

TREATMENT OUTCOMES OF
ERECTILE DYSFUNCTION:
*INFORMATION FOR YOUR
PATIENTS*

Shubha De
Dr. Grantmyre
State of the Art Presentation
June 8, 2011

Case:

- ▣ 59y/o male:

- ▣ Engineer, father of 2
- ▣ New relationship 10 months
- ▣ Now having 'sex troubles'

has to work for an erection, doesn't last

- ▣ Has heard there are pills and other things

“Doc, what are the chances they will work for me?”

- ▣ PMHX

- DMII

- DMII+Obesity

- Prostate Ca +Brachy

- Prostate Ca +RRP

Case:

- ▣ 59y/o male:

- ▣ Engineer, father of 2
- ▣ New relationship 10 months
- ▣ Now having 'sex troubles'

has to work for an erection, doesn't last

- ▣ Has heard there are pills and other things

“Doc, what are the chances they will work for me?”

- ▣ PMHx

○ **NONE**

Newly diagnosed organ confined PCa

“Don't ruin my new relationship”

Objectives

- ▣ Discuss the background of ED
- ▣ Cover the some less frequent treatment options and their efficacy and indications for use
- ▣ To apply these treatment options to unique patient populations
- ▣ To put treatment in context of a patient's relationship

ED Epidemiology

- ▣ Between 15-60% of men over 40y/o are affected
 - Massachusetts Male Aging Study 52% 40-70yo
 - ▣ 65% mild, 25% mod, 10% complete
- ▣ 58% of males with ED will seek treatment
 - 40% of them will initiate treatment
 - ▣ 16% will continue with treatment
- ▣ 525,000 clinic visits
- ▣ 30,000 hospital admission
- ▣ Viagra most profitable drug to date (1.4billion/y)

ED Epidemiology

Varying rates based on risk factors

- ▣ Age
- ▣ Comorbidities
- ▣ Geographically/Culturally
 - \$100 million /year (England)
 - \$90 million / year Japan
 - \$500 million/year (US)
 - \$0/year Sierra León

Consequences of ED

- ▣ Depression, loss of self esteem, mental health conflict
- ▣ Deterioration of sexual and overall quality of life experiences
- ▣ Female Partner
 - Decreased sexual desire
 - Decreased levels of arousal, orgasm frequency, and satisfaction following ED onset
 - More likely to have sexual dysfunction, relationship problems, and completely stop sexual activity (as compared to those in a relationship without ED)

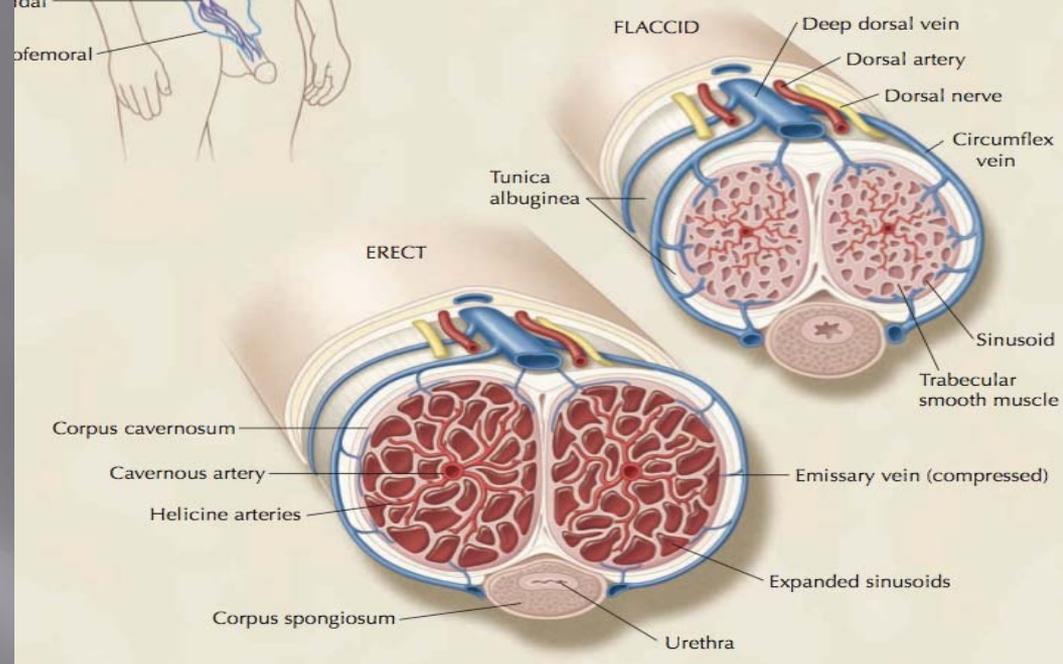
Erections: How they work

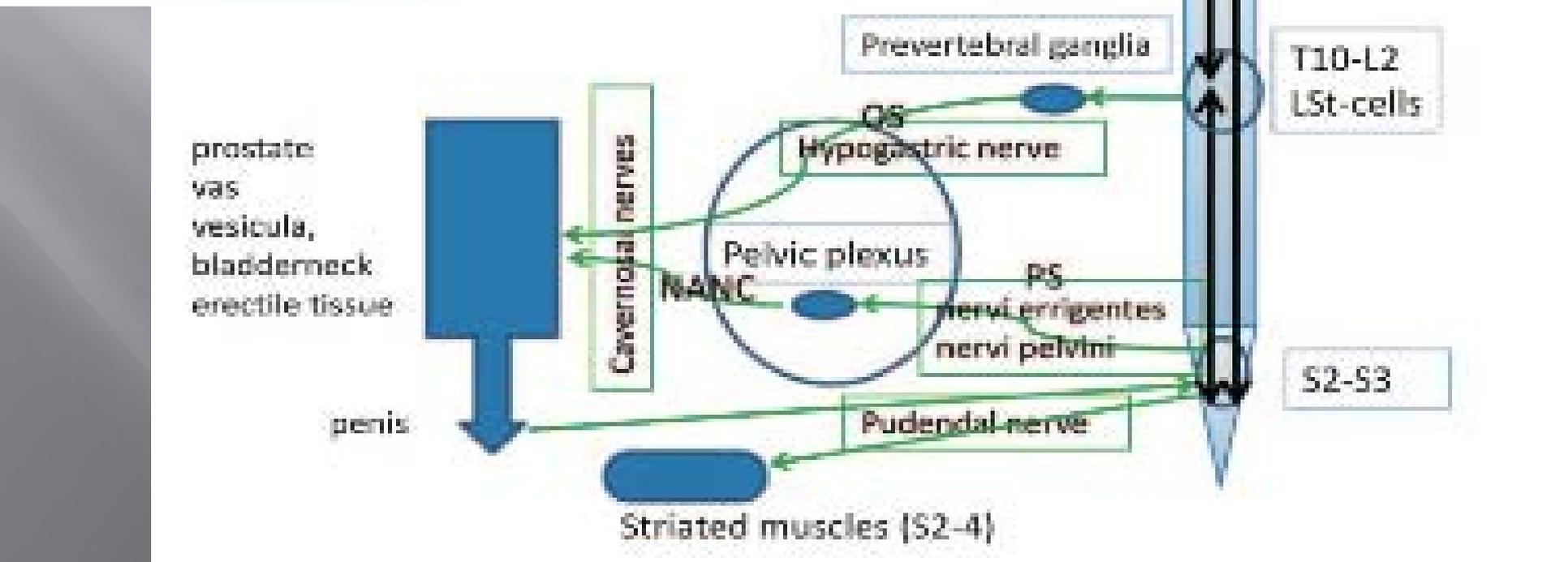
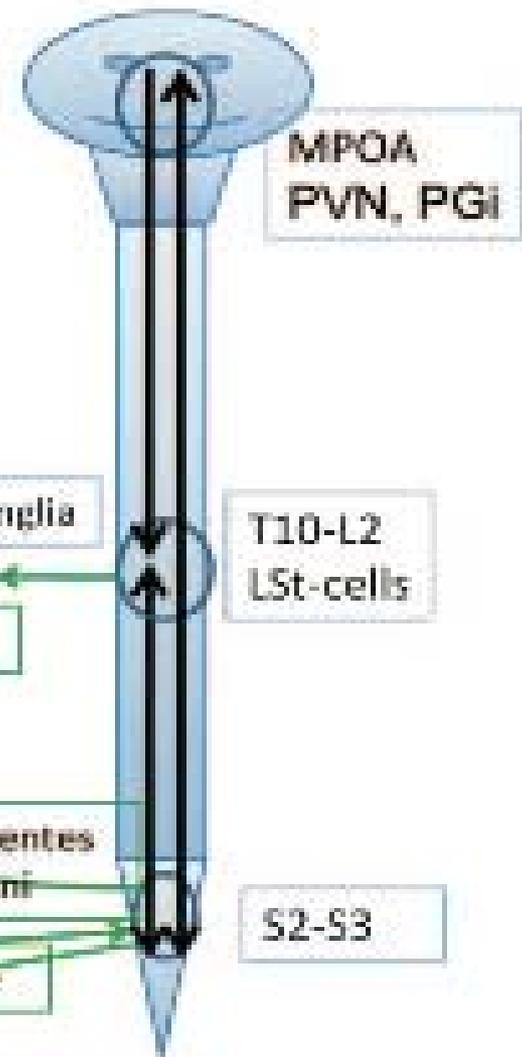
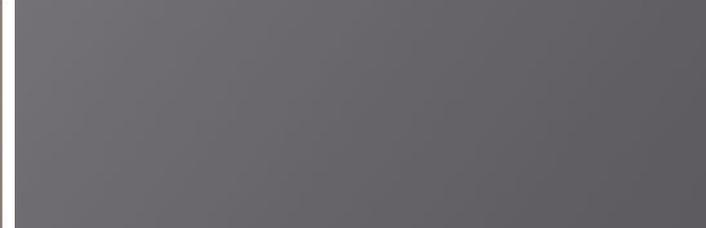
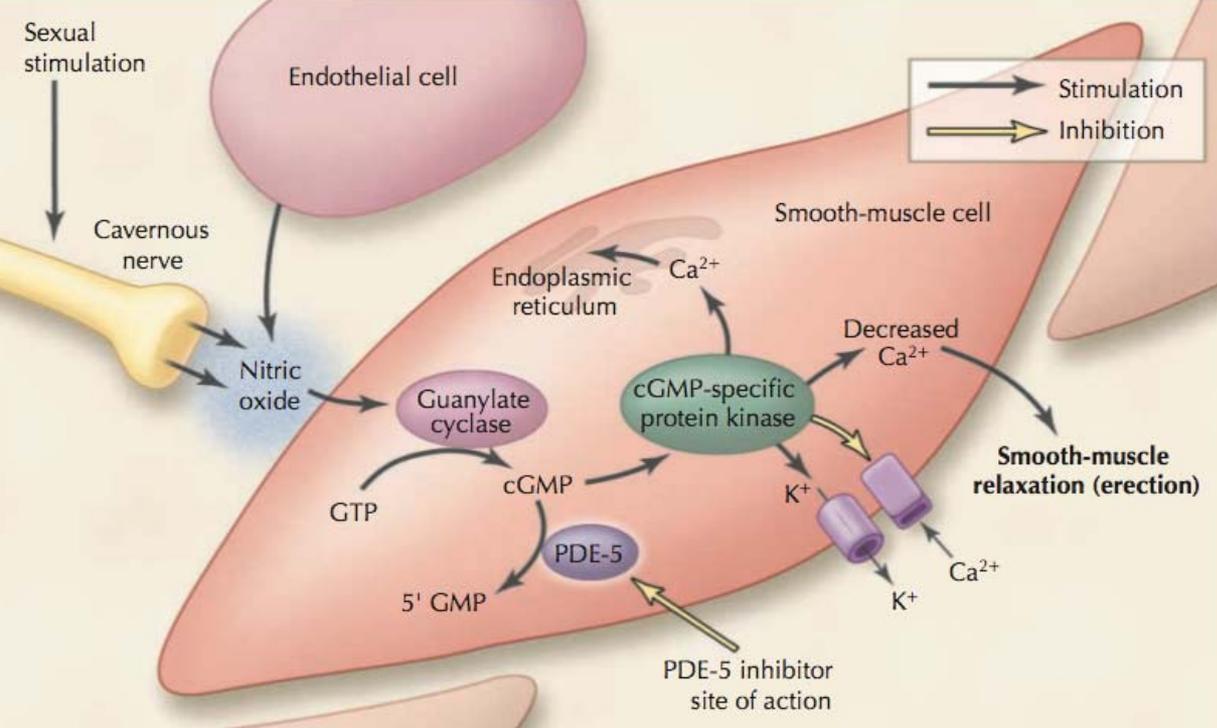
Vascular component

Macroscopic View:

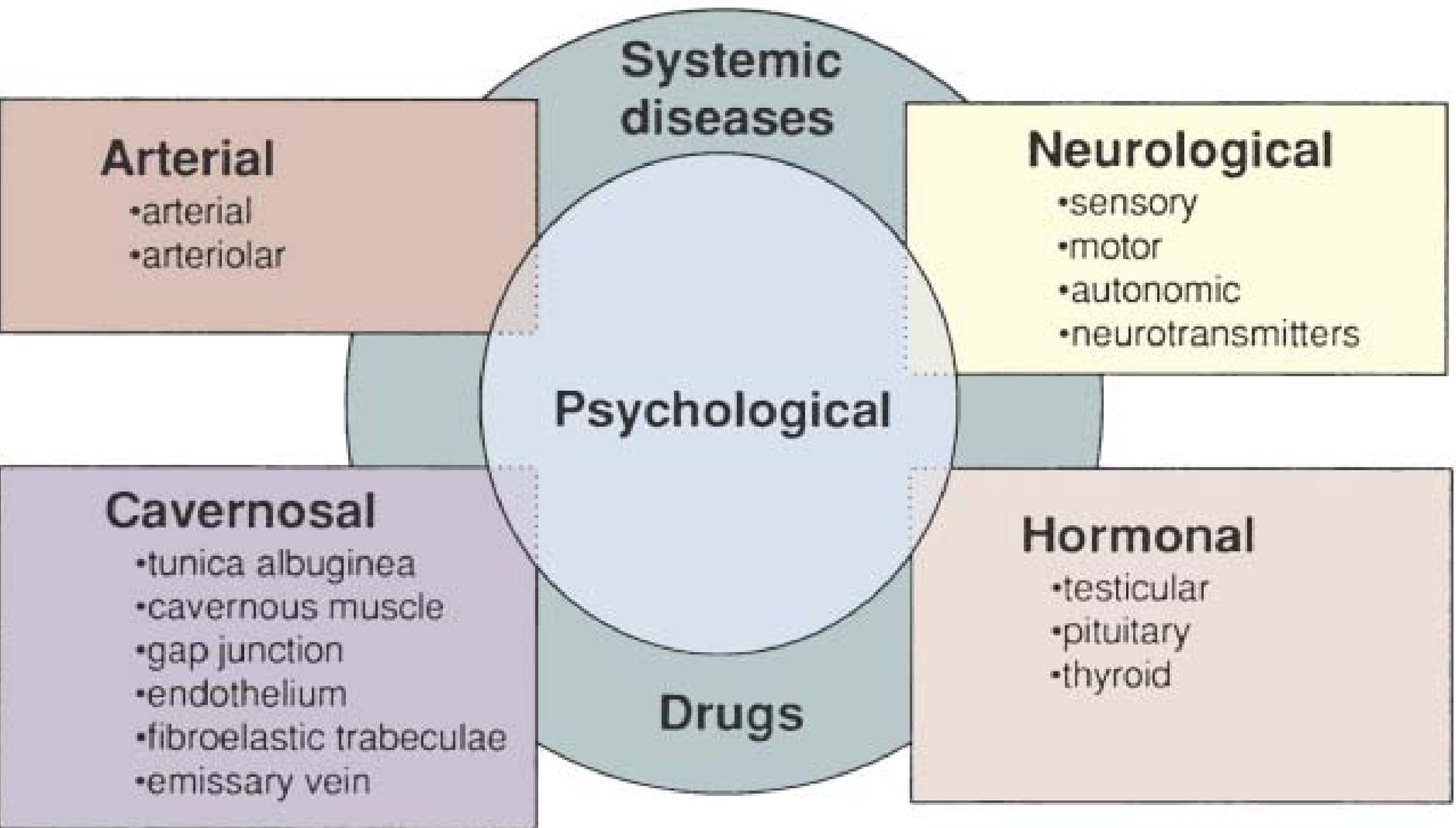
▣ Inflow > outflow

- ▣ Pudendal a. → Cavernosal a. → Sinusoids of trabecular smooth muscle within the corpora → Emissary v.
- ▣ Distension of the corpora cause mechanical compression of the peripheral emissary veins against the non-distensible tunica, leading to penile rigidity





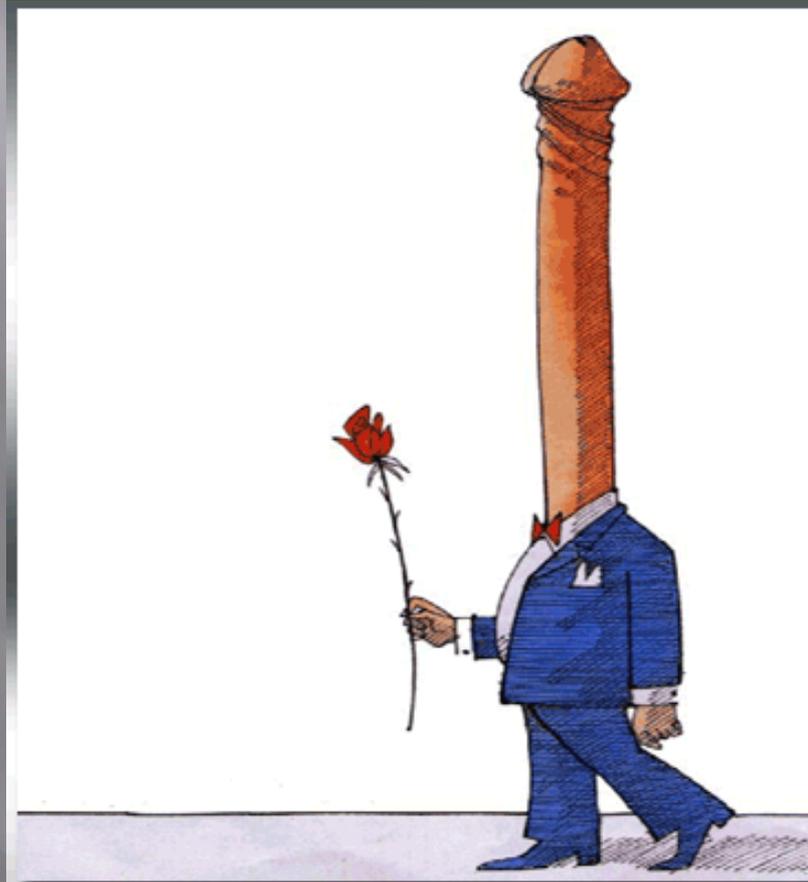
Classification of ED





Your Problem Is
OBVIOUS!!!

