Managing Sexual Dysfunction in Cancer Patients

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Faculty/Presenter Disclosure

Relationships with commercial interests in the last 20 years

Speaker: Stacy Elliott, MD

- Holder of Stocks/Shares

none

– Grants/Research Support :

CIHR, Neurotrauma funds, Pfizer (female SCI)

– <u>Speakers Bureau/Honoraria/Consulting Fees</u>:

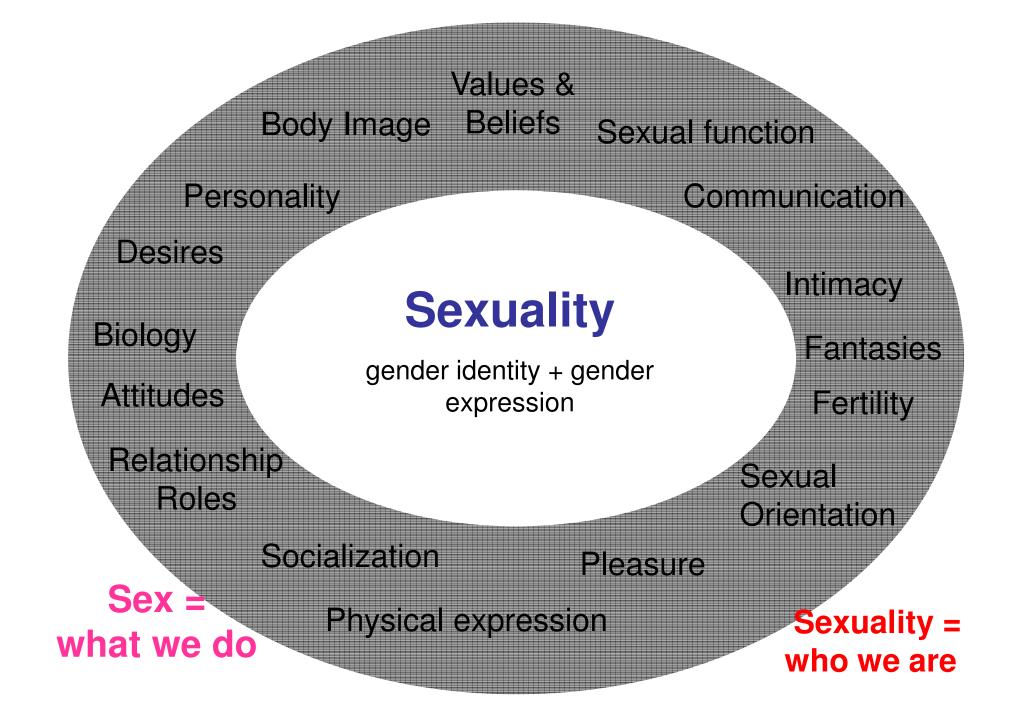
Mylan (testosterone)

Other:

Employee of Vancouver Hospital and Faculty at the University of British Columbia

Mitigating Potential Bias

- All the recommendations involving clinical medicine are based on evidence from well-designed clinical trials published in peer-reviewed journals.
- The faculty of this course and UBC CPD has in no way influenced the information in this talk.
- I have received no direct payment from pharmaceutical companies for this talk.
- All products available in Canada for sexual dysfunction will be discussed



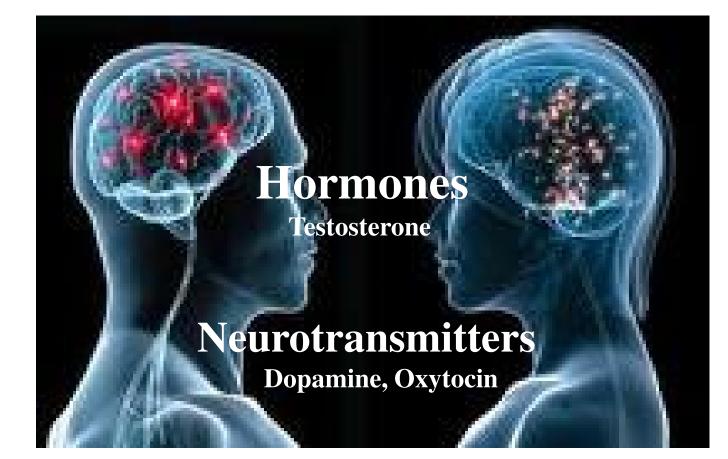
Objectives

- Describe the components of sexual function
- Summarize a Sexual Rehabilitation Framework (SRF) to manage the complexity of changes
- Identify appropriate options for management

Objectives

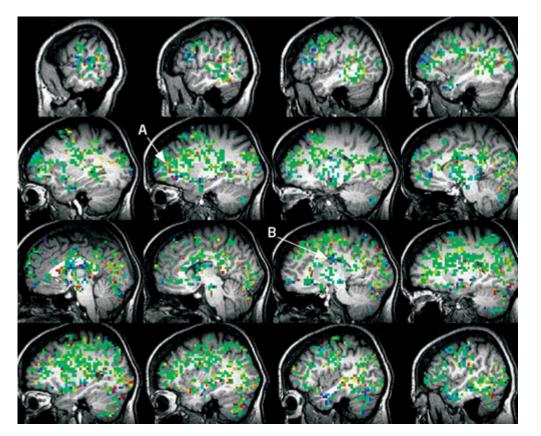
Describe the components of sexual function

Arousal = Brain activation



Brain Sex

Medial Preoptic Area (MPOA) of hypothalamus = pivotal position



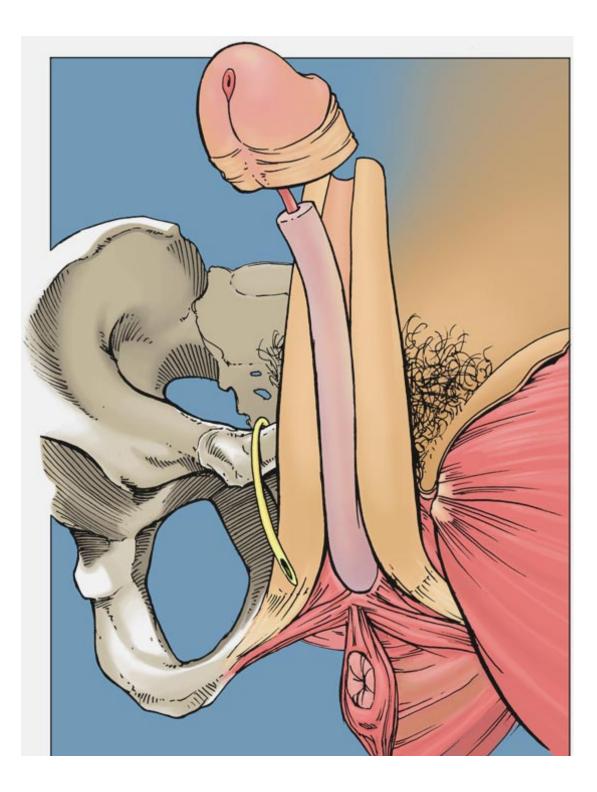
MPOA projects to the -Hypothalamic paraventricular nucleus (HPN) --midbrain (ventral tegmental area) -brainstem nuclei (raphe and gigantocellular)

