Erectile Dysfunction – After Prostate Cancer Treatment

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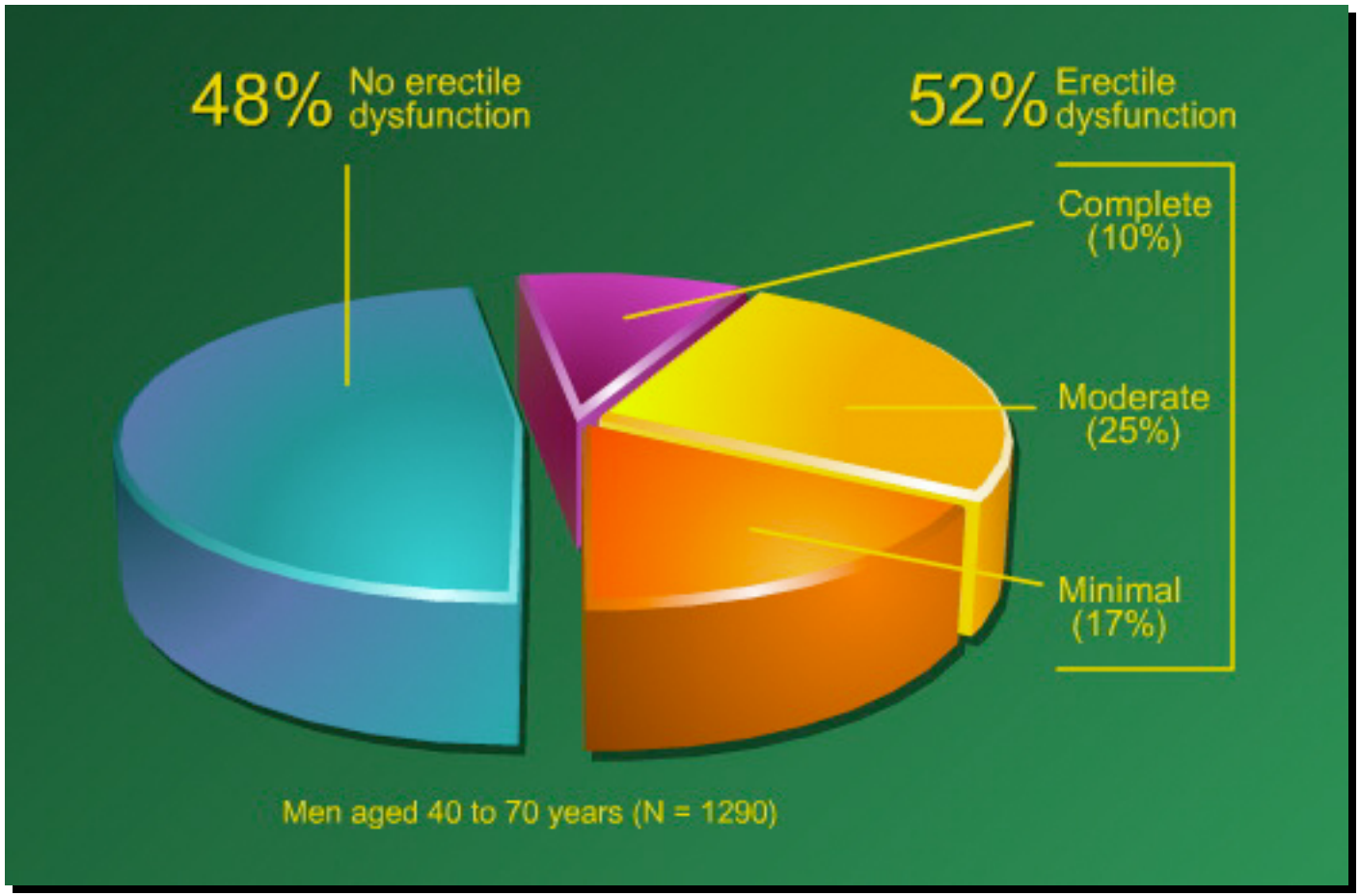
Erectile Dysfunction

- Definition: “. . .the consistent or recurrent inability of a man to attain and/or maintain a penile erection sufficient for sexual performance”[1]
- Multifactorial – may impact total health and quality of life[2,3]

