Sexual Dysfunction in Men

Causes, Diagnosis, & Treatment Options

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Sexual dysfunction:

Physical or psychological problems that prevents sexual satisfaction

Desire or arousal

Psychological cause

Low testosterone

Insufficient dopamine

Decreased oxytocin

Medication side effects

Insomnia, OSA

Orgasm disorder

Premature ejaculation—occurs before or too soon for preference

Inhibited or delayed ejaculation

Retrograde ejaculation—ejaculate forced back into bladder

Erectile dysfunction

Psychological cause

Pornography overuse/abuse

Vascular dysfunction

Medication side effects

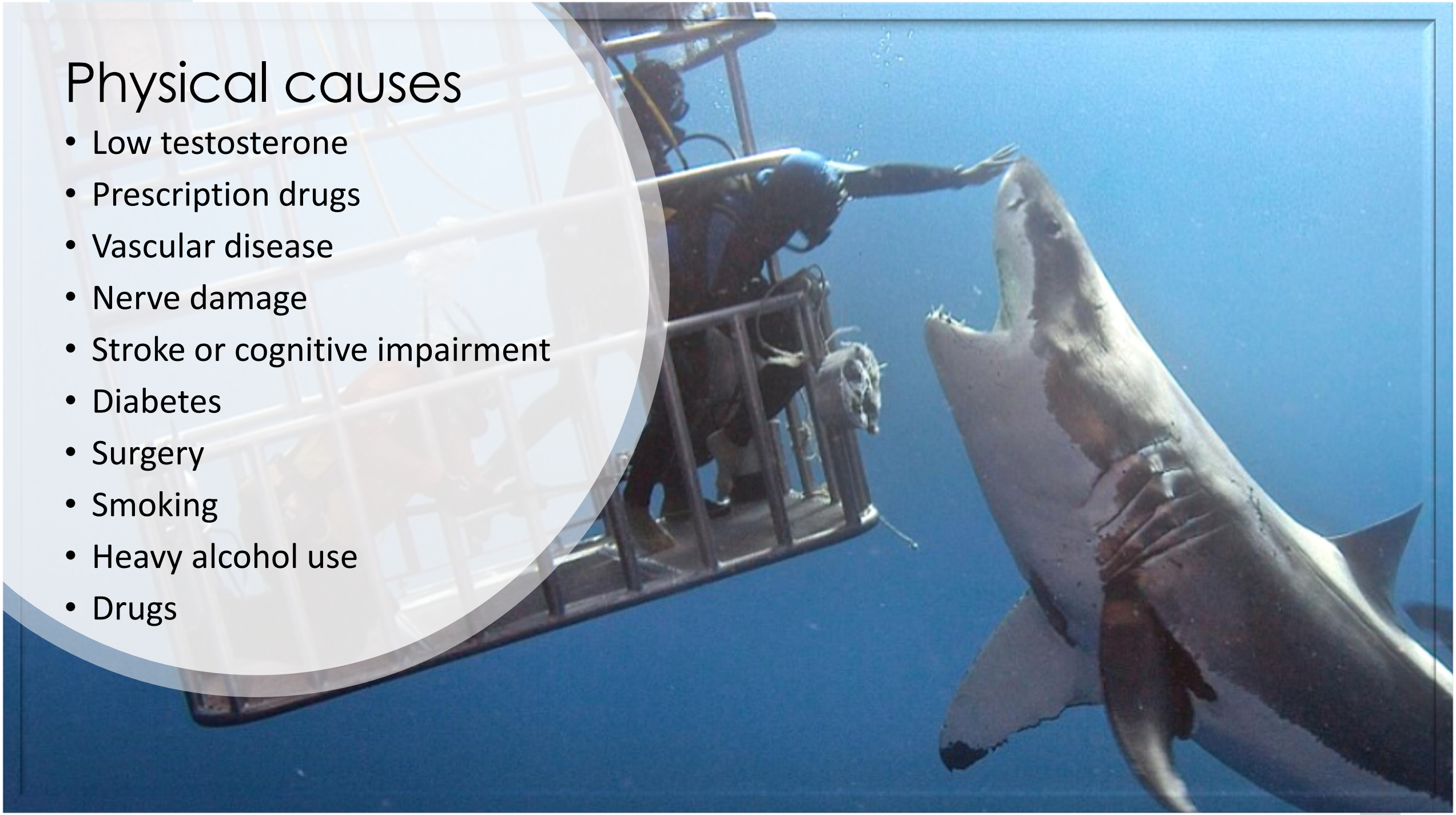
Neurological problem

Psychological causes

- Performance anxiety
- Sexual trauma or PTSD
- Relationship problems
- Depression
- Feelings of guilt
- Anxiety
- Low self-confidence or self-esteem
- Stress

Physical causes

- Low testosterone
- Prescription drugs
- Vascular disease
- Nerve damage
- Stroke or cognitive impairment
- Diabetes
- Surgery
- Smoking
- Heavy alcohol use
- Drugs



Desire or arousal problem:
inhibition, low libido, hypo & hypersexual desire


Photo credit: Simon Matzinger

Expectation

Sexual frequency (2010 AARP survey of 1,670 men & women ≥ 45 yo)[1]

- Sex at least 1 x week
  - 41% of men in 50s
  - 24% of men in 60s
  - 15% of men ≥ 70s
- 34% of men masturbate at least once a week
- 48% of single currently dating (6% of respondents) have sex at least once a week vs 36% married people (54% of respondents)
- 60% singles satisfied with their sex lives vs 52% married
- 20-30% of men & women remain sexually active into their 80s[2]

Genital self-image & self-confidence

Kinsey study 2,500 men

- Average flaccid penis 1-4”
- Average erect penis: 5-6.5” long, 4-5” circumference
  - There was a slight underestimation of penis size compared to actual measurement[3]

Micropenis: <2.8” in length when stretched

  - 0.6% of men, caused by low testosterone at late stage of fetal development

Male Genital Self-Image Scale (MGSIS)[4]

Better genital self-image, better scores on International Index of Erectile Function (IIEF)

Heterosexual men had better scores than those choosing "other" for sexual orientation

>90% of men comfortable with partner viewing their genitals

~25% comfortable with medical exam

20% of men dissatisfied with penis size

Sexual desire occurs in the brain

Limbic system (amygdala, hippocampus, dentate & cingulate gyrus)

- Common to all mammals & is one of the oldest areas of the brain
- Regulates emotion & attempts to avoid pain & seek pleasure

Activation of amygdala triggers erections, sexual feelings, pleasure, & sexual memories

Sexually-pleasing visual stimuli activate amygdala & hypothalamus more in men than women[5]

Sexual desire occurs in the brain

Input from amygdala travels to ventral striatum (nucleus accumbens, putamen, medial caudate nucleus)

Nucleus accumbens large concentration of dopaminergic neurons

- Pleasure & reward area

During orgasm, mesodiencephalic transition zone activated[6]

- Involved in variety of rewarding behaviors
- “Ejaculation parallels heroin rush”
- Also rCBF increases in cerebellum (plays a role in emotional processing)

Dopamine

Synthesized in brain & kidneys

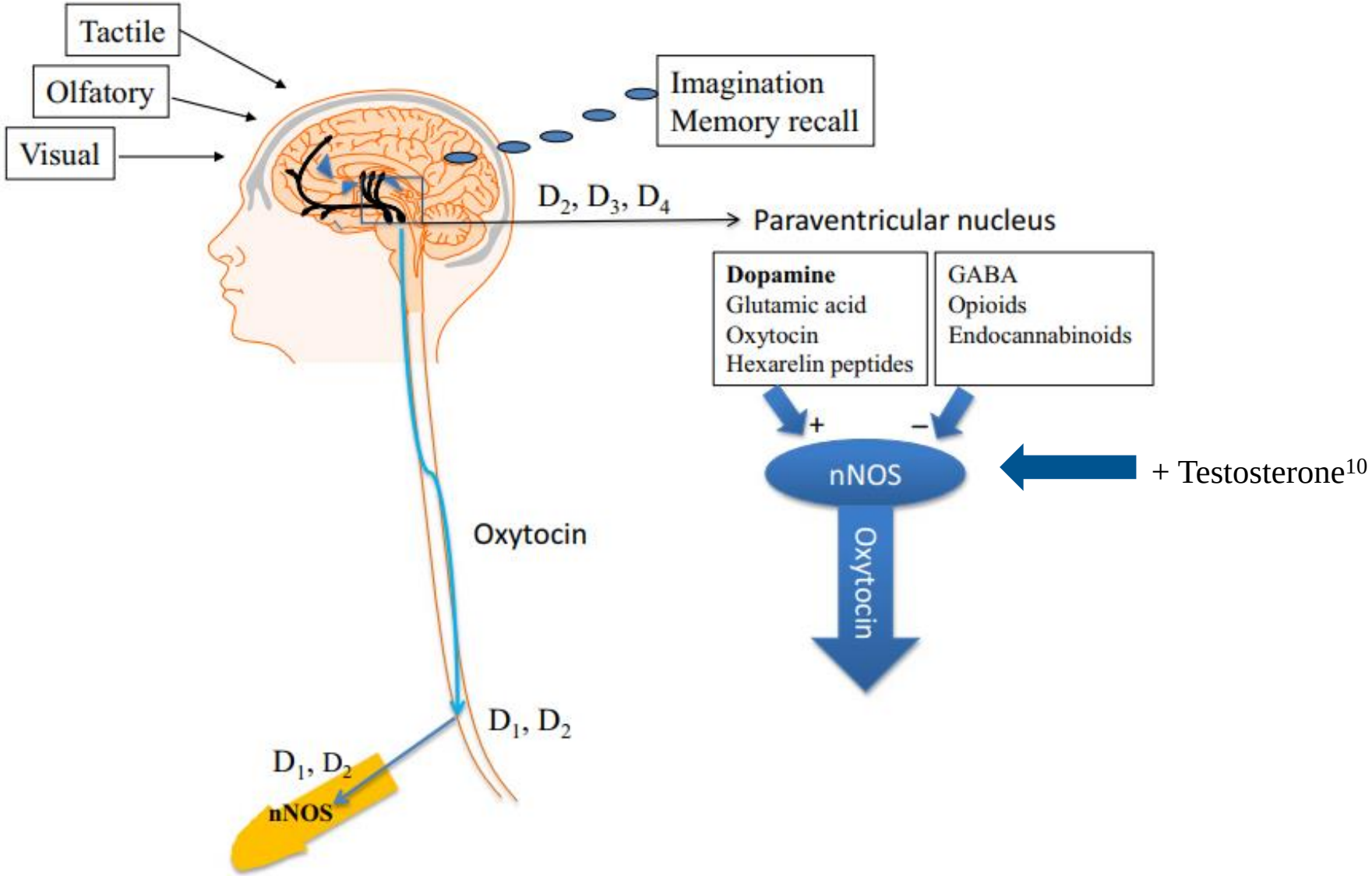
Reward-mediated behavior & reinforcement

Anticipation triggers release

Main neurotransmitter that facilitates sexual motivation, intercourse, & genital reflexes[7,8]

Can trigger erections by acting on oxytocinergic neurons in the paraventricular nucleus (PVN) of hypothalamus

Activation of dopamine receptors in lumbosacral parasympathetic nerves of spinal cord facilitate erections[9]



Simonsen U, et al. (2016). Modulation of dopaminergic pathways to treat erectile dysfunction. Basic Clin Pharmacol Toxicol. 119(Suppl3):63-74.

Oxytocin

Peptide hormone & neuropeptide made by hypothalamus, released by posterior pituitary during kissing, hugging, sexual arousal, & possibly orgasm[11-13]

Attachment, bonding, mb monogamy

- Activates nucleus accumbens & ventral tegmental area (VTA)
- Intranasal oxytocin increases attractiveness of partner compared to other females[14]

Promotes erections

- Oxytocin injected into PVN & VTA of male rats induces erections & increases dopamine in nucleus accumbens & PVN[15,16]

Hippocampus whitei

Photo credit: Pat Morris

Oxytocin

Regulated by other hormones & neurotransmitters

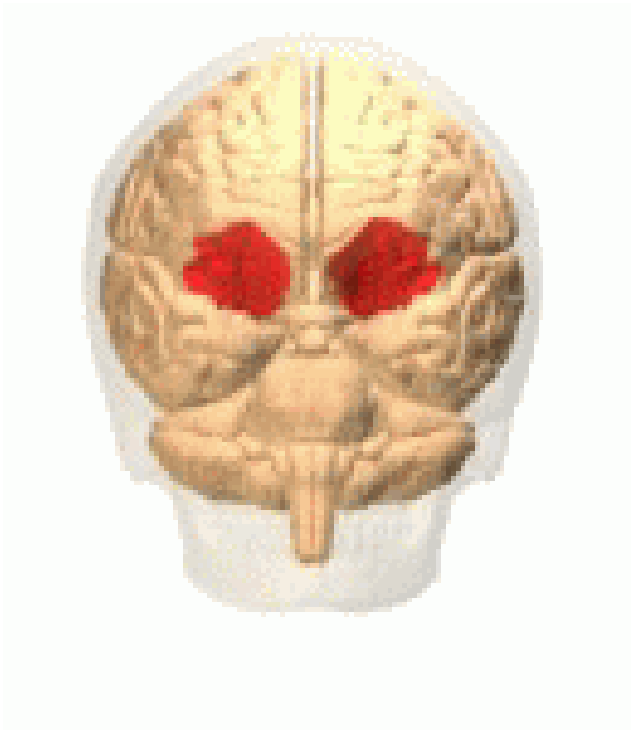
- Inhibited by endogenous opioids, GABA, endocannabinoids
- Stimulated by dopamine

