IS IT YOUR MAN OR YOUR MEDICATION?

MEDICATIONS THAT IMPACT SEXUALITY

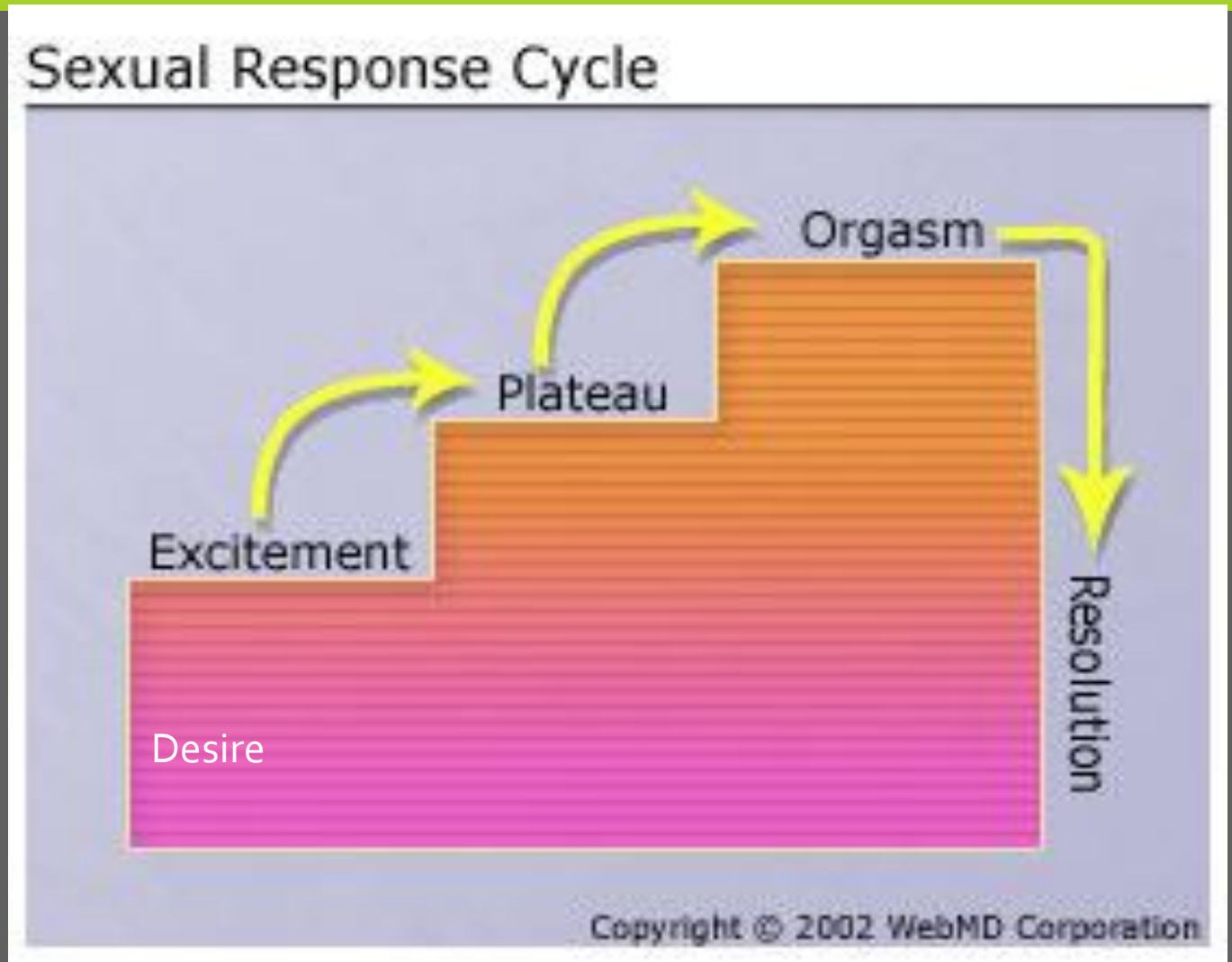
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OBJECTIVES

- To understand the stages of sexuality.
- To understand the mechanism of drugs that impact sexuality.
- To know alternative drugs/treatment that do not effect sexuality