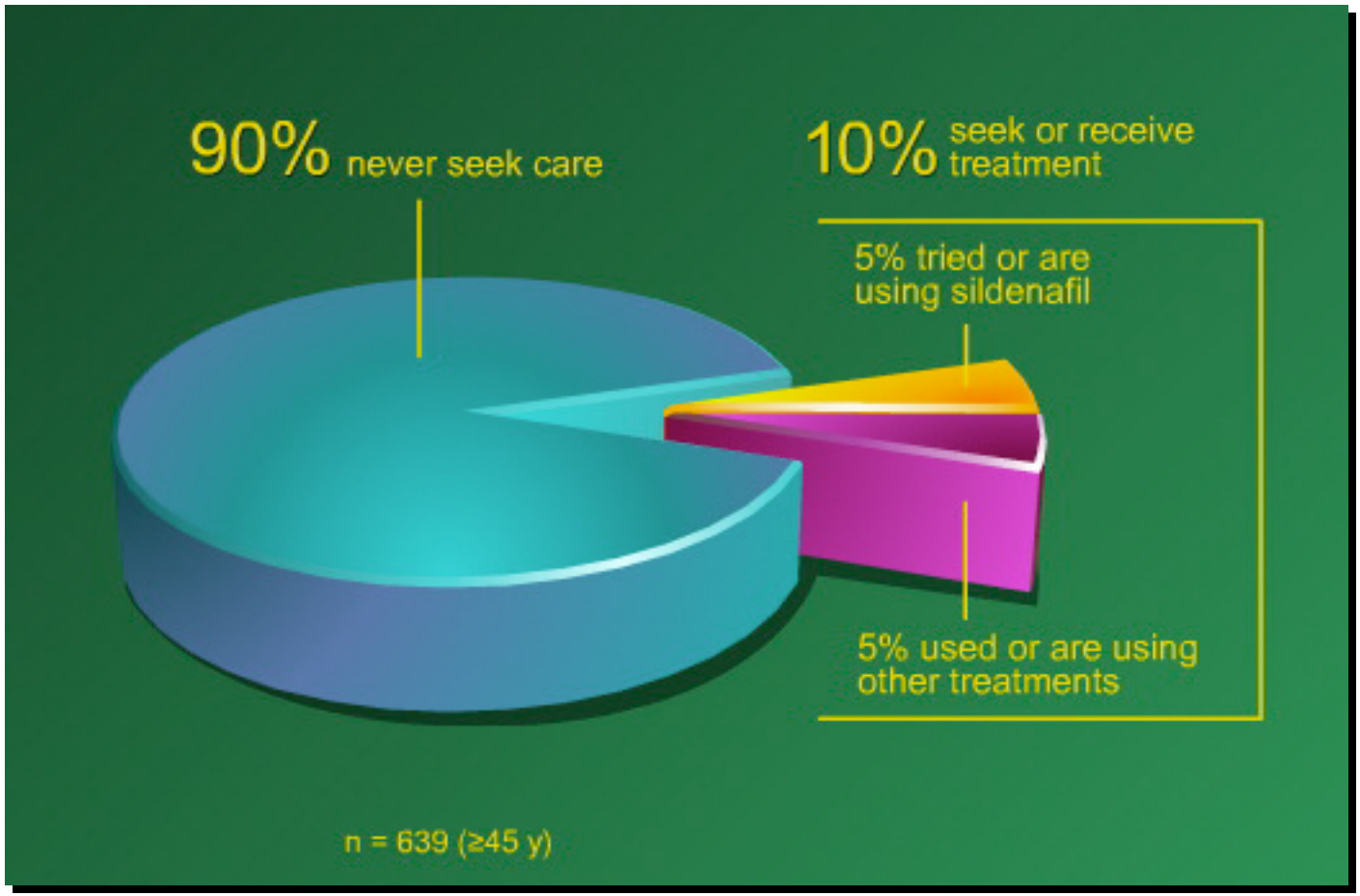
1. Recommendations of the 1st International Consultation on Erectile Dysfunction. In: *Erectile Dysfunction*; Jardin A, et al, eds. Plymouth, UK: Health Publication, Ltd; 2000:711-726. **2.** Laumann EO, et al. *JAMA*. 1999;281:537-544. **3.** Jonler M, et al. *Br J Urol*. 1995;75:651-655.

Massachusetts Male Aging Study:Prevalence of ED



Adapted with permission from Feldman HA, et al. *J Urol*. 1994;151:54-61.

Undertreatment of ED



Adapted with permission from McKinlay JB. *Int J Impot Res*. 2000;12 (suppl 4):S6-S11.
Based on data from the American Association of Retired Persons. *Modern Maturity Magazine*, Washington DC, 1999.

Impact of ED on the Relationship

- Partners feel they are to blame
- Marital distress and sexual dysfunction are related
- ED reduces intimacy, closeness in a couple
- ED increases depression, anger, anxiety, which affect couple

Importance of Outcomes to ED Therapy – Patient Perspective*

1. Cure for ED
2. Pleasure
3. Partner satisfaction
4. Reproduction
5. Naturalness
6. Control
7. Duration
8. Spontaneity
9. Penetration
10. Frequency per week

* Top 10 items cited

n = 50

Hanson-Divers C. J Urol 1998;159:1541

What Do Men Think When They Have ED?