Life experiences affect the methylation of the oxytocin receptor gene & its expression[17]

- Social isolation reduces expression of oxytocin receptor

Plays a role in muscle regeneration[18]

- Genetic lack of oxytocin causes premature sarcopenia



Hypoactive sexual desire disorder (HSDD)

Orbitofrontal cortex

First place where olfactory & taste information converge

Large network of connections projecting to hippocampus, ventral tegmental area, & amygdala

Involved in learning, prediction, & decision making for emotional & reward-related behaviors[19]

Increased activity in medial orbitofrontal cortex in HSDD[20]

Can also be dt limbic system damage[21]

Photo credit: Linus Nylund

Hypoactive sexual desire disorder (HSDD)

Persistent or recurrent deficient or absent sexual/erotic thoughts or fantasies & low or absent desire for sexual activity

Causes distress or impairs man's life or interpersonal relationships

Not attributable to another psychiatric disorder, substance use (drugs or medications), or medical conditions

HSDD prevalence & causes

15% of men (National Health & Social Life Survey), up to 40% older men[22,23]

Causes (lifelong, situational, acquired): [24]

- Gender identity or sexual orientation
- Paraphilia (“abnormal” sexual desires)
- Trauma
- Difficulty in new or long-term relationship
- Testosterone deficiency
- Neurotransmitter imbalance[25]

Photo credit: Vlad Tcompalov

Hypersexual disorder

Recurrent, intense sexual fantasies, urges, & behavior ≥ 6 months w/ ≥ 4 of the following:

- Excessive time spent fantasizing about sex, planning for & engaging in sexual behavior
- Repetitively engaging in
  - Sexual fantasies, urges, & behavior in response to dysphoric mood states (e.g., anxiety, depression, boredom)
  - Sexual fantasies, urges, and behavior in response to stress
  - Sexual behavior while disregarding the risk for physical or emotional harm to self or others
- Unsuccessful efforts to control or reduce these sexual fantasies, urges, & behavior

Photo credit: Pietro Jeng

Hypersexual disorder

"Sex addiction" dx controversial

Similar to other addictions—addicts crave euphoria from sex & use it to escape from unpleasant or painful emotions (a form of self-medicating)

Cycle of indulging, feeling guilt and remorse, desire to change, giving into craving

Causes & risk factors:

- Childhood or prior sexual abuse
- Co-occurring psychiatric disorder (impulse control, BPD, bipolar disorder, anxiety)
- Co-occurring substance abuse/addiction
- Brain injury
  - Limbic or temporal lobe injury
  - Bilat damage to hypothalamus[26]
  - Injury to prefrontal cortex
  - Temporal lobe epilepsy[27]

Photo credit: Kyaw Tun

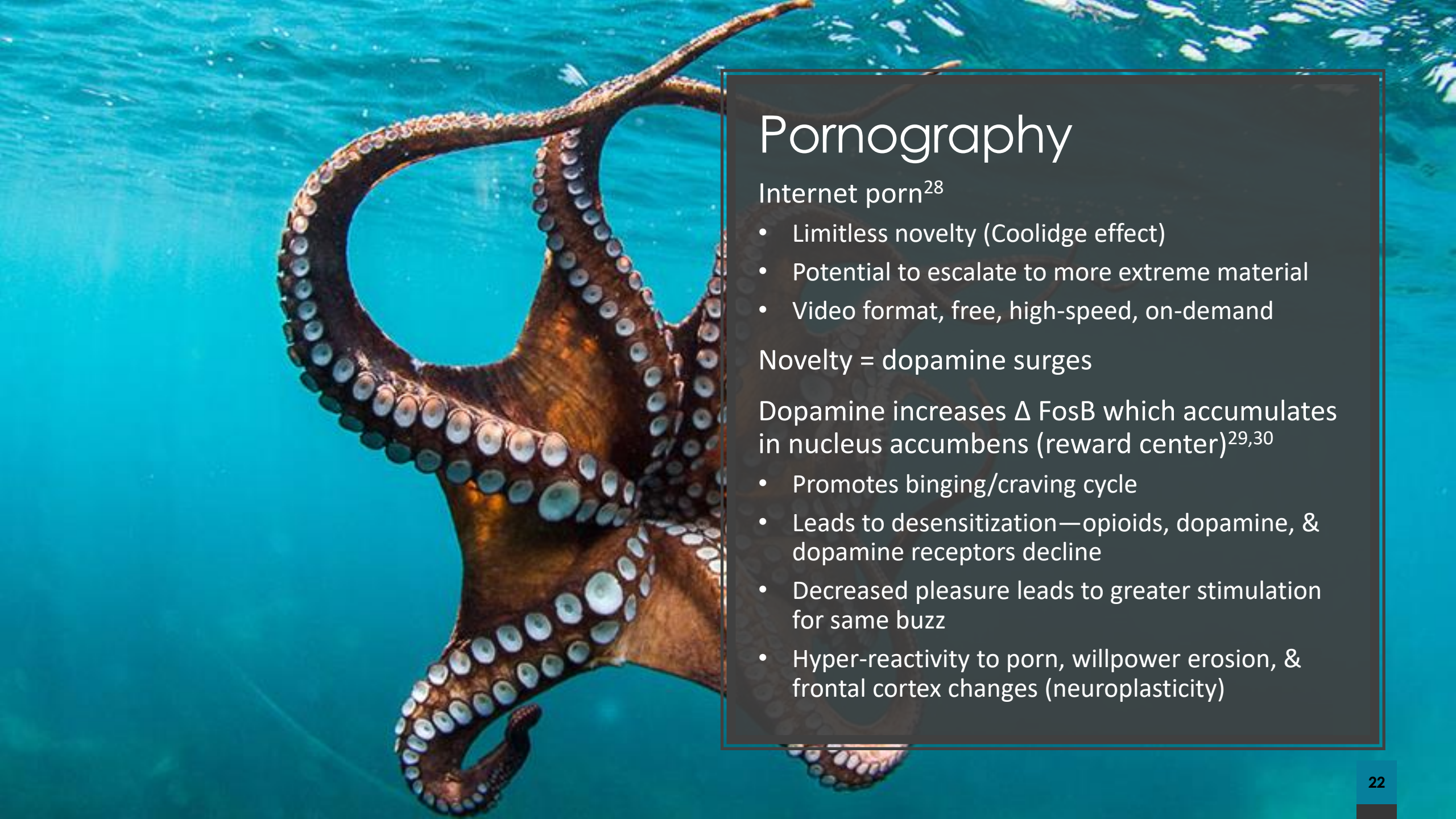
Photo credit: Pratik Mehta

Coolidge Effect

Coined by Frank Beach, psychologist & founder of behavioral endocrinology

> *President Coolidge and his wife were individually shown around a farm. When Mrs. Coolidge came to the chicken yard she noticed a rooster who mated repeatedly & asked how often it happened. When told "dozens of times each day" she said, "Tell that to the President when he comes by."*
>
> *Upon being told, the President asked, "Same hen every time?" The reply was, "Oh, no, Mr. President, a different hen every time." President: "Tell that to Mrs. Coolidge."*

Definition: males exhibit renewed sexual interest if introduced to different receptive sexual partners. Possible evolutionary benefit so a male can fertilize multiple females.



Pornography

Internet porn[28]

- Limitless novelty (Coolidge effect)
- Potential to escalate to more extreme material
- Video format, free, high-speed, on-demand

Novelty = dopamine surges

Dopamine increases Δ FosB which accumulates in nucleus accumbens (reward center)[29,30]

- Promotes binging/craving cycle
- Leads to desensitization—opioids, dopamine, & dopamine receptors decline
- Decreased pleasure leads to greater stimulation for same buzz
- Hyper-reactivity to porn, willpower erosion, & frontal cortex changes (neuroplasticity)

Most common Rxs that inhibit libido

TCAs: amitriptyline, doxepin, imipramine, nortriptyline

SSRIs: fluoxetine, sertraline, paroxetine, citalopram, escitalopram

Diuretics: spironolactone, thiazides

α-adrenergic blockers: terazosin, prazosin

β-blockers: propranolol, metoprolol, carvedilol

Hormone blockers: Lupron, Zoladex

Ejaculation problems

Premature, Delayed, Retrograde

Premature

Ejaculation prior to or soon after vaginal penetration w/inability to delay ejaculation & negative consequences (e.g., distress, avoidance of sexual intimacy)

Most common sexual complaint by men

- Internationally 20-30% of men[31]
- Probably under-reported & undertreated[32]

Occasional PE is normal. Ave time from beginning of intercourse to ejaculation is 5 min.

Causes: psychological, environmental, endocrine, neurobiological, possibly genetic (5-HT1 receptor polymorphism)[33]

PE Treatment

CBT or sex therapy

Yoga (= fluoxetine)[34]

SSRIs (off-label) esp. paroxetine

Dapoxetine 30 or 60 mg (phase III trials in US)[35]

- 1st drug specifically developed for PE
- Serotonin, dopamine, NE reuptake inhibitor
- Can be used “on demand” – peaks in 60 min
- Mean half-life 1.4 hrs (vs 21 h-4 d with other SSRIs)[36]
- Doesn’t accumulate with multiple doses[37]
- Don’t combine with MAO inhibitors, SNRIs, other SSRIs
- Okay to use with PDE5i[38]

If ED plus premature ejaculation, treat ED first (PE may not be a problem after ED treated)[39]

Photo credit: Fabrizio Frigeni

Delayed ejaculation

Delay in, infrequency of, or absence of ejaculation ≥75% of occasions for ≥ 6 mos

Least studied/understood male sexual dysfct[40]

Can be lifelong (primary) or acquired (secondary); Prevalence 1-4%

Increases with age—3% of men in their 40s, 43% of men in their 70s[41]

Causes:

- Psychological
- Neurological damage (stroke, MS, spinal cord injury)
- DM
- Endocrine (hypogonadism, hyperprolactinemia)
- Chronic prostatitis/chronic pelvic pain syndrome
- PC, BPH/LUTS surgery
- Medications (SSRIs, tamsulosin, finasteride, spironolactone)
- Heavy ETOH & marijuana use [42]

Delayed ejaculation treatment

Masturbation retraining

CBT

Penile vibratory stimulation (vibrators)

Testosterone therapy (low T assoc w/DE, high T assoc w/PE[43]

- 60 mg topical T to axillar for 4 mos ineffective[44]

Medications (all off-label)[45]

- Amantadine, cabergoline, apomorphine (dopamine agonists)
- Buproprion
- Cyproheptadine (serotonin & histamine antagonist)

Concurrent ED, treat with PDE5i

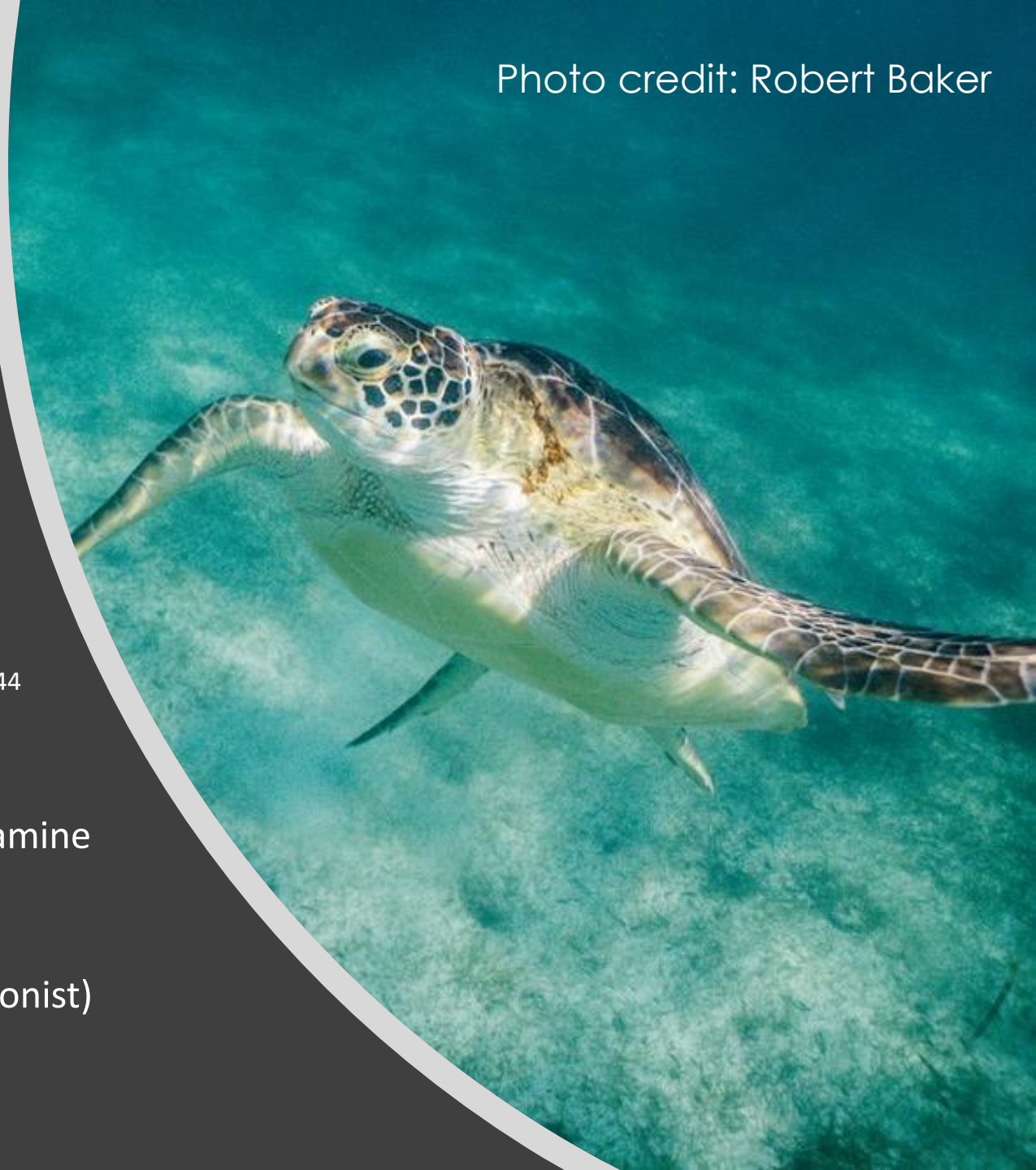


Photo credit: Robert Baker

Retrograde

Reduced ejaculation or dry orgasms

Causes:[46]