MASTERS & JOHNSON'S LINEAR MODEL



SEXUAL RESPONSE CYCLE

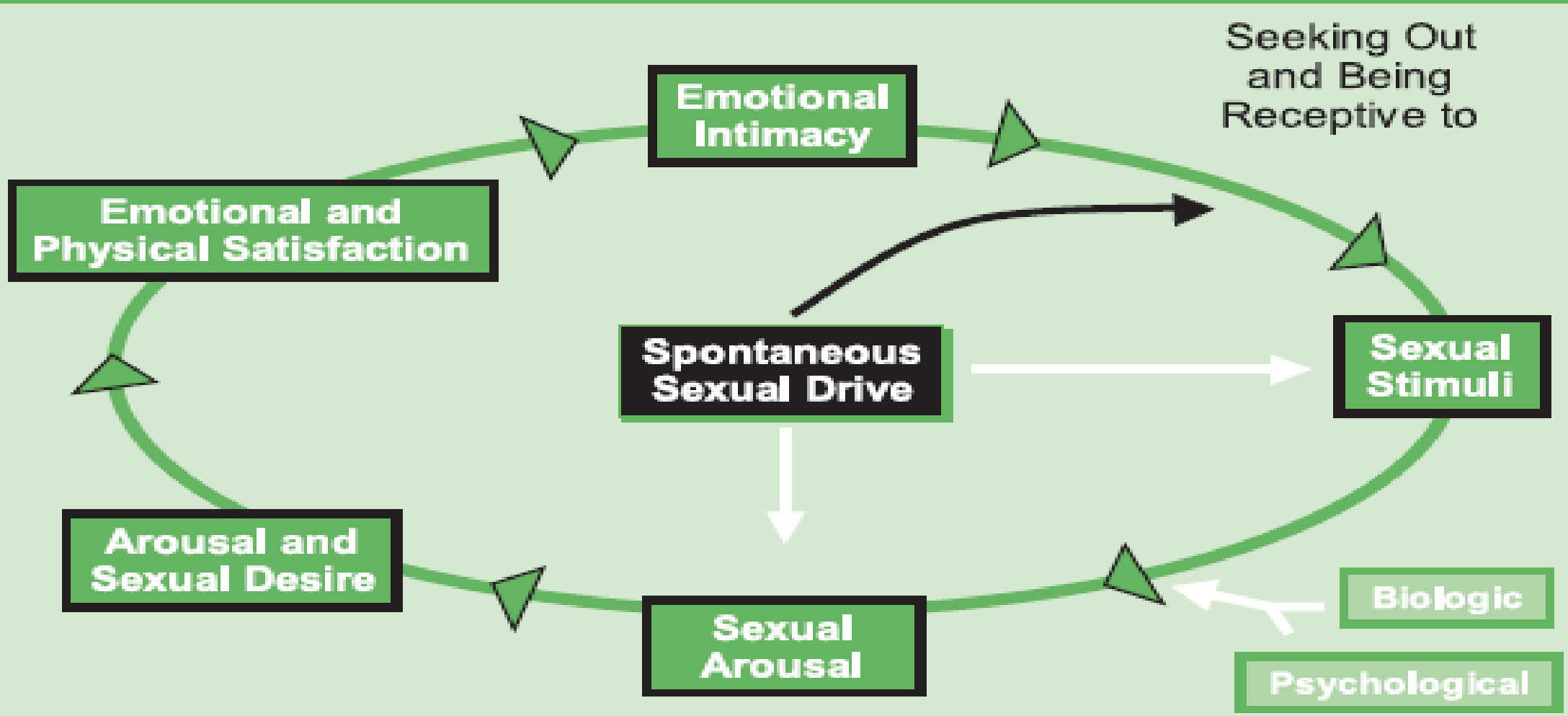
- Desire (libido) – desire to have sexual activity, including sexual thoughts, images, and wishes
- Arousal (excitement) – subjective sense of sexual pleasure accompanied by physiologic changes, including genital vasocongestion and increases in heart rate, blood pressure, and respiratory rate
- Orgasm – peaking of sexual pleasure and release of sexual tension, with rhythmic contractions of the perineal muscles and reproductive organs
- Resolution – muscular relaxation and a sense of general well-being following sexual activity

*for many women, the phases may vary in sequence, overlap, repeat, or be absent during all or some sexual encounters. It is helpful to know where in the sexual response cycle a problem occurs

PROBLEMS WITH MASTERS AND JOHNSON'S

- It assumes that men and women have similar sexual responses, and in so doing may pathologize normal behavior in women
- women may not even experience all of the phases
- has been criticized because it does not take into account non-biologic experiences such as pleasure and satisfaction or place sexuality in the context of the relationship

FIGURE 3. Non-linear Model of Female Sexual Response Developed by Basson[6]



Basson's non-linear model acknowledges how emotional intimacy, sexual stimuli, and relationship satisfaction affect female sexual response.