"I've lost my manhood"

"I feel like the centre has been taken out of me"

"I'm a fraud"

"I can't cut it anymore"

"I feel like an absolute nothing"

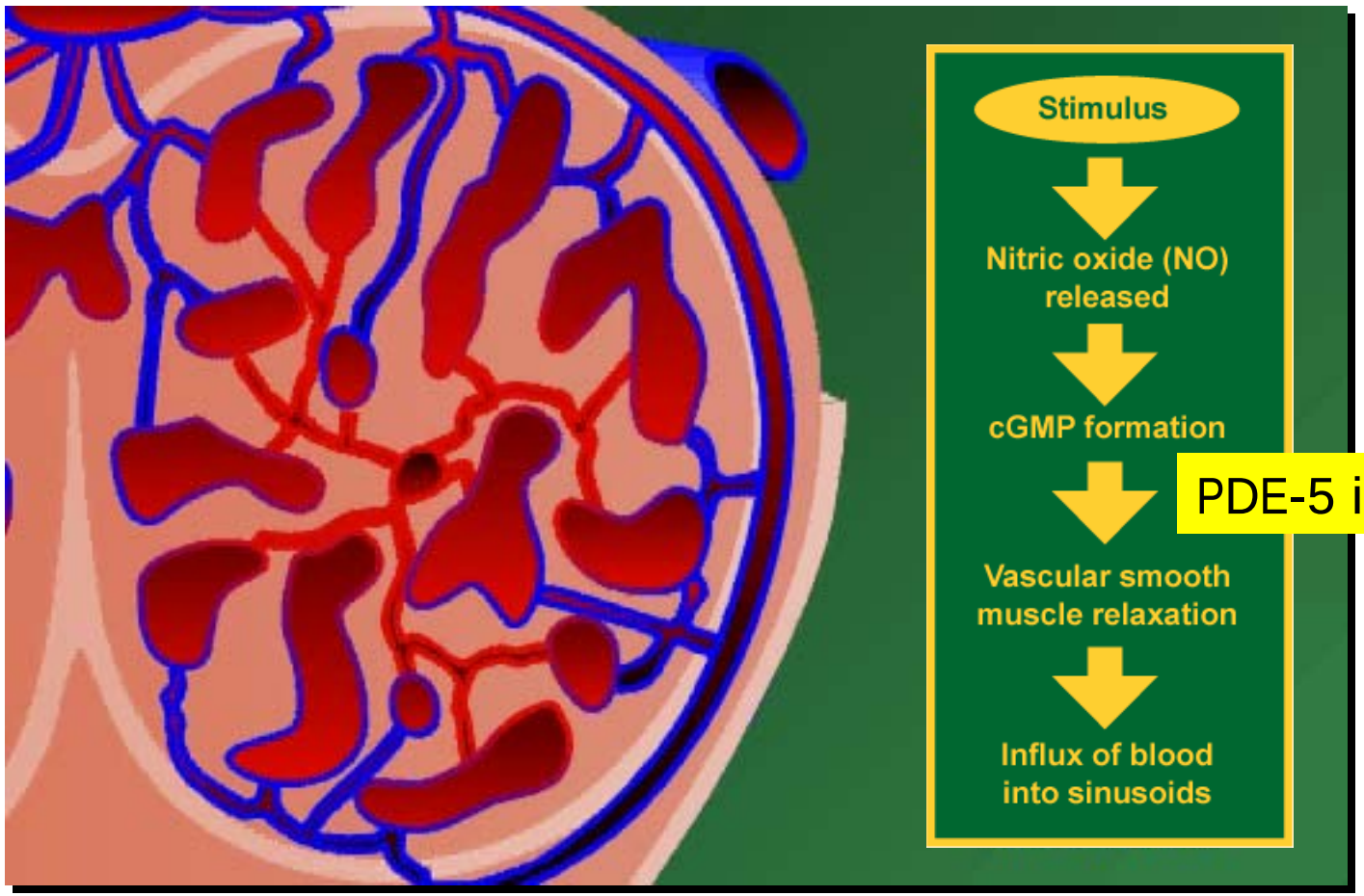
Zilbergeld B. The new male sexuality 1999. p. 302, 303

Epidemiology and Impact of ED:

Summary

- ED is common – 52% of men > 40 years
- ED prevalence increases with age
- Risk factors include diabetes, vascular disease, smoking, neurologic disease, pelvic surgery
- ED causes depression, anxiety, frustration
- ED affects the man, his partner, and the relationship

Physiology of Erection



Adapted with permission from Miller TA. *Am Fam Physician*. 2000;61:95-104, 109-110.