- Congenital
- Prostate surgery (TURP)
- Bladder neck damage
- Spinal cord injuries

Medications

- Alpha-adrenergic blockers
- Psychotropics

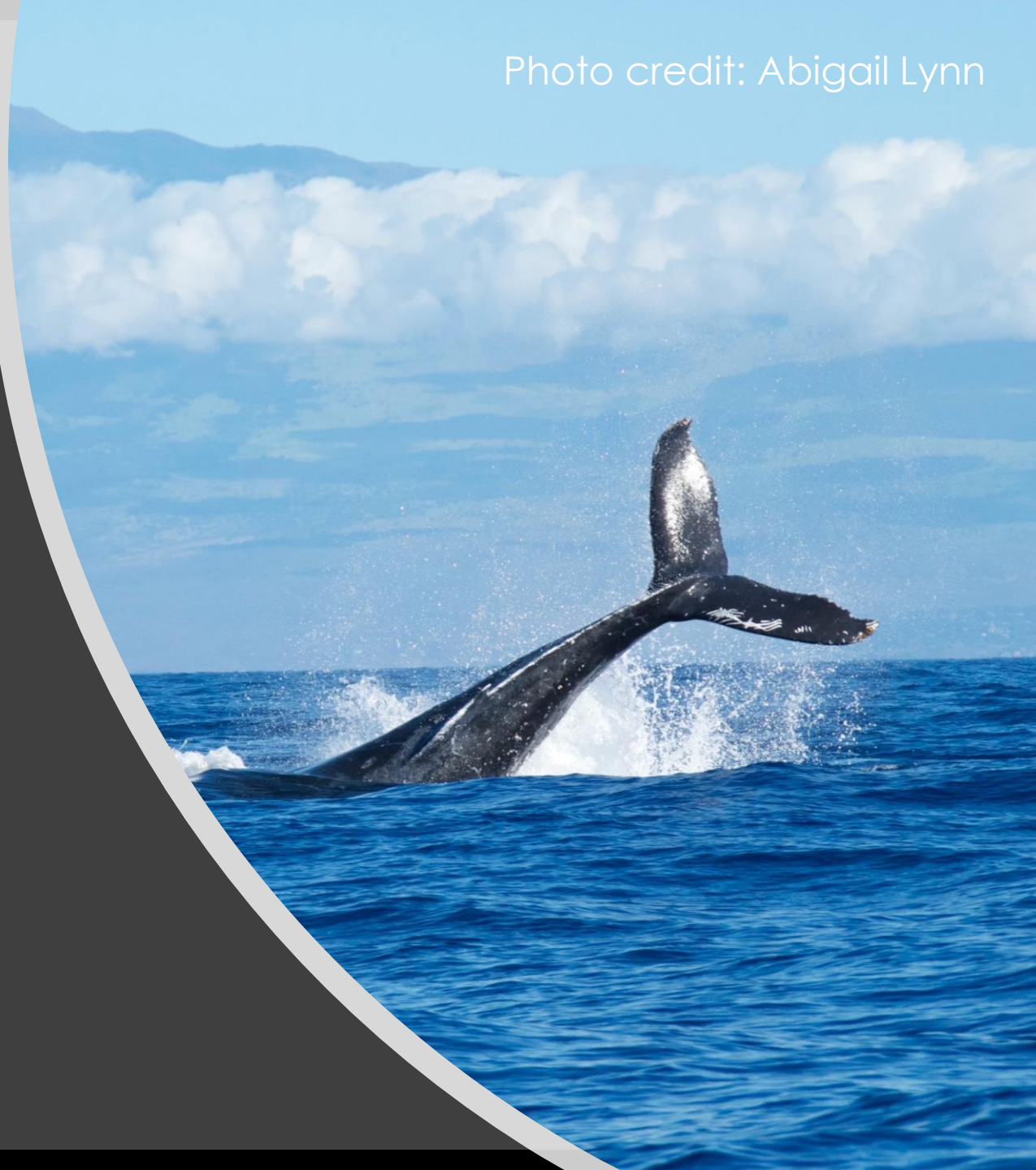
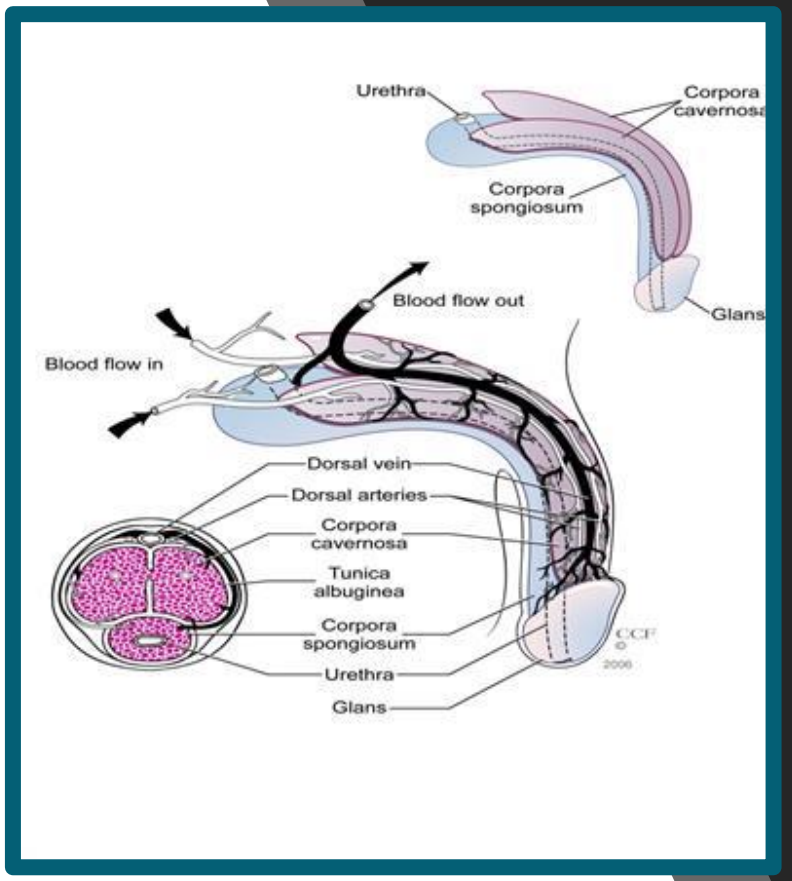


Photo credit: Abigail Lynn

Erectile dysfunction

Erectile physiology



Sexual stimulation → parasympathetic nerves release Ach → endothelial cells release NO → cGMP

Smooth muscle relaxation in arteries/arterioles of corpus cavernosa & spongiosum → rapid filling & expansion of sinusoidal system

Blood trapped in corpus caverona by occlusion of venous plexuses & tunica albuginea

Full erection intercavernous pressure 100 mmHg. Ischiocavernosus muscles compress blood-filled cavernosa. Perineal muscles contract causing final rigidity.

Ejaculation—vascular inflow & outflow temporarily cease & penile intracavernous pressure reaches several hundred mmHg

Erectile neurotransmitter release stops, PDE enzymes break down cGMP, SNS discharge during ejaculation → detumescence.

Nerves

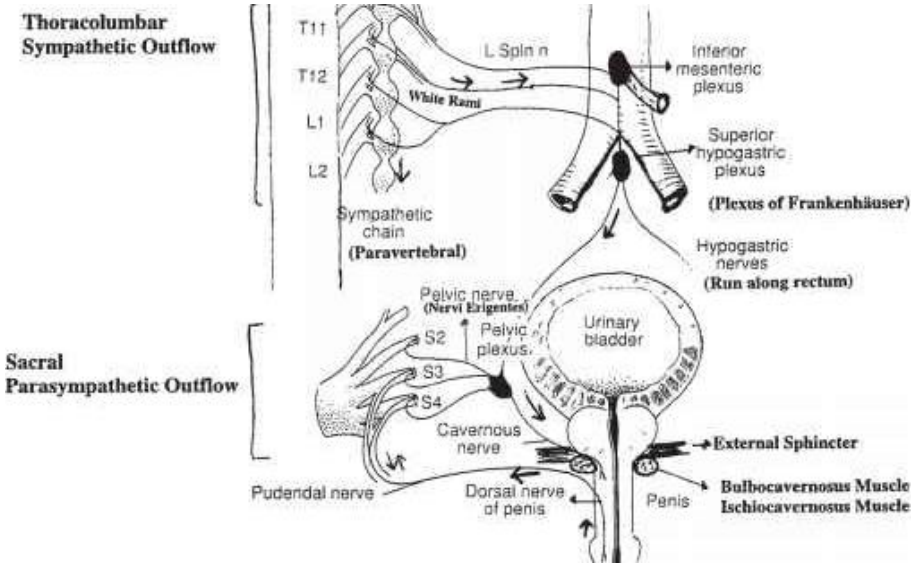
Autonomic (sympathetic & parasympathetic) and somatic (sensory & motor)

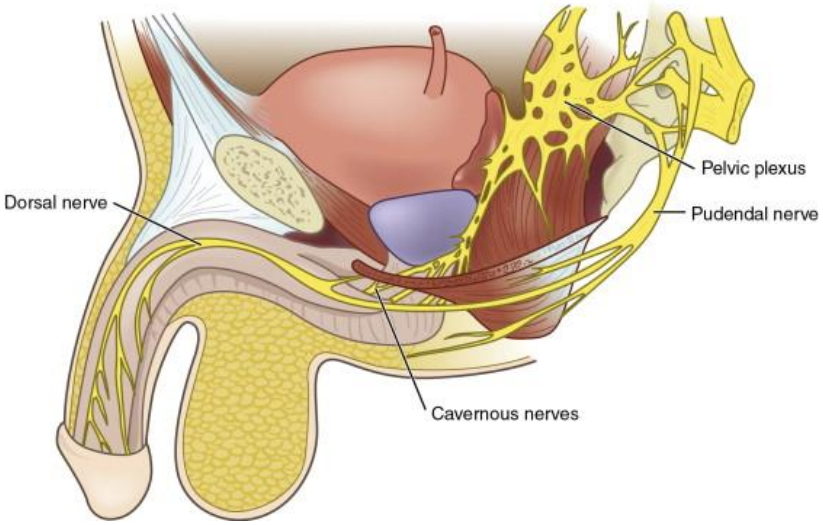
- Sympathetic (T11-L2): anti-erectile; control ejaculation & detumescence
- Parasympathetic (S2-S4): pro-erectile

Sympathetic & parasympathetic nerves merge to form cavernous nerves, which enter the corpora cavernosa, corpus spongiosum, and glans penis—regulate blood flow during erection

Pudendal nerve:

- Somatic sensory to entire pelvis
- Motor: all sphincters, pelvic floor, rigidity muscles





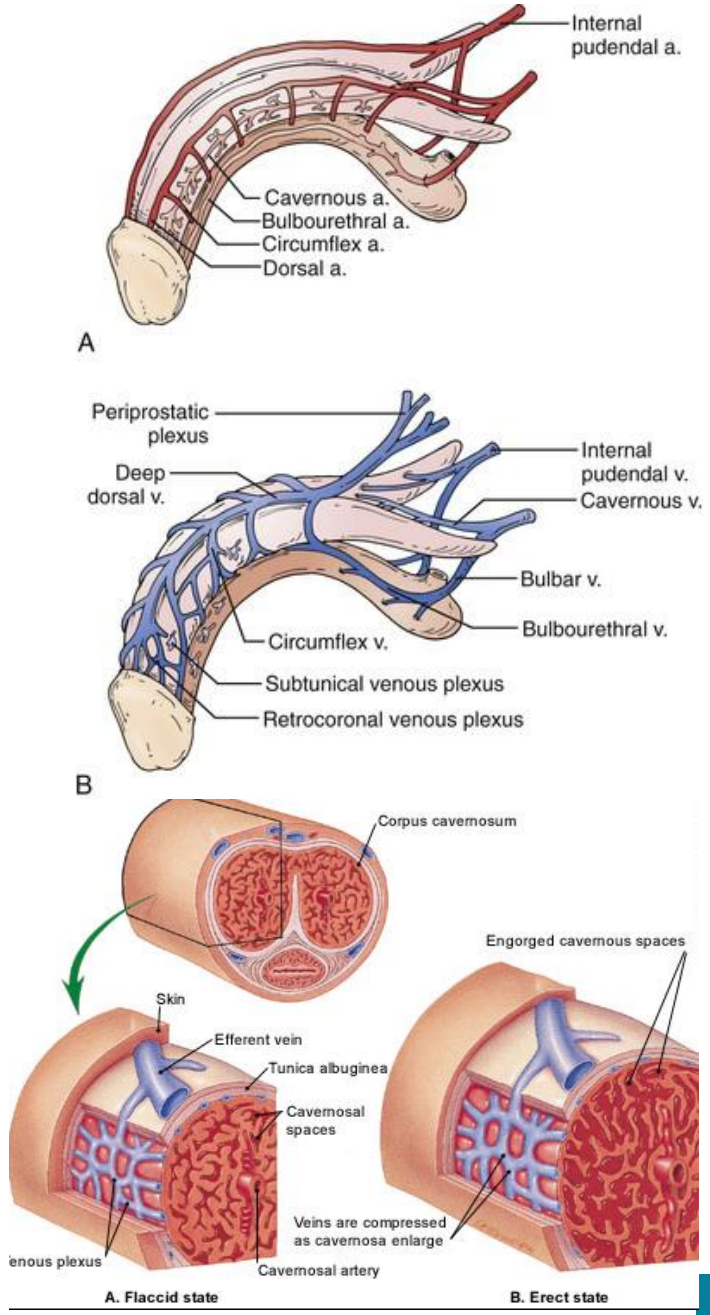
Vascular System

Internal pudendal arteries provide blood flow to the penis

Bulbourethral artery passes through the deep penile (Buck) fascia—supplies the bulb of the penis & penile (spongy) urethra