BASSON'S NON LINEAR FEMALE MODEL

- Female sexual functioning proceeds in a more complex and circular manner
- dramatically and significantly affected by numerous psychosocial issues (e.g., satisfaction with the relationship, self-image, previous negative sexual experiences
- most women in long-term relationships do not frequently think of sex or experience spontaneous hunger for sexual activity.
- desire for increased emotional closeness and intimacy from a partner may predispose a woman to participate in sexual activity
- Once she is aroused, sexual desire emerges and motivates her to continue the activity
- the goal of sexual activity for women is not necessarily orgasm but **rather personal satisfaction**, which can manifest as physical satisfaction (orgasm) and/or emotional satisfaction (a feeling of intimacy and connection with a partner)

FEMALE SEXUAL DYSFUNCTIONS

- one or more phases of the sexual response cycle
- must be recurrent or persistent and cause personal distress or interpersonal difficulty.
- strongly affected by relationship and sociocultural factors
- Depression and anxiety are strongly associated with female sexual dysfunction.
- Cancer, urinary incontinence, vaginal atrophy, end stage renal disease, alcohol or other substance abuse, anemia, thyroid disorders and diabetes are also associated
- Spontaneous desire is unusual in women, except in new relationships,
- Desire in women typically is responsive, commonly triggered by emotional factors, exposure to erotic images, or physical proximity
- before making a Dx: note that not only is a problem present, but also that it is associated with personal distress or interpersonal difficulty.

WHAT CAUSES FEMALE ORGASMIC DISORDER (FOD)?

- Both physical and psychological factors can contribute to female orgasmic disorder:
- **Medical conditions**. Diabetes, vascular disease, multiple sclerosis, spinal cord injury and certain pelvic conditions may interfere with a woman's ability to reach orgasm. FOD has also been associated with arthritis, thyroid problems, and asthma.
- **Medications**. Antidepressants [particularly serotonin reuptake inhibitors (SSRIs)], antipsychotics, and drugs taken for cancer, high blood pressure, and heart disease can have sexual side effects that affect orgasm.
- **Sexual inexperience**. Some women have not yet learned what types of stimulation bring them to orgasm. Or, they might not know how to talk to their partner about what gives them pleasure.
- **Guilty feelings about sex**. Women may have been brought up to believe that they shouldn't enjoy sex, so they feel guilty or "wrong" for doing so.
- **Anxiety and depression**. A woman may feel so anxious about sex that she is unable to relax enough to have an orgasm. Or, she may focus so much on negative events that she is unable to be "in the moment" and enjoy stimulation. For some women, poor body image causes anxiety. Others fear losing self-control during orgasm.
- **Relationship issues**. Conflict with her partner can make a woman less likely to reach orgasm. This could be due to sexual problems in the relationship, general relationship problems, anger, mistrust, or inability to communicate.
- **Past abuse**. Women who have been physically, psychologically, or sexually abused often have trouble with orgasm.

DISTRACTIONS

- the relationship with the partner is a principal determinant of sexual satisfaction
- Men tend to get distracted during sex by worries about performance
- women are distracted by concerns about appearance, produce anxiety and guilt, and diminish sexual arousal and pleasure
- The principle of mindfulness holds that it's better to tend fully to what is actually going on—the rich details of the event as it happens—without jumping forward in time to labeling, judgment, and worry, or backward to comparisons, remorse, or guilt.

TAKE-HOME MESSAGES FOR WOMEN

- Sexual pleasure and satisfaction **are not** reliant on orgasm though orgasm may be a nice bonus.
- Sexual desire doesn't always have to come before sexual activity or arousal…sometimes getting physical and experiencing arousal will elicit desire.
- External factors such as relationship dynamics, intimacy, and weighing rewards and costs of sexual experience may play an important role in sexual response.
- Only 25% of women reliably experience orgasm during intercourse-no matter: how long it lasts, what size the man's penis, or how the woman feels about the man or the relationship
- Men have sex to relax, women need to be relaxed to want sex.