Major Risk Factors for ED

- Aging
- Chronic disease

  Heart disease, hypertension, peripheral vascular, diabetes, and depression

  Medications, eg, thiazide diuretics and

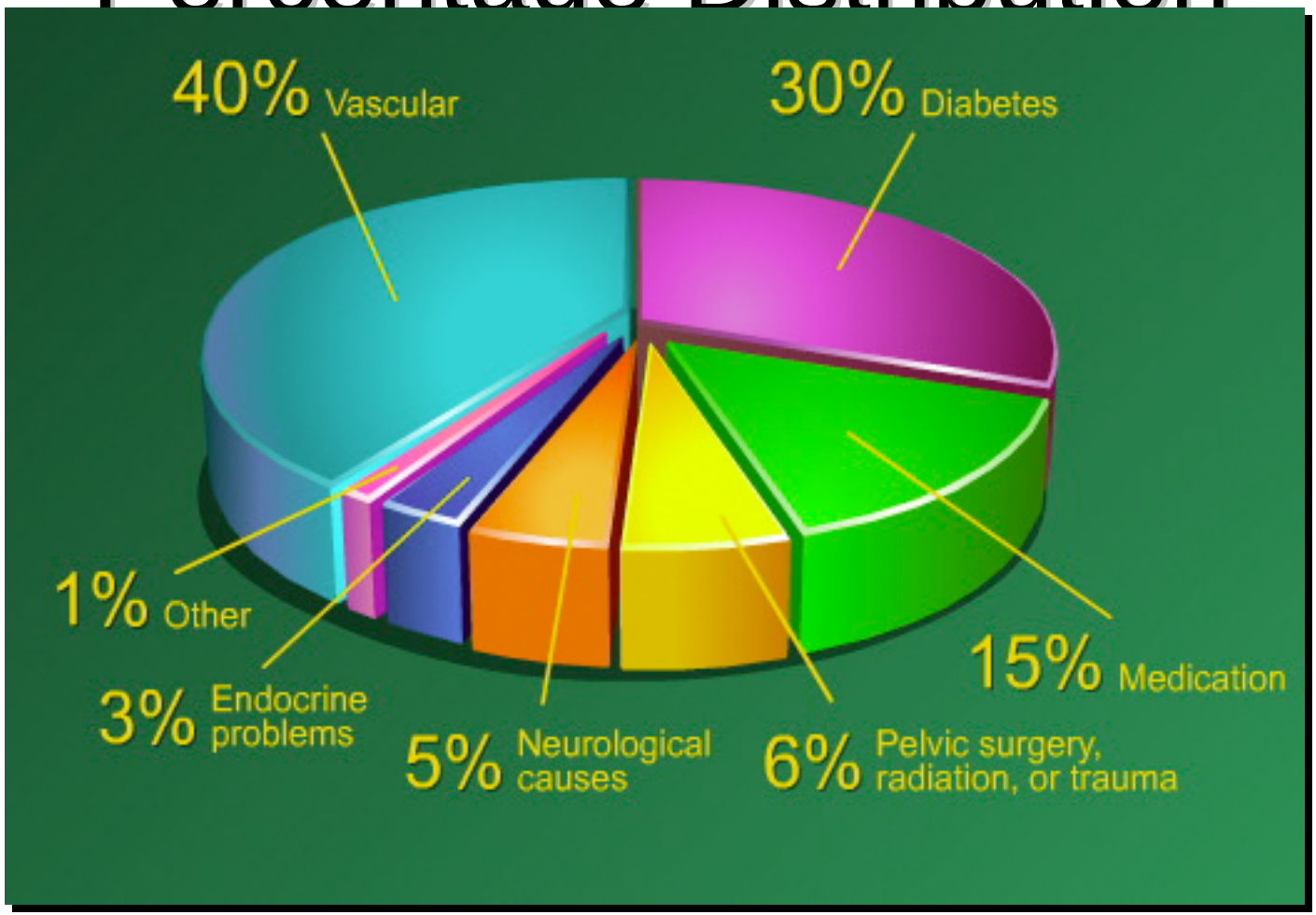
  β-blockers
- Lifestyle

  Stress, alcohol and drug abuse,
  and smoking

Psychogenic Causes of ED[1-5]

1. Lue TF. *N Engl J Med.* 2000;342:1802-1813. **2.** Usta MF, et al. *Urology*. 2001;57:758-762. **3.** Tiefer L, Schuetz-Mueller D. *Urol Clin North Am.* 1995;22:767-773. **4.** Araujo AB, et al. *Am J Epidemiol*. 2000;152:533-541. **5.** Rosen RC. *Urol Clin North Am.* 2001;28:269-278.

Organic Causes of ED: Percentage Distribution



Adapted with permission from Goldstein I and the Working Group for the Study of Central Mechanisms in Erectile Dysfunction. *Sci Am.* August 2000;70-75.

ED and Radiation Tx

- Incidence of ED less after Radiation vs. Surgery.
- However, with time incidence of ED increases.
- No real difference between External Beam and Brachytherapy.
- Response to PDE5 inhibitors is good to excellent but depends on other medical problems.

ED and Radical Prostatectomy

- Incidence highest in older men with medical problems, less in healthy young men.
- Cause is nerve injury and decreased blood flow.
- Results best in bilateral nerve sparing surgery.
- Response to PDE5 inhibitors best in bilateral nerve sparing surgery in young healthy men.

HIFU

- Can map the nerves to reduce or prevent injury.
- Theoretically very precise.
- Rate of ED is 25-35%
- Multiple other factors are involved (ie HTN, CAD etc.)

First-Line Therapy

- Lifestyle/drug therapy modification
- Psychosocial counseling and education
- Androgen replacement therapy
- Oral therapy

Recommendations of the 1st International Consultation on Erectile Dysfunction.
In: Jardin A, et al, eds. *Erectile Dysfunction*. Plymouth, UK: Health Publication Ltd; 2000:711-726.