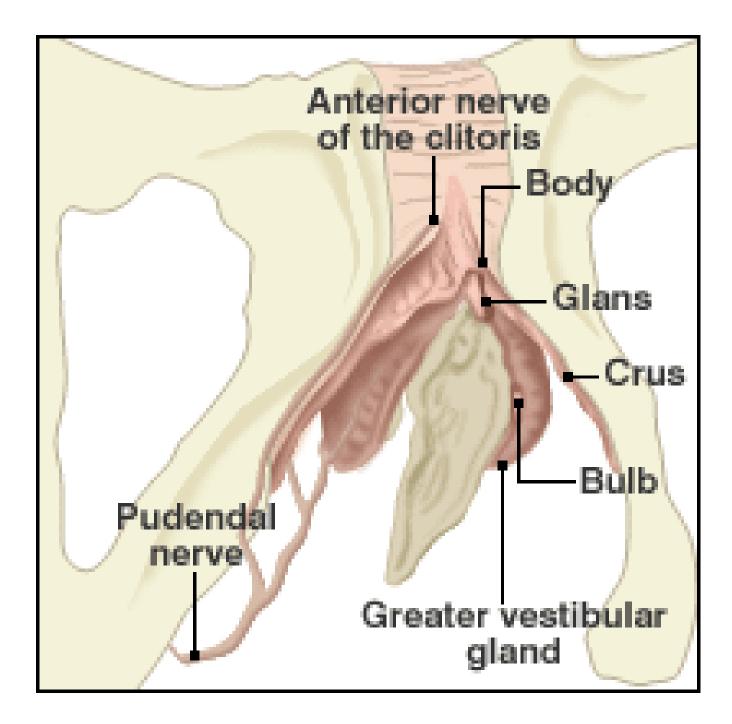
These then, project to the autonomic and somatic spinal centers commanding the peripheral nerves

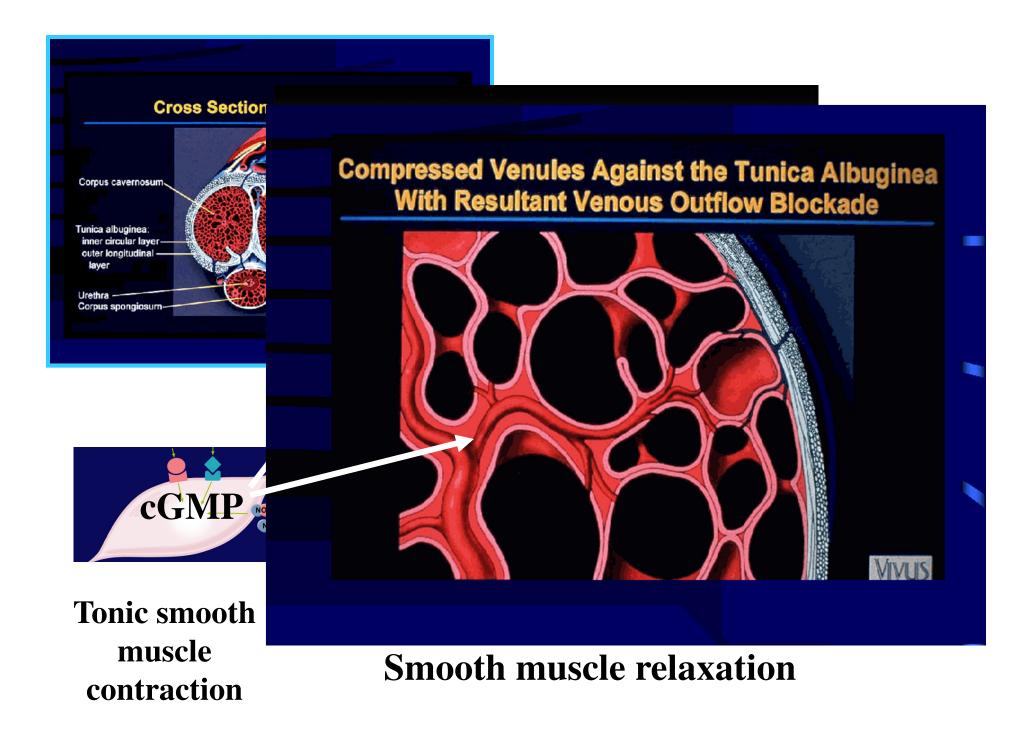


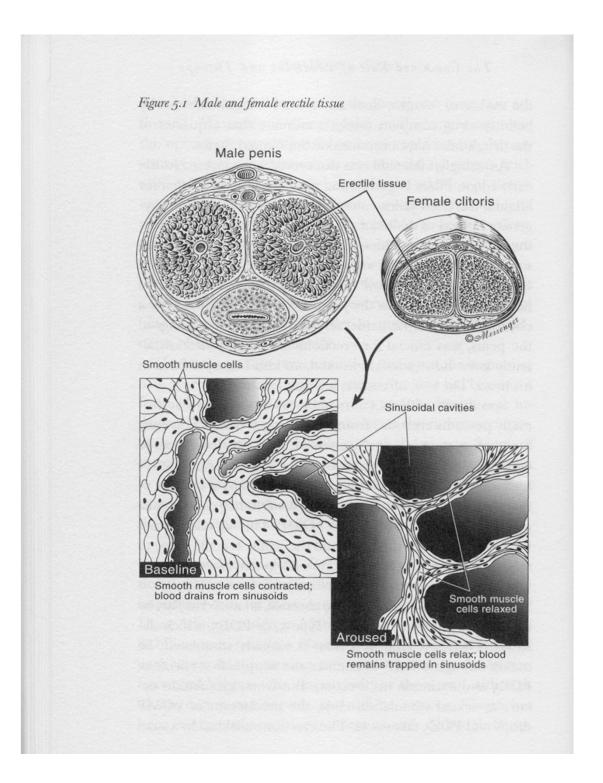
Psychological Control

Physical Stimulus

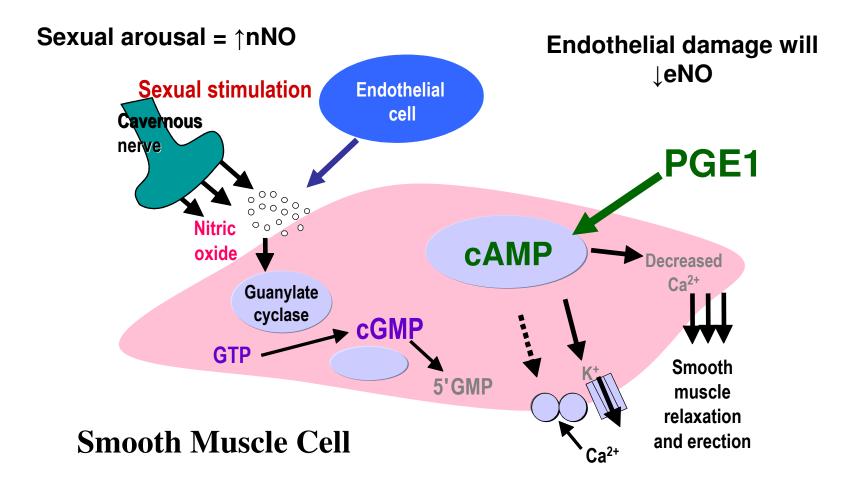








Penile Erection: NO-cGMP Mechanism and PDE5



Ignarro L. J Pharmacol Exp Ther 1981;218:739

Ejaculation and Orgasm

Ejaculation:

- the process of sperm transport from the testes to the urethral meatus (neurology defined)

Orgasm:

- the combination of a local, learned reflex and/or the brain's interpretation of it (neurology unclear)

- usually accompanies ejaculation

Orgasm in both sexes

- We don't know the neurology
- Women who have experienced reinforcement of their orgasmic reflex have an easier time regaining
- Loss of sensation, spasm, pain all interfere with signalling
- Lack of sexual drive or impaired genital arousal makes hitting the threshold very difficult
- Reduced testosterone increased threshold

Sex Response Cycle



Sympathetic

Orgasm

(ejaculation:men)

Parasympathetic

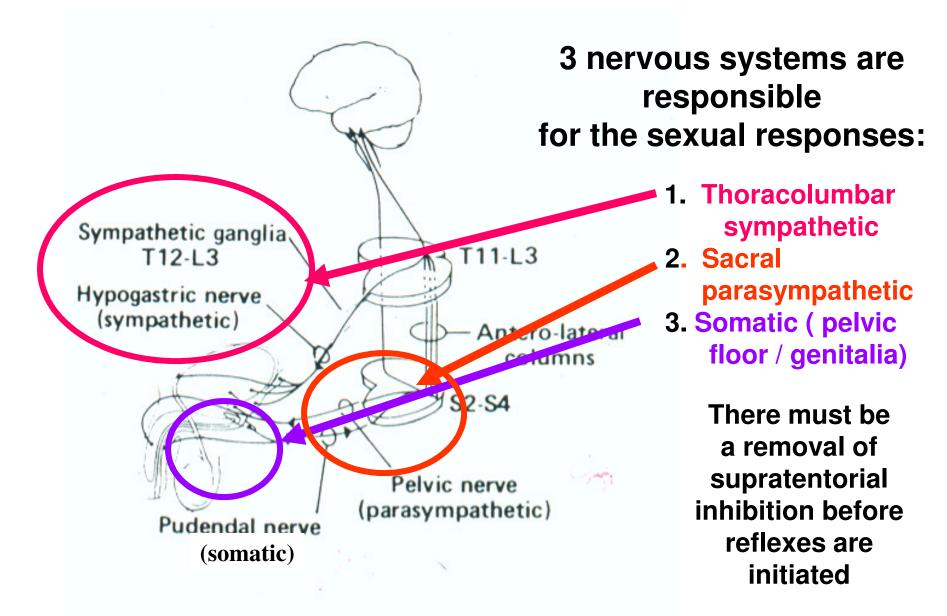
Arousal

Refractory period (men)

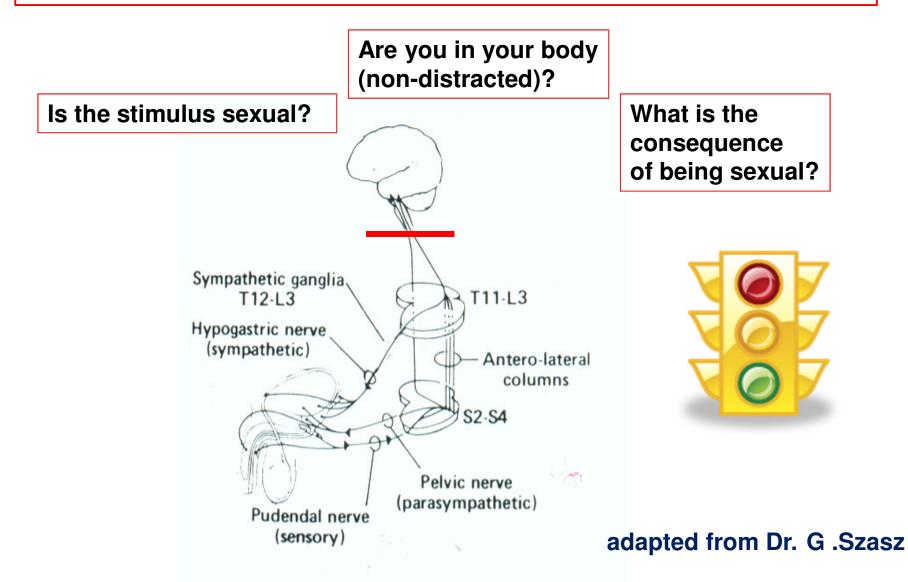
Age-Related Changes in Sexual Response

- Excitement phase takes longer to achieve
 - \downarrow vaginal blood flow and genital engorgement
 - Slower tumescence and less rigidity of erections
- Plateau phase prolonged
 - \downarrow vasocongestion of nipples and nipple erection
 - \downarrow uterine elevation
 - Harder to achieve ejaculation
- Orgasm retained
 - \downarrow number and intensity of vaginal contractions
 - Faster detumescence and prolonged refractory period

Sexual Neurophysiology



Prerequisites for removal of supratentorial inhibition from the brain



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1°,2°,3° ways of looking at sexual dysfunction in cancer patients

- Primary: *direct* physiological impairments from the disease process itself
- Secondary : *indirectly* related to physical disorders concerning illness or disease itself and medication effects
- Tertiary: consequence of cultural, social, emotional and psychological effects

Cancer and Sexual Dysfunction

- Primary : anatomical disruption, direct alterations secondary to nerve changes, small and large vessel disease
- Secondary: anemia, fatigue, hormonal alterations, incontinence, increased renal or CV effects, depression
- Tertiary : social isolation with surgical scarring, weight changes

Cancer affects...

- Biopsychosocial aspects of sexuality
- Doesn't need to be genital or breast surgery to have a huge impact
- Silent scars as well as obvious scars
- Sexual self esteem affected by changes to body image and health
- May have to accept a new sexual body

What do you need to know?

Think ...

..... Sexual Rehabilitation Framework... too overwhelming otherwise!

Sexual Rehab is...

- Part of a comprehensive rehab program
- The process of supporting individuals to move towards optimal sexual well-being
- Focuses on the emotional, spiritual and physical
- Respects individual values and beliefs and stage of "readiness"



"Taking a sexual history and thinking beyond sexual (genital) function to the factors that influence sexuality within the practicality of a table helps reduce the intimidating task of addressing the complexity of sexuality."