Its all in your head....



Your Problem Is
OBVIOUS!!!

Treatment options

TREATMENT STRATEGY OF ERECTILE DYSFUNCTION (ALGORITHM)

Treatment of erectile dysfunction

The objective of treatment is to restore a satisfactory sexual relationship, not only a rigid erection

A Educate the patient about risk factors and comorbidities

Together with

B Counsel the patient and partner if available
Consider treatment options

C **Initiate medical treatment**
Treatment is selected taking into account the medical and psychosocial contraindications and patient preference and availability

Other oral treatments

PDE-5 inhibitors*

Local therapies
• Pharmacological
• Mechanical

Not satisfied

Not satisfied

Not satisfied

2 **Reevaluate and adjust therapy**
• Dose titration
• Instruct patient on optimal use of treatment

Not satisfied

3 Consider alternative oral or local therapy as above

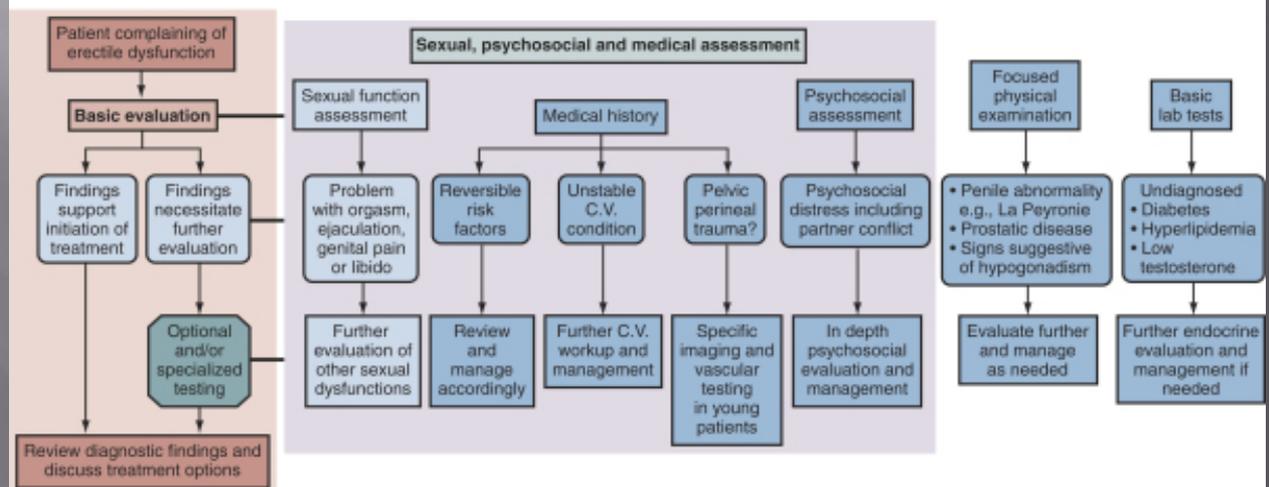
Not satisfied

4 **Refer to a specialist**

Depending on the predominant etiology and circumstances the specialist could be a:

- **Urologist:** penile prosthesis, penile revascularization or correction of penile deformity
- **Psychosocial therapist or psychiatrist:** treatment of complicated psychosexual problems
- **Other medical specialist**

ALGORITHM FOR DIAGNOSTIC EVALUATION OF ED



*PDE-5 inhibitors are the preferred treatment option in the large majority of patients

Conservative management

Medication Changes

- ▣ Diuretics: Thiazide (self report studies)
- ▣ Beta blockers: Older B1/B2 non specific agents may act centrally and in penis (10% of adrenoceptors in the penis are beta)
- ▣ ACE inhibitors
- ▣ CCB
- ▣ Statins: Worsening of atherosclerosis will lead to negative outcomes
- ▣ Opiates: hypogonadotropic hypogonadism
- ▣ Alcohol: small amounts vs. chronic use

Medication Changes

- ▣ Antipsychotics: Dopaminergic blockade
- ▣ Antidepressants
 - Tricyclics:
 - MAOI:
 - SSRI:
 - Mirtazapine/nefazodone
- ▣ Anxiolytics
 - Benzodiazepines: GABA, dopamine and serotonin

Urologists Medications

- ▣ Alpha blockers: Help SM relaxation, improved
- ▣ Antiandrogens (ARA)
 - Effectively antagonize androgen receptors, and may have complete or no effect on normal function
 - T, and DHT
- ▣ 5ARI
 - Least effect on circulating testosterone, 5% complain of decreased desire and ED at 5mg
 - 1mg no sexual dysfunction
 - 70-80% have decreased libido
- ▣ LHRH: profound loss of sexual desire + ED

Lifestyle management

- ▣ Physical activity
 - Greater than 16MET hours per week 30% lower risk
 - Higher activity associated with lower rates of ED
- ▣ Weight loss
- ▣ Smoking: No randomized data
 - Some evidence to believe NO, endothelial dysfunction
 - Associated improvements in CV status and ED at 6m
- ▣ Reversible risk factors
 - DM, dyslipidemia
 - HTN

Psychosocial Therapy

- ▣ Cochrane Review
 - 9 RTC, and 2 'quasi-RTC' reviewed including 398 men (psychotherapy +/- medication, vacuum devices, control groups)
 - **Psychotherapy** reduced the amount of 'persisting erectile dysfunction' over **No Intervention** (RR 0.40, NNT 1.61), with lasting effects at 6 months
 - **Psychotherapy + Viagra vs. Viagra**, had lower attrition rates and greater reductions in persistent ED
 - **Group therapy vs. Viagra** (one study) favored group therapy with significant IIEF score improvements
 - Treatment responses vary in subgroup analyses
 - ▣ Age, relationship type, severity of ED

Medical Options 2nd line

The Cost of Erections

Table 22-3 -- Treatment Options for ED: Costs, Advantages, and Disadvantages

<i>Treatment</i>	<i>Cost (\$)</i>	<i>Advantages</i>	<i>Disadvantages/Side Effects</i>
Counseling	500-2000	Noninvasive; resolves conflict	High recurrence rate of ED
Oral drugs (phosphodiesterase inhibitors)	10/pill	Noninvasive; 60%-70% efficacy	Systemic side effects; nitrate contraindications
Vacuum devices	200-550	Minimally invasive	Unnatural erection; absence of spontaneity; petechiae, pain; cold penis
Intracavernous injection	40-200/mo	90% efficacy	More invasive; priapism, fibrosis, pain
Prosthesis	20,000-30,000	High success rate	Requires surgery, anesthesia; infection, fibrosis
Vascular surgery	15,000-30,000	Restores natural erection	Low efficacy of venous surgery; arterial bypass limited to select patients; requires anesthesia and extensive workup

PDE5 Inhibitors

- ▣ Most profitable pharmaceutical to date
- ▣ Most counterfeited medication globally. Usually with no active ingredient
- ▣ Differences in MOA
- ▣ Most commonly used PRN

Table 2: Pharmacokinetic characteristics of PDE-5 inhibitors used in the treatment of erectile dysfunction

Parameter	Sildenafil	Vardenafil	Tadalafil
Oral dose, mg	100	20	20
Median time to peak concentration, min	60	40–60	120
Half-life, h	3–4	4–5	17.5
Maximum concentration, µg/L	411	17	378
Area under the erectile curve, µg·h/L	1691	67	8066
Volume of distribution, L	105	208	63
Food interaction	Yes with high-fat foods; possible with low-fat foods	Minimal with low-fat foods; delay in time to peak concentration with high-fat foods	None
Alcohol interaction	None	None	None
Age > 65 yr	Half-life ↑ Dose adjustment may be needed	Half-life ↑ Dose adjustment may not be needed	Half-life ↑ Dose adjustment may not be needed

Note: PDE-5 = phosphodiesterase type 5.

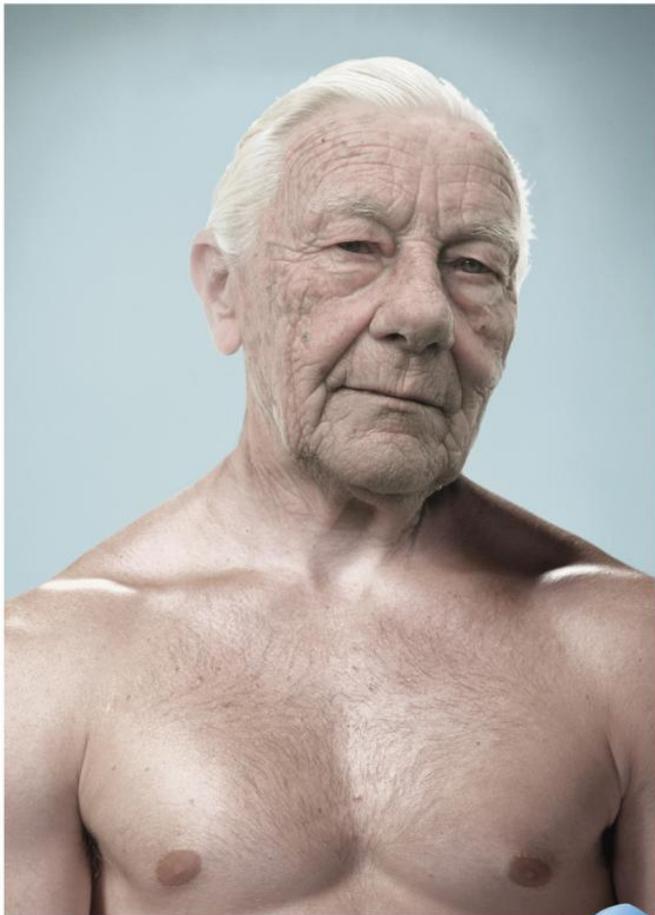
Pills that Changed Expectations...

- ▣ Viagra released in 1998 to large ethical and sociologic conflicts
 - “medicalization of social life events”
 - the medicalization and illness approach to normal common life experiences (child birth, puberty, hair loss, menopause)
 - “the anti-decline narrative of men”
 - “sexual intimacy is reduced to vaginal penetration”
 - “public support of private affairs”
- ▣ Have they changed our way of thinking?

Two Types of Ad Campaigns

Exaggerated Need
(humorous/farcical)

Normalizing
(youthful/celebratory)



Two Types of Ad Campaigns

Exaggerated Need
(humorous/farcical)



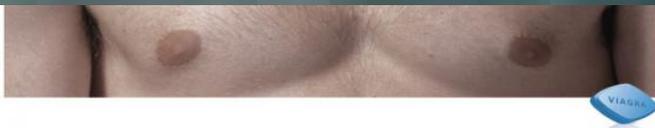
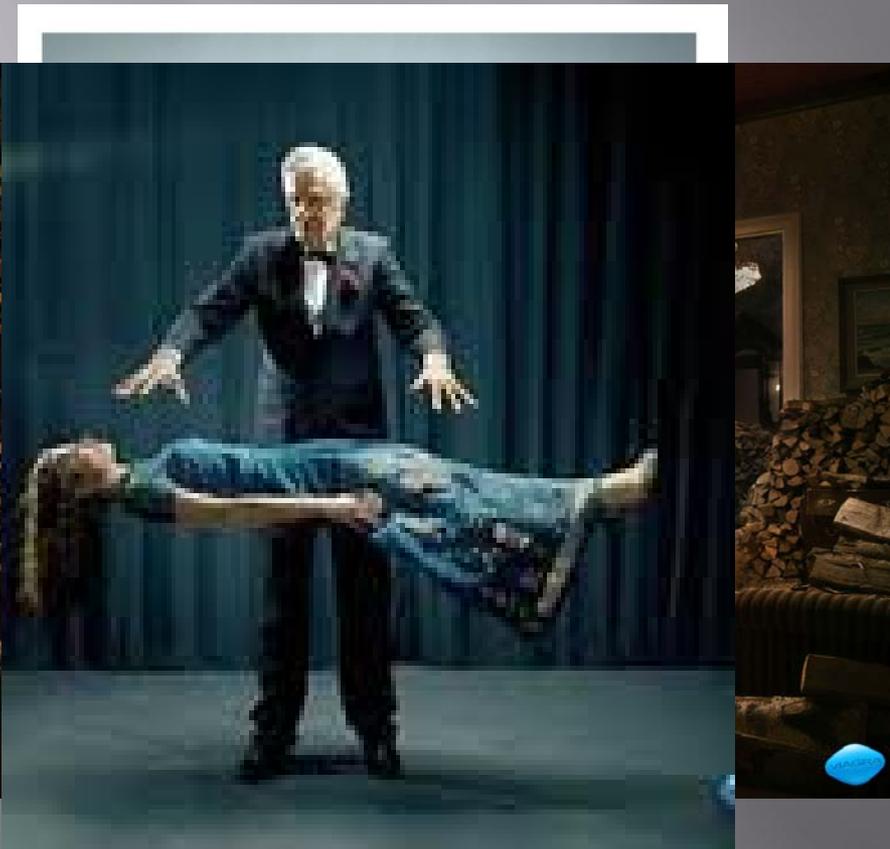
Normalizing
(youthful/celebratory)



Two Types of Ad Campaigns

Exaggerated Need
(humorous/farcical)

Normalizing
(youthful/celebratory)



Two Types of Ad Campaigns

Exaggerated Need
(humorous/farcical)