First-Line Therapy: Oral PDE5 Inhibitors

- Phosphodiesterase type 5 (PDE5) inhibitors[1,2]
  - Sildenafil
  - Tadalafil (prn or once per day)
  - Vardenafil

1. Lue TF. *N Engl J Med*. 2000;342:1802-1813. **2.** Padma-Nathan H, Giuliano F. *Urol Clin North Am*. 2001;28:321-334.

PDE5 Inhibitors: Onset and Duration of Activity*

PDE5 Inhibitor	Onset (min)	Duration (h)
Sildenafil[1,2]	30-60*	4*
Tadalafil[3]	30-45*;16†	24-36*†
Vardenafil[4]	30-60	3-5

*RigiScan® with visual sexual stimulation; oral dosing, empty stomach.
†Home setting; stopwatch recording.
.

1. Viagra prescribing information, January 2000. **2.** Boolell M, et al. *Int J Impot Res*. 1996;8:47-52. **3.** Padma-Nathan H. *J Urol*. 2001;165(suppl):224, Abstract 923. **4.** Sorbera LA, et al. *Drugs Future*. 2001;26:141-144.

First-Line Therapy: Oral Agents

- α-adrenergic blockers[1]
  - Yohimbine
  - Phentolamine*
- Apomorphine SL[1-3†]
- L-arginine + yohimbine[4‡]
- Trazodone[1*]
- OTC herbal remedies[5§]

*Not FDA approved for treatment of ED.
†Approved and used in Europe.
‡In clinical development.
§No proof of efficacy/safety.

1. Lue TF. *N Engl J Med*. 2000;342:1802-1813. **2.** Padma-Nathan H, Giuliano F. *Urol Clin North Am.* 2001;28:321-334. **3.** Dula E, et al. *Eur Urol*. 2001;39:558-564. **4.** Jardin A, et al, eds. *Erectile Dysfunction.* Plymouth, UK: Health Publication Ltd; 2000:243-278. **5.** Moyad MA, et al. *Semin Urol Oncol*. 1999;17:103-110.

Sildenafil
Efficacy Summary

- Restores impaired erectile function and works only following sexual stimulation.
- 78% of patients receiving VIAGRA reported improved erections compared to 20% with placebo.
- Works in a wide variety of etiologies (hypertension, diabetes, depression, spinal cord injury and radical prostatectomy).
- One year open-label extension trial, 88% of patients reported improved erections

Safety Summary

- In clinical trials:

  Adverse events (AEs) transient and mild-to-moderate

  Headache (15.8%), flushing (10.5%), dyspepsia (6.5%), and nasal congestion (4.2%) were most frequently reported AEs.

  Discontinuation rates due to AEs comparable for VIAGRAand (2.6% and 2.3%, respectively)

  No cases of priapism were reported.

- Contraindicated with nitric oxide donors or nitrates in any form.

Sildenafil (VIAGRA™)
Dosing & Administration

- Recommended dose is 50 mg taken as needed approximately 60 minutes before sexual activity.
- Based on efficacy and tolerance, the dose may be increased to 100 mg or decreased to 25 mg.

Optimizing PDE5 Inhibitor Therapy

Incorrect use ⇒ treatment failure

- Patients should be advised that:
  - Sexual stimulation is needed[1]
  - A number of drug trials may be required
  - Sildenafil may be taken with food but onset of action may be delayed

1. Sadovsky R, et al. *Int J Clin Pract*. 2001;55:115-128.

Summary

Tadalafil significantly improves erectile function

Onset of effectiveness as early as 16 minutes with most at 30 minutes

Period of effectiveness for up to 24-36 hours

No interaction with food

Incidence of MI Across All Studies

	Age-standardized male population	*Placebo-treated patients*	*Tadalafil-treated patients*		
			Double-blind studies	*Open-label safety studies*	*All studies*
Total number of patients	–	> 1200	> 2500	1376	> 4000
Total patient exposure as patient-years	–	184.9	384.4	1155	1539.4
Number of patients with MI	–	2	1	5	6
Rate of MI per 100 patient-years	0.6*	1.1	0.28	0.43	0.39

* Sadovsky R. Int J Clin Pract 2001;55:115

Emmick J. Eur Heart J Suppls 2002:4(Suppl H):H32

Hutter A. 17th Annual Scientific Session of the American Society of Hypertension 2002

α-blocker	PDE 5 Inhibitor		
	Tadalafil	**Vardenafil HCI**	**Sildenafil citrate**
Tamsulosin	No limitations	No limitations	Precaution
Alfuzosin	Precaution	Precaution	Precaution
Terazosin	Precaution	Not recommended	Precaution
Doxazosin	Precaution	Not recommended	Precaution

Data from separate Product Monographs

NAION

- Most common cause of blindness
- 1-10/100,000 incidence

- Risk factors:
  - Age >50
  - Diabetes mellitis
  - Hypertension
  - Hyperlipidemia
  - Cup to lens ratio

NAION AND VIAGRA

- Reported by ophthalmologist (Pomeranz,USA) - case series of 7
- All had been on Viagra
- Unknown when blindness occurred in relation to Viagra
- All patients >50, hypertension, poorly controlled DM