Elliott, SL, Hocaloski S, Carlson M. Multidisciplinary Approach to Sexual and Fertility Rehabilitation: The Sexual Rehabilitation Framework *Top Spinal Cord Inj Rehabil* 2017;23(1):49–56.

The 3-Step Method

- 1. Many men/women who are living with _____ have concerns or questions about the sexual part of their lives
- 2. Have you thought about this at all?
- 3. Would you like to talk to someone about it?

Sexual Rehabilitation Framework

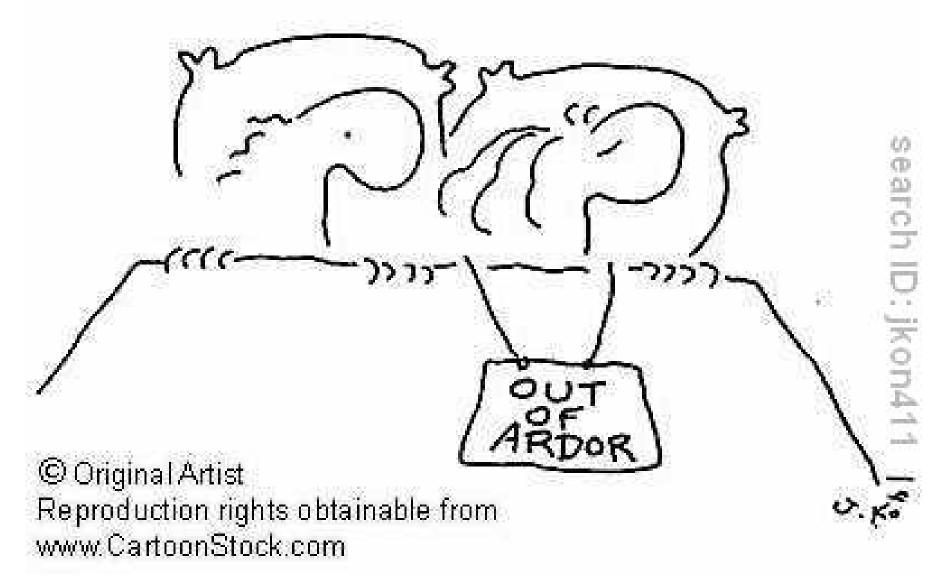
Sexual Area	Consequences	Comments
Sexual Drive/interest		
Sexual Functioning abilities		
Fertility & Contraception		
Factors re the condition		
Motor & sensory influences		
Bladder & bowel influences		
Sexual Self-view and Self-esteem		
Partnership Issues		

Sexual Rehabilitation Framework

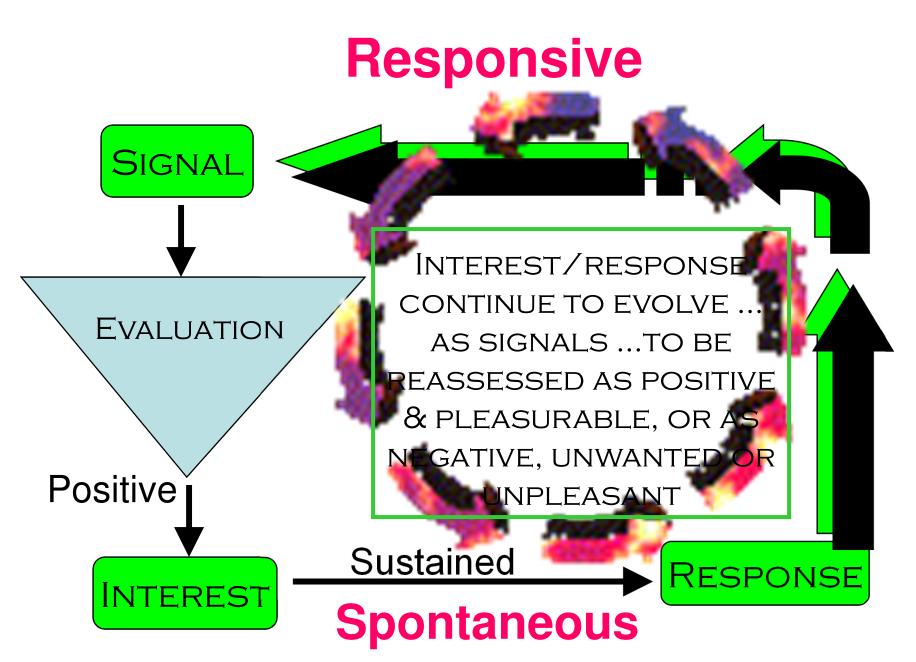
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Sexual Interest/Libido

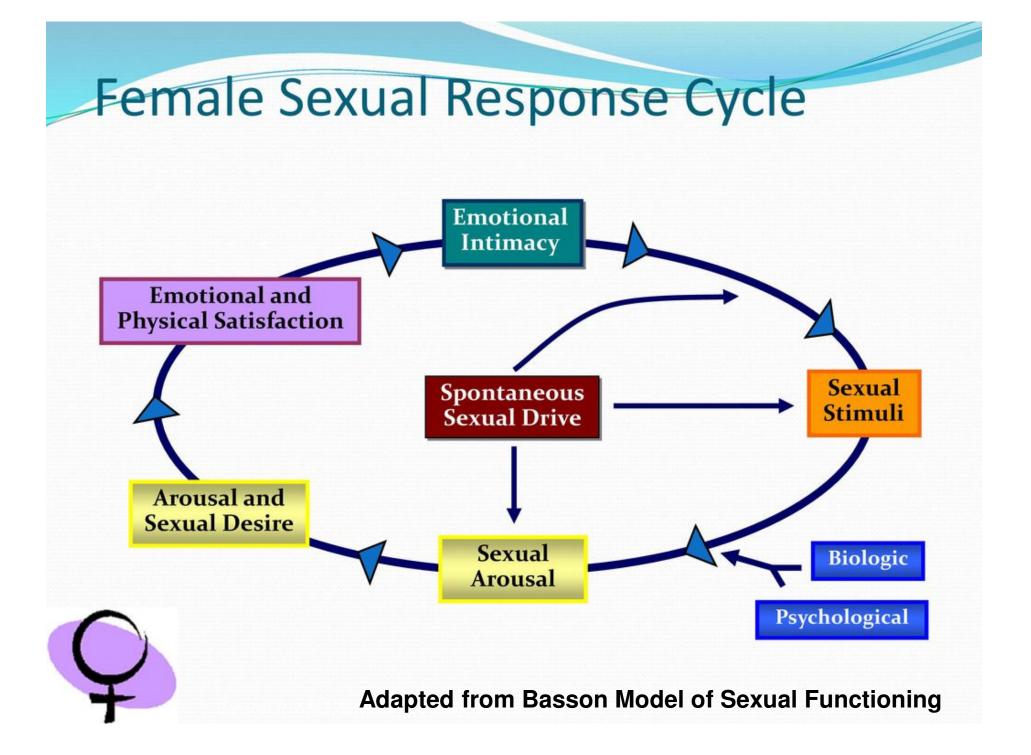
Complex interaction of *biological urge* (driven by testosterone, mood and chemical brain factors) and *motivational factors* (what the sexual payoff is perceived to be)