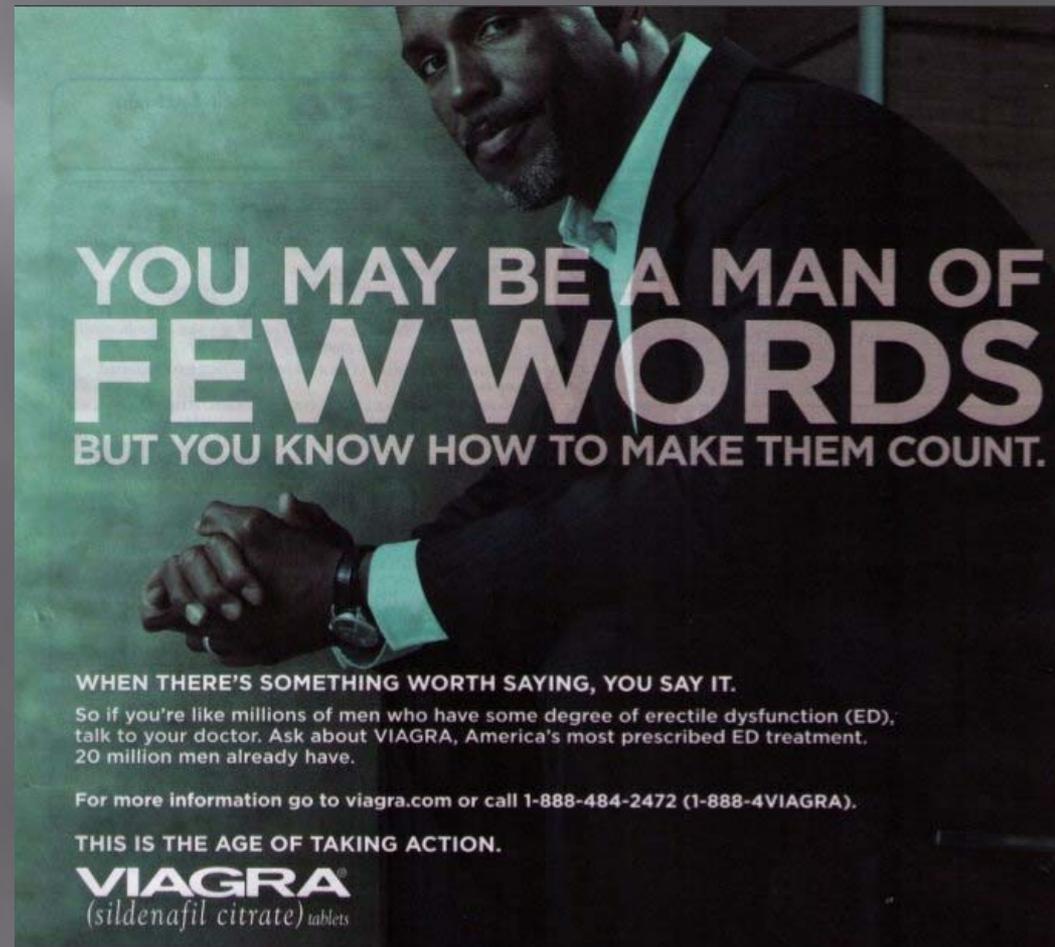
Normalizing
(youthful/celebratory)



Two Types of Ad Campaigns

Exaggerated Need
(humorous/farcical)

Normalizing
(youthful/celebratory)



**YOU MAY BE A MAN OF
FEW WORDS
BUT YOU KNOW HOW TO MAKE THEM COUNT.**

WHEN THERE'S SOMETHING WORTH SAYING, YOU SAY IT.
So if you're like millions of men who have some degree of erectile dysfunction (ED), talk to your doctor. Ask about VIAGRA, America's most prescribed ED treatment. 20 million men already have.

For more information go to viagra.com or call 1-888-484-2472 (1-888-4VIAGRA).

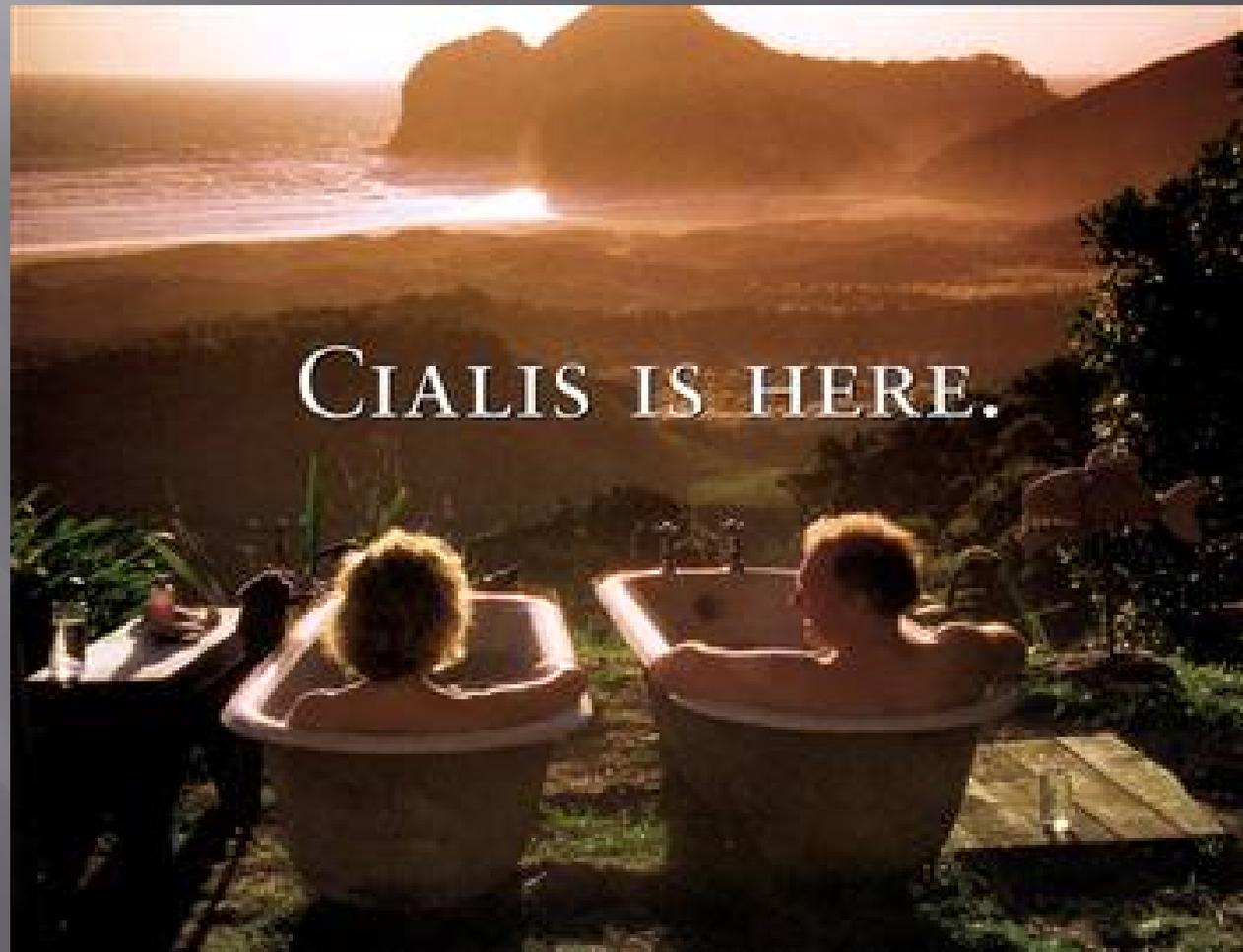
THIS IS THE AGE OF TAKING ACTION.

VIAGRA
(sildenafil citrate) tablets

Two Types of Ad Campaigns

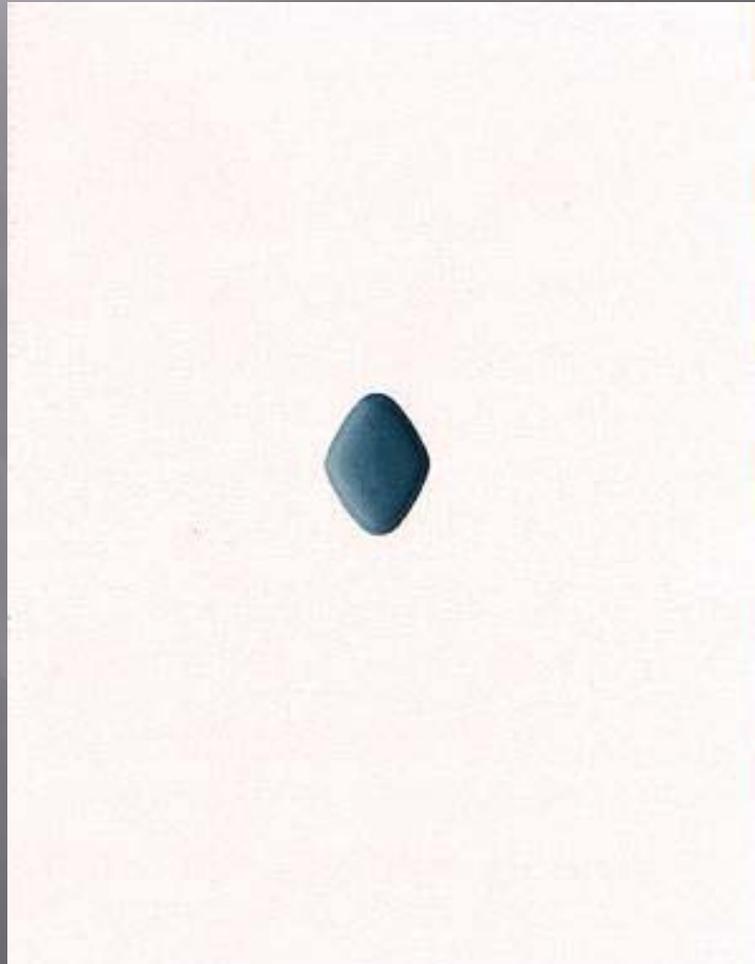
Exaggerated Need
(humorous/farcical)

Normalizing
(youthful/celebratory)



Two Types of Ad Campaigns

Exaggerated Need
(humorous/farcical)



Normalizing
(youthful/celebratory)



Two Types of Ad Campaigns

Exaggerated Need
(humorous/farcical)

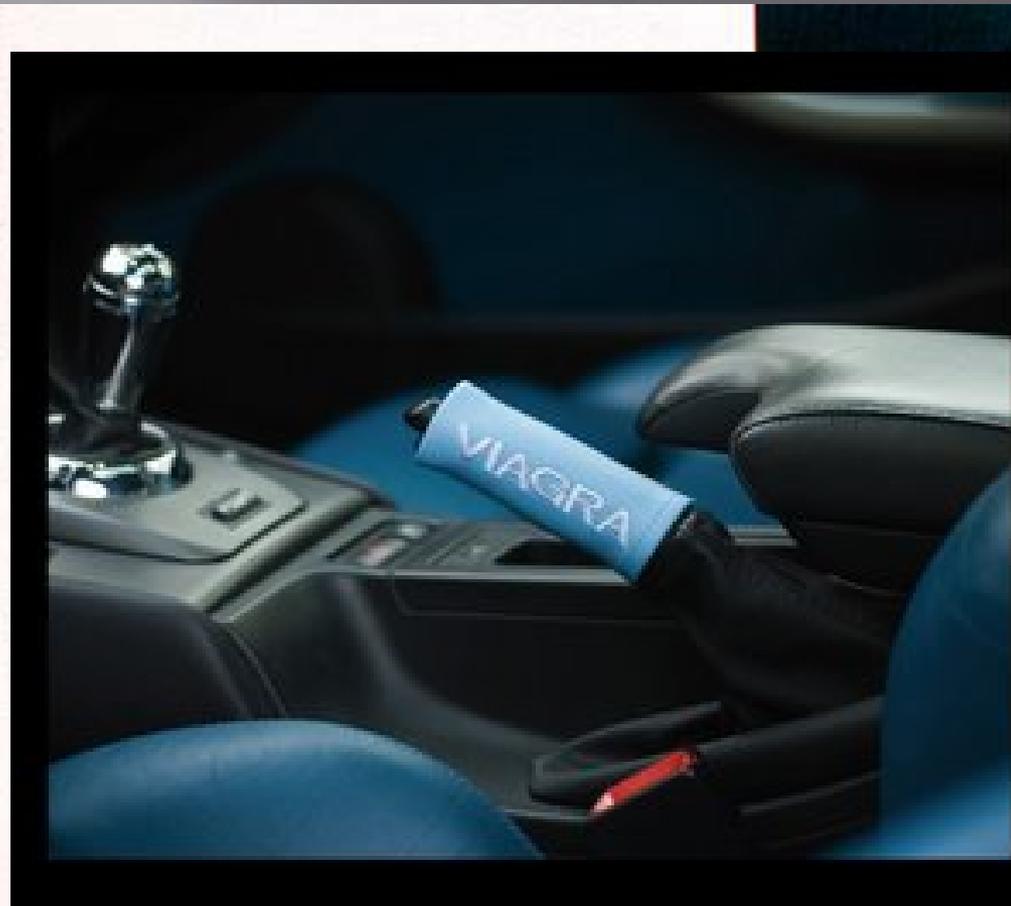
Normalizing
(youthful/celebratory)



Two Types of Ad Campaigns

Exaggerated Need
(humorous/farcical)

Normalizing
(youthful/celebratory)



Challenge
In the male-ego driven Arab world, sexual impotence is a very serious issue. And due to cultural and religious restraints, you can't show any sexual content.

Strategy
We had to show objects that would reflect male potency and explain the effect of Viagra while conveying it in a light manner, hence the usage of the hand brake.

Results
The giveaway has just been distributed and it's too soon to gather any sort of quantitative information. However, word from respective pharmacies is that men are accepting it with a smile.

Two Types of Ad Campaigns

Exaggerated Need
(humorous/farcical)

Normalizing
(youthful/celebratory)



Two Types of Ad Campaigns

Exaggerated Need
(humorous/farcical)

Normalizing
(youthful/celebratory)



Male Sexual Lifecyle *(Sheeny, 1999)*

15-30y/ o: Race Car Sex

- Narcissistic attitude of instant gratification

30-40y/ o: Dutiful Sex

- Procreation and relationship building

40-55: Masters Tournament Sex

- The virtuoso peak of a mans sexual life cycle when control, choreograph, prolong and savor each erotic encounter

55-70: Surfing Sex

- Erectile function changes most notable

>70: Snuggling Sex

- Touching and tenderness are central to intimacy

Male Sexual Lifecyle *(Sheeny, 1999)*

15-30y/ o: Race Car Sex

- Narcissistic attitude of instant gratification

30-40y/ o: Dutiful Sex

- Procreation and relationship building

40-55: Masters Tournament Sex

- The virtuoso peak of a mans sexual life cycle when control, choreograph, prolong and savor each erotic encounter

55-70: Surfing Sex

- Erectile function changes most notable

>70: Snuggling Sex

- Touching and tenderness are central to intimacy



Couple's dynamics over time

Classic

- ▣ Changes with age
 - “decline attitude” was pervasive with sexual activity
 - The older people are, the less they are supposed to have sex.

Now

- ▣ Libido Mismatch:
 - Male sex drive is touted as being more robust than females
 - Psychological distress is reported when feel they are lacking in comparison to their partners
 - Females may feel a sharp change in libido match when viagra is unilaterally sought by their partner
- ▣ His viagra for her
 - A limiting factor was male performance capabilities
 - A large number of women's QoL and sexual function indices improve with penetrative sexual activity as they age

PDE5 Inhibitors: Daily dosing

- ▣ Typical dosing is Low Dose:
 - Viagra 25mg
 - Cialis / Levitra 5, 10mg
- ▣ Daily dosing has been studied in vasculogenic ED
 - HTN
 - Dyslipidemia
 - Atherosclerosis
 - DM
- ▣ Same side effects
 - Head ache
 - Flushing
 - Dyspepsia
 - Rhinitis
 - Visual disturbances
 - Back pain

Daily Dosing

- ▣ Randomized crossover study
 - Cialis 20mg PO q2nd Day vs. 20mg PRN
 - Periodic blood work and U/S done
 - At 15d follow up
 - ▣ Decreased CRP, VCAM, ET-1
 - ▣ Increased cavernous artery diameter and carotid artery diameter, peak systolic velocity
 - ▣ Improved morning erections
 - ▣ Improved Sexual function (4 points, 35% of patients improved by category)

If Unsuccessful

- ▣ Rotate agents, after several attempts at usage
 - No clear guidelines to number, or frequency
 - Likely class effect to moderate-severe side effects
- ▣ Unsuccessful PDE-5 use, in a patient felt to be secondary to hypo-gonadal state, testosterone therapy is indicated
 - DHT may enhance production of NO, increasing PDE5 clinical effect

Penile Injection

- ▣ Locally acting vasodilator
 - Alprostadil (prostoglandin E1)
 - Phentolamine (not supported by makers for ICI)
 - Papaverine (not supported by maker for ICI)
- ▣ All are sympatholytics, increase arterial flow and dilate smooth muscle
- ▣ Efficacy 70-80%
- ▣ Large user attrition rate (30-60%)



Prosthesis Counseling

- ▣ Several different types of implants
- ▣ Risks of reoperation
 - Infection 1-3%
 - Erosion
 - Mechanical failure 5-15%
 - Revision/replacement
 - Unilateral implant placement
 - Urethral injury
 - Penile shortening
 - Non-reversible destruction of erectile tissue

Malleable

- ▣ Simplest for insertion and use
- ▣ Permanent erection
- ▣ Cost effective
- ▣ Less than 10% of all inserted prostheses
- ▣ Difficult to conceal, most painful post operative course during healing

Inflatable prosthesis

- ▣ Two piece have mechanical advantage of less parts, and easier implantation
 - Less realistic tumescence/detumescence
- ▣ Three piece prosthetics achieve best tumescence/detumescence, with girth/length expansion
 - Require a separate reservoir.
 - Have more parts, and therefore have more room for technical and mechanical error, requiring revision
 - Devise survival: 74% at 10y
 - devise survival free of failure: 81% at 10y

The right fit for your patients

- ▣ Personal preference and perception of function and cosmesis
- ▣ “limited mental or manual dexterity” should be offered a malleable
- ▣ Those with decreased sensation should have inflatable devices due to skin and urethral erosions due to undetected pressures with rods

Special Populations



The Sugar Diabetes

- ▣ 25% of all people diagnosed w ED have DM
- ▣ Prevalence of ED 3x higher (DMI), 1.9x (DMII)
- ▣ Occurs at earlier ages. Within 10y of diagnosis
- ▣ CAD and PVD significantly increases risk
- ▣ All dimensions of sexual health affected
 - Sex drive, ejaculation, satisfaction
- ▣ Etiology of ED
 - Psychological
 - CNS
 - Androgen secretion
 - Peripheral nerve activity
 - Endothelial cell dysfunction
 - Smooth muscle contractility
- ▣ DM1 is well studied, however DM2 is less clear. 90% of adult cases of DM2 are NIDDM

The Sugar Diabetes

- ▣ Adiposity (Waist to hip ratio, waist circumference, BMI) all increase risk by 1.5-3x, added to DM,
- ▣ Hypogonadism can be found in DM2 with low/normal testosterone, though Metabolic syndrome compounds these findings.
- ▣ Advanced glycation end products, bind to vascular collagen, and are highest in corpora
 - Generate free radicals
 - Decreased NO synthase and guanylyl cyclase
 - Increase ET1 (potent vasoconstrictor)
- ▣ Neuropathic damage through microvascular complications.