Dorsal artery travels between the dorsal nerve & deep dorsal vein & gives off circumflex branches that accompany the circumflex veins—terminal branches are in the glans

Deep penile (cavernosal) artery enters the corpus cavernosum at the crus and runs the length of the penile shaft—supply helecine arteries



ED causes & contributing factors

Psychological	• Depression & low libido • Performance anxiety • PTSD
Pornography	• Limitless novelty (Coolidge effect) • Cycle of binging and craving • Down-regulation of dopamine & dopamine receptors
Neurological	• Neurological disease (Parkinson's, AD) • Stroke • Damage to nerves (biking, prostate surgery)
Hormonal	• Hypogonadism • Thyroid dysfunction • T2DM, hyperinsulinemia/IR
Drugs	• Antihypertensives • SSRIs • ETOH & tobacco
Vascular	• HTN • Diabetes • Atherosclerosis

Depression & Anxiety

Mild-to-moderate depression plus ED—when ED improves with treatment, depression may improve[47]

Performance anxiety—first described by Masters & Johnson in 1970[48]

PTSD & hyperactive amygdala:

- ED in 85% of veterans w/PTSD vs 22% of veterans w/o PTSD[49]

Psychogenic ED Dx: erectile function normal with masturbation, with a different partner, or with different stimuli.

- Nocturnal or morning erections often normal.
- Often abrupt onset or associated w/stress (e.g., job loss, death of relative, financial problems)

See “The Great Porn Experiment” – Ted Talk, Gary Wilson

Porn-induced ED

2002 meta-analysis of ED studies reported consistent rates of 2% in men under 40.[50]

This was before Internet “porn tube sites” which appeared in 2006.

ED much more common in younger men now

- 2012 Swiss study: 30% of men 18-24 yo[51]
- 2013 Italian study: 25% of men <40 yo[52]
- 2014 Canadian study: 25% of men 16-21 yo[53]

Photo credit: Masaaki Komori

Photo credit: Jason Leung

Neurogenic

10% to 19% of all causes of ED[54]

- MS, Parkinson's
- Diabetes (also vascular)
- Stroke
- Surgery (radical prostatectomy: 18-24 mos dt cavernous nerve neuropraxia)
- Spinal cord injury
- Long-distance cycling?
  - Compression of pudendal nerve & blood vessels b/n saddle & pubic symphysis decreases blood flow & oxygen to penis[55,56]
  - ED mb temporary
  - Swimmers & runners same ED as cyclists[57]
  - Cyclists higher urethral strictures

Spinal Cord Injuries

WWII soldiers with severe or complete cervical or thoracic spinal cord injuries—still able to achieve complete erections[58]

- Physical penile stimulation sends sensory signals via the pudendal nerve to sacral nerves.
- Incoming signals activate connector nerve cells (interneurons) to stimulate nearby parasympathetic neurons.
- These neurons then transmit signals from the sacral spine to the penile blood vessels.
- As long as this reflex arc remains intact, an erection is possible.

Photo credit: Samuel Zeller


Photo credit: David Clode

Hormonal

Hypogonadism

- Minimal level testosterone necessary to maintain erectile function unknown (probably varies)[59]
- Testosterone decreases with age & ED prevalence increases with age (50% age 50, 60% age 60, 70% age 70)[60]

Hyperestrogenism—interdependent risk factor for ED? Increase in serum estradiol or increased estradiol-to-testosterone ratio?[61]

Hypo or hyperprolactinemia[62,63]

Hypo & hyperthyroidism—ED common[64]

- More in hyperthyroidism[65]

Hyperinsulinemia, IFG, T2DM—ED may be first clinical sign of metabolic disease & CVD[66]

Medication side effects

Alpha-adrenergic blockers: tamsulosin (Flomax)

Beta-blockers: carvedilol, atenolol, metoprolol

H2 receptor blockers: cimetidine (Tagamet), ranitidine (Zantac), Pepcid

Diuretics: HCTZ, spironolactone, triamterine

CNS depressants: alprazolam, diazepam, codeine

CNS stimulants: cocaine, amphetamines (Ritalin, Adderall)

Diuretics, such as furosemide (Lasix), spironolactone

SSRIs

Synthetic hormones: Lupron (Eligard)

Vascular dysfunction

Erectile dysfunction—harbinger of systemic disease[67]

ED increases risk of CVD, stroke, all-cause mortality[68]

ED & CVD same risk factors:

- Obesity
- HTN
- Smoking
- Physical inactivity
- Dyslipidemia
- Prediabetes, diabetes
- Standard American Diet (SAD)

ED as big a risk factor for future events as smoking & FH MI[69]

Underlying mechanism for ED & CAD is endothelial dysfunction (ED = ED)[70.71]

ED may be due to generalized or focal arterial disease[72]

Venom-occlusive dysfunction may contribute

Peyronie's

Prevalence 0.5-9% of men[73-75]

Risk factors: age, DM, smoking, genetics (20% of PD have Dupuytren's)

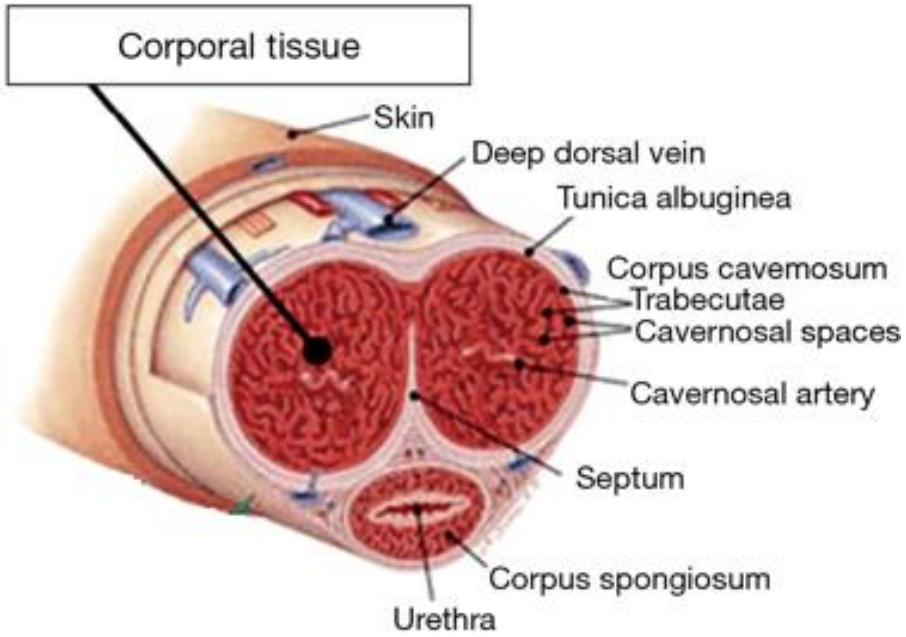
Tunica albuginea is mainly collagen with 5% elastin—allows penis to expand & lengthen during erection

Trauma or micro trauma to tunica albuginea combined with abnormal wound healing causes fibrotic nodules/plaques to form[76]

May cause ED dt scar preventing full expansion of corpus cavernosa and compression of veins, allowing venous leakage

- 32-80% also have ED

Penile curvature may make penetration difficult



Treatment

Nothing—natural course over 12 mos[77]

- Nearly all complete pain resolution
- Curvature:
  - 12% improve
  - 40% remain stable
  - 48% worsen

Collegenase clostridium histolyticum (Xiaflex)—only FDA-approved, non-surgical treatment

- MOA: selectively binds collagen, unravels fibril structure of plaques, breaks peptide bonds
- After 52 weeks, 33-35% change in erect penile curvature compared with 18-22% in placebo[78]

Plaque excision, esp when curvature >60° or w/severe narrowing (“hinging”) or plaque is large or calcified

Possibly effective treatments

Coenzyme Q10 (300 mg)[79]

Intralesional verapamil injection[80-85]

- Younger age and larger baseline curvature may respond better[84]
- Possibly better diluted (10 mg verapamil/20 mL)

L-carnitine (2 g/d) plus intralesional verapamil (10 mg x 10 wks)[86]

Interferon injections[87]

Vacuum pump[88]

Extracorporeal shock wave therapy (ESWT)[89,90]

- Improves pain, but may not improve curvature or plaque size
- Possibly better with 5 mg daily tadalafil)[91]

PRP or stem cell intercavernosal injections[92]

Ineffective treatments

Vitamin E (mb combined with verapamil, topical diclofenac, antioxidants)[93]

Colchicine[94]

Tamoxifen

Carnitine

Serrapeptase and nattokinase

Diagnosis

- Labs
- Imaging
- Questionnaires

Desire, Orgasm, ED

Take a good history

- Psychosocial issues (expectations, stressors, relationship)
- Health conditions (neurological issues, metabolic syndrome, DM, HTN, CVD, liver or kidney disease)
- Smoking
- ETOH & other drug use
- Medications

Questionnaires:

- Health Inventory (SHIM): 5 questions
- The International Index of Erectile(IIEF-15): 15 questions, validated in 32 languages[95]
  - IIEF-5: 5 questions[96]

Sexual Health Inventory for Men (SHIM)

OVER THE PAST 6 MONTHS						
1. How do you rate your confidence that you could get and keep an erection?		VERY LOW	LOW	MODERATE	HIGH	VERY HIGH
		1	2	3	4	5
2. When you had erections with sexual stimulation, how often were your erections hard enough for penetration (entering your partner)?	NO SEXUAL ACTIVITY	ALMOST NEVER OR NEVER	A FEW TIMES (MUCH LESS THAN HALF THE TIME)	SOMETIMES (ABOUT HALF THE TIME)	MOST TIMES (MUCH MORE THAN HALF THE TIME)	ALMOST ALWAYS OR ALWAYS
	0	1	2	3	4	5
3. During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?	DID NOT ATTEMPT INTERCOURSE	ALMOST NEVER OR NEVER	A FEW TIMES (MUCH LESS THAN HALF THE TIME)	SOMETIMES (ABOUT HALF THE TIME)	MOST TIMES (MUCH MORE THAN HALF THE TIME)	ALMOST ALWAYS OR ALWAYS
	0	1	2	3	4	5
4. During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?	DID NOT ATTEMPT INTERCOURSE	EXTREMELY DIFFICULT	VERY DIFFICULT	DIFFICULT	SLIGHTLY DIFFICULT	NOT DIFFICULT
	0	1	2	3	4	5
5. When you attempted sexual intercourse, how often was it satisfactory for you?	DID NOT ATTEMPT INTERCOURSE	ALMOST NEVER OR NEVER	A FEW TIMES (MUCH LESS THAN HALF THE TIME)	SOMETIMES (ABOUT HALF THE TIME)	MOST TIMES (MUCH MORE THAN HALF THE TIME)	ALMOST ALWAYS OR ALWAYS
	0	1	2	3	4	5
Add the numbers corresponding to questions 1–5.						TOTAL:
The Sexual Health Inventory for Men further classifies ED severity with the following breakpoints: 1–7 severe ED 8–11 moderate ED 12–16 mild to moderate ED 17–21 mild ED						

International Index of Erectile Function (IIEF-5)

Over the past six months:						
1	How do you rate your **confidence** that you could get and keep an erection?	Very low	Low	Moderate	High	Very high
		1	2	3	4	5
2	When you had erections with sexual stimulation, how often were your erections hard enough for penetration?	Almost never/never	A few times (much less than half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always/always
		1	2	3	4	5
3	During sexual intercourse, **how often** were you able to maintain your erection after you had penetrated (entered) your partner?	Almost never/never	A few times (much less than half the time)	Sometimes (about half the time)	Most time (much more than half the time)	Almost always/always
		1	2	3	4	5
4	During sexual intercourse, **how difficult** was it to maintain your erection to completion of intercourse?	Extremely difficult	Very difficult	Difficult	Slightly difficult	Not difficult
		1	2	3	4	5
5	When you attempted sexual intercourse, how often was it satisfactory for you?	Almost never/never	A few times (much less than half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always/always
		1	2	3	4	5

[a] The IIEF-5 score is the sum of the ordinal responses to the five items; thus, the score can range from 5 to 25.