Desire discrepancy



Adapted from Stevenson and Elliott 2007



Sexual Rehabilitation Framework

	Sex Response Cycle		
Sexual Area	Co		
Sexual Drive/interest	orgasm		
Sexual Functioning abilities	Genital		
Fertility & Contraception	Arousal		
Factors re the condition			
Motor & sensory influences	 Women – vaginal lubrication and accommodation, orgasm, freedom from sexual pain 		
Bladder & bowel influences			
Sexual Self-view and Self-esteem	Men – attain and maintain an Erection, ejaculation, orgasm,		
Partnership Issues	freedom from sexual pain		

Sexual Rehabilitation Framework

Consequences	Comments
Hormones	
Hand function	
	2
	Getty Stock Photo
	1 Ball
	Hormones

nttp://business.sn24.org.uk/service-news/2016/12/14/contraceptioncuts

Sexual Area	Consequences	Comments	
Sexual Drive/interest			
Sexual Functioning abilities	Very important – think BIG ! Medication affect Depression & meds Fatigue Skin problems Pain & pain meds		
Fertility & Contraception			
Factors re the condition			
Motor & sensory influences			
Bladder & bowel influences	Mode of cancer treatment Specific system failures		
Sexual Self-view and Self-esteem			
Partnership Issues			

Sexual Area	Consequences	Comments
Sexual Drive/interest		
Sexual Functioning abilit		Paner Hadd with.
Fertility & Contraception		
Factors re the condition		
Motor & sensory influences	https://nypost.com/2018/04/25/mom-discovers	
Bladder & bowel influences	Neuropathic pain Ambulation difficult	ies
Sexual Self-view and Self-esteem	Poor abduction for v	women
Partnership Issues	Metastatic disease r	

Sexual Area	Consequences	Comments
Sexual Drive/interest		-
Sexual Functioning abilities		POOP
Fertility & Contraception		T's in the (colostomy) bag.
Factors re the condition		
Motor & sensory influences	https://www.ca	fepress.com/+colostomy+t-shirts
Bladder & bowel influences		
Sexual Self-view and Self-esteem		
Partnership Issues		

Sexual Area	Consequences	Comments	
Sexual Drive/interest	A CONTRACT OF		
Sexual Functioning abilities			
Fertility & Contraception	X	The second se	
Factors re the condition	10		
Motor & sensory influences		Access Sex One 2007 Photography with Sarah Murray	
Bladder & bowel influences	Sense of masculinity/fe	emininity	
Sexual Self-view and Self-esteem	Grieving for losses		
Partnership Issues	Ability to persist with s		

Sexual Area	Consequences	Comments
Sexual Drive/interest	the start of the	II
Sexual Functioning abilities		
Fertility & Contraception	and the second second	
Factors re the condition	https://greatergood.berkeley.edu/article/item/what_we_c	an_learn_from_the_best_marriages
Motor & sensory influences	Single/partnered/hov	w one identifies
Bladder & bowel influences	Losses — Gains	
Sexual Self-view and Self-esteem	Role reversals Caregiver- lover syndrome	
Partnership Issues		

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Bladder & bowel influences		
Sexual Self-view and		
Self-esteem		
Partnership Issues		

Arousal = Brain activation



Hormone-related Anatomic Changes in the Female Genitourinary Tract

- Genitourinary syndrome of <u>menopause</u> (GSM) is highly prevalent
- Reduction of pubic hair
- Loss of fat and subcutaneous tissue of mons pubis
- Atrophy of genitourinary epithelium
- Atrophy of labia majora
- Atrophy of Bartholin's glands
- Shortening and \downarrow elasticity of the vagina
- Increased bladder infections

Safety of vaginal estrogen for GSM

- A recent report^[4] from the Nurses' Health Study provides important new information regarding the safety of vaginal estrogen. In this large, long-term cohort study, the mean duration of vaginal estrogen use was almost 3 years.
- The incidence of cardiovascular outcomes, including <u>myocardial</u> <u>infarction</u>, <u>stroke</u>, and venous <u>thromboembolism</u>, was similar in users and nonusers of vaginal estrogen.^[4] Likewise, the risk for invasive cancer, including endometrial and <u>breast cancer</u>, was similar in users and nonusers.^[4]
- Current guidance from the American College of Obstetricians and Gynecologists^[5] as well as the North American Menopause Society recommends that in appropriate candidates, low-dose vaginal estrogen can be used indefinitely without concomitant progestin therapy.^[6] The findings of

this important study support these recommendations.

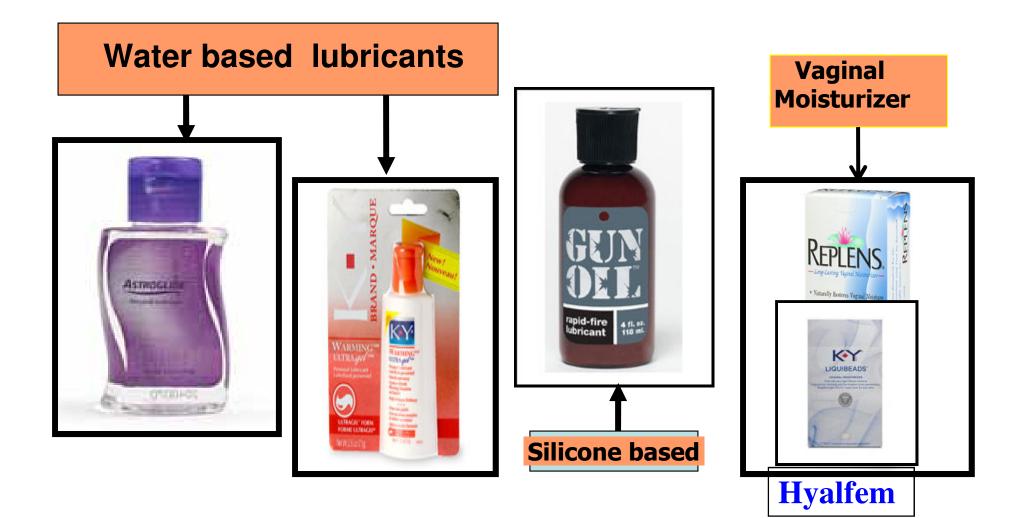
4 Bhupathiraju SH, et al. Vaginal estrogen use and chronic disease risk in the Nurses' Health Study. Menopause. 2018 Dec 17. [Epub ahead of print] 5. Management of menopausal symptoms. ACOG Practice Bulletin No. 141. American College of Obstetricians and Gynecologists. Obstet Gynecol. 2014;123:202-216.

6 Management of symptomatic vulvovaginal atrophy: 2013 position statement of The North American Menopause Society. Menopause. 2013;20:888-902.