The Sugar Diabetes

- ▣ Decreased success of all ED treatments (oral to implants)
- ▣ Complications of DM compound the risk and severity of ED
 - Duration of disease
 - limb loss
 - retinopathy,
 - nephropathy,
 - uncontrolled HTN
- ▣ Correct modifiable risk factors
 - Atherosclerotic and vascular disease
 - Glycemic control is directly proportional to ED risk.
 - BMI lipids
 - Smoking, EtOH, recreational drugs

The Sugar Diabetes

Medical management

- ▣ Viagra improved erections and intercourse in diabetic patients, with titration up to 100mg (dose reduction in renal/hepatic impairment)
- ▣ Other PDE5's are considered safe and efficacious
 - Most studies selected for well controlled diabetics, without end organ dysfunction
- ▣ ICI: effective long term treatment of DM1, DM2
- ▣ Vacuum: satisfactory erection in 70% of DM, 30% d/c rate due to poor rigidity, pain, failure to ejaculate, aesthetics, partner issues
- ▣ Testosterone: increasing NO synthase expression, and NO affinity
 - Not commonly required in DM

Obesity

- ▣ 1/3 of American men are obese (2006), 3% are morbidly obese
- ▣ Obesity has dose dependant effect
- ▣ Obesity has similar risk factors to DM in ED
- ▣ Italian weight loss study (Giomini, 2009)
 - Randomized 110 men to exercise or education Improved lifestyle
 - Psychosocial
 - Improved mood and self-esteem
 - Endothelial function
 - NO bioavailability
 - Decreased inflammation
 - Increased testosterone

Obesity

- ▣ The key is weight loss
 - Activity, lifestyle management
 - Surgery
- ▣ Gastric bypass
 - Randomized controlled trial (n=20)
 - ▣ Intense nutritional education and physical activity followed by Bypass surgery, vs. general multidisciplinary weight loss plan
 - ▣ Bypass (delta 22kg/m², delta 1.7kg/m²)
 - ▣ IIEF scores improved (19 → 23) at 20m
 - ▣ FT, TT increased and PRL decreased in the intervention group



Diabetes + Obesity

- ▣ Look AHEAD study (2006):
 - Multicenter RCT including 5100 patients randomized to Intense Lifestyle intervention
 - ▣ 55-74, diabetic, BMI>25, sexually active at enrollment
 - IIEF at initiation and 1year

Results at 1y

- Intense group: significantly more weight loss (9.9% vs. 0.6%), greater fitness increases, improvements in HgbA1c, BP, HDL
- IIEF 17.2→18.6 vs. 18.3→18.4

Diabetes and Obesity

□ Erectile function:

	worsening	equivalent	improved
Intense activity group	8%	70%	22%
Diabetic education group	20%	57%	23%

- Strongest predictors of improvement in EF scores
 - Lower initial baseline EF scores
 - Magnitude of weight loss
- Weight loss pooled analysis:
 - Those who lost weight had better erectile function
 - Those who gained weight had worse erectile function
 - Not a dose-response effect

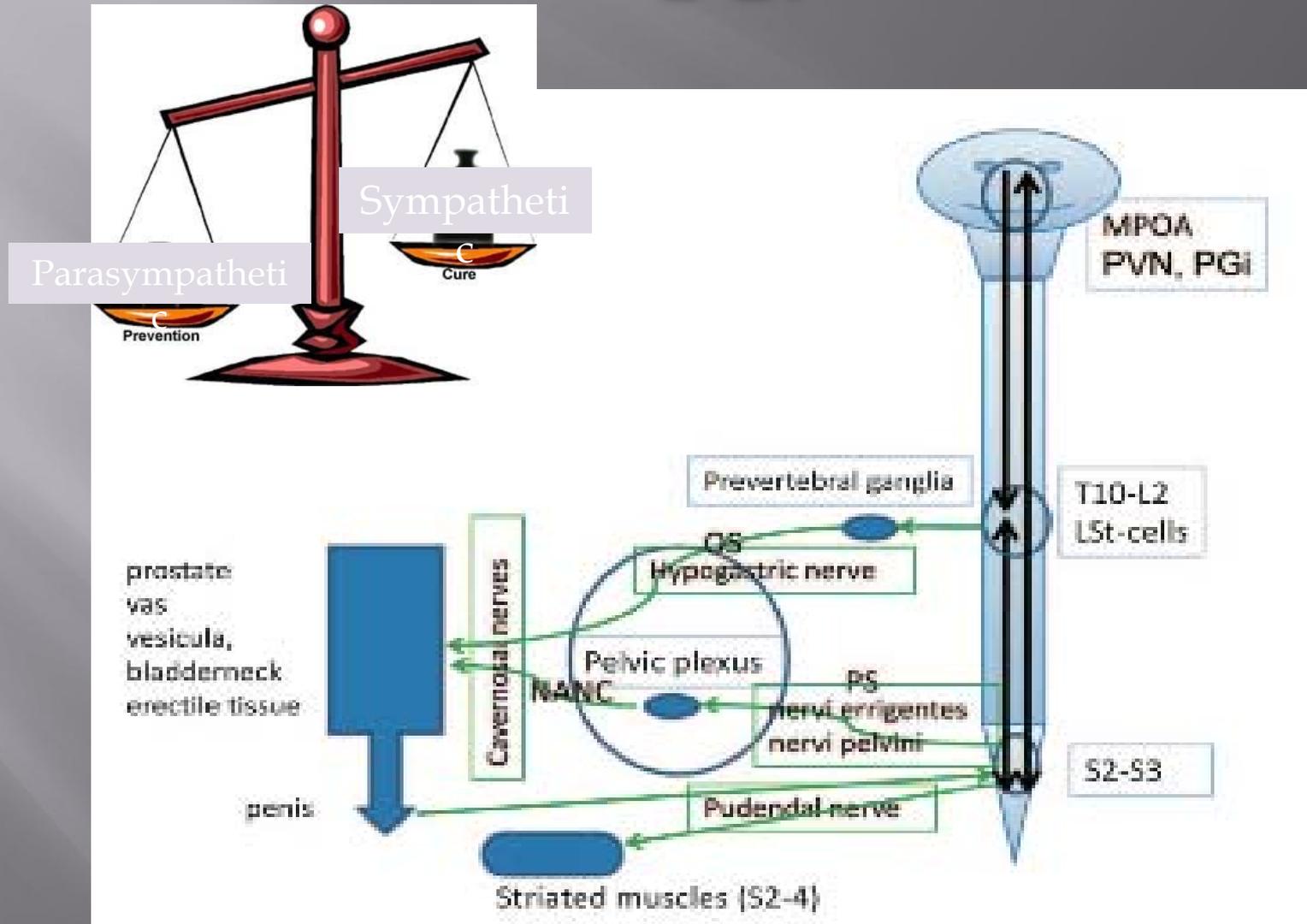
CRF

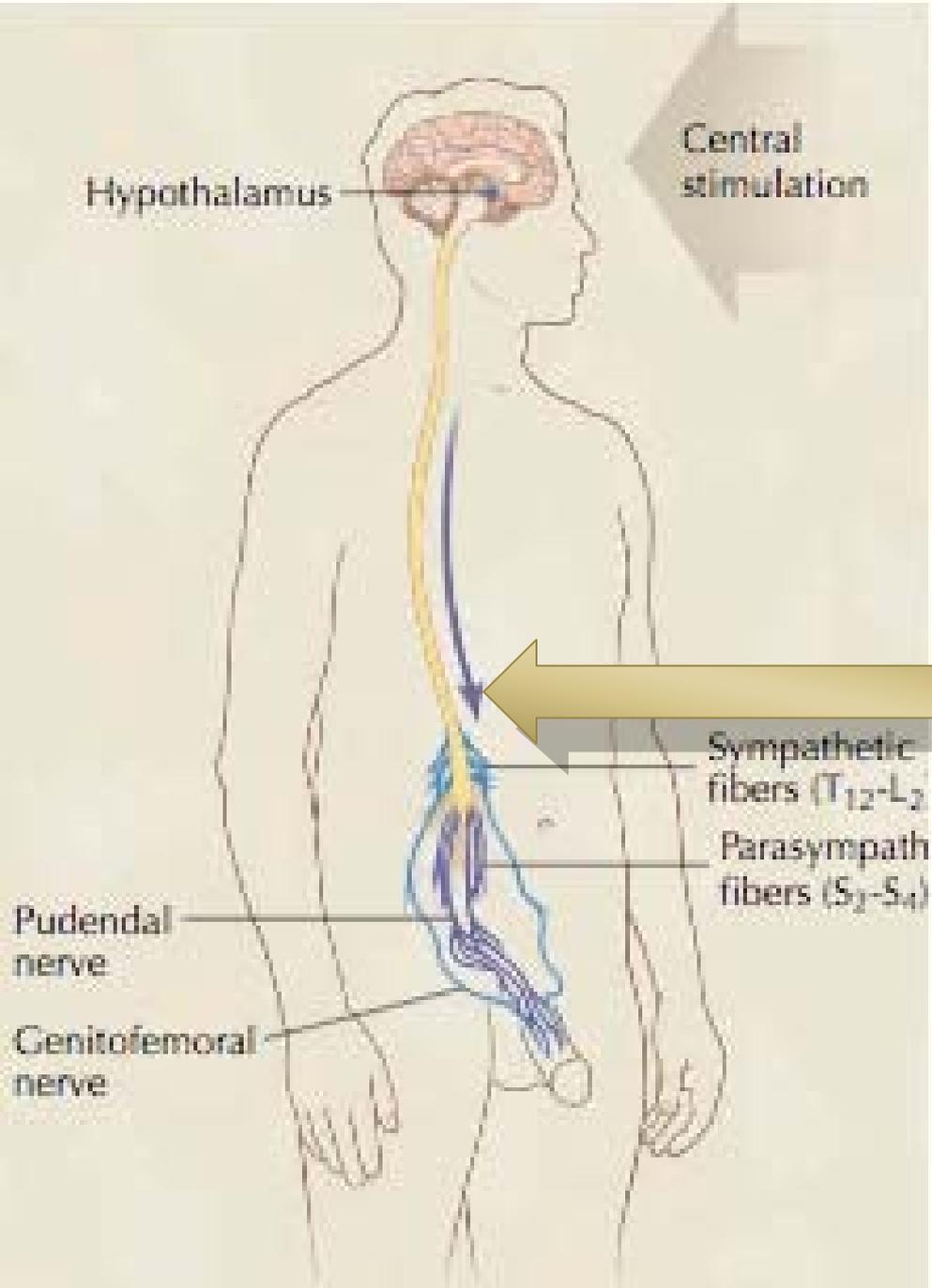
- ▣ 50-80% of Men with CRF have ED
 - Decreased libido
 - Delayed orgasm
- ▣ Inversely related to GFR
- ▣ Chronic renal failure
 - Hypothalamic-pituitary-testis axis
 - Testis changes (leydig cell dysfunction, seminiferous tubules fibrosis, arrested maturation)
 - Psychological factors (depression)
 - Autonomic dysfunction
- ▣ Improves with transplant
 - Decreased PRL beta-estrogen, increased testosterone
 - Improved IIEF 6mos after transplant

CRF

- ▣ Cochrane Review:
 - 114, filtered to 15 RTC
 - ▣ Zinc: oral delivery mildly improves testosterone, no change in sexual function
 - ▣ PDE 5 safe with significant sexual function benefits
 - ▣ No ICI, no prosthesis studies
- ▣ ESRD patients and ED
 - Quoted 70-80% efficacy of Viagra in ESRD
 - All-comers HD patients, Viagra efficacy <50%
 - ▣ Equal benefit in IIEF and HRQoL scores

SCI

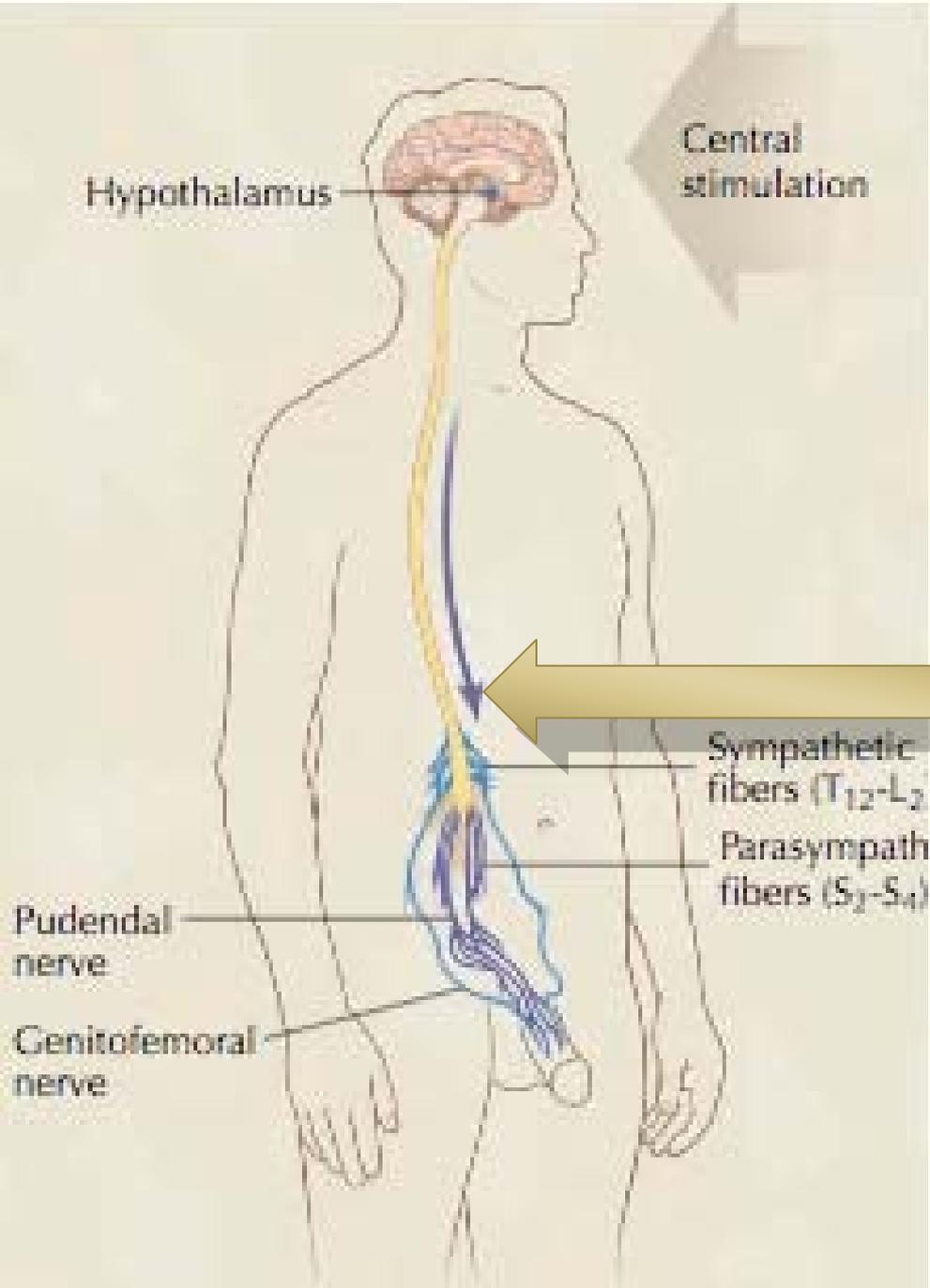




□ Afferents

- Pudendal (S₂-4)
 - Dorsal penile n.
- Scrotum
 - Ilioinguinal
 - Genitofemoral

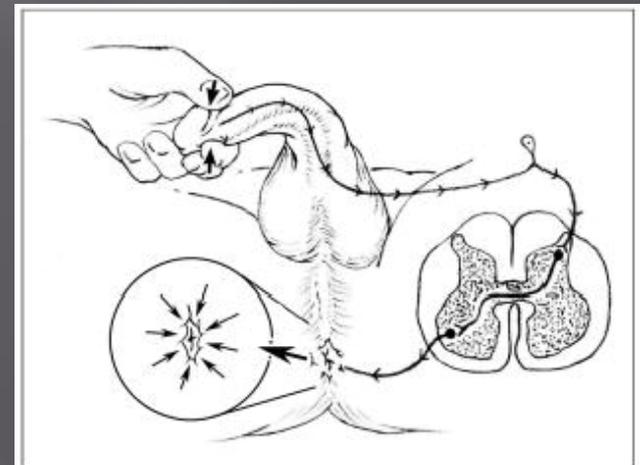
Lesions above sacral cord:
no sensory testing
available via pinprick,
light touch, temp