- 38 cases reported in US

NAION and LEVITRA/CIALIS

- Health Canada/FDA state warning, BUT NO CAUSAL RELATIONSHIP

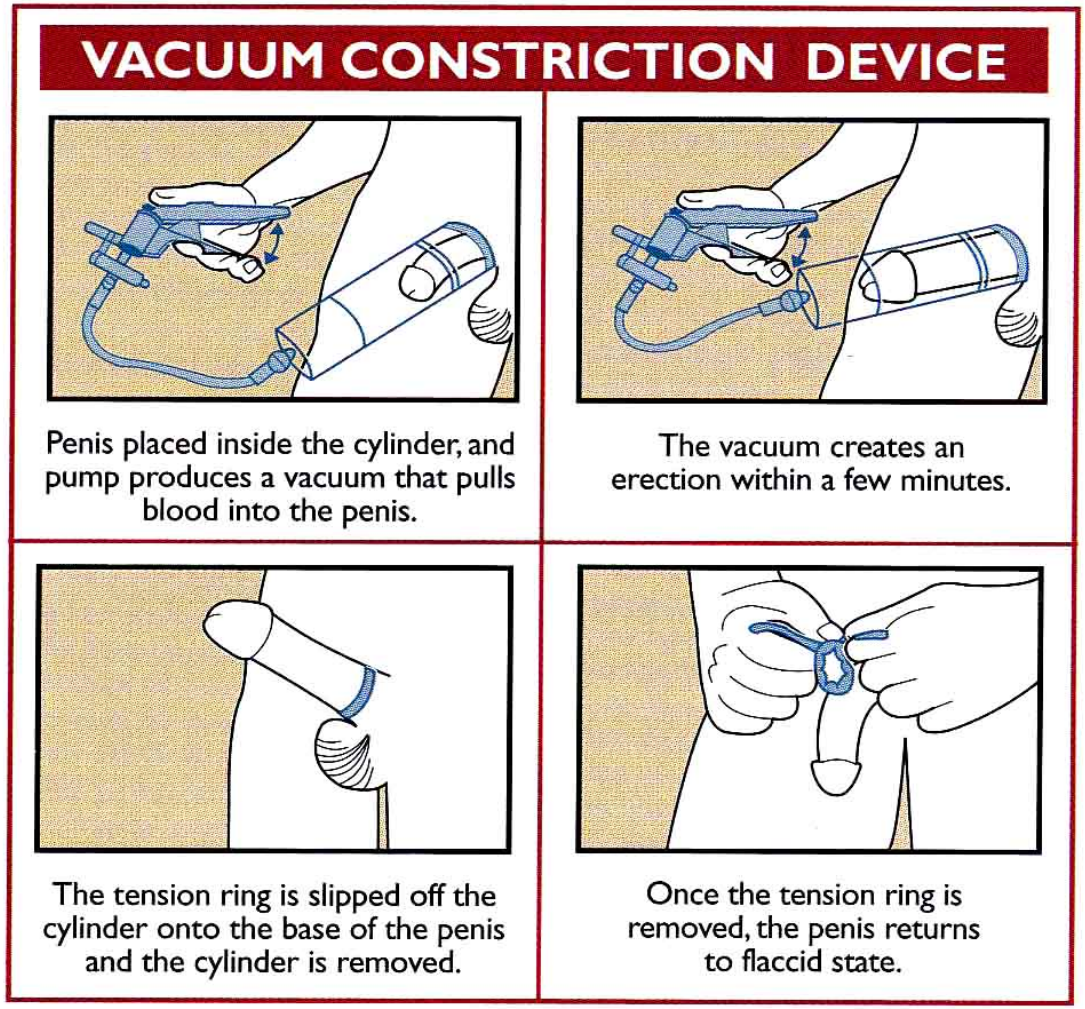
Second-Line Therapy for Management of ED

- Vacuum constriction device[1]
- Intracavernosal injection
  - Alprostadil[1]
  - Drug mixture* (trimix: papaverine, phentolamine, alprostadil)[1]
- Transurethral alprostadil (MUSE®)[1-3]
- Topical therapy–creams/gels[4,5]

*Not FDA approved for intracavernosal delivery.

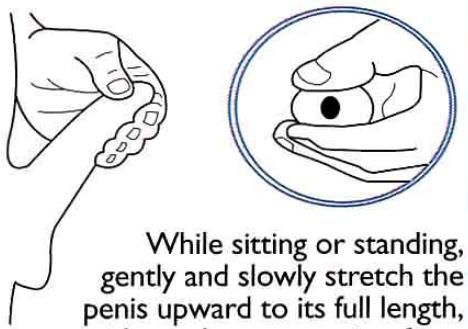
1. Lue TF. *N Engl J Med.* 2000;342:1802-1813. **2.** Padma-Nathan H, et al. *N Engl J Med*. 1997;336:1-7.
3. Lewis R. *Int J Impot Res.* 2000;12(suppl 4):S86-S90. **4.** Goldstein I, et al. *Urology*. 2001;57:301-305.
5. McVary KT, et al. *J Urol*. 1999;162:726-731.