Help for dysparunia in the breast cancer patients

- Moisturizers can be used 1-3 times a week
- Non- hormonal lubricants, e.g., coconut oil, sesame oil
- Use of intravaginal DHEA
- Failure of above, then it is reasonable to use hormonal, low dose vaginal estrogen if
 - consultation with the patient's oncologist
 - low risk of recurrence
 - -? no use of aromatase inhibitors

Lubrication difficulties & Dyspareunia

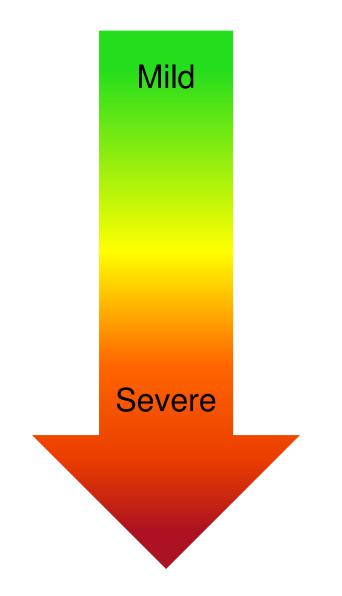


Dysparunia

- Complex (differentiate superficial, mid and deep dysparunia) and psychological components
- Should be assessed by sexual medicine specialists (BC Center for Sexual Medicine, Diamond gynecology)
- Referral to Gynecology, Vulvar pain clinics?
 Pelvic floor physiotherapy ?
- Chronic pelvic pain in men needs to be seen by urology and possibly PF specialists

Signs and Symptoms of TDS

Order of Appearance



Decreased libido

- Decreased vitality
- Fatigue
- Mood changes
- Insomnia
- Anemia
- Delayed ejaculation
- Flushes
- Erectile dysfunction
- Decreased muscle mass
- Increased visceral body fat
- Testicular atrophy
- Weakness
- Osteopenia/osteoporosis
- Loss of facial, axillary and pubic hair

Sexual Symptoms of androgen deficiency are varied and include:

- decreased sexual interest
- diminished erectile quality, particularly of nocturnal erections
- muted, delayed or absent orgasms
- decreased genital sensation
- reduced sexual pleasure

Morales A: 2003 & 2004 , Nieschlag E, 2005; Jockenhovel F 2004; Gooren LJ, 2004; Schulman C 2002

Who is at risk for Low T?

- Low T is a general sign of poor health
- Glucocorticoid or opioid therapy
- Liver or renal disease, COPD, traumatic brain injury or SCI, HIV, MS
- Metabolic syndrome or diabetes
- Anemia, sarcopenia

Replacing hormones for sexual QoL ??

- Risk / benefit
- Assess reduced or no systemic absorption and safety
- Myths: TRT for hypogonadism causes prostate cancer or worsens the risk of aggressive prostate cancer
- Truths: men with low T have more aggressive PCa and found at later stage

Testosterone Replacement Therapy (TRT)

- Goals:
 - Symptom improvement
 - Achievement of physiological T levels
- Several safe and effective formulations available

Newest: Natesto



No TRT for men wanted kids!



Women and Androgens

- Serum androgen levels do not correlate with sexual symptomatology
- Much more complex than just hormones
- Testosterone is aromatized to estrogen
- Debate on androgen replacement value in women except for specific cases
- Long term use no safety data

Some Medications Affecting Sexual Function

Drug class	Arousal	Desire	Orgasm	Vaginal dryness/ED
Antihistamines	X			
Anti-hypertensives	X	X		
Anti-lipid, cholesterol lowering agents		X		
Anti-ulcer		X		
Anticholinergics	X			X
Antidepressants	X	X	X	X
Antipsychotics	X	X	X	
Amphetamines			X	
Sedatives	X	X	X	
Tobacco, alcohol		X		(tobacco)
Steroids, Narcotics		X		
SERMs, GNRH agonists, Flagyl	X		X	

Drugs for Female Sexual Dysfunction

- Biopsychosocial model is essential to understand whether a candidate drug induces meaningful effect over placebo
- Vasoactive agents, hormone therapy and psychoactive drugs have been investigated
- Before 2015, randomized placebo-controlled trials showing efficacy and safety, however, did not convince the FDA to approve either transdermal testosterone patch in postmenopausal women or the serotoninergic agent flibanserin in premenopausal women, for the treatment of hypoactive sexual desire disorder (ie nonlife threatening condition).

Addyi – not in Canada yet

- Flibanserin is a novel multifunctional serotonin agonist and antagonist (MSAA) that improves sexual functioning in premenopausal women who suffer from reduced sexual interest and desire.
- Now sold under the trade name Addyi, is a medication approved for the treatment of premenopausal women with <u>hypoactive sexual</u> desire disorder (HSDD). The medication increases the number of satisfying sexual events per month by about one half to one over placebo from a starting point of about two to three.

Therapies for erectile dysfunction

Oral medications : PDE5i

- Viagra prn
- Levitra prn
- Cialis prn and daily
- Mechanical
- Vacuum erection devices : VED
- Penile rings
- Intraurethral medications: MUSE
- Intracavernosal injections : ICI
- Penile prosthesis :PP