CHILD BIRTH/MENOPAUSE

- 83 % reported sexual problems at 3 months postpartum and 64 % at 6 months
- physical recovery and breastfeeding, as well as fatigue and the demands of parenting, often decrease sexual desire.
- Low estrogen levels after delivery and local injury to the genital area at delivery may result in pain with sexual activity.
- parous women were not more likely to have sexual dysfunction than those who were nulliparous
- It is estimated as many as 1 in 3 postmenopausal women experience painful sex due to estrogen levels decline dramatically.

RISK FACTORS FOR SEXUAL PROBLEMS

- **Personal well-being** — A woman's sense of personal well being is important to sexual interest and activity. A woman who does not feel her best physically or emotionally may experience a decrease in sexual interest or response.
- **Relationship issues** — An emotionally healthy relationship with **current and past sexual partners** is the most important factor in sexual satisfaction. Stress or conflict between a woman and her partner, and current or past emotional, physical, or sexual abuse often influence a woman's sexual desire and response. In addition, even good relationships can become less exciting sexually over time.
- **Male sexual problems** — For women with a male sexual partner, sexual dysfunction in the partner can affect her sexual response. Male sexual problems, (erectile dysfunction, diminished libido, or abnormal ejaculation), can occur at any time, but become more common with advancing age. In addition, women tend to live longer than men, resulting in a shortage of healthy, sexually functional partners for older women.

MEDICATIONS

OVERVIEW OF MEDICATIONS THE IMPACT SEXUALITY

- Anti-anxiety drugs
- Antiepileptic drugs
- Antidepressants
- Antihistamines
- Antipsychotics
- Benzodiazepines
- Blood pressure medications, including diuretics (water pills)
- Chemotherapy drugs
- Estrogen-containing drugs
- Finasteride
- Non-steroidal anti-inflammatory drugs (NSAIDs)
- Opioids
- Oral contraceptives
- Parkinson's disease medications
- Prostate cancer medications

- Alcohol and recreational drugs (such as marijuana, cocaine, heroin, nicotine, and methadone) can also have sexual side effects.

International Society of Sexual Medicine. https://www.issm.info/sexual-health-qa/what-types-of-drugs-have-general-sexual-side-effects/

PSYCHIATRIC AND NEUROLOGIC DISEASE

1

Depression present in 17 to 26 % of women who complain of low sexual desire

2

(SSRIs) can cause low desire and difficulty with orgasm in women.

3

Antipsychotic's inhibit dopamine, which may serve as a central neuromodulator of sexual function.

4

It is also possible that a resultant increase in prolactin, causing gonadal suppression, affects sexual function



BENZODIAZEPINES



- thought to lessen sexual interest, excitement and sensation. [1]
- may also interfere with the production of testosterone, important for sexual desire in women as well as men.[1]
- The sexual problems most frequently associated with benzodiazepines are diminished orgasms, pain during intercourse, ED and ejaculation problems.[1]

ANTIEPILEPTIC'S

- Sexual dysfunction is common in patients on antiepileptic drugs.
- Topiramate, pregabalin and gabapentin may cause SD,
- Topiramate can elicit different patterns of SD, especially anorgasmia in women and erectile dysfunction in men, even with a therapeutic dose.
- whereas oxcarbazepine, lamotrigine and levetiracetam may improve sexual function









ANTIEPILEPTIC'S

- these drugs can lower testosterone levels, which can depress desire and interfere with arousal (erection problems for men, lubrication problems for women). [1]
- impair the ability to have orgasms[1]

ANTIDEPRESSANTS



blocking the action of three brain chemicals that relay signals between nerve cells: acetylcholine, serotonin and norepinephrine



Up to 70% of patients with depression have sexual dysfunction, which can affect any phase of sexual activity[7]



Providers consistently underestimated the prevalence of antidepressant-associated sexual dysfunction



it may be difficult to distinguish the effects of the illness on sexual function from the effects of the drugs used for treatment.

ANTIDEPRESSANTS

- SSRI and SNRI inhibit desire, cause erectile dysfunction and decrease vaginal lubrication.[7]
- They also impair orgasm in 5–71% of patients
- Tricyclic antidepressants inhibit sexual desire and orgasm[7]
- the odds of having sexual dysfunction 4 to 6 times greater with SSRIs or venlafaxine XR than with bupropion SR.