Workup

- ✓Lab work: CBC, CMP, lipid panel, insulin, HbA1c, total & free testosterone, LH, estradiol, TSH, free T4, free T3, possibly prolactin, DHEA-S, cortisol
- ✓PE: BP, evidence of CVD (peripheral vascular disease, carotid bruit, JVD), waist circumference, liver enlargement, penile & testicular exam, pelvic floor muscle strength
- ✓Imaging (reserved for potentially surgical intervention)
  - Duplex doppler ultrasound
  - Penile arteriography (injecting dye to see blood flow in penile arteries)
  - Magnetic resonance imaging (MRI)

Porn Induced ED?

Porn vs anxiety-related ED:

1. On one occasion masturbate to your favorite porn (or simply recall it).
2. On another masturbate with no porn/porn fantasy. (no recalling of porn).
    - Compare quality of erection & time it took to orgasm. A healthy young man should have no trouble attaining a full erection & reaching orgasm without porn or porn fantasy**.**
    - If you have a strong erection in #1, but ED in #2, then you have porn-induced ED.
    - If #2 is strong, but you have trouble with a real partner, then you have anxiety-induced ED.
    - If you have problems during #1 & 2, may be severe porn-induced ED or an organic problem.

www.yourbrainonporn.com/how-do-i-know-if-my-ed-porn-related-test

Photo credit: David Clode

Other symptoms associated with porn dependency or addiction

1. Delayed ejaculation
2. Greater sexual excitement w/porn than w/partner
3. Decreased penile sensitivity
4. Ejaculating when only partly erect or getting totally erect only with ejaculation
5. Needing to fantasize to maintain erection or interest with sexual partner
6. Losing interest in earlier genres of porn
7. Decreasing sexual arousal w/sexual partner(s)
8. Losing erection while attempting penetration
9. Inability to maintain erection or ejaculate with oral sex

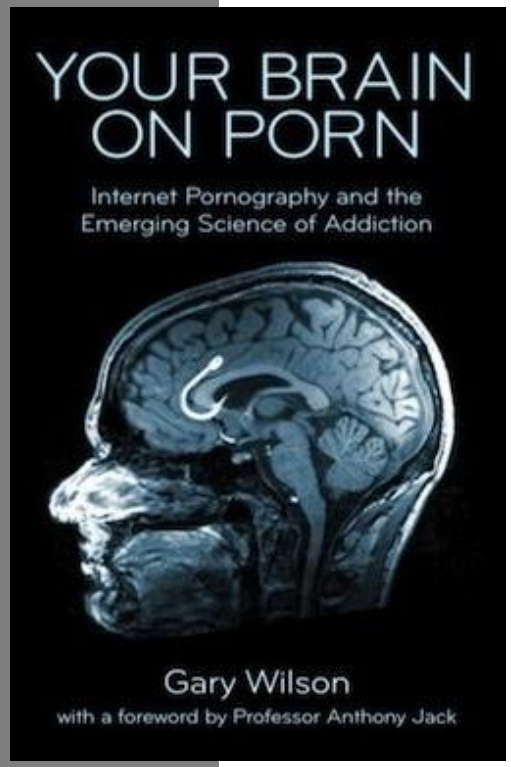
Treatment

Tolle causam
Treat whole person

Mental & physical health

- CBT
- EMDR
- Sex addicts anonymous (SA)
- Diet
- Exercise
- Weight loss

Treating Porn-induced low libido or ED



1. Eliminate porn, porn substitutes, & recalling porn (all artificial sexual stimulation)
2. Rewire sexual arousal to real people

How long will it take?

- 2 mos for men >50 (older guys didn't start on Internet porn when young & brain most vulnerable to addiction)
- 2-5 mos younger men

May experience withdrawal symptoms:

- Mood swings
- Anxiety including panic attacks
- Agitation/irritability
- "Flatline"—little or no libido

Prepare to confront deniers. Many men don't believe internet porn has caused their ED until they stop using it & recover erectile function.

Diet

Beets, leafy greens high in nitrates convert to nitrites. Increase NO & endothelial function, lower BP[97-99]

Pomegranate seeds, juice decrease ox & glyc LDL & reduce IMT.[100.101] Improve NO & lower inflammation & BP[102, 103]

Flavonoids from berries improve endothelial function[104]

HFCS & soft drinks increase metabolic syndrome, atherosclerosis, DM, & ED[105]

Advanced glycation end products (AGEs) contribute to DM, CVD, ED[106-108]

- Highest AGEs: bacon, fast food hamburgers, hot dogs, cheese, pizza, fried food (esp meat, chicken, potatoes)

Salt impairs vasodilation & endothelial function[109, 110]

4 clinical trials show MedDiet & lifestyle influence sexual function[111]

MedDiet in diabetic men delays sexual dysfct & lowers inflammation[112]

Exercise

Improves:[113-118]

- Visceral fat loss
- Endothelial function
- BP
- Inflammation
- Insulin sensitivity
- Lipoproteins

Increases endothelial progenitor cells (EPCs)[119]

Improves ED[120]

Photo credit: David Clode

Lose the fat

Fat tissue secretes >35 adipokines—nearly all promote inflammation, insulin resistance, & vascular disease[121,122]

Weight loss improves erectile function[123]

- Nutritional counseling & exercise advice
- Monthly meetings 1st year; bimonthly second year
- Goal: 10% weight loss; outcome 15% weight loss
- Increase activity ~ 3 hours per week
- Ave 33 lbs in 2 yrs
- Decreased IL-6, CRP

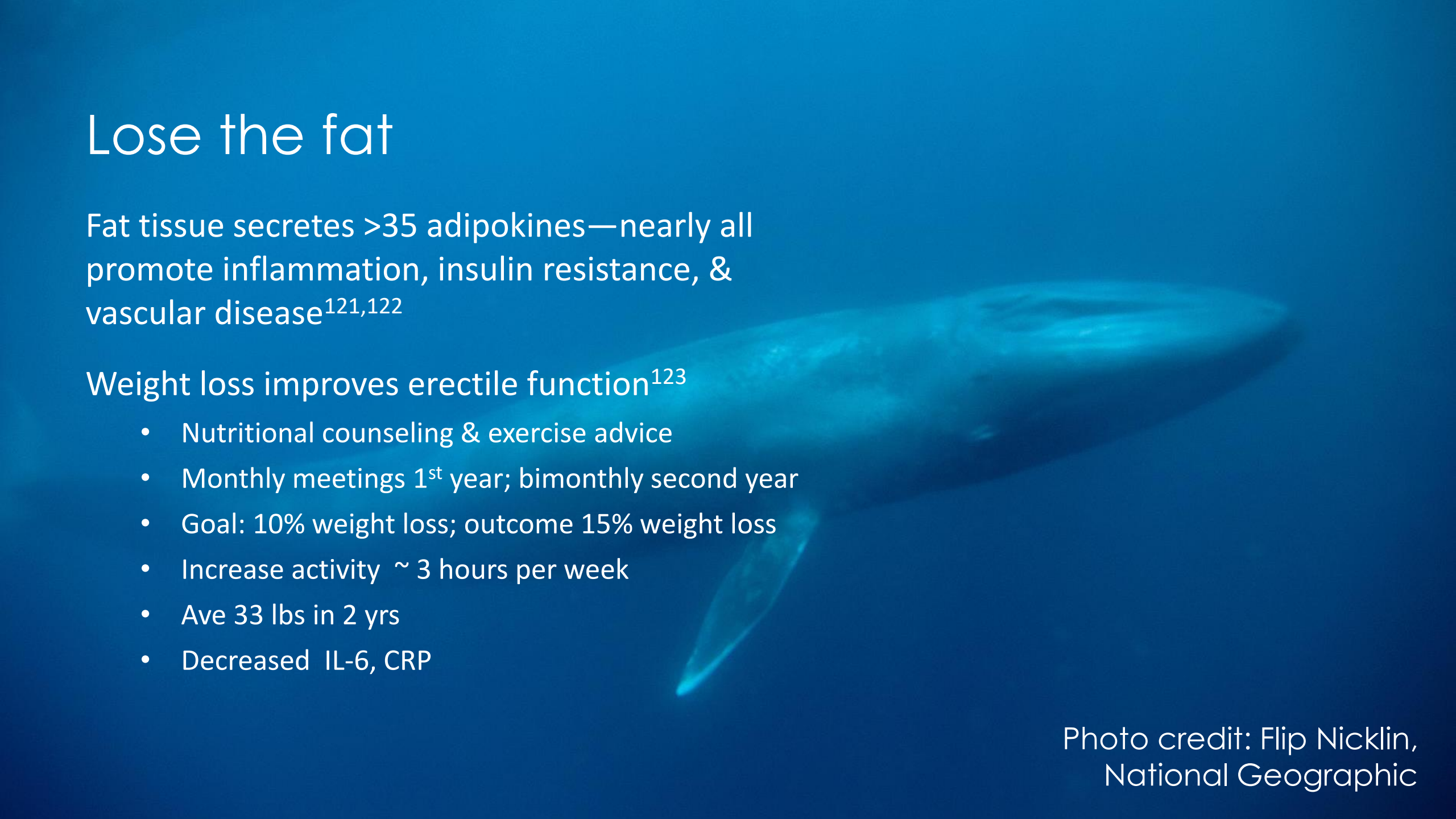
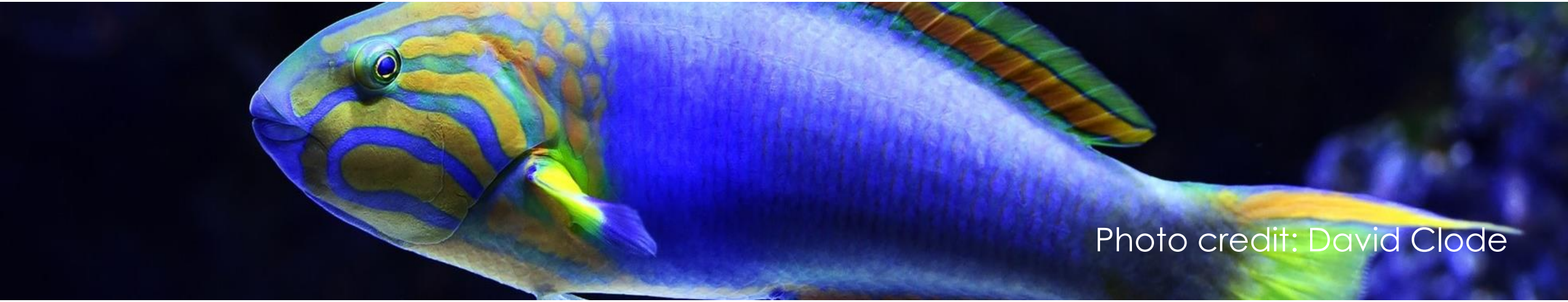


Photo credit: Flip Nicklin, National Geographic

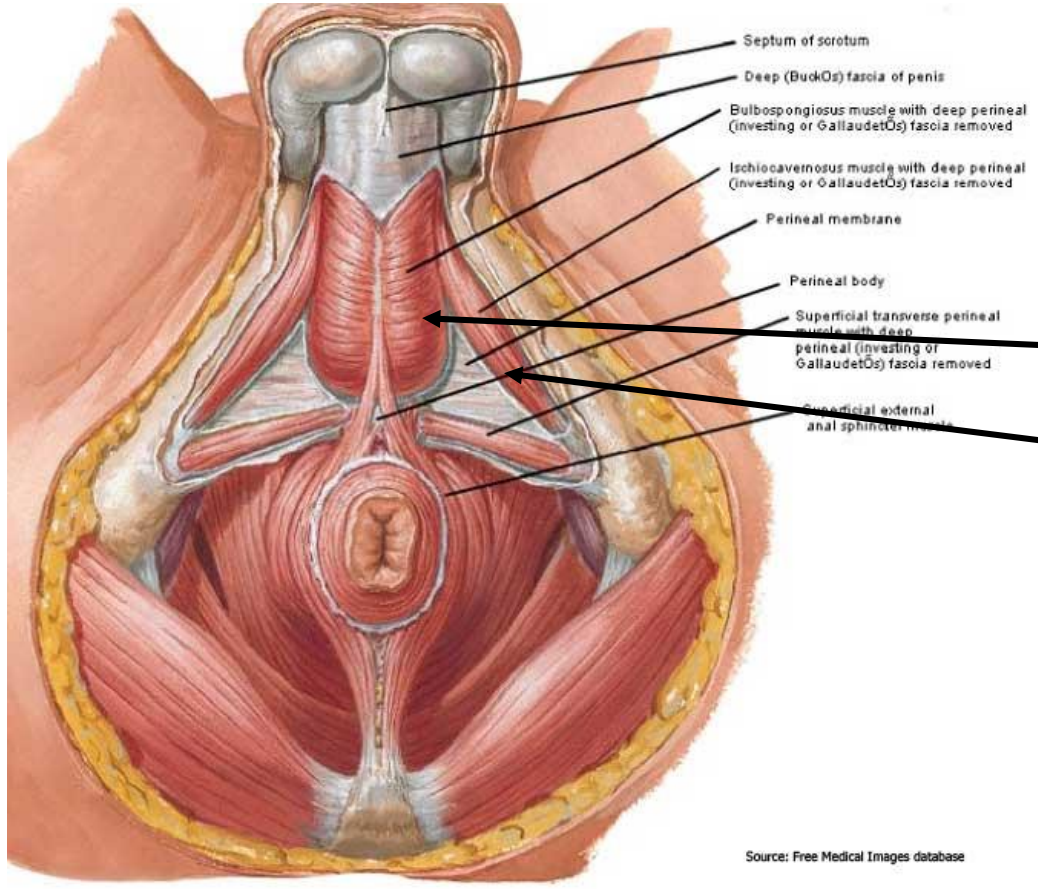
Physical & manual therapy



Physical therapy

Penis pump

Improve pelvic floor muscle tone/strength



Maintenance of erection (not done by NO alone)

Get weaker with age

Pelvic floor therapy improves ED (up to 75% of men may improve or resolve ED sx in 6 mos)[124]

Retract penis & lift scrotum (bulbocavernosus & ischiocavernosus muscle function)

1. Maximum contraction: 3 x lying, 3 x sitting, 3 x standing BID
2. Tighten pelvic floor muscles strongly after voiding urine

Also cured dribbling in 66% of men

Kegel exercise[125]

- Stop urine midstream several times during urination. These are the muscles you'll use.
- Perform Kegel holding for 5 seconds, 10-20 times, 3 x day
- Breathe and relax (no clenching buttocks or other muscles or holding breath)

Arnold Kegel, MD, 1894-1981

Vacuum constriction device (penis pump)

Geddins Osbon developed a “youth equivalent device” in 1960s. He personally used the device for more than 20 years without failure. First VCD device (Erecaid) FDA approved in 1982.

3 parts: vacuum cylinder, battery or manually operated pump, & constriction rings. Directions:

1. Place correct constriction ring over the open end of vacuum cylinder.
2. Apply water-soluble lubricant to base of penis & place vacuum cylinder over penis.
3. Generate negative pressure (100–225 mmHg) by hand or battery-operated pump to create an erection.
4. Move constriction ring onto the base of the penis to maintain erection. Do not leave on > 30 min dt risk of ischemia.

Supplements

Herbs

Amino acids

Yohimbe (*Pausinystalia yohimbe*)

Evergreen native to central Africa

- Bark contains 3 alkaloids: yohimbine (most active), rauwolscine, & corynanthine

Effective for ED[126-129]

My help with delayed/inability to ejaculate[130]

Dosage: 15-30 mg, up to 100 mg qd

- Onset 10-15 min; half life 35 min
- S/E: GI, tachycardia, HTN, anxiety

OTC brands not reliable

- 49 most popular brands—0 to 12.1 mg yohimbine/serving[131]
  - 19 brands no rauwolscine & corynanthine
  - 11 brands listed a specific quantity of yohimbine on the label--most were inaccurate
  - 2 brands accurate quantity of yohimbine & listed S/E

Tribulus terrestis

Grows in Europe, Asia, Africa, & Middle East

Root & fruit used in Chinese & Ayurvedic medicine

Doesn't raise testosterone (IV in primates does)[132-135]

May improve libido

May increase NO & improve erectile function(rats, rabbits)[136,137]

One human RCT (500 mg Tribulus terrestris, standardized to furostanol saponins, not less than 112.5 mg, TID pc): improved libido, ED, intercourse satisfaction, orgasmic function. No adverse effects.[138]

Eurycoma longifolia (Malasian ginseng, Tongkat Ali)

Chinese review of 11 RCTs & pilot trials: improved ED, semen volume, libido, & testosterone[139]

Mild increase in libido (8-10%)[140]

May increase testosterone, especially free T[141,142]

Improves ED[143,144]

Lowers cortisol & increases testosterone in stressed subjects & athletes[145]

Increases muscle strength[142]

Water root extract safe at high doses & long-term

Dosage: 200-300 mg QD or BID, patented form 22% eurypeptides & 40% glycosaponins

Photo credit: Steven Foster

Epimedium (Horny goat weed)

Farmers noted that goats & sheep became amorous after eating the weed

>60 species from Berberidaceae family

Icariin, assumed active ingredient--prenylated flavonoid

Improves erectile function (rats)[146]

PDE5 inhibitor[147,148]

May increase NO[149,150]

Dosage 900-1,500 mg qd

L-arginine & L-citrulline

L-arginine conditionally essential AA (if arginase enzyme increased, DM, renal failure[151,152]

- Used by enterocytes of intestine, liver, or converted into L-citrulline or L-ornithine
- 6 g PO absorption ~68%; 10 g absorption ~20%[153,154]
- L-citrulline → arginine in kidneys & > absorption[155]

When converted to citrulline, NO is byproduct

- Citrulline may increase plasma arginine > arginine supplementation[156]

May improve ED—5,000 mg (esp if low urinary NOx)[157]

- Increased ADMA inhibits eNOS. L-arginine supplementation may re-establish L-arginine:ADMA ratio to improve NO production/endothelial function.[158]

More effective for ED combined w/yohimbine or pycnogenol (pine bark of *Pinus pinaster*)[159-161]

S/E: Herpes activation & unsafe with recent MI (9g QD increased mortality)[162]

Boosting Dopamine

Exercise[163,164]

- Exercise requiring learning new skill better than sustained exercise for increasing synaptic connections[165-167]

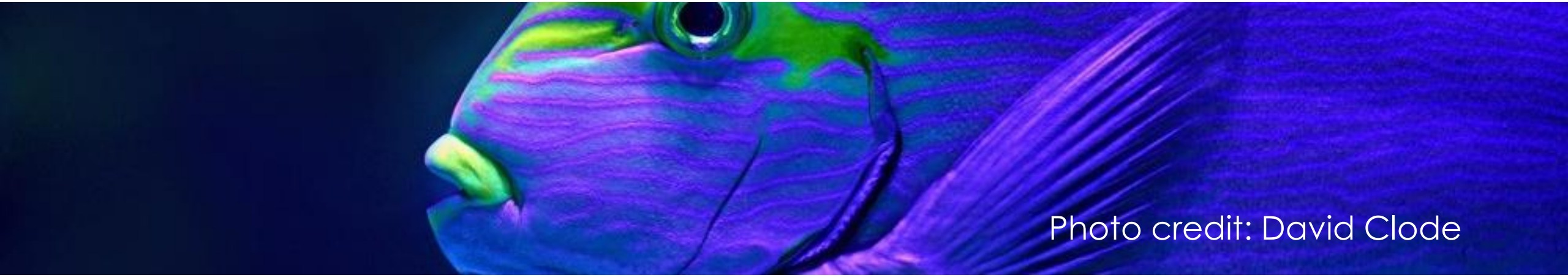
Meditation—increases theta activity correlated w/increased dopamine release[168]

AA precursors & cofactors to increase dopamine synthesis

- Amino acid precursors (L-phenylalanine → L-tyrosine→ L-dopa → dopamine → NE → epinephrine)
- Cofactors for production (tetrahydrobiopterine or BH_4, iron, B6)
- *Mucuna pruriens* improves sexual behavior in diabetic rats[169]
- Hypersexuality is S/E dopamine agonists (pramipexole & ropinirole)[170]

Photo credit: David Clode

Medications & hormones



SSRIs for premature ejaculation (dapoxetine under FDA review)

Testosterone

Oxytocin

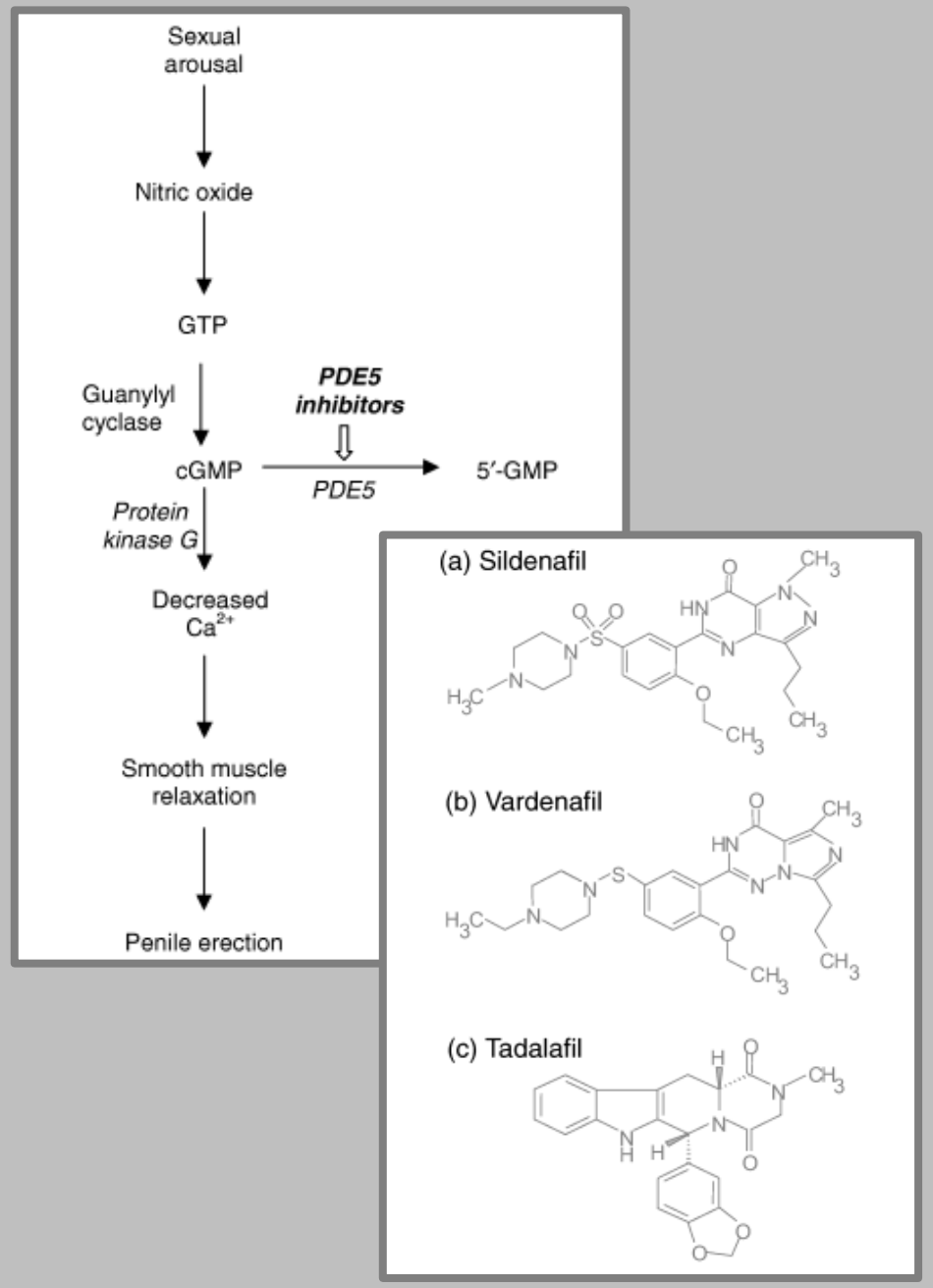
PDE5i

Apomorphine

Intercavernosal injections

Phosphodiesterase 5 Inhibitors (PDE5i)

- Sildenafil (Viagra®) – Pfizer, 1998 (patent expires 04/2020 but Teva & Greenstone (subsidiary of Pfizer) marketing generic since 12/ 2017)
- Vardenafil (Levitra®) – Bayer, 2003 (patent expires Oct. 31, 2018)
- Tadalafil (Cialis®) – Eli Lilly, 2003
- Avanofil (Stendra®) – Vivus, 2012
- Lodenafil (Hellavu—not FDA-approved)
- Udenafil (not FDA-approved)
- Miradenafil (Mvix—not FDA approved)



Mechanism of Action

1. Sexual arousal > NO release in corpus cavernosum & spongiosum
2. cGMP produced from GTP accumulates
3. Causes smooth muscle relaxation leading to an erection
4. PDE5i prevent cGMP breakdown, increasing NO activity

PDE5i have different selectivities for PDE isozymes (11 identified).[171]

- PDE6 enzyme in the retina transfers light into nerve impulses. Inhibition of this enzyme causes color perception disturbances.
- Vardenafil 3x, sildenafil 7 x, tadalafil 700 x more selective for PDE5 than for PDE6.

PDE5i Comparison

No head-to-head trials. Differences in onset, duration of action, & S/E/[172]

Sildenafil onset 30-60 min; half-life 4 hrs; duration 12 hrs (don't use within 4 hrs tamsulosin)

Tadalafil onset 60-120 min; half-life 17.5 hrs; duration 36 hrs

Vardenafil onset 30-60 min; half-life 4 hours; duration 10 hrs

Avanafil onset 15-30 min; half-life 3 hrs; duration 6 hrs

Hepatic metabolism via CYP3 A4

Side effects

Headache (10%-20%)

Flushing (5%-15%)

Dyspepsia (4%-12%)

Nasal congestion (1%-10%)

Dizziness (2%-5%)

Priapism (rare)

Vision abnormalities (6%)—"chromatopsia" dt PDE6 retinal phototransduction enzyme, more common with sildenafil & vardenafil)

Caused by cross-reactivity with other PDE isoenzymes esp. vascular, visceral, & pulmonary smooth muscle

High concentration of PDE5 in smooth muscle of corpora cavernosa

- **Contraindicated with nitrates (remember Jack Nicholson in Something's Gotta Give?)**

Apomorphine

Used since 1869 for Parkinson's (Apokyn®)

Derived from morphine—doesn't contain morphine or bind opioid receptors

High affinity for dopamine D4 receptor; moderate affinity for D2, D3, D5, & adrenergic α1D, α2B, α2C receptors.

- RE libido & erections, probably via D2 in hypothalamus & limbic system[173]

Marketed (Uprima®, Ixense®) in Austria, Germany, France, Italy; withdrawn from EU in 2004

Dosage: compounded 2-3 mg SL

- As effective as 4-6 mg without S/E. Can combine w/sildenafil or tadalafil.

Erections 10-25 minutes after use firm enough for penetration in ~50% vs ~ 30 baseline[173,174]

S/E: nausea, headaches, dizziness. Caution with antiemetics such as Zofran dt hypotension & possible LOC

Intercavernosal injections

Introduced in 1983

Modulates endothelial function

87-93% effective (alprostadil)[175,176]

97.6% effective with bi, tri, quadmix[177]

Options:

- Prostaglandin E1 (compounded alprostadil or FDA Caverject Impulse®, Edex®)—pain 48.5%
- Bimix (phentolamine, papaverine)—no E1
- Trimix (PGE1, phentolamine, papaverine)—pain 2.9%
- Quadmix (PGE1, phentolamine, papaverine, atropine)—pain 0%

See excellent Medscape article: Intracavernosol Injection Algorithm by Jeffrey A. Albaugh: http://www.medscape.com/viewarticle/551563_1

Intercavernosal injections

PGE1: 10, 20, or 40 mcg/mL N saline

Bi-Mix (per mL N saline):

- Phentolamine 0.5, 1, 2, or 3 mg
- Papaverine 30 mg

Trimix (per mL N saline)

- PGE1 5, 8.3, or 10 mcg
- Phentolamine 0.5, 0.83, or 1.0 mg
- Papaverine 15, 22.5, or 30 mg

Quad-mix(per mL N saline)

- PGE1 10, 20, or 60 mcg
- Phentolamine 1 or 2 mg
- Papaverine 30 mg
- Atropine 0.15 mg

Dose:

No history ED age <55: 0.1-0.2 ml
History of ED or age ≥ 55: 0.1-0.3 ml
Increase by 0.1-0.3 ml if needed

1 ml syringe, 27 or 30-gauge 1/2 or 5/8-inch needle.

Inject lateral shaft (10 o'clock and 2 o'clock) from base of penis to two-thirds toward glans. Avoid corpus spongiosum, urethra, glans. Rotate site.

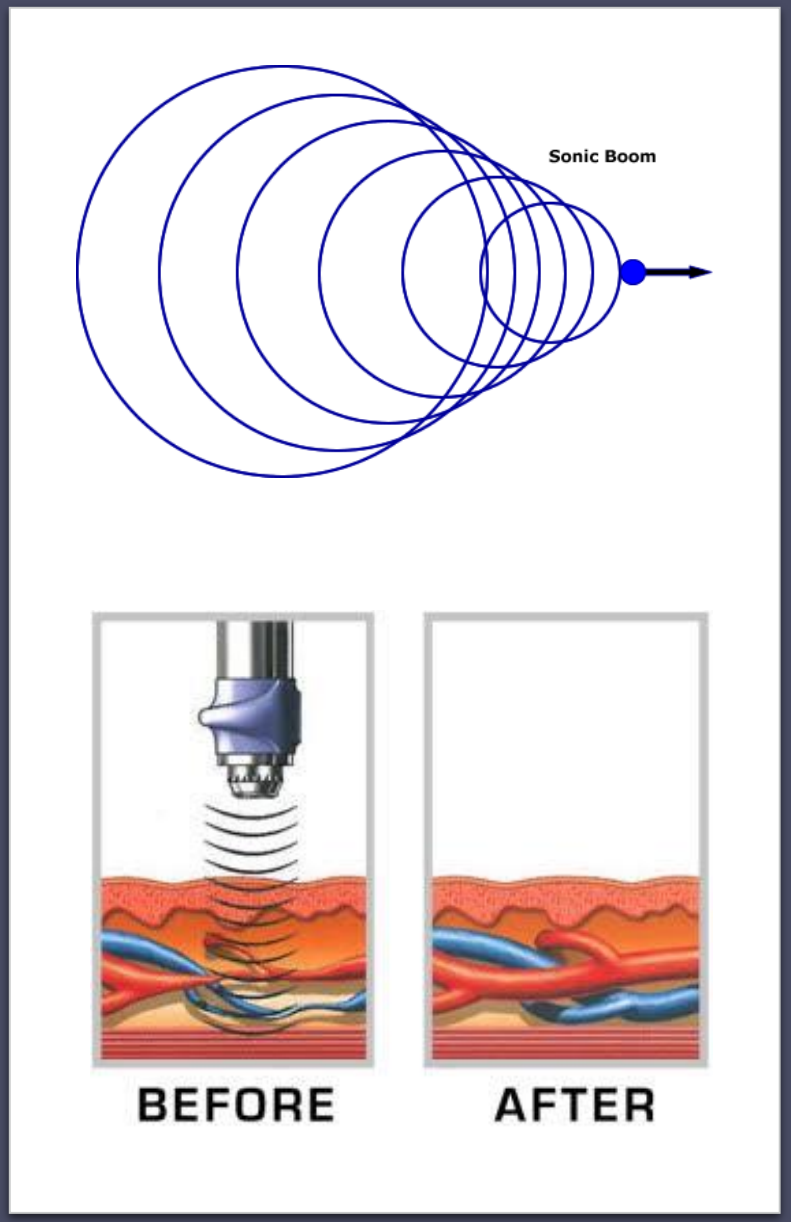
Risk of Peyronie's & priapism—ER if >3 hour erection

Low-intensity extracorporeal shockwave therapy

What is it?

Research

Who's a good candidate?



Low-intensity extracorporeal shockwave (LI-ESW)

High energy sound waves, not electrical shocks

When acoustic wave reaches the speed of sound, air cannot easily move out of the way—a shock wave is formed & energy dissipates

- When object moves faster than sound, resulting sound travels behind the object (sonic boom)

Shock wave travels unchanged through fluid & soft tissue until it encounters significant change in tissue structure

Pressure from shockwaves transfers to tissue causing micro cavitation

LI-ECSW variables: energy flux density, total number of pulses, frequency (number of pulses per second, Hz)

LI-ESWT

Originated in 1990s. Ultrasound induced angiogenesis in rat wounds—increased expression of vascular endothelial growth factor (VEGF)[178]

MOA for ED: promotes regeneration of penile nNOS-positive nerves, endothelium, & smooth muscle by recruiting endogenous mesenchymal stem cells.[179]

Also may activate local penile progenitor cells[180]

Not currently FDA-approved for ED (off-label use)

First ED efficacy study[181]

2010, Israel

20 men, non-responders to PDE5-I, ave age 56

2 sessions per week for 3 weeks

LI-ESW to the penile shaft and crura at 5 different sites

Results: improvement in erectile function, duration of erections, & penile rigidity at 1 month; sustained at 6 months

Significant increases in IIEF-ED domain scores in all men

11/29/2016 Can low-intensity extracorporeal shockwave therapy improve erectile function? A 6-month follow-up pilot study in patients with organic erectile dys... - ...

PubMed

Format: Abstract

Full text links

ELSEVIER FULL-TEXT ARTICLE

Eur Urol. 2010 Aug;58(2):243-8. doi: 10.1016/j.eururo.2010.04.004. Epub 2010 May 6.

Can low-intensity extracorporeal shockwave therapy improve erectile function? A 6-month follow-up pilot study in patients with organic erectile dysfunction.

Vardi Y[1], Appel B, Jacob G, Massarwi O, Gruenwald I.

Author information

Abstract

BACKGROUND: Low-intensity extracorporeal shockwave therapy (LI-ESWT) is currently under investigation regarding its ability to promote neovascularization in different organs.

OBJECTIVE: To evaluate the effect of LI-ESWT on men with erectile dysfunction (ED) who have previously responded to oral phosphodiesterase type 5 inhibitors (PDE5-I).

DESIGN, SETTING, AND PARTICIPANTS: We screened 20 men with vasculogenic ED who had International Index of Erectile Function ED (IIEF-ED) domain scores between 5-19 (average: 13.5) and abnormal nocturnal penile tumescence (NPT) parameters. Shockwave therapy comprised two treatment sessions per week for 3 wk, which were repeated after a 3-wk no-treatment interval.

INTERVENTION: LI-ESWT was applied to the penile shaft and crura at five different sites.

MEASUREMENTS: Assessment of erectile function was performed at screening and at 1 mo after the end of the two treatment sessions using validated sexual function questionnaires, NPT parameters, and penile and systemic endothelial function testing. The IIEF-ED questionnaire was answered at the 3- and 6-mo follow-up examinations.

RESULTS AND LIMITATIONS: We treated 20 middle-aged men (average age: 56.1 yr) with vasculogenic ED (mean duration: 34.7 mo). Eighteen had cardiovascular risk factors. At 1 mo follow-up, significant increases in IIEF-ED domain scores were recorded in all men (20.9 +/- 5.8 vs 13.5+/- 4.1, $p<0.001$); these remained unchanged at 6 mo. Moreover, significant increases in the duration of erection and penile rigidity, and significant improvement in penile endothelial function were demonstrated. Ten men did not require any PDE5-I therapy after 6-mo follow-up. No pain was reported from the treatment and no adverse events were noted during follow-up.

CONCLUSIONS: This is the first study that assessed the efficacy of LI-ESWT for ED. This approach was tolerable and effective, suggesting a physiologic impact on cavernosal hemodynamics. Its main advantages are the potential to improve erectile function and to contribute to penile rehabilitation without pharmacotherapy. The short-term results are promising, yet demand further evaluation with larger sham-control cohorts and longer follow-up.

https://www.ncbi.nlm.nih.gov/pubmed/20451317 1/2

RCTs in PDE5i responders

2012, Vardi et al[182]

67 men, all PDE5i responders

After 1 mo PDE5i-washout, 12 sessions of LI-ESW or sham treatment

Erectile function & penile hemodynamics assessed before 1st treatment & after final treatment

~50% treated men able to achieve erections firm enough for penetration & had improved penile blood flow.

No adverse effects

2015, Srini et al[183]

135 men, all DPE5i responders

1 mo PDE5i washout

12 sessions vs sham treatment

F/U 1, 3, 6, 9, 12 mos

78% at 1 mo, 71% at 5 mos initially unable to achieve erections firm enough for penetration able to do so. None in placebo group.

Very high dropout rate (58% sham, 42% treatment arm) at 12 mos

No adverse effects

PDE5i non-responders may become responders

2012, Gruenwald et al[184]

Open-label single-arm prospective study

29 men, all PDE5i non-responders

2 treatments per week x 3 weeks; repeated after 3-week no-treatment interval (12 total treatment)

15,000 pulses, 120 shocks/min

ED improved slightly at 1 mo. PDE5i given at that time. 72% able to achieve erections firm enough for penetration at second month

2016, Kitrey et al[185]

RCT

58 men, all PDE5i non-responders

12 sessions, 15,000 pulses, 120 shocks/min vs sham treatment

54.1% of treatment group able to achieve erections firm enough for penetration (EHS score) at 1 mo using PDE5i; 40.5% improved IIEF-EF score

0% improved in sham group

Open-label trial, PDE5i non-responders, 1 y f/u[186]

Vascular risk factors: DM, HTN, dyslipidemia, CAD

50 men, considered non-responders if correct dosage of PDE5i, correction of risk factors & testosterone level, improved sexual stimuli, proper diet training

Ave age 64.8 yrs, ED duration ave ~ 6 yrs

14,400 shockwaves over 4 weeks

Success = improvement in Erection Hardness Score (EHS), ED severity (IIEF-EF), Sexual Encounter Profile ("Penis hard but not enough for penetration & hard enough for penetration but not completely hard"), Global Assessment Question (GAQ) "Has tx improved quality of your erections?"

60% positive response

OUTCOMES ASSESSMENT

Twelve-Month Efficacy and Safety of Low-Intensity Shockwave Therapy for Erectile Dysfunction in Patients Who Do Not Respond to Phosphodiesterase Type 5 Inhibitors

Amado Bechara, MD, PhD, Adolfo Casabé, MD, Walter De Bonis, MD, and Pablo Gomez Ciciclia, MD

ABSTRACT

Introduction: Low-intensity shockwave therapy (LISWT) has recently emerged as a promising method in the treatment of erectile dysfunction (ED).

Aim: To assess the long-term results of the effectiveness and safety of LISWT in patients with ED who are non-responders to phosphodiesterase type 5 inhibitor (PDE5i) treatment.

Methods: This open-label, longitudinal, and observational study investigated an uncontrolled population of 50 consecutive patients whose ED was unresponsive to PDE5i treatment. Patients were treated with a four-session LISWT protocol. During active treatment and follow-up, all patients remained on their regular high on-demand or once-daily PDE5i dosing schedules.

Main Outcome Measures: Effectiveness was assessed according to the International Index of Erectile Function erectile function domain, questions 2 and 3 of the Sexual Encounter Profile, Erection Hardness Scale, and Global Assessment Question scores at baseline and at 3, 6, 9, and 12 months after treatment. Patients were considered responders whenever they showed improvement in erection parameters in all four assessments and responded positively to the Global Assessment Question. Adverse events were recorded. Statistical variables were applied and findings were considered statistically significant at a P value less than $< .05$.

Results: Eighty percent (mean age = 64.8 years) completed the 12-month follow-up. Positive response rates were 60% of available subjects at the end of the study and 48% of the intent-to-treat population. After the 12-month follow-up, 91.7% of responders maintained their responses. No patient reported treatment-related adverse events.

Conclusion: LISWT in patients with ED unresponsive to PDE5i treatment was effective and safe in 60% of patients treated. The efficacy response was maintained for 12 months in most patients.

Key Words: Low-Intensity Extracorporeal Shockwave Therapy; Erectile Dysfunction; Phosphodiesterase Type 5 Inhibitor

INTRODUCTION

Erectile dysfunction (ED) is a medical entity that is highly prevalent in men older than 50 years whose history of vascular risk factors (VRFs) has been a common denominator in the origin of this symptom.[1]

Many studies have stressed the status of ED as a potential indicator of cardiovascular disease, although other clinical trials have found a high incidence of ED in men with VRFs such as metabolic syndrome, diabetes, and hypertension.[2,3]

Since 1998, the phosphodiesterase type 5 inhibitor (PDE5i) has introduced a change in the treatment paradigm for patients with ED because approximately 60% of patients can recover their erectile function and lead a satisfactory sex life.[4]

Despite the effectiveness of PDE5i in the treatment of ED, 40% to 50% of patients—depending on the etiology of the dysfunction—do not respond to this drug therapy, even after optimization approaches such as treatment combinations have been implemented.[5–10]

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Instituto Medico Especializado, Buenos Aires, Argentina

http://dx.doi.org/10.1016/j.esxm.2016.06.001

RCT with 6 mo f/u[187]

2015, Olsen et al

112 men

5 sessions over 5 weeks

At 10 weeks, placebo received active tx

57% active group able to have intercourse without medication

At 6 mos, 19% active group, 23% active placebo group still able to have intercourse without medication (~20% “penile rehabilitation”?)

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ORIGINAL ARTICLE

Can low-intensity extracorporeal shockwave therapy improve erectile dysfunction? A prospective, randomized, double-blind, placebo-controlled study

Anne B. Olsen[1], Marie Persiani[1], Sidsel Boie[2], Milad Hanna[3] and Lars Lund[1,4,5]

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Abstract

Objective. The aim of this study was to investigate whether low-intensity extracorporeal shockwave therapy (LI-ESWT) can be used as a treatment for men with erectile dysfunction of organic origin. *Materials and methods.* This prospective, randomized, blinded, placebo-controlled study included 112 men unable to have intercourse either with or without medication. Erectile dysfunction was assessed at screening and 5, 12 and 24 weeks after treatment. Assessment was performed by interview and using the Erection Hardness Scale (EHS) and the International Index of Erectile Function (IIEF-15) questionnaire. The men were randomly assigned either to LI-ESWT (n = 51, active group) or placebo (n = 54, placebo group). They received five treatments over 5 weeks. Both the participants and the doctors were blinded to the treatment. After 10 weeks, the placebo group received active treatment (active placebo group). *Results.* Twenty-nine men (57%, active group) were able to obtain an erection after treatment and to have sexual intercourse without the use of medication. In the placebo group, only five men (9%) showed similar results (p = 0.0001). The EHS after 5 weeks showed that men in the active group experienced a significant improvement in their erectile dysfunction, but no significant result was found with the use of the IIEF – Erectile Function domain. *Conclusions.* This placebo-controlled study over 5 weeks shows that 57% of the men who suffered from erectile dysfunction had an effect from LI-ESWT. After 24 weeks, seven (19%, active group) and nine (23%, active placebo group) men were still able to have intercourse without medication. This study shows a possible cure in some patients, but more research, longer follow-up in the placebo group and an international multicentre randomized study are needed.

Keywords:
Erectile dysfunction, extracorporeal shockwave, penis

History
Received 26 January 2014
Revised 31 July 2014
Accepted 30 October 2014

Introduction

Erectile dysfunction is a male sexual dysfunction defined as a consistent or recurrent inability to attain or maintain an erection sufficient for sexual intercourse [1,2]. Erectile dysfunction is a common disorder of middle-aged men that profoundly affects their quality of life [3,4]. For the past 15 years, oral treatment with phosphodiesterase-5 (PDE-5) inhibitors or intracavernosal injection therapy with vasodilating agents has been the preferred treatment for erectile dysfunction [2].

Extracorporeal shockwave therapy (ESWT) has been used for many years in different fields. In 1980, the clinical use of extracorporeal shockwave lithotripsy as a treatment for stone disease in the upper urinary tract began and proved effective [5–7]. Throughout the years, ESWT has been modified for use in other specialities, such as in the treatment of gallstones, sialolithiasis and Peyronie's disease [8–10]. Animal studies have demonstrated neoangiogenesis in myocardial tissue and skin flaps [11,12], which invites the hypothesis that erectile dysfunction of vascular origin could be treated by ESWT [11–14].

Recent studies have shown promising results of low-intensity extracorporeal shockwave therapy (LI-ESWT) on patients suffering from mild to severe erectile dysfunction [15–17]. A randomized, double-blind, controlled study of men allocated in a two-to-one ratio to LI-ESWT or sham operation showed positive short-term clinical and physiological effects of LI-ESWT on erectile function in PDE-5 inhibitor responders [17].

The aim of the present study was to evaluate LI-ESWT given to men with erectile dysfunction in a one-to-one ratio, and then to investigate and monitor the effects of treatment on erectile function.

Materials and methods

Study population

During the period 2012–2013, 112 men with erectile dysfunction of organic origin who had responded to PDE-5 inhibitors were included in this prospective, randomized, blinded, placebo-controlled study and followed for 5 weeks.

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RCT with 12 mo f/u[188, 189]

2017, 2018 Fojecki et al, Danish hospital

126 men, ave age 65

5 session over 5 weeks or sham

After 4 week break, both groups received 5 treatments over 5 weeks (so initial treatment group got 10 sessions over 14 weeks vs 5 sessions in sham)

Success based on IIEF-EF score of at least 5 points: 38.3% in sham group vs 37.9% in ESWT group

2 cycles (10 sessions) of LI-ESWT not superior to 1 cycle (5 sessions) at 6 & 12 mo f/u:

THE JOURNAL OF SEXUAL MEDICINE

REVIEW PAPERS

Effects of Low-Intensity Extracorporeal Shockwave Therapy on Erectile Dysfunction: A Systematic Review and Meta-Analysis

Raul I. Clavijo, MD,[1,*] Taylor P. Kohn, MD,[2,*] Jaden R. Kohn, BS,[2] and Ranjith Ramasamy, MD[3]

ABSTRACT

Introduction: Low-intensity extracorporeal shock wave therapy (Li-ESWT) has been proposed as an effective non-invasive treatment option for erectile dysfunction (ED).

Aim: To use systematic review and meta-analysis to assess the efficacy of Li-ESWT by comparing change in erectile function as assessed by the erectile function domain of the International Index of Erectile Function (IIEF-EF) in men undergoing Li-ESWT vs sham therapy for the treatment of ED.

Methods: Systematic search was conducted of MEDLINE, EMBASE, and ClinicalTrials.gov for randomized controlled trials that were published in peer-reviewed journals or presented in abstract form of Li-ESWT used for the treatment of ED from January 2010 through March 2016. Randomized controlled trials were eligible for inclusion if they were published in the peer-reviewed literature and assessed erectile function outcomes using the IIEF-EF score. Estimates were pooled using random-effects meta-analysis.

Main Outcome Measures: Change in IIEF-EF score after treatment with Li-ESWT in patients treated with active treatment vs sham Li-ESWT probes.

Results: Data were extracted from seven trials involving 602 participants. The average age was 60.7 years and the average follow-up was 19.8 weeks. There was a statistically significant improvement in pooled change in IIEF-EF score from baseline to follow-up in men undergoing Li-ESWT vs those undergoing sham therapy (6.40 points; 95% CI = 1.78−11.02; I^2 = 98.7%; $P < .0001$ vs 1.65 points; 95% CI = 0.92−2.39; I^2 = 64.6%; $P < .0001$; between-group difference, $P = .047$). Significant between-group differences were found for total treatment shocks received by patients ($P < .0001$).

Conclusion: In this meta-analysis of seven randomized controlled trials, treatment of ED with Li-ESWT resulted in a significant increase in IIEF-EF scores.

J Sex Med 2017;14:27−35.

Key Words: Erectile Dysfunction; Shock Waves; Randomized Controlled Trial; Meta-Analysis

INTRODUCTION

Erectile dysfunction (ED) is when a man is unable to achieve or maintain an erection for satisfactory sexual performance. ED is estimated to affect one in every five men and, given the aging male population and increasing prevalence of comorbid conditions, it is likely to become even more prevalent.[1] Phosphodiesterase type 5 inhibitors (PDE5is) are often effective in treating patients with ED and are associated with few side effects; however, a significant proportion of men do not respond to therapy.[2] In men who do not respond to PDE5is or cannot tolerate them because of side effects, options such as medicated urethral suppositories for erection, intracorporal injections, and penile prostheses are available.[3] Although these treatment options can be effective, long-term usage rates are hindered by side effects and potential complications.[4] Furthermore, these treatments attempt to improve erectile function without treating the underlying pathophysiology of ED.[5]

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Open-label, 2 yr f/u[190]

2018, Kitrey et al

156 men

1 mo, treatment successful in 63.5%

2 yr effective in 53.5%

Severe ED had earlier failure

All patients with DM and severe ED lost effect

Mild ED without DM, 76% preserved effectiveness

Low Intensity Shock Wave Treatment for Erectile Dysfunction—How Long Does the Effect Last?

Noam D. Kitrey,* Yoram Vardi, Boaz Appel,† Arik Shechter, Omar Massarwi, Yasmin Abu-Ghanem and Ilan Gruenwald

From the Urology Department, Sheba Medical Center (NDK, YV, YA-G), Ramat-Gan and Ruth and Bruce Rappaport Faculty of Medicine, Technion (YV) and Neurourology Unit, Rambam Healthcare Campus (BA, OM), Haifa (AS, IG), Israel

Purpose: We studied the long-term efficacy of penile low intensity shock wave treatment 2 years after an initially successful outcome.

Materials and Methods: Men with a successful outcome of low intensity shock wave treatment according to the minimal clinically important difference on the IIEF-EF (International Index of Erectile Function-Erectile Function) questionnaire were followed at 6, 12, 18 and 24 months. Efficacy was assessed by the IIEF-EF. Failure during followup was defined as a decrease in the IIEF-EF below the minimal clinically important difference.

Results: We screened a total of 156 patients who underwent the same treatment protocol but participated in different clinical studies. At 1 month treatment was successful in 99 patients (63.5%). During followup a gradual decrease in efficacy was observed. The beneficial effect was maintained after 2 years in only 53 of the 99 patients (53.5%) in whom success was initially achieved. Patients with severe erectile dysfunction were prone to earlier failure than those with nonsevere erectile dysfunction. During the 2-year followup the effect of low intensity shock wave treatment was lost in all patients with diabetes who had severe erectile dysfunction at baseline. On the other hand, patients with milder forms of erectile dysfunction without diabetes had a 76% chance that the beneficial effect of low intensity shock wave treatment would be preserved after 2 years.

Conclusions: Low intensity shock wave treatment is effective in the short term but treatment efficacy was maintained after 2 years in only half of the patients. In patients with milder forms of erectile dysfunction the beneficial effect is more likely to be preserved.

Key Words: penis, erectile dysfunction, extracorporeal shock wave therapy, treatment outcome, risk factors

Abbreviations and Acronyms

CVD = cardiovascular disease
CVRF = cardiovascular risk factors
DM = diabetes mellitus
ED = erectile dysfunction
IIEF-EF = International Index of Erectile Function-Erectile Function
LIST = low intensity shock wave treatment
MCID = minimal clinically important difference
PDE5I = phosphodiesterase type 5 inhibitor

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The corresponding author certifies that, when applicable, a statement(s) has been included in the manuscript documenting institutional review board, ethics committee or ethical review board study approval; principles of Helsinki Declaration were followed in lieu of formal ethics committee approval; institutional animal care and use committee approval; all human subjects provided written informed consent with guarantees of confidentiality; IRB approved protocol number; animal approved project number.

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† Financial interest and/or other relationship with Medispec.

Low intensity extracorporeal shock wave therapy is a new treatment modality for ED. The efficacy of this technique using various types of energy (electrohydraulic, electromagnetic or piezoelectric), several protocols and devices has already been published. The short-term results of most studies are encouraging.[1–8] LIST is effective even in patients with severe ED in whom the response to PDE5Is has stopped.[9] While the mechanism of action is not fully understood, animal studies have shown that the shear stress exerted by this energy induces the release of angiogenic factors and results in revascularization.[10,11] Since one of the underlying causes of ED is

RCT for Peyronie's, 2009[191]

100 men with Peyronie's < 12 mos

4 weekly treatments, 2000 shock waves

Plaque size, penile curvature, and quality of life

After 12 wks., pain, erectile function, & QoL improved in treatment group; stable at 24 weeks

Plaque size and curvature degree unchanged in active group but slightly increased in placebo group

After 24 wks., plaque size and curvature degree worse in the placebo group

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EUROPEAN UROLOGY

Andrology

A First Prospective, Randomized, Double-Blind, Placebo-Controlled Clinical Trial Evaluating Extracorporeal Shock Wave Therapy for the Treatment of Peyronie's Disease

*Alessandro Palmieri, Ciro Imbimbo, Nicola Longo, Ferdinando Fusco, Paolo Verze, Francesco Mangiapia, Massimiliano Creta *, Vincenzo Mirone*

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Extracorporeal shock wave therapy
Peyronie's disease

Abstract

Background: Extracorporeal shock wave therapy (ESWT) is a conservative therapy for patients with Peyronie's disease (PD).
Objective: To investigate the effects of ESWT in patients with PD.
Design, setting, and participants: One hundred patients with a history of PD not >12 mo who had not had previous PD-related treatments were enrolled in a prospective, randomized