Managing Sexual Dysfunction in Cancer Patients

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Oncology CME Webcast Series

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Speaker:  Stacy Elliott, MD

- **Holder of Stocks/Shares**
  
  none

- **Grants/Research Support**:
  
  CIHR, Neurotrauma funds, Pfizer (female SCI)

- **Speakers Bureau/Honoraria/Consulting Fees**:
  
  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
Sexuality

gender identity + gender expression

Sex = what we do

Sexuality = who we are
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

Hormones
- Testosterone

Neurotransmitters
- Dopamine
- Oxytocin
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
Tonic smooth muscle contraction

Smooth muscle relaxation

Compressed Venules Against the Tunica Albuginea With Resultant Venous Outflow Blockade

cGMP
Figure 5.1 Male and female erectile tissue

- Male penis
- Erectile tissue
- Female clitoris
- Smooth muscle cells
- Sinusoidal cavities
- Smooth muscle cells contracted; blood drains from sinusoids
- Aroused
- Smooth muscle cells relax; blood remains trapped in sinusoids
Penile Erection: NO-cGMP Mechanism and PDE5

Sexual arousal = \( \uparrow \text{nNO} \)

Endothelial damage will \( \downarrow \text{eNO} \)

Sexual stimulation

Endothelial cell

GTP

Nitric oxide

Cavernous nerve

Nitric oxide

Smooth Muscle Cell

Decreased Ca\(^{2+}\)

Smooth muscle relaxation and erection

PGE1

\( \downarrow \text{eNO} \)

Sexual stimulation

Endothelial cell

GTP

Nitric oxide

Cavernous nerve

Nitric oxide

Smooth Muscle Cell

Decreased Ca\(^{2+}\)

Smooth muscle relaxation and erection

PGE1

\( \downarrow \text{eNO} \)

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

- Desire
- Orgasmic threshold
- Orgasm (ejaculation: men)
- Refractory period (men)
- Parasympathetic
- Sympathetic
- Arousal
Age-Related Changes in Sexual Response

• Excitement phase takes longer to achieve
  • ↓ vaginal blood flow and genital engorgement
  • Slower tumescence and less rigidity of erections

• Plateau phase prolonged
  • ↓ vasocongestion of nipples and nipple erection
  • ↓ uterine elevation
  • Harder to achieve ejaculation

• Orgasm retained
  • ↓ number and intensity of vaginal contractions
  • Faster detumescence and prolonged refractory period
Sexual Neurophysiology

3 nervous systems are responsible for the sexual responses:

1. Thoracolumbar sympathetic
2. Sacral parasympathetic
3. Somatic (pelvic floor / genitalia)

There must be a removal of supratentorial inhibition before reflexes are initiated.
Prerequisites for removal of supratentorial inhibition from the brain

Is the stimulus sexual?

Are you in your body (non-distracted)?

What is the consequence of being sexual?

adapted from Dr. G. Szasz
Objectives

• Describe the components of sexual function

• Summarize a Sexual Rehabilitation Framework (SRF) to manage the complexity of changes
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.”

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

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<td>Fertility &amp; Contraception</td>
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<td>Factors re the condition</td>
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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
Signal Evaluation Positive Interest

Sustained Interest/response continues to evolve ... as signals ... to be reassessed as positive & pleasurable, or as negative, unwanted or unpleasant

Responsive Spontaneous

Adapted from Stevenson and Elliott 2007
Female Sexual Response Cycle

Adapted from Basson Model of Sexual Functioning
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**Sex Response Cycle**

**Women** – vaginal lubrication and accommodation, orgasm, freedom from sexual pain

**Men** – attain and maintain an Erection, ejaculation, orgasm, freedom from sexual pain
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<td>Sexual Drive/interest</td>
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<td>Hand function</td>
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http://business.sh24.org.uk/service-news/2016/12/14/contraceptioncuts
# Sexual Rehabilitation Framework

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<td>Very important – think BIG!</td>
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<td>Depression &amp; meds</td>
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<td>Specific system failures</td>
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<td>Sensory increase or loss</td>
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<td>Poor abduction for women</td>
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<td>Metastatic disease mechanics</td>
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https://www.cafepress.com/+colostomy+t-shirts
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<td><strong>Sexual Self-view and Self-esteem</strong></td>
<td>Sense of masculinity/femininity</td>
<td>Grieving for losses</td>
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<td>Sexual appeal to others and self</td>
<td>Ability to persist with sexual exploration</td>
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<td>Lack of support</td>
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<td>Losses</td>
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https://greatergood.berkeley.edu/article/item/what_we_can_learn_from_the_best_marriages
Objectives

• Describe the components of sexual function

• Summarize a Sexual Rehabilitation Framework (SRF) to manage the complexity of changes

• Identify appropriate options for management
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</table>
Arousal = Brain activation

Hormones

Neurotransmitters
Hormone-related Anatomic Changes in the Female Genitourinary Tract

- Genitourinary syndrome of menopause (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 ↓ elasticity of the vagina
- Increased bladder infections
A recent report 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 myocardial infarction, stroke, and venous thromboembolism, was similar in users and nonusers of vaginal estrogen. Likewise, the risk for invasive cancer, including endometrial and breast cancer, was similar in users and nonusers.

Current guidance from the American College of Obstetricians and Gynecologists 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. The findings of this important study support these recommendations.

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

Water based lubricants

Vaginal Moisturizer

Silicone based

Hyalfem
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

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

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<thead>
<tr>
<th>Drug class</th>
<th>Arousal</th>
<th>Desire</th>
<th>Orgasm</th>
<th>Vaginal dryness/ED</th>
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<tr>
<td>Antihistamines</td>
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<td>Anti-hypertensives</td>
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<td>Anti-lipid, cholesterol lowering agents</td>
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<td>Anti-ulcer</td>
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<td>Steroids, Narcotics</td>
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<td>SERMs, GNRH agonists, Flagyl</td>
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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 non-life 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 pre-menopausal women with hypoactive sexual 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
Available PDE5i 2019

- **Sildenafil**
- **Vardenafil**
- **Tadalafil**
- **Staxyn**
- **Cialis daily**
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
Prostaglandin E1 most utilized medication (through CAMP mechanism)

Bimix:
Papaverine & Phentolamine

Trimix:
Prostaglandin & Papaverine & Phentolamine
Spongiosal delivery of PGE1

MUSE
(intraurethral)

VITAROS
Topical solution via the glans only
Treating Erectile Dysfunction
Physical Methods

- Vacuum device - rehabilitative function
- Constrictor bands
Treating Erectile Dysfunction with Surgical Methods
Pelvic floor potential

Male pelvic floor

Female pelvic floor

Bladder
Vagina
Rectum
Pelvic Floor
Anal Sphincter

Pelvic muscle
Obturator internus
Adductor magnus
Adductor longus
Biceps femoris
Gastrocnemius
Soleus
Sartorius
Rectus femoris
Adductor brevis
Quadriceps femoris
Hamstring muscles
Medial head of gastrocnemius
Lateral head of gastrocnemius
Biceps femoris
Sartorius
Rectus femoris
Adductor muscles
Adductor longus
Adductor brevis
Adductor magnus
Quadriceps femoris
Hamstring muscles
Vibrators
Vibrators for men

Hitachi Magic Wand and others

Viberect FDA approved

WAHL

Ferticare FDA and HC approved for SCI
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

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

Mindfulness:
Being still, becoming aware, living fully in the present moment

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?
- **Question**: 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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