ANTIDEPRESSANTS

Decreased Desire

- amitriptyline
- clomipramine
- fluoxetine
- imipramine
- paroxetine
- phenelzine
- sertraline

Decreased Arousal

- amitriptyline
- citalopram
- clomipramine
- doxepin
- fluoxetine
- imipramine
- nortriptyline
- paroxetine
- phenelzine
- sertraline
- tranylcypromine

Orgasm/ejaculatory Difficulties

- citalopram
- clomipramine
- doxepin
- escitalopram
- fluoxetine*
- fluvoxamine
- imipramine
- nortriptyline
- paroxetine*
- sertraline*
- tranylcypromine
- venlafaxine

ANTIDEPRESSANT MEDICATION WITH NO/LESS SIDE EFFECTS

- bupropion (Wellbutrin),
- mirtazapine (Remeron),
- duloxetine (Cymbalta)
- vortioxetine (Trintellix)

serotonin modulators

- nefazodone (Serzone), treat major depression and PMS
- vilazodone (Viibryd) treat major depression
- (Trazadone) treat major depression, functional dyspepsia & as a hypnotic for insomnia

FIXES

- evidence supports adding bupropion to SSRI therapy to improve desire and frequency of sexual activity.[7]
- lower the antidepressant dose to the minimum effective dose[7]
- Switching to another antidepressant with a lower risk for sexual dysfunction; such agents include bupropion, mirtazapine, nefazodone, and vilazodon[7]
- drug holiday to improve sexual dysfunction. A small study evaluated the effect of SSRI discontinuation 1-2 days before anticipated sexual activity [7]

- Bupropion SR maybe useful in treatment of orgasmic delay/inhibition and possibly disorders of sexual arousal

ANTIPSYCHOTIC

- antipsychotic drugs block dopamine, a brain chemical that helps regulate emotional responses and control the brain's reward and pleasure centers. They also increase levels of the hormone prolactin, which can lead to ED, reduced libido and difficulties achieving orgasm. [1]
- the incidence of sexual dysfunction associated with antipsychotic drugs ranges in different studies from 45 percent to as high as 90 percent.[1]

ANTIPSYCHOTICS

- Men: report erectile dysfunction, decreased orgasmic quality with delayed, inhibited or retrograde ejaculation, and diminished interest in sex.
- Women experience decreased desire, difficulty achieving orgasm, changes in orgasmic quality and anorgasmia.
- Dyspareunia, secondary to estrogen deficiency, can result in vaginal atrophy and dryness.
- Galactorrhea is experienced in both sexes

THE RELATIVE IMPACT OF ANTIPSYCHOTIC DRUGS ON SEXUAL FUNCTION

- **Effect on sexual function**

Least



Most

Antipsychotic

- aripiprazole
- quetiapine
- clozapine
- olanzapine
- haloperidol
- risperidone

BLOOD PRESSURE MEDICATION

- In women, it can lead to vaginal dryness, a decrease in desire, and difficulties achieving orgasm.[2]
- Some diuretics, not only interfere with blood flow to the sex organs but increase the body's excretion of zinc, which is needed to produce testosterone. [1]
- And beta-blockers can sabotage a satisfying sex life at least three ways — by making you feel sedated and depressed, by interfering with nerve impulses associated with arousal and by reducing testosterone levels [1]
- a benzodiazepines calcium channel blocker is often the best choice, and drugs in this class have been shown to cause fewer adverse sexual effects [1]

HYPERTENSIVES: MEN

- In men, the decreased blood flow can reduce desire and interfere with erections and ejaculation[2]
- In an international survey, 20% of men using beta blockers (beta adrenoceptor antagonists) for hypertension had erectile dysfunction.[5]
- Centrally acting alpha agonists (clonidine) and diuretics have also been implicated in impairing sexual function.[5]
- The aldosterone receptor blocker spironolactone also blocks the androgen receptor and is associated with erectile dysfunction and gynecomastia.[5]