Sildenafil

Vardenafil

Tadalafil











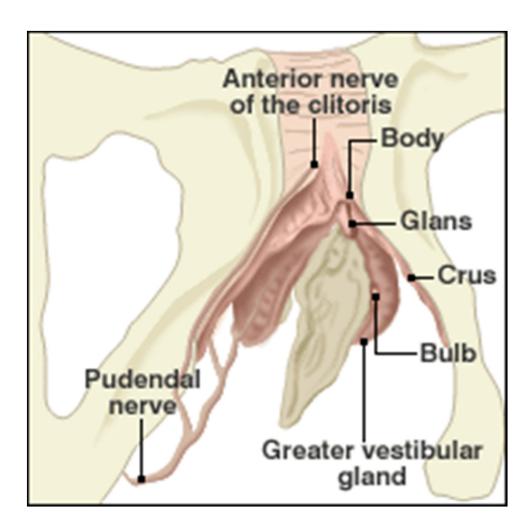


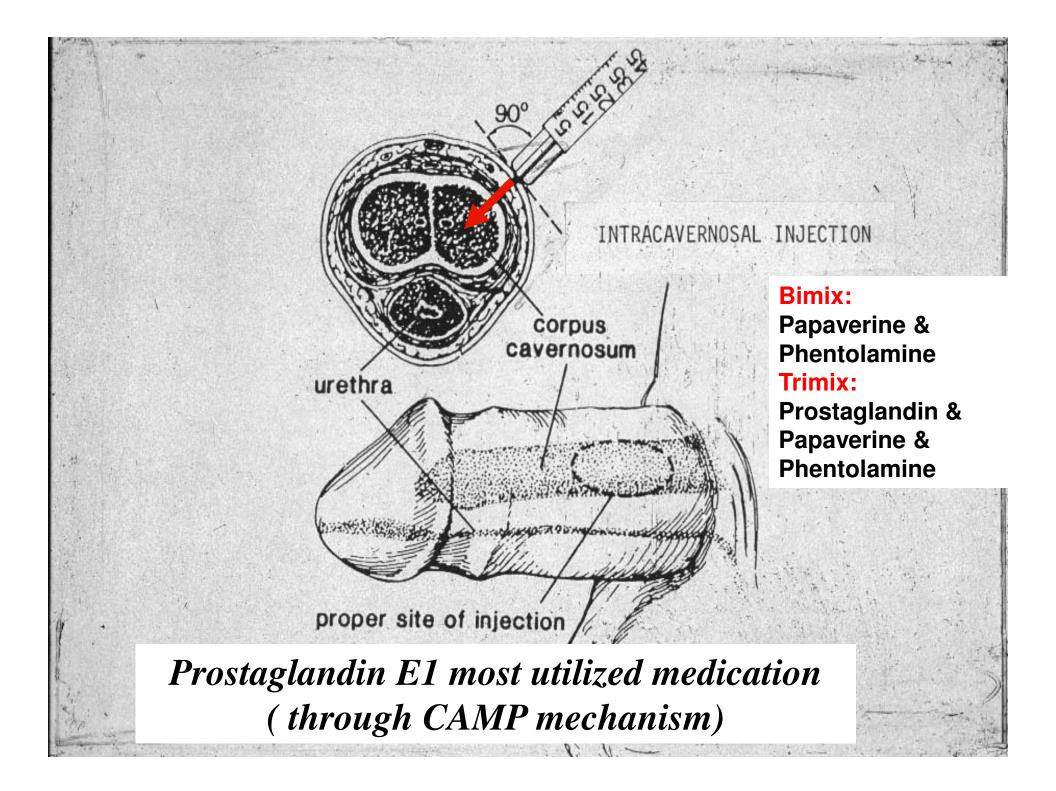
Only erectile tissue will be effected by PDE5i

Most of the time clitoral smooth muscle is maximally relaxed anyway

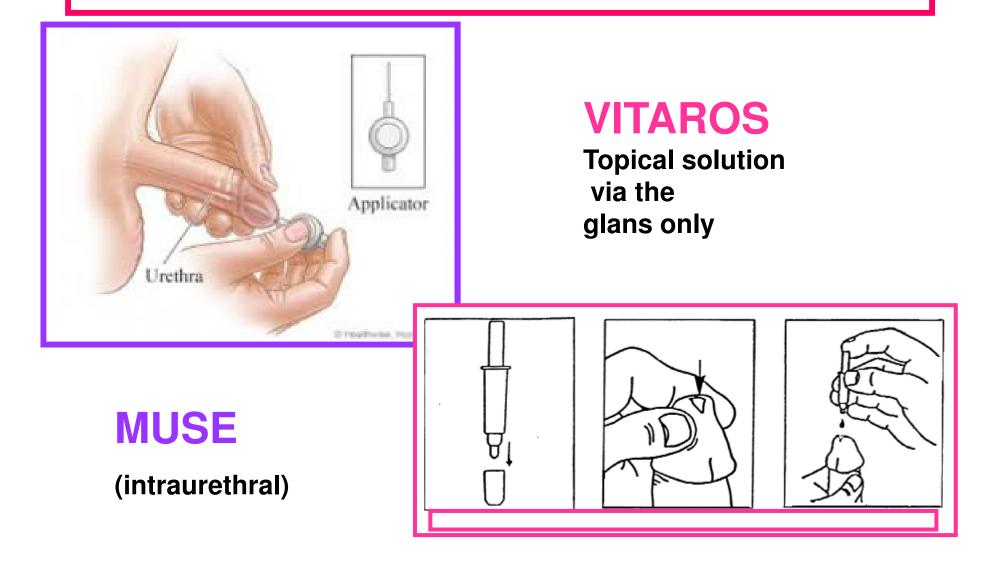
PDE5i may increase perceived sensation due to vasocongestion in women with compromised genital sensation or substantial atherosclerosis

While this has been seen in women with MS and incomplete SCI, it has not been tested in women with cancer

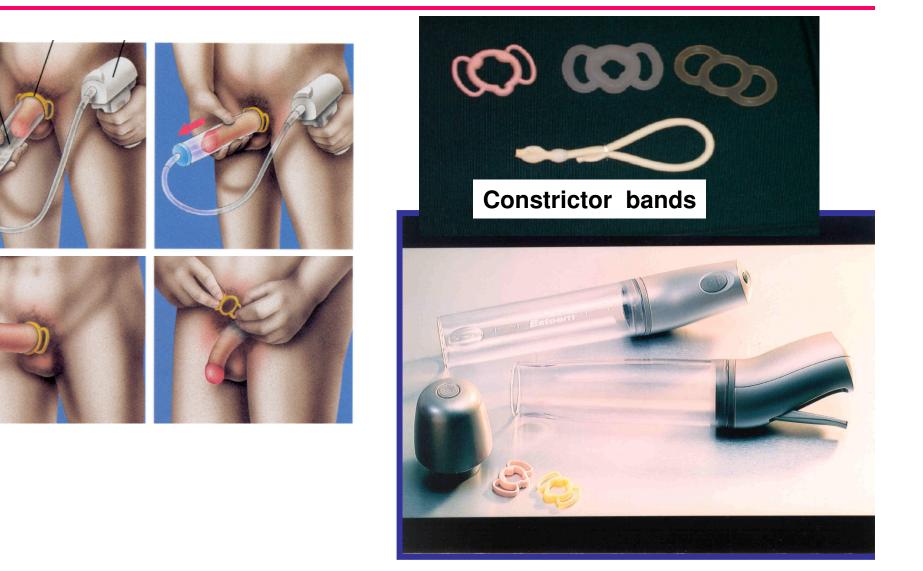




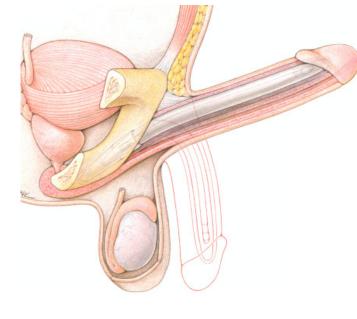
Spongiosal delivery of PGE1

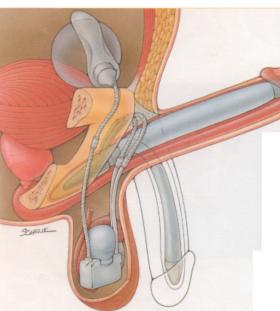


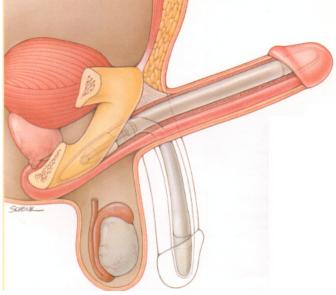
Treating Erectile Dysfunction Physical Methods