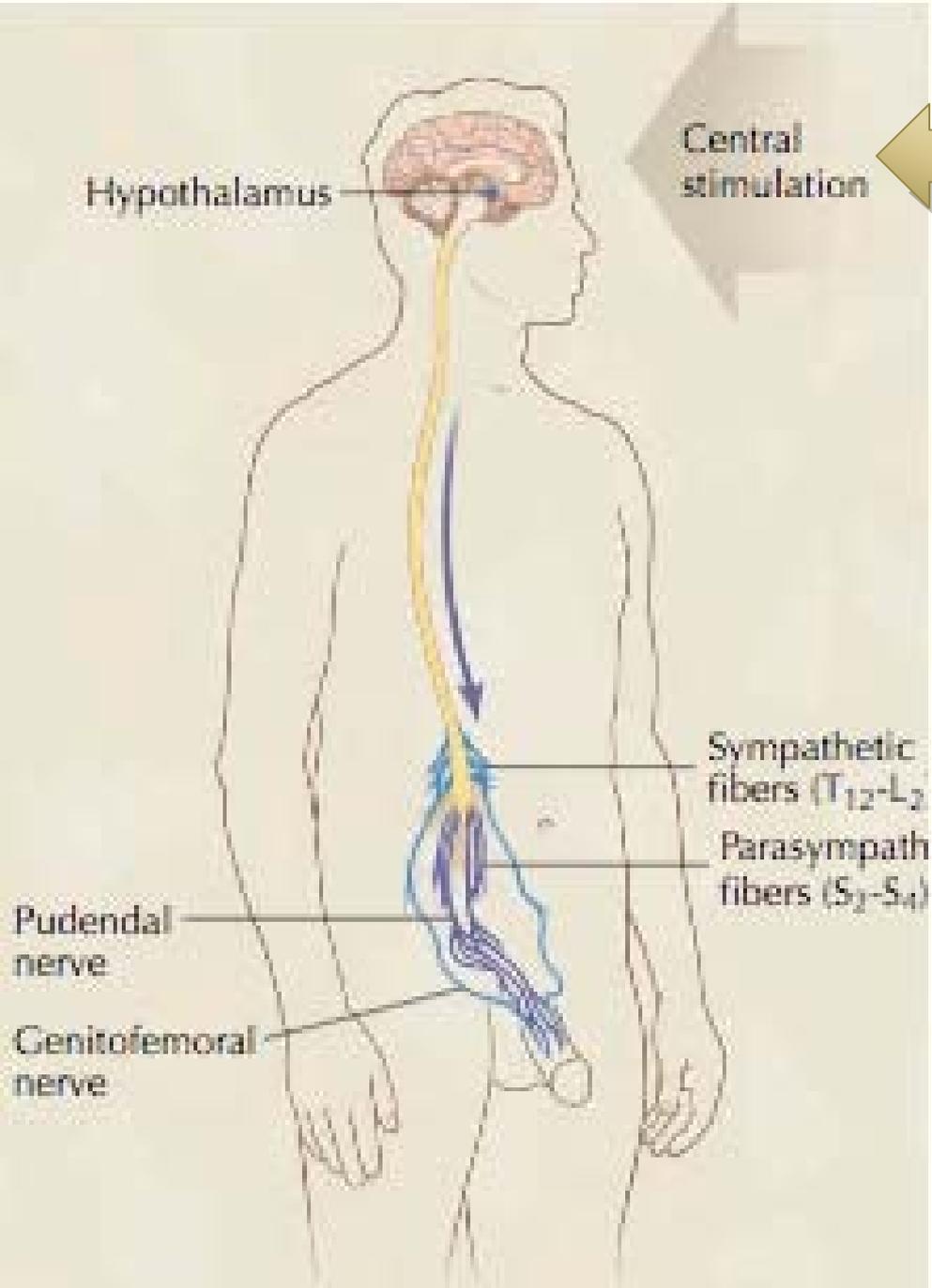


□ Afferents

- Pudendal (S₂-4)
 - Dorsal penile n.
- Scrotum
 - Ilioinguinal
 - Genitofemoral

Lesions above sacral cord:
no sensory testing
available via pinprick,
light touch, temp



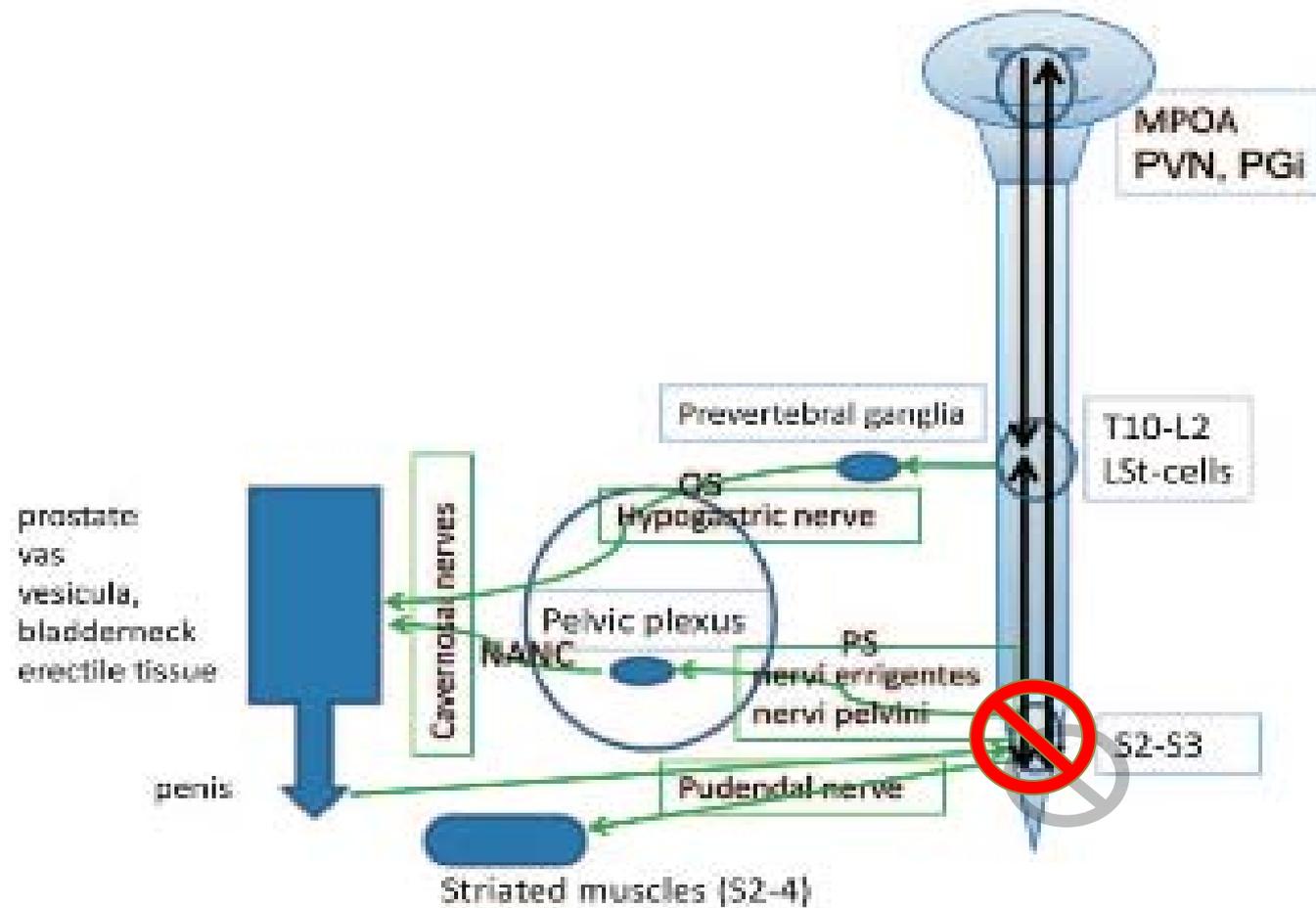


▣ Afferents

- ▣ 'Central afferents'
 - ▣ Tactile stimulation from higher dermatomes
 - ▣ AV
 - ▣ Olfactory
 - ▣ Emotional/Imaginary
- ▣ Processed cortically, then to the hypothalamus, then to the thoracolumbar and sacral centers
- ▣ Psychogenic Erection

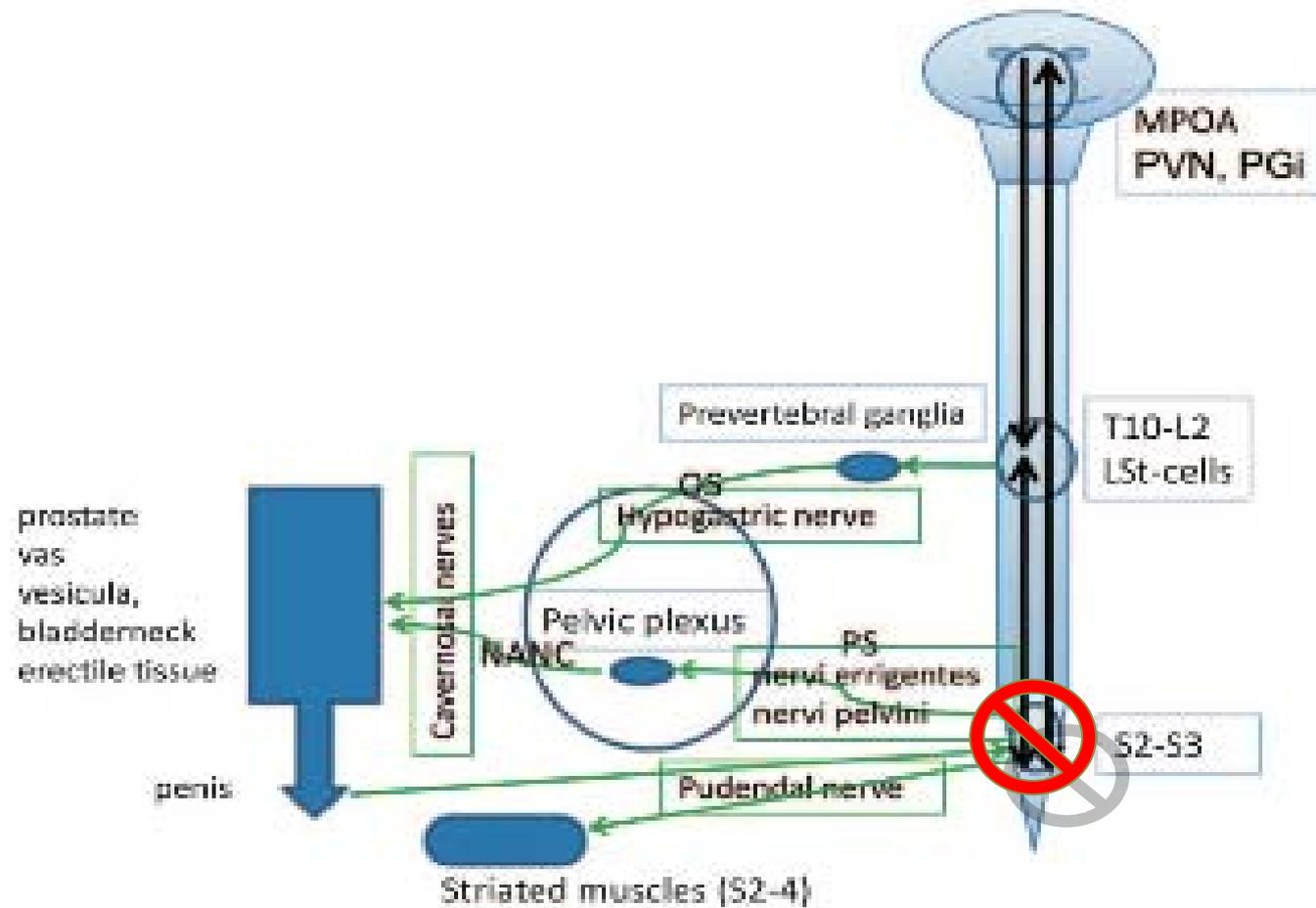
Efferents

- ▣ Sacral Cord (s2-4)
 - parasympathetic
 - ▣ Acetylcholine to modulate NO release
 - ▣ Inhibit noradrenalin release
 - Non-adrenergic non-cholengeric fibers (NANC)
 - ▣ NO, VIP release
- ▣ Thoracolumbar (T12-L2)
 - Sympathetic
 - Through the **hypogastric nerve** to the pelvic plexus then to the cavernous nerve
 - Directly from the S. chain to **pudendal nerve**



Penile Reflex

- Pudendal afferents from penis
- Parasympathetic and NANC relaxing SM
- Sympathetic (hypogastric n.) contracting SM



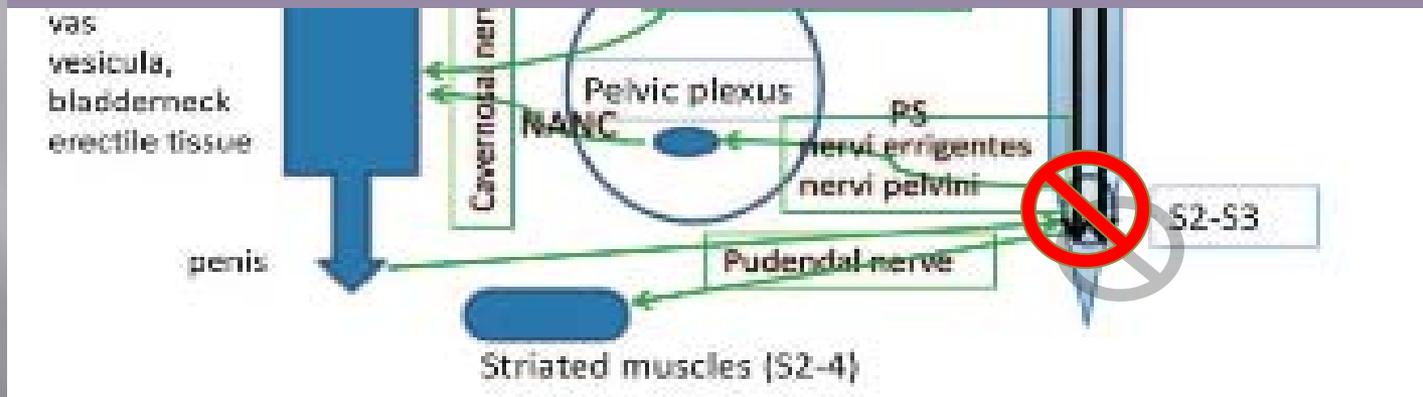
- Sacral lesion should have **NO ERECTILE FUNCTION**
 - Report no reflexive erections
 - Tend to have psychogenic erections

