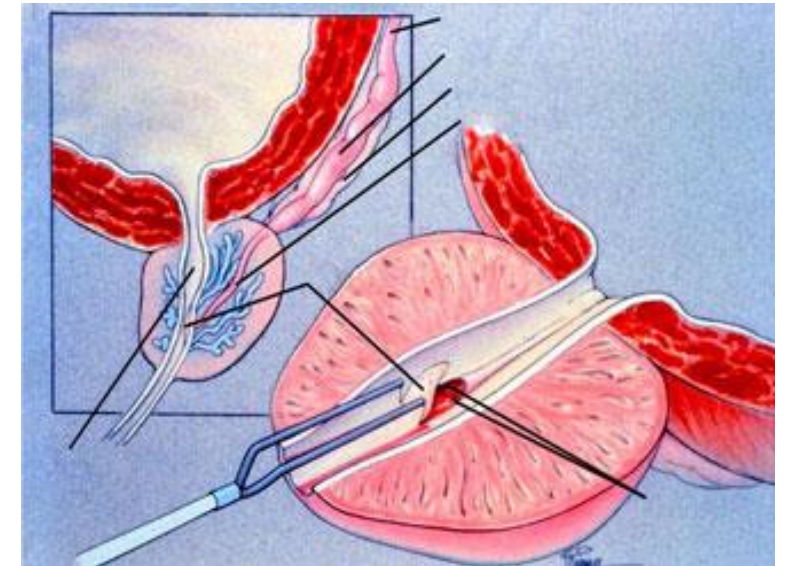
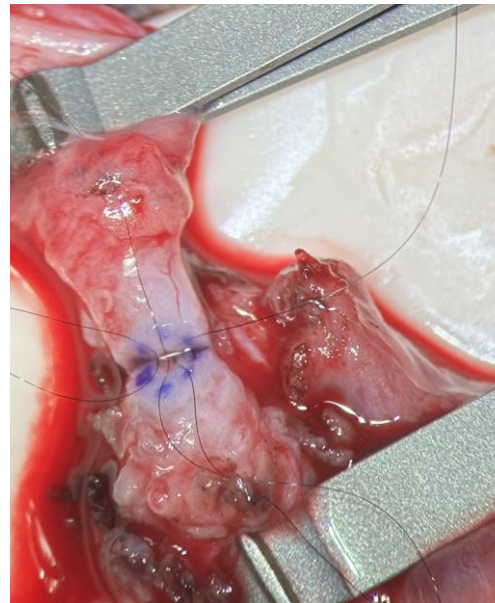
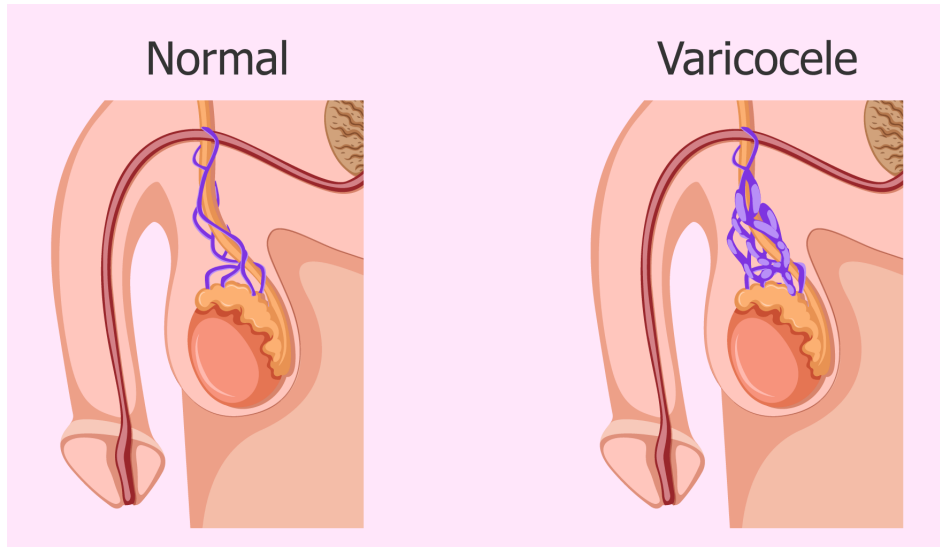
Male Infertility

Hormone Optimization

- hCG
 - LH analog → stimulates Leydig cells → increases intratesticular T
- FSH
 - Direct Sertoli cell stimulation → spermatogenic maturation
- Clomiphene/enclomiphene
 - Estrogen receptor antagonism at hypothalamus → increases GnRH → increases LH and FSH
- Aromatase inhibitors
 - Decreases conversion from testosterone to estradiol

Corrective Surgery

- Varicocelectomy to improve semen parameters and testosterone
- Vasectomy reversal
- Correction of ejaculatory duct obstruction



Contact Information

Thank You!



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Patrick Dougherty



Austin Dittrich



 **214-645-8765**