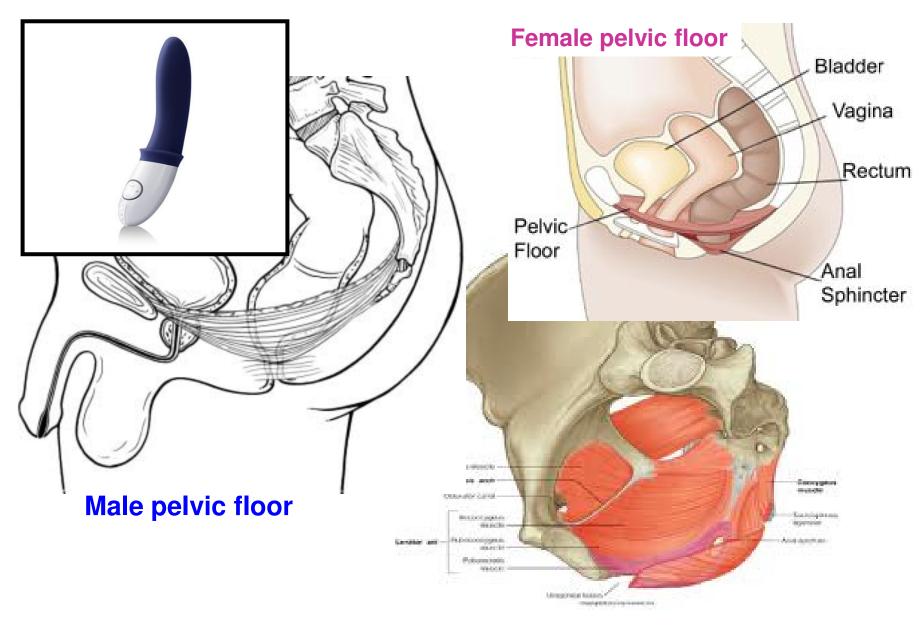
Treating Erectile Dysfunction with Surgical Methods







Pelvic floor potential



Vibrators



Vibrators for men



Conditions that Facilitate Sexual Pleasure and Orgasm

- Relaxation, meditation, dreams
- Fantasy, recalling positive experiences
- Breathing, going with the flow
- Trust or being with a partner who is trusted
- MINDFULNESS
- Addition of nongenital touch, plenty of time, added stimulation of a vibrator



ISCOS 2015 POSTER SIP75

Lived Experiences : Tepper ISSWSH 2002

Pleasure Principle

"Pleasure is the authentic, abiding satisfaction that makes us feel like complete human beings" - Virginia Johnson

Adds meaning to life

Antidote to physical and mental pain

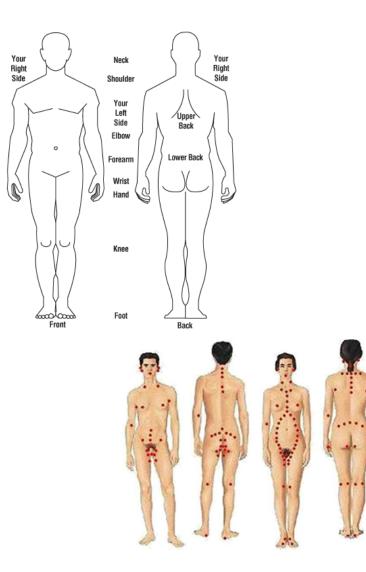
Enhances intimacy

Increases a sense of connectedness

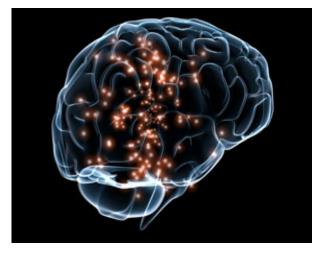
Decreases stress

Lived Experiences : Tepper ISSWSH 2002

Afferent recruitment

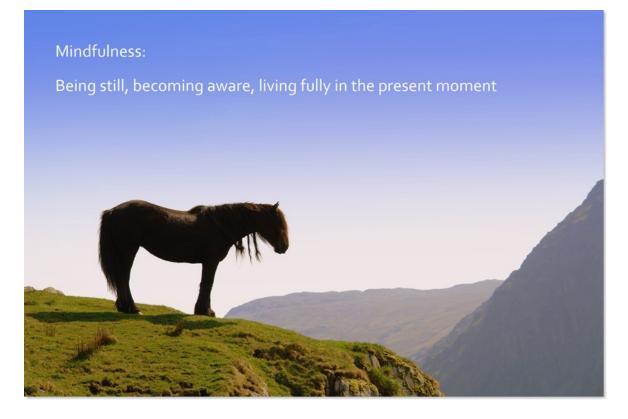






What is Mindfulness?

Non-judgmental, present moment awareness



Jon Kabat -Zinn

Benefits of 'Mindfulness' in Sexual Rehab

- Body remapping
- Improve mind body connection
- Improve self-view
- Present moment awareness
- Pain management
- Stress reduction
- Self-compassion
- Quality of life



Tara Brach, Jon Kabat-Zinn, Jack Kornfield, Zindel Segal,

Sexual Rehab Principles

- Maximize Potential
- Adapt to limitations
- Remain positive and open minded



S.Elliott 2010

Talking Sex as a Physician: What gives you confidence?

Knowing how to take a **10 minute history**

- Having a schemata in your head to get going and do a basic assessment : is this going to be straightforward or not?
- Relax: don't try to do everything in one appointment
- Knowing therapeutics
- Practice and experience

Screening vs. assessment

Different attitudes

- Don't ask don't tell?
- Likelihood of presentation by women > men
- Routine screening in physicals or related to genital or relationship concerns
- Screen for problems in high risk patients only?
- <u>Question</u>: is it a sexual dysfunction or a something else presenting in the sexual arena?

Talking Sex

- If you can talk bladder and bowel, you can talk sex
- This isn't personal: no one can read your mind
- Use the proper words over and over
- Don't use slang (with a few exceptions)
- Don't bluff : ask if you don't know
- Remember: you know more than you think

Ten minute sexual history

- 1. Clarify : What's the main concern?
- 2. Classify : Onset and duration? Situational or generalized?
- 3. Context
- 4. Rest of sexual response
- 5. Partner's sexual response
- 6. Reaction
- 7. Previous treatment
- 8. Motivation

Decide

- What are you comfortable with?
- What is your education?
- What are you willing to learn more about?
- What are your limitations?
- Practice
- Financial reimbursement
- Professional fulfillment : QOL vs life-threatening

Referral sources

BC Centre for Sexual Medicine

- 604 875-4705

2nd floor Blusson, 818 West 10th Avenue Vancouver

Prostate Cancer Supportive Care Program - 604 - 875 – 4495

Room 6259 Gordon and Lesley Diamond Building , VGH

Sexual Health Rehabilitation Service

- 604-737-6233 (25th and Oak)
- 604 875 4111 x 69402 (Blusson)





Thank you for listening! Questions?

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