- **Supra T9 Lesions**

- Have reflexive erections
- No psychogenic erections

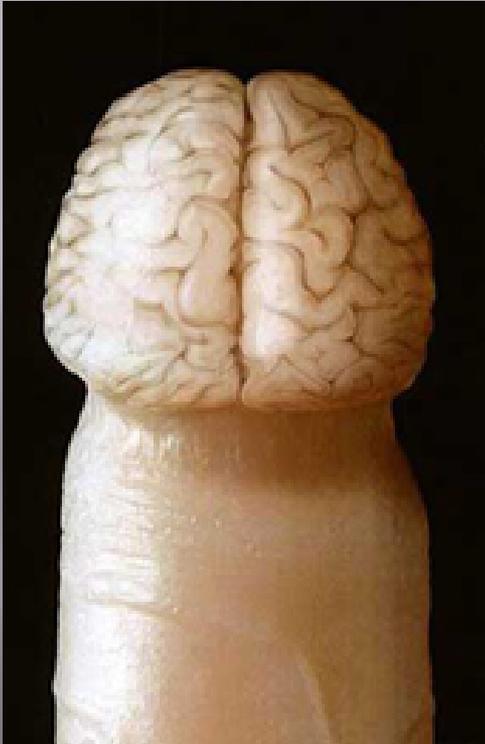


Sensation is about completeness

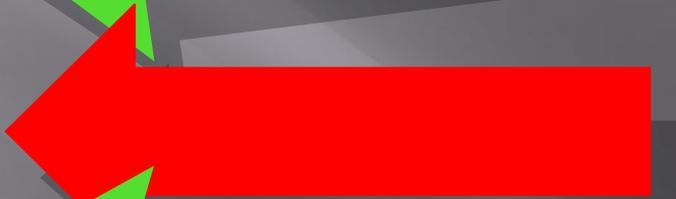


- ▣ **Sacral lesion should have NO ERECTILE FUNCTION**
 - Report no reflexive erections
 - Tend to have psychogenic erections

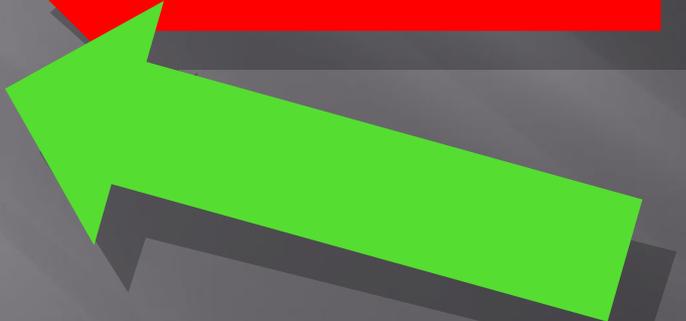
Central Regulation



Catecholamine:
L-dopa
amphetamines
MAOI



Serotonin:
generally inhibitory



Dopamine:
May inhibit or
stimulate erections

Treatment Options

▣ Implants

- Three advantages:
 1. Keep an condom catheter on (semi-rigid)
 2. Keep penis upright for self catheter with decreased dexterity (hinged, semi-rigid)
 3. Penetration during intercourse (inflatable)
- Patient specific factors need to be considered, dexterity, duration of use (implantation at relatively early ages), reoperation rates, body image, sexual dysfunction, etc
- Increased complication rates in SCI
 - ▣ 5y follow up 13% complication
 - ▣ Overall infection rate 10%
 - ▣ Extrusion (Semi-rigid 19%, inflatable 2.4%)
- Decreased sensation can lead to pressure and abrasion trauma

SCI Treatment Options

- ▣ Vacuum Device
 - Patients have quite successful (>90%) experiences with erectile function with the vacuum, though satisfaction drops over time.
 - Its is felt to improve sexual relationships, though there is universal dissatisfaction with the device because of the lack of spontaneity
 - Low risk (edema, petechia, abrasions, discomfort)
 - May have diminished penile sensation, therefore constriction rings removal has been forgotten
- ▣ MUISE: 65% efficacy in UMN lesions
 - Alprostadil may cause significant hypotension, which is concerning for <T6 lesions (due to low baseline sBP)

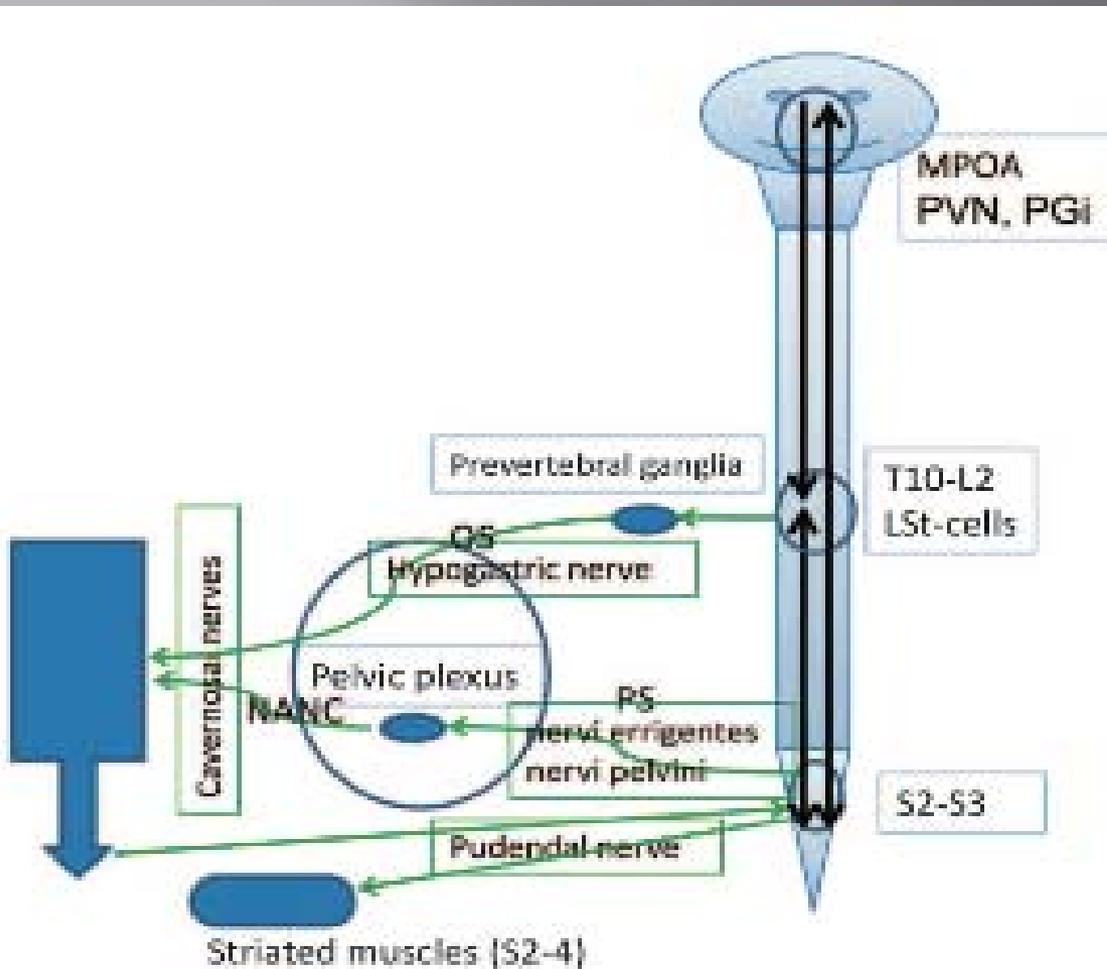
SCI Treatment Options

- ▣ PDE 5: Well studied in UMN lesions with reflexive erectile and psychogenic function
 - Therefore requires either thoracolumbar or sacral sparing
 - Sacral lesions and cauda equina do poorly
 - 75%-94% efficacy, no significant difference between agents in washout studies
 - Higher QoL scores for Cialis due to the increased length of action and spontaneity of activity
 - Same dose usually adequate
 - Same SE profile (HA, flushing) and incidence (2%), may mimic AD
 - ▣ Nitrites cannot be used to treat AD
 - ▣ Alpha blocker may potentate hypotension *caution*
 - Orthostatic symptoms are a concern in <T6 lesions
 - ▣ 26mmHg dec in sBP, 16mmHg in dBP

SCI Treatment Options

ICI

- ▣ Most common agents
 - Prostaglandin E (expensive)
 - Papaverine/phenotlamine
- ▣ Partner involvement is critical due to dexterity issues
- ▣ Priapism: nonSCI 0-3.4%, SCI 15%
 - most common papaverine/phentolamine
 - must start very low doses and titrate up



- Higher than T6, or Sacral lesion (LMN)
 - ICI

- Lower than T6
 - PDE5

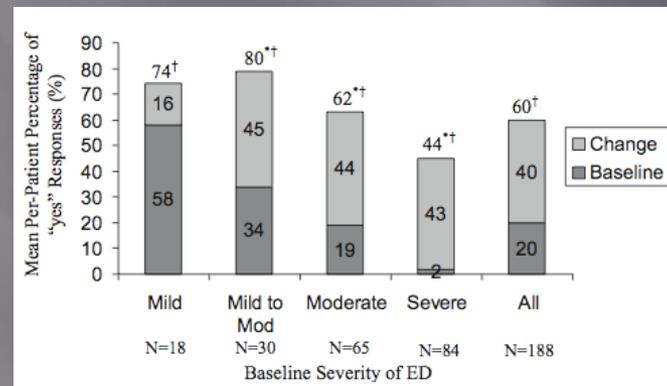
- Prosthesis
 - Bladder
 - Sexual dys.

THE AGING MAN

- ▣ Changes in older men's penises
 - greater latency to erection
 - less turgidity
 - loss of forceful ejaculation
 - decreased volume of ejaculate
 - longer refractory period
 - decreased frequency and duration of nocturnal erection with increasing age
- ▣ Endothelial dysfunction
- ▣ Reduced NO bioavailability
- ▣ Dec libido, sexual activity
- ▣ Increased collagen deposition in the corpora over time
- ▣ Increased medication requirements, increased comorbidities with less room for reversibility to baseline

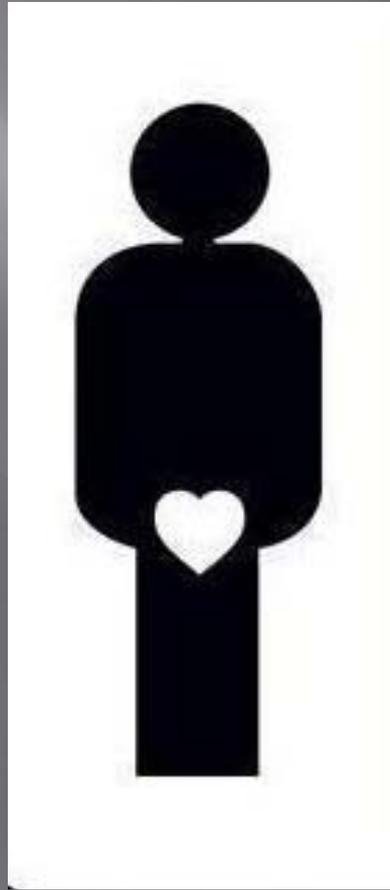
The Aging Man

- ▣ Multi-centre Cialis study for >65y/o with no comorbidities
 - 1900 patients with 12w of PRN use 20mg Cialis
 - 187 centers participated
 - Improvement from 12.8 to 20.1 IIEF score



- 73% of patients had successful intercourse within the 36hrs
 - ▣ 64% had successful intercourse between 24-36hr

Heart vs. Penis



The Cardiovascular Risk

Broken heart ? Mended penis

- ▣ ACS in US: 1542/1million (men 55-62)
 - Predicted 52 MIs in the PDE5 population. Only 15 were documented
- ▣ The risk of PDE 5 inhibitors is related to the functional capacity of the patient then the medication
- ▣ PDE5 present in vascular tissue, therefore causes both arterial and venous dilation, resulting in a clinically insignificant drop in systolic and diastolic BP.
- ▣ QT interval prolongation is a marker of lengthened ventricular repolarization, and can lead to V tach.
 - Levitra causes boarderline QT prolongation at 80mg

Risk of Cardiac Event

Adverse Cardiovascular Events

- ▣ Cialis: MI and CVA reporting's were less than the expected 0.6 MI/100pt years
 - ▣ Placebo Arms had increased MI's when patients had concomitant DM or HTN
- ▣ Viagra: no difference in 30 RTC for MI and CVA between placebo and viagra
- ▣ Levitra: No difference in Placebo and Tx arms in MI, Stroke, Angina events

Risk of Cardiac Event

- ▣ Sex on the heart
 - Equal to mild/moderate activity
 - ▣ Pre-orgasm 2-3mets, Orgasm 4mets
 - ▣ Shoveling driveway, 10-12mets
 - HR <130, sBP <170
- ▣ Sexual dysfunction after MI, Angina, CHF, CABG, PCI:
 - 25% to baseline
 - 25% no sexual function
 - 50% deteriorated from baseline
 - *30% improvement in transplant patient
- ▣ Death during sex: 0.6% of all sudden death cases

Safe sex in cardiac patients?

Risk Stratify to council (Princeton Consensus Panel)

- ▣ Low risk: <3 factors: Any treatment is indicated
 - recent (<2w) MI, Stable angina, mild CHF, HTN, valve disease
- ▣ Intermed risk (>3 factors): Should be evaluated prior to therapy
 - Pass stress test at 5 mets, no restrictions
- ▣ High risk: refer for eval prior to resuming sexual activity. 1.10%/year of MI
 - unstable angina, uncontrolled HTN, severe CHF, MI<2wks ago, sig arrhythmias, valve dz, cardiomyopathy
 - MI post Sexual activity
(20/1million vs. 6/1million with no risk factors)

Caution with PDE5

- ▣ AHA/ACC guidelines caution use of PDE5i in:
 1. active ischemia, sig CHF, sig Hypotension
 2. Multidrug antihypertensive therapy
 3. Liver/Renal failure
 4. Cimetidine or erythromycin (cyp3A4)

Mended Ticker ? Mended Pecker

- ▣ ED precedes angina by 2-3 years
 - Precedes MI by 3-5 years
- ▣ Testosterone deficiency is linked to
 - All cause mortality
 - Cardiovascular mortality
 - DMII, Met Syndrome, dyslipidemia,

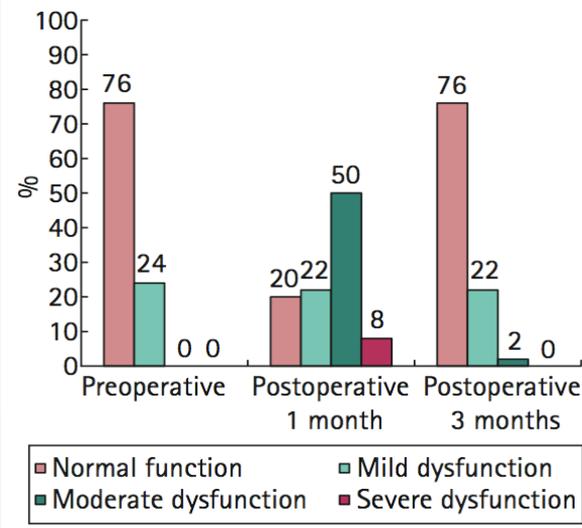
“Testosterone testing should be performed in all with ED, especially with obesity, DM, CHF, or those that do not respond to PDE5” (Jackson, 2010)
- ▣ PCI, CABG, Transplant, improve sexual dysfunction, allows freedom from anti-HTN and nitro. No conclusive effect on erectile function
- ▣ Adding a Statin to a PDE 5 failure
 - Modest but significant gains (2-3 IIEF points) after 3 months
- ▣ Improving cardiac health through modifiable RF

Doc, what did you do to me?