HYPERTENSIVES: WOMEN

- Sexual dysfunction more common in women with hypertension (before treatment) compared to normotensive women (42% vs 19%). [3]
- poorly studied in women, these drugs may have similar adverse effects on the arousal phase as in men, leading to failure of swelling and lubrication.[4]
- Decreased sexual desire (41% of women) and sexual pleasure (34%) have been reported [4]
- Alpha adrenergic drugs such as (clonidine and prazosin) also **reduce desire and arousal**. [5]
- The angiotensin II receptor antagonist, **valsartan**, was associated with **improved sexual desire and fantasies** when **compared** with the beta blocker **atenolol** in women with hypertension. [5]

CARDIOVASCULAR DRUGS

Decreased Desire

- clonidine
- digoxin
- hydrochlorothiazide
- methyldopa
- spironolactone

Decreased Arousal

- beta blockers
- clonidine
- digoxin
- hydrochlorothiazide
- methyldopa
- perhexilene
- spironolactone

Conaglen, H.M and Conaglen, J.V. (2013) . Drug induced sexual dysfunction in men and women. Aust. Prescriber (30, p 42-45.

ALTERNATIVES

- Lozol (indapamide) appears to be less of a problem than some of the other common water pills and impotence dropped from 75.3 % to 11.8%.[9]
- Capoten (captopril)

Angiotensin-converting enzyme inhibitor or angiotensin receptor blocker (ACEI/ARB) had higher odds of sexual activity in women [10]

- calcium channel blockers such as
  - Cardene (nicardipine),
  - Cardizem (diltiazem) or
  - Plendil (felodipine)

THE ANSWER….

- Alpha blockers, ACE inhibitors and calcium channel blockers are **not** considered to **cause erectile dysfunction**

- studies have suggested that angiotensin II receptor antagonists may even improve sexual function.[9,10]

STATINS

- that by limiting the availability of cholesterol, a building block of hormones, these drugs likely interfere with the production of testosterone, estrogen and other sex hormones.
- may cause erectile dysfunction (ED).
- men and women taking statins reported increased difficulty achieving orgasm.
- In one study, people's levels of sexual pleasure dropped along with their levels of LDL cholesterol.

ALTERNATIVE TO STATINS[1]

- slightly elevated cholesterol with a combination of:
- sublingual (under-the-tongue) vitamin
- B_{12}(1000 mcg daily),
- folic acid (800 mcg daily) and vitamin
- B_6 (200 mg daily).

H2 BLOCKERS

- H2 blockers can cause impotence (as well as breast enlargement in men) when taken at high doses for a long period of time.[1]

- Cimetidine (Tagamet) is associated with decreased libido, reduced sperm count and ED than other H2 blockers, including ranitidine (Zantac), famotidine (Pepcid) and nizatidine (Axid). [1]

ALTERNATIVES TO H2: HOME REMEDY

- apple cider vinegar and honey (one tablespoon of each in a glass of water), taken throughout the day, along with melatonin at bedtime.[1]

OTHER MEDICATIONS

Decreased desire

- Cimetidine

Decreased Arousal

- Antihistamines
- cimetidine
- cyproterone
- disulfiram
- gonadotrophin-releasing
- hormone agonists
- propantheline
- pseudoephedrine

Orgasm or Ejaculatory Difficulties

naproxen

NSAIDS AND MUSCLE RELAXANTS

- Naproxen (Anaprox, Naprelan,Naprosyn)
- Indomethacin (Indocin)

- Cyclobenzaprine (Flexeril)
- Orphenadrine (Norflex)

ANTIHISTAMINES

- **Dimehydrinate** (Dramamine)
  Diphenhydramine (Benadryl)
  Hydroxyzine (Vistaril)
  Meclizine (Antivert)
  Promethazine (Pheregan)
- Temporary loss of libido[4]

PARKINSON'S DISEASE MEDICATIONS

- Biperiden (Akineton)
  Benztropine (Cgentin)
  Trihexyphenidyl (Artane)
  Procyclidine (Kemadrin)
  Bromocriptine (Parlodel)
  Levodopa (Sinemet)

CANCER

- long-acting gonadotrophin-releasing hormone agonists used for prostate and breast cancer result in hypogonadism, with subsequent reduction in sexual desire, erectile dysfunction in men,
- vaginal atrophy and dyspareunia in women as well as orgasmic dysfunction

- Prostate cancer
- **Flutamide** (Eulexin)
  Leuprolide (Lupron)

- Chemotherapy
- **Busulfan** (Myleran)
  Cyclophosphamide (Cytoxan)

BIRTH CONTROL PILLS

- ALL OCP: lower estrogen (and testosterone) in the body by suppressing the ovaries' and therefore may also affect libido.
- increase the amount of SHBG x7 ,more testosterone will bind to it, which means less is left in the active form.
- According to Hormones and Behavior, Canadian researchers report that women with higher levels of testosterone climax more often than those with lower hormone levels
- The adrenaline rush of a budding relationship can also override the effects of low testosterone.