Second-Line Therapy for Management of ED



Second-Line Therapy for Management of ED

MUSE® - Intraurethral Therapy



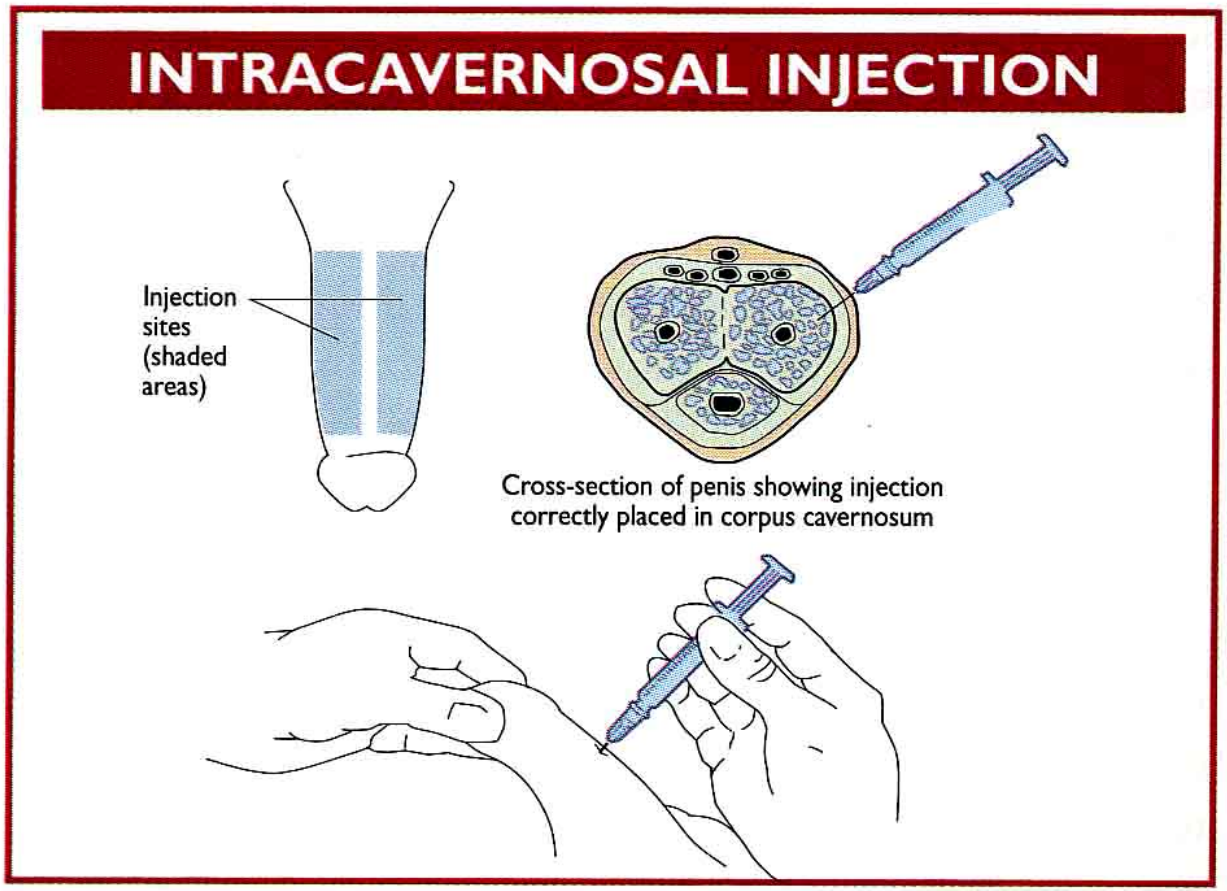
While sitting or standing, gently and slowly stretch the penis upward to its full length, with gentle compression from top to bottom of the glans. This straightens and opens the urethra.

Slowly insert the applicator stem into the urethra up to the collar. Insertion up to the collar is very important to ensure proper absorption of the medicated pellet.

Holding the penis upright and stretched to its full length, roll the penis firmly between your hands for at least 10 seconds. This will ensure that the medication is adequately distributed along the walls of the urethra.

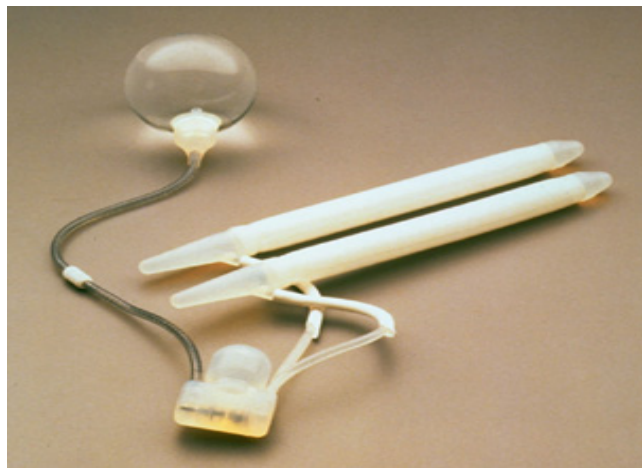
Stand up and walk around for 10 minutes while the penis becomes erect. This activity increases blood flow to the penis and will improve the quality of your erection. Do not begin sexual intercourse for at least 10 minutes.