- 50 men followed prospectively after cysto/URS procedures
 - 76% Normal EF, 12% mild EF at baseline
 - Compared all procedures, including stented +/- string

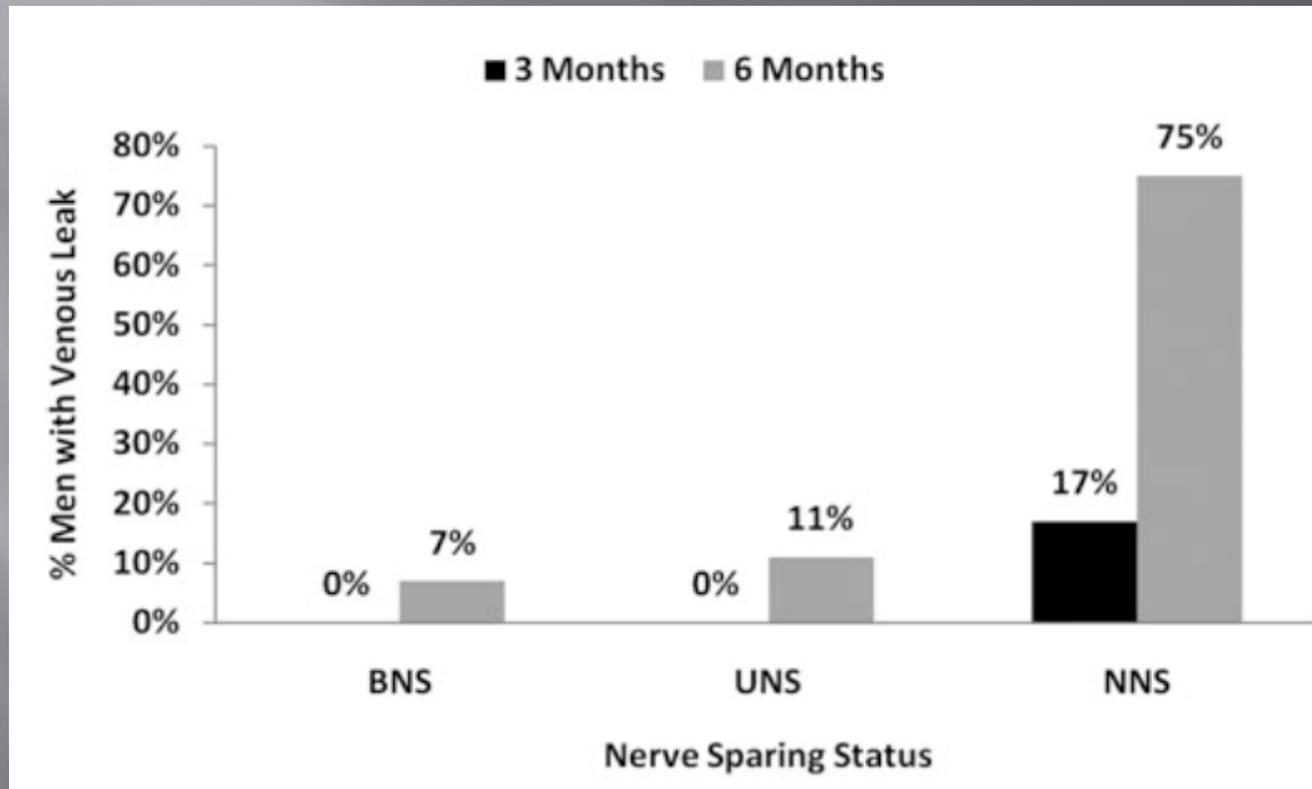
FIG. 1. Changes in ED distribution over time.



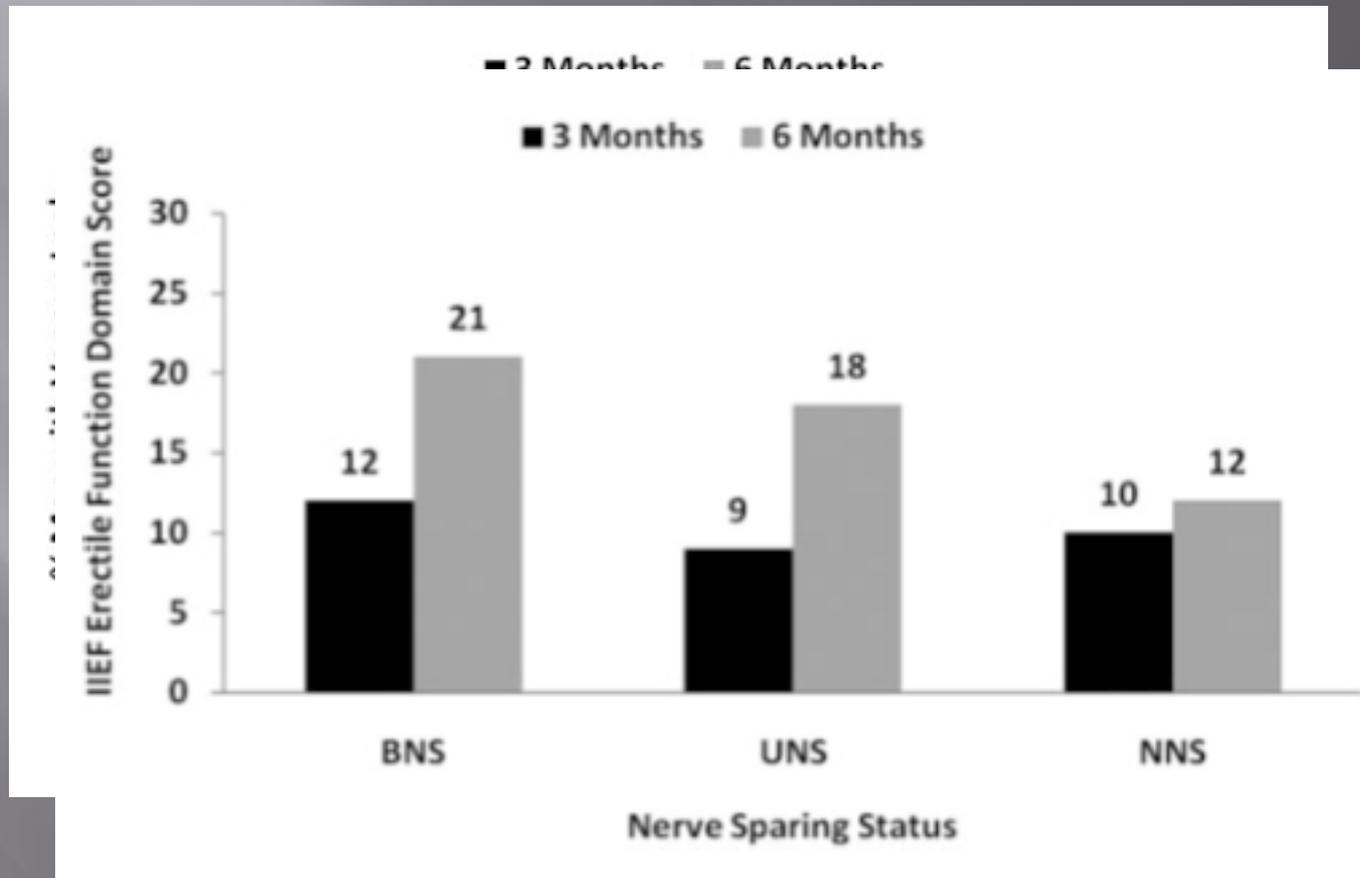
Prostate Cancer-RRP

- ▣ Up to 50% of patients for RRP have baseline ED
- ▣ 20% of patients have up to 15% penile shrinkage after RRP (0.4– 2cm between 1-2y)
- ▣ HR-QoL recover within 6m of surgery, however sexual function remains significantly affected at >1y
- ▣ With bilateral nerve sparing RP 14-90% of patients show full return to baseline
 - Meta-analysis bilat nerve sparing ~55%, under 60y.o. 77%, older 60 61%, unilat 47%
 - Non Nerve sparing 0-14%
- ▣ Dysfunction is due to nerve signal interruption, and venous leak from fibrosis and proximal venous shunts
 - Decreased nerve supply may lead to smooth cell apoptosis, increased collagen, decreased elastin, ultrastructural changes in tunica
 - Poor innervation = venous leak

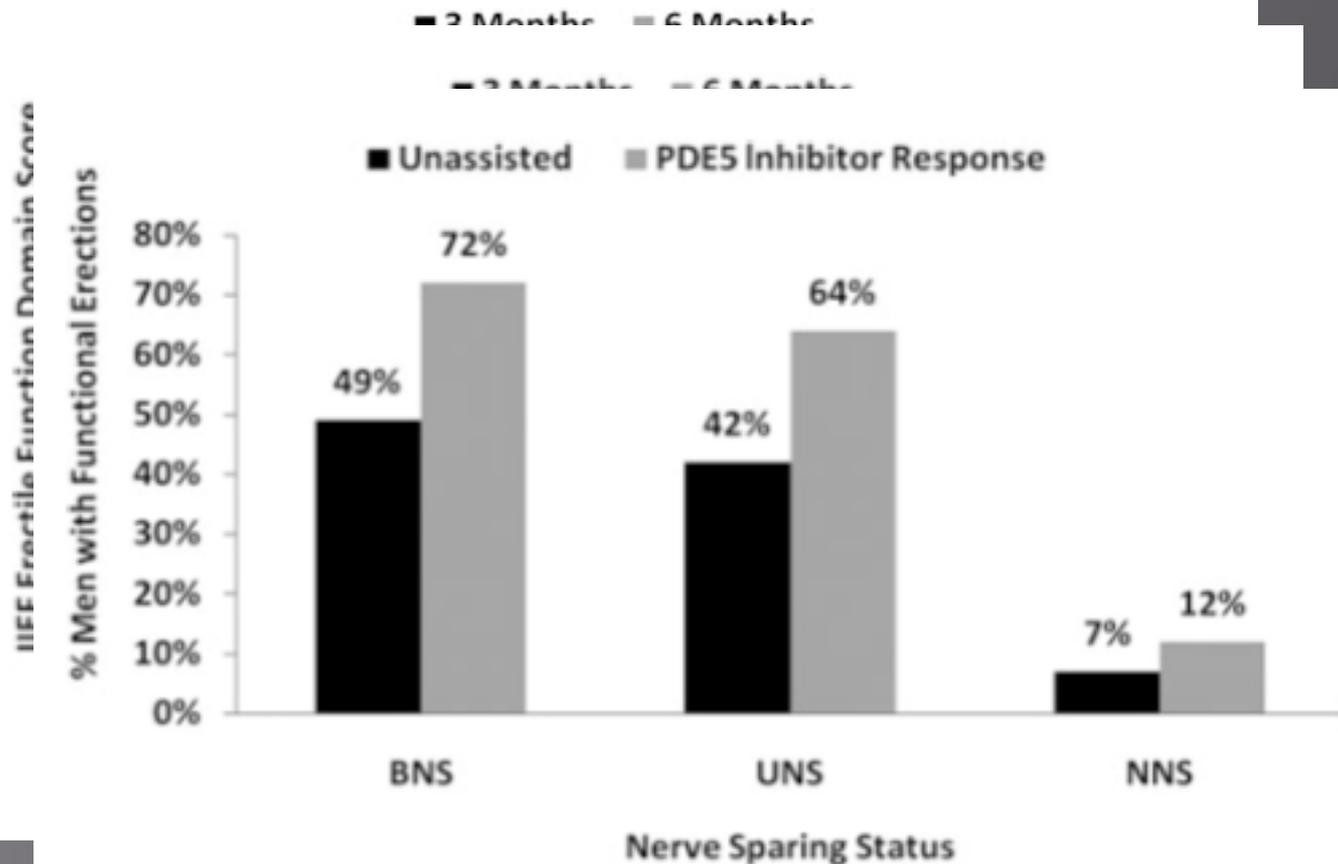
ED and RRP



ED and RRP



ED and RRP



Penile/Erectile Rehabilitation

- ▣ Penile rehabilitation has been researched with no long term evidence on efficacy
- ▣ Several different protocols
 - On demand PDE5
 - Daily lower dose PDE5 +/- Oral PRN
 - Regular ICI 3/week
 - ▣ Oral Scheduled
 - ▣ Oral PRN
 - ICI or Oral 3/week to achieve erection
 - Daily Vacuum devices
 - ▣ Immediate vs. Delayed

	Intervention	Design	n	Significant Findings
Schwartz 2004	PRN PDE5	Prospective	21	Stable Smooth muscle on Bx in 50mg, increased in 100mg
Bannowski 2008	Daily PDE5 (BNS responders)	RCT (No tx)	41	Higher IIEF and spontaneous, effective erections (47% vs. 28)
McCullogh 2008	Daily PDE5	RCT	54	Increased rigidity and spontaneous erections
Nadipati 2006	Daily PDE5, ICI 3/week	prospective	22	Lower ICI doses, early return to activity, increased satisfaction
Mulhall 2005	Erections 3/week PDE or ICI	Prospective	132	Increased spontaneous erections, higher IIEF scores
Montorsi 1999	ICI 3/week	RCT	30	Increased spontaneous erections
Raina 2006	Daily Vacuum	RCT	109	Improved sexual satisfaction, increased spont. erections
Kohler 2007	Daily Vacuum Delayed/immed	RCT	28	No difference in when to start vacuum for penile shortening or

Penile/Erectile Rehabilitation

Oral PDE5

- ▣ Biopsy studies pre/post prostatectomy with dose response to viagra showed increased SM growth at 100mg
- ▣ On demand, and daily viagra tends to double spontaneous erections and the quality of erections at one year. Daily viagra has higher spontaneous erection rates, and patients tend to have earlier return of erections.
- ▣ Higher doses (100mg) of daily viagra may have more sustained findings after a washout period of 2months, compared to lower doses
- ▣ Tolerability and safety were not an issue in any study

Penile/Erectile Rehabilitation

- ▣ Vacuum devices
 - May help with penile shrinking, though studies have shown length loss is $<0.5\text{cm}$ in 15-20% of men, and most rapid loss happens between time of surgery and catheter removal
 - For rehabilitation have been used starting at one month or six months, daily for 10 minutes without constriction ring. Penile shorting was not fully reversed in delayed group
 - NNS patients: 60-80% have functional erections with vacuum, and increased rates of spontaneous erections (17% vs. 10% for control)

Penile/Erectile Rehabilitation

- ▣ ICI (two studies)
 - RTC (alprostadil 3/week vs. no treatment)
 - ▣ 12 weeks of ICI, 80% completion, 17% complication rate
 - ▣ Functional erection without ICI (67% vs. 20%)
 - ▣ Improved frequency of spontaneous erections
 - Prospective series (Viagra or ICI 3/w vs. PRN viagra)
 - ▣ Functional erections (52% vs. 19%)
 - ▣ Higher IIEF scores*with both groups using aids

Radiation

EBRT: Progressive arterial damage (loss of SM, intimal thickening, occlusion after 5d*)

- Typically normal neuro exam, abnormal doppler study
- Dose dependant effect to the penile bulb causing arterial dysfunction and fibrosis
- Time dependant, late complication (36-50%)
- 27% after 1y, 36% after 2y
- 80% have venous leak at high doses
- Age, HTN, DM are poor predictors of ED after EBRT
- IMRT has more accurate radiation targeting, and can decrease cavernous tissue exposures by 40-50%

PDE5 are effective in EBRT, but will show reduced efficacy over time (80% at 1y, 40% at 3y)**

Radiation

Brachytherapy: Multifocal etiology of ED by mechanical needle injury, rad toxicity (bulb and nerves)

- 76% with functional erections (at 1y) in meta-analysis of 5 studies
- Those who start with good erections show the largest change in function
- Viagra post BT: 85% response rate, correlating strongly to pre-treatment IIEF

ADT

- ▣ Orchiectomy > LHRH
- ▣ Incidence of sexual dysfunction is poorly studied
- ▣ Decreased libido and erectile function, QoL
 - Theoretically reversible with cessation of tx
 - SEER database
 - ▣ 70% of men developed ED
 - ▣ 51% who had some sexual interest prior had none after
 - ▣ 75% of men stopped all sexual activity
- ▣ 44% response rate to PDE5, and 47% response rate to combination tx (PDE+ICI)
- ▣ Age<70, DM were found to predictive of ED

Social Factors: The Partner

More than the Man: Partner Influence

- ▣ Men are more likely to seek help if partner is unhappy
- ▣ Men believe ED threatens relationships
- ▣ Couples which pursue ED treatment typically continue to use it longer than those who do not
- ▣ Improvement in sexual dysfunction of one partner improves satisfaction of sex in the other partner

How do partners influence treatment?