HORMONE ALTERNATIVES

- In women, estrogen cream can alleviate local symptoms such as atrophic vaginitis and dyspareunia.
- If a woman complains of sexual dysfunction while on an injectable progestogen, another form of contraceptive can be considered.[6]
- ospemifene (Osphena), acts like estrogen on vaginal tissues to make them thicker and less fragile, resulting in a reduction in the amount of pain women experience with sexual intercourse.[8]

OTHER "DRUGS"

- **Alcohol**: it does not directly increase libido. It causes sexual promiscuity, produces an illusion of confidence.
- **Illegal Drugs:** Anabolic steroids, unnaturally promote muscle growth and athletic performance, but they also cause an increase in sexual desire. "Party drugs" that increase libido include marijuana, amphetamines and cocaine
- Sildenafil Bodybuilders and other athletes take it as a performance-enhancing substance:

VYLEESI (BREMELANOTIDE): A MELANOCORTIN-RECEPTOR-4 AGONIST

- In premenopausal women with female sexual dysfunctions, self-administered, as desired,
- subcutaneous BMT was safe, effective, and well tolerated
- is meant to be used as needed, 45 minutes before sexual activity
- Major Side effects: **nausea** but was relatively mild and did not get worse over time

Global HealthCare. 2019. Bremelanotide expected to find adherents, say experts. *Pharmaceutical Today*. *https://www.pharmaceutical-technology.com/comment/bremelanotide-fda-approval/*

FLIBANSERIN (ADDYI)

- Originally developed as an antidepressant
- Works by enhancing downstream release of dopamine and norepinephrine while reducing serotonin release in the brain circuits that mediate symptoms of reduced sexual interest and desire
- approved by the FDA as a treatment for low sexual desire in **premenopausal women.**
- A daily pill, may boost sex drive in women who experience low sexual desire and who find the experience distressing.
- 0.5-1 more satisfying sexual experience /month
- Potentially serious side effects include low blood pressure, sleepiness, nausea, fatigue, dizziness and fainting, particularly if the drug is mixed with alcohol.
- Experts recommend that you stop taking the drug if you don't notice an improvement in your sex drive after eight weeks.

(Mayo Clinic , 2016, Addyi Prescribing information https://hcp.addyi.com/

FLIBANSERIN (ADDYI)
CONS

- with combined oral contraceptives and strong CYP2C19 inhibitors (e.g., proton pump inhibitors, selective serotonin reuptake inhibitors, benzodiazepines, antifungals) may increase the risk of hypotension, syncope, and CNS depression.
- Only available only through a restricted program called the *Addyi* REMS Program, because of the increased risk of severe hypotension and syncope due to an interaction between *Addyi* and alcohol.
- CNS depressants (e.g., diphenhydramine, opioids, hypnotics, benzodiazepines) may increase the risk of CNS depression (e.g., somnolence)
- you can not take a Diflucan within two days of starting the drug and within two weeks of finishing it
- ***Use of ADDYI and alcohol increases the risk of severe hypotension and syncope; therefore, alcohol use is contraindicated.***
- 4 of 23 people needed medical attention because their had such a profound drop in blood pressure or fainted.
- All of your patients will receive their first 8 weeks of Addyi FREE, regardless of insurance coverage. Then $25/$99/month

(Mayo Clinic , 2016), Addyi prescribing https://hcp.addyi.com/

STRATEGIES TO MANAGE SEXUAL DYSFUNCTION

- Taking a phosphodiesterase type 5 inhibitor in anticipation

of intercourse has become the standard of care for men. It improves erections in about 70% of men with hypertension.

- However, phosphodiesterase type 5 inhibitors are contraindicated in men using nitrates

- In women, sildenafil has shown promise for reversing the inadequate lubrication and delayed orgasm induced by SSRI

(Mayo Clinic , 2016)

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