Second-Line Therapy for Management of ED



Inflatable Penile Prostheses: Reliability/Patient Satisfaction

Long-term, US multicenter study AMS 700CX 3-piece inflatable penile prostheses
86% mechanical reliability after 5 y (n=372)
91% erection suitable for coitus (n=172)
>85% would undergo
surgery again and/or
recommend procedure
to a friend (n=178)



Carson CC, et al. *J Urol.* 2000;164:376-380.

Conclusions

- ED is common with multifactorial etiology
- Initiate first-line therapy including lifestyle modification and oral drugs as the least invasive therapeutic option
- Sildenafil and Tadalafil (PDE5 inhibitors) may offer effective treatment for most patients
- For patients with treatment failures or contraindications to therapy, the second- and third-line approaches may apply

1. DeBusk R, et al. *Am J Cardiol.* 2000;86:175-181.

Question 1(Touch Pad)

The treatment of Erectile Dysfunction should be primarily performed by Primary Care Physicians.

1. Yes

2. No

Question 1 (Touch Pad)

I feel very comfortable treating patients with Erectile Dysfunction and only refer patients when they fail therapy.

1. Yes

2. No

Question 2 (Touch pad)

When I see a patient with incontinence I refer them immediately to:

1. A Urologist
2. A Gynecologist
3. A Urogynecologist
4. A nurse incontinence specialist
5. I don’t refer but treat them initially

Question 4 (Touch pad)

There is no reasonably successful treatment for stress incontinence available.

1. True
2. False

Question 3 (Touch pad)

My biggest concern when I see a patient with a scrotal lesion or complaint is that:

1. I am going to miss a testicular torsion?
2. I don’t feel comfortable examining the scrotum because I am not confident of the anatomy?
3. I am embarrassed to examine that region?

Objectives:

- To learn how to make the diagnosis of erectile dysfunction
- To learn how to treat erectile dysfunction
- To learn about the new treatments available for erectile dysfunction

Major Risk Factors for ED: Diabetes Mellitus

- Contributing factors:[1]
  - Increased age
  - Increased duration of diabetes
  - Poor glycemic control [1,2]
  - Diabetic complications
    eg, neuropathy

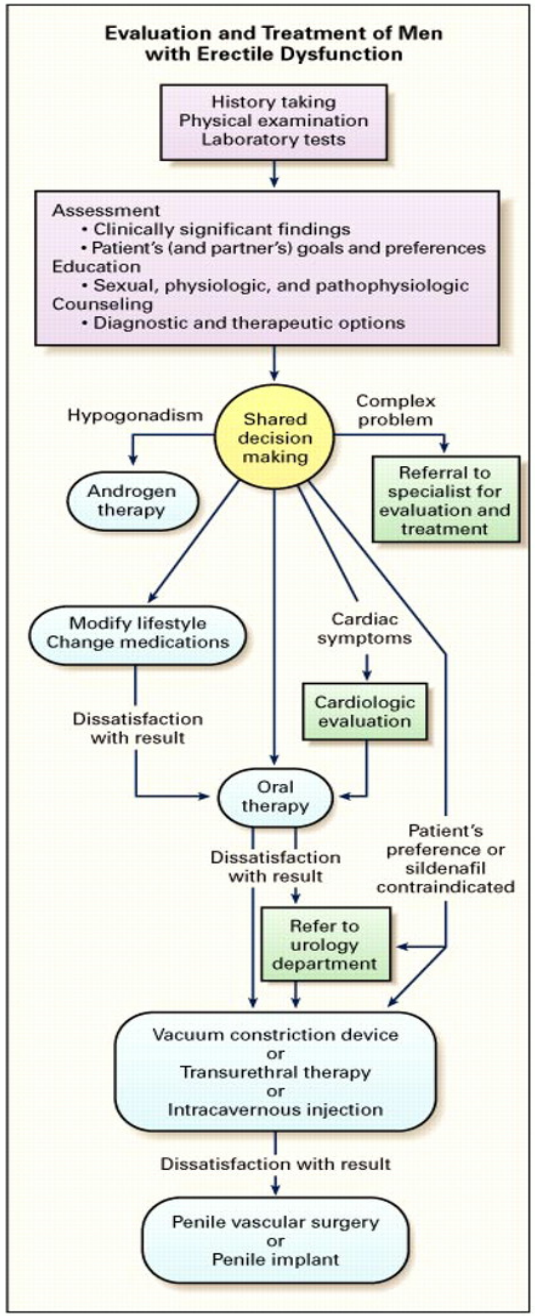
1. Klein R, et al. *Diabetes Care*. 1996;19:135-141. **2.** Romeo JH, et al. *J Urol.* 2000;163:788-791.

Classification of ED: Psychogenic or Organic?

Psychogenic	Organic
Sudden onset	Gradual onset
Complete immediate loss	Incremental progression
AM erections present	Lack of AM erections
Varies with partner and under circumstance stimulating	Lack of erections most sexually circumstances

Adapted from Ralph D, et al. *BMJ.* 2000;321:499-503.

Evaluation and Treatment



Lue T. NEJM 2000; 342:1802-1813