FEMALES Study

- ▣ Partners of men enrolled in the MALES population based ED study were questioned using a 65pt questionnaire (77% response, 430 women)
- ▣ 46% US, 40% European, 14% SA, 91% married/common law
- ▣ Female partner beliefs which increase men's likelihood of seeking treatment were concordant with men's beliefs

FEMALES study questionnaire

Nature of ED

- ▣ Permanent
- ▣ Severity
- ▣ Acknowledgment

Cause of ED

- ▣ associated ED with illness/meds
- ▣ associated ED with psychiatric illness

Attitudes to Sexual Activity before onset of ED

- ▣ More satisfied with sexual activity

Perception of impact of ED on QoL

Attitudes to medical treatment

Contact with Health Care professionals

Couples sex life satisfaction:

ORIGINAL RESEARCH—COUPLES' SEXUAL DYSFUNCTION

Vardenafil Improves Sexual Function and Treatment Satisfaction in Couples Affected by Erectile Dysfunction (ED): A Randomized, Double-Blind, Placebo-Controlled Trial in PDE5 Inhibitor-Naïve Men with ED and Their Partners

David Edwards, MB, BS,* Geoff Hackett, MD, John Curram, PhD[†]

*The White House Surgery, Chipping Norton, Oxfordshire, UK

ORIGINAL RESEARCH—COUPLES' SEXUAL DYSFUNCTIONS

Improvement in Quality of Sexual Life in Female Partners of Men with Erectile Dysfunction Treated with Sildenafil Citrate: Findings of the Index of Sexual Life (ISL) in a Couple Study

Marie Chevret-Méasson, MD,* Emmanuel Lavallée, MSc,[†] Sylvie Troy, MD,[‡] Benoit Arnould, PhD,[‡] Séverine Oudin, PhD,[§] and Beatrice Cuzin, MD, MSc[¶]

, France; [†]Mapi Values, Lyon, France; [‡]Mapi-Naxis,

Sexual Medicine

Associate Editor
Michael G. Wyllie

Editorial Board
Ian Eardley, UK
Jean Fourcroy, USA
Sidney Glina, Brazil
Julia Heiman, USA

Chris McMahon, Australia
Bob Millar, UK

Alvaro Morales, Canada
Michael Perelman, USA

Marcel Waldinger, Netherlands

The COUPLES-project: a pooled analysis of patient and partner treatment satisfaction scale (TSS) outcomes following vardenafil treatment

Raymond C. Rosen, William A. Fisher*, Manfred Beneket†, Martin Homering‡ and Thomas Evers‡

*New England Research Institutes, Watertown, MA, USA; *University of Western Ontario, London, Ontario, Canada; †Bayer Vital GmbH, Leverkusen, and ‡Bayer HealthCare AG, Wuppertal, Germany*

Accepted for publication 17 November 2006

Couples Sex Life Satisfaction:

- ▣ Open label vs. Double blinded studies
- ▣ IIEF5: 5 domains of erectile function
- ▣ EDITS: satisfaction of treatment
- ▣ TSS: ease with erection, erectile function satisfaction, pleasure from sexual activity, satisfaction with orgasms, confidence to complete sexual act, satisfaction with medication
- ▣ SEP 2, 3: were you able to insert your penis, did your erection last long enough to have successful intercourse
- ▣ SEAR: Sexual confidence, Sexual relationship
- ▣ ISL: female sexual life satisfaction, sex drive, general life satisfaction

Couples sex life satisfaction

- ▣ Improved aspects of erectile function
- ▣ Improved sexual experiences between partners
- ▣ Improved pleasure with sexual activity
- ▣ Improved sex drive
- ▣ Significant satisfaction of treatment
- ▣ Significant satisfaction with orgasms

Couples Sex Life Satisfaction:

- ▣ Open label vs. Double blinded studies
- ▣ Conducted by physicians, and funded by drug companies
- ▣ One study per drug per continent + subgroup analysis (SA, Europe, Asia, Australia)
- ▣ Advertised recruitment via newspaper and radio advertisements

Couples ... life Satisfaction

ORIGINAL RESEARCH—ED PHARMACOTHERAPY

The South Australian Couples Sildenafil Study: Double-Blind, Parallel-Group Randomized Controlled Study to Examine the Psychological and Relationship Consequences of Sildenafil Use in Couples

James Hundermark, MBBS, FRANZCP,* Adrian Esterman, MSc, PhD, AStat,[†]
David Ben-Tovim, PhD, MBBS, FRANZCP,[‡] Mary-Anne Austin, Dip Appl Sc (Nsg),[§] and
Melissa Dougherty, BA (Hons) Psych[‡]

- ▣ Randomized double blinded study measuring relationship satisfaction after six months of viagra vs. placebo
- ▣ 39 couples randomized. IIEF-5 scores improved in viagra group

ORIGINAL RESEARCH—ED PHARMACOTHERAPY

The South Australian Couples Sildenafil Study: Double-Blind, Parallel-Group Randomized Controlled Study to Examine the Psychological and Relationship Consequences of Sildenafil Use in Couples

- ▣ Dyadic Adjustment Scale (DAS) questionnaire measured couple's relationship satisfaction
 - Dyadic Consensus
 - Dyadic Cohesion
 - Dyadic Satisfaction
 - Affectionate Expression
- ▣ No difference in those with improved erectile function (IIEF5), improved sexual satisfaction (EDITS) of the Viagra group and placebo group in terms of DAS scores

In this together?

Patients Responding to Phosphodiesterase Type 5 Inhibitor Therapy—What Do Their Sexual Partners Know?

Theodor Klotz, MD, MPH,* Mike Mathers, MD,[†] Rosemarie Klotz, MD,[‡] and Frank Sommer, MD[§]

*Department of Urology, Klinikum Weiden, Weiden, Germany; [†]Urological Ambulatory, Remscheid, Germany; [‡]Internal Medicine Ambulatory, Munich, Germany; [§]Institute of Men's Health—Department of Urology, University of Hamburg, Hamburg, Germany

DOI: 10.1111/j.1743-6109.2008.00346.x

- ▣ German study looking at all responders to PDE5 inhibitors after three months of use
- ▣ The less severe the ED (on IIEF-5 questionnaire), the younger the patient, the more frequent use
- ▣ Large proportion of men in stable relationships do not disclose use to their partners
 - Severe ED: 7% have not told their partner
 - Moderate ED: 53% have not told their partner
 - Mild ED: 79% have not told their partner

...in this together?

- ▣ More likely to seek help if spouse was supportive
- ▣ Spouse influences decision to seek treatments and adherence to use
- ▣ Dissatisfaction or failure to support treatment leads to increased attrition

What to tell patients

What to Tell Patients

- ▣ Encourage partner participation
- ▣ Explore psychogenic aspects of ED
 - Group therapy and psychotherapy are effective and
- ▣ Educate: Natural history, treatment options
- ▣ Risk: Age 40, 15% + 10-15%/decade
 - Add 15% for each significant risk factor
- ▣ Lifestyle modification
 - What are your weight goals – direct improvement
 - HgbA1c – direct improvement
- ▣ Identify special risk populations

Don't Bother...

ORIGINAL RESEARCH—ED PHARMACOTHERAPY

Five Years After the Launch of Viagra in Korea: Changes in Perceptions of Erectile Dysfunction Treatment by Physicians, Patients, and the Patients' Spouses

60 Urologists, 60 Internists/GP's were surveyed

- ▣ After Viagra release
 - 10% rise in Urologists ED visits
 - 35% rise in Internist/GP visits

Five Years After the Launch of Viagra in Korea: Changes in Perceptions of Erectile Dysfunction Treatment by Physicians, Patients, and the Patients' Spouses

- ▣ Reason for increased visits:
 1. Heightened patient awareness
 2. Perception of need for treatment
 3. Convenient drug administration
- ▣ Primary care physicians then:
 - Took more interest in ED physiology
 - Became more confident in treatment
 - Initiated discussions on ED
- ▣ 90% of patients who presented to primary care, presented with a different chief complaint

Thank You

1. O'Connor E, McCabe M, Conaglen H, Conaglen J. Attitudes and experiences: Qualitative perspectives on erectile dysfunction from the female partner. *J Health Psychol*. 2011. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/21586642>. Accessed May 30, 2011.
2. Yildiz N, Gokkaya NKO, Koseoglu F, Gokkaya S, Comert D. Efficacies of papaverine and sildenafil in the treatment of erectile dysfunction in early-stage paraplegic men. *Int J Rehabil Res*. 2011;34(1):44-52.
3. Dimitriadis F, Karakitsios K, Tsounapi P, et al. Erectile function and male reproduction in men with spinal cord injury: a review. *Andrologia*. 2010;42(3):139-165.
4. Chevret-Méasson M, Lavallée E, Troy S, et al. Improvement in quality of sexual life in female partners of men with erectile dysfunction treated with sildenafil citrate: findings of the Index of Sexual Life (ISL) in a couple study. *J Sex Med*. 2009;6(3):761-769.
5. Chevret-Méasson M, Lavallée E, Troy S, et al. Improvement in quality of sexual life in female partners of men with erectile dysfunction treated with sildenafil citrate: findings of the Index of Sexual Life (ISL) in a couple study. *J Sex Med*. 2009;6(3):761-769.
6. Tophill PR, Linton KD. Letter to the editor on "Sildenafil in spinal cord injury" by Khorrami et al. (2009). *Int. J. Androl*. 2010;33(6):865.
7. Everaert K, de Waard WIQ, Van Hoof T, et al. Neuroanatomy and neurophysiology related to sexual dysfunction in male neurogenic patients with lesions to the spinal cord or peripheral nerves. *Spinal Cord*. 2010;48(3):182-191.
8. Klotz T, Mathers M, Klotz R, Sommer F. Patients responding to phosphodiesterase type 5 inhibitor therapy: what do their sexual partners know? *J Sex Med*. 2007;4(1):162-165.
9. Tatarevic E. Re: testosterone levels among men with spinal cord injury: relationships between time since injury and laboratory values. *Am J Phys Med Rehabil*. 2009;88(12):1033-1035.
10. Khorrami MH, Javid A, Moshagh D, et al. Sildenafil efficacy in erectile dysfunction secondary to spinal cord injury depends on the level of cord injuries. *Int. J. Androl*. 2010;33(6):861-864.
11. Ramos AS, Samsó JV. Specific aspects of erectile dysfunction in spinal cord injury. *Int. J. Impot. Res*. 2004;16 Suppl 2:S42-45.
12. Lombardi G, Macchiarella A, Cecconi F, Del Popolo G. Ten-year follow-up of sildenafil use in spinal cord-injured patients with erectile dysfunction. *J Sex Med*. 2009;6(12):3449-3457.
13. Sakamoto H. The neurobiology of psychogenic erectile dysfunction in the spinal cord. *J. Androl*. 2010;31(6):519-526.
14. Hundertmark J, Esterman A, Ben-Tovim D, Austin M-A, Dougherty M. The South Australian couples sildenafil study: double-blind, parallel-group randomized controlled study to examine the psychological and relationship consequences of sildenafil use in couples. *J Sex Med*. 2007;4(4 Pt 2):1126-1135.
15. Watkins Bruner D, James JL, Bryan CJ, et al. Randomized, double-blinded, placebo-controlled crossover trial of treating erectile dysfunction with sildenafil after radiotherapy and short-term androgen deprivation therapy: results of RTOG 0215. *J Sex Med*. 2011;8(4):1228-1238.
16. Mulhall JP, Bella AJ, Briganti A, McCullough A, Brock G. Erectile function rehabilitation in the radical prostatectomy patient. *J Sex Med*. 2010;7(4 Pt 2):1687-1698.
17. Soh J, Kaiho Y, Kikuchi E, et al. Characteristics and management of erectile dysfunction after various treatments for prostate cancer. *Int. J. Urol*. 2010;17(8):689-697.
18. Reich O. What do we know (or think we know) about erectile dysfunction following laser treatments for lower urinary tract symptoms? *Eur. Urol*. 2010;58(2):212-213.
19. Chen Y, Dai Y, Wang R. Treatment strategies for diabetic patients suffering from erectile dysfunction. *Expert Opin Pharmacother*. 2008;9(2):257-266.
20. Hatzichristou D, Gambla M, Rubio-Aurioles E, et al. Efficacy of tadalafil once daily in men with diabetes mellitus and erectile dysfunction. *Diabet. Med*. 2008;25(2):138-146.
21. Anon. A statement on the use of sildenafil in the management of sexual dysfunction in patients with cardiovascular disease. Heart and Stroke Foundation of Canada. Canadian Cardiovascular Society. *Can J Cardiol*. 1999;15(4):396-399.
22. Wang C, Nieschlag E, Swerdloff R, et al. Investigation, treatment, and monitoring of late-onset hypogonadism in males: ISA, ISSAM, EAU, EAA, and ASA recommendations. *J. Androl*. 2009;30(1):1-9.
23. Seyam R, Mohamed K, Akhras AA, Rashwan H. A prospective randomized study to optimize the dosage of trimix ingredients and compare its efficacy and safety with prostaglandin E1. *Int. J. Impot. Res*. 2005;17(4):346-353.
24. Montague DK, Jarow J, Broderick GA, et al. AUA guideline on the pharmacologic management of premature ejaculation. *J. Urol*. 2004;172(1):290-294.
25. Hackett G, Kell P, Ralph D, et al. British Society for Sexual Medicine guidelines on the management of erectile dysfunction. *J Sex Med*. 2008;5(8):1841-1865.
26. Hatzimouratidis K. Can we cure erectile dysfunction? *Eur. Urol*. 2010;58(2):249-250.
27. Montague DK, Jarow JP, Broderick GA, et al. Chapter 1: The management of erectile dysfunction: an AUA update. *J. Urol*. 2005;174(1):230-239.
28. Montague DK, Barada JH, Belker AM, et al. Clinical guidelines panel on erectile dysfunction: summary report on the treatment of organic erectile dysfunction. The American Urological Association. *J. Urol*. 1996;156(6):2007-2011.
29. Padma-Nathan H. Diagnostic and treatment strategies for erectile dysfunction: the "Process of Care" model. [University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School]. *Int. J. Impot. Res*. 2000;12 Suppl 4:S119-121.
30. Wespes E, Amar E, Hatzichristou D, et al. EAU Guidelines on erectile dysfunction: an update. *Eur. Urol*. 2006;49(5):806-815.
31. Fazio L, Brock G. Erectile dysfunction: management update. *CMAJ*. 2004;170(9):1429-1437.
32. Anon. [Guideline for diagnosis and therapy of libido and erection disorders. Guidelines of the German Society of Urology]. *Urologe A*. 2001;40(4):331-339.
33. Wespes E, Amar E, Hatzichristou D, et al. Guidelines on erectile dysfunction. *Eur. Urol*. 2002;41(1):1-5.
34. Hatzimouratidis K, Amar E, Eardley I, et al. Guidelines on male sexual dysfunction: erectile dysfunction and premature ejaculation. *Eur. Urol*. 2010;57(5):804-814.
35. Qaseem A, Snow V, Denberg TD, et al. Hormonal testing and pharmacologic treatment of erectile dysfunction: a clinical practice guideline from the American College of Physicians. *Ann. Intern. Med*. 2009;151(9):639-649.
36. Hellstrom WJG, Montague DK, Moncada I, et al. Implants, mechanical devices, and vascular surgery for erectile dysfunction. *J Sex Med*. 2010;7(1 Pt 2):501-523.
37. Garber BB. Inflatable penile prostheses for the treatment of erectile dysfunction: an update. *Expert Rev Med Devices*. 2008;5(2):133-144.
38. Lightfoot AJ, Rosevear HM, Kreder KJ. Inflatable penile prostheses: an update. *Curr Opin Urol*. 2010;20(6):459-464.
39. Vecchio M, Navaneethan SD, Johnson DW, et al. Interventions for treating sexual dysfunction in patients with chronic kidney disease. *Cochrane Database Syst Rev*. 2010;(12):CD007747.
40. Kimoto Y, Nagao K, Sasaki H, et al. JSSM Guidelines for erectile dysfunction. *Int. J. Urol*. 2008;15(7):564-576.
41. Heidelbaugh JJ. Management of erectile dysfunction. *Am Fam Physician*. 2010;81(3):305-312.
42. Munarriz R. Penile microvascular arterial bypass surgery: indications, outcomes, and complications. *ScientificWorldJournal*. 2010;10:1556-1565.
43. Simmons M, Montague DK. Penile prosthesis implantation: past, present and future. *Int. J. Impot. Res*. 2008;20(5):437-444.
44. Aversa A, Greco E, Bruzziches R, et al. Relationship between chronic tadalafil administration and improvement of endothelial function in men with erectile dysfunction: a pilot study. *Int. J. Impot. Res*. 2007;19(2):200-207.
45. Montorsi F, Adaihan G, Becher E, et al. Summary of the recommendations on sexual dysfunction in men. *J Sex Med*. 2010;7(11):3572-3588.
46. Siddiqi K, Lewis RW. Surgical therapy for the treatment of erectile dysfunction. *Nat Clin Pract Urol*. 2008;5(4):174-175.
47. Sharlip ID, Shumaker BP, Hakim LS, et al. Tadalafil is efficacious and well tolerated in the treatment of erectile dysfunction (ED) in men over 65 years of age: results from Multiple Observations in Men with ED in National Tadalafil Study in the United States. *J Sex Med*. 2008;5(3):716-725.
48. Eid JF. What is new for inflatable penile prostheses? *Curr Opin Urol*. 2009;19(6):582-588.

Questions?

Name _____

Unscramble the words to make a sentence.
about each sentence.

1



is pen in goat My a

My pen is

in a goat.

2



god

My

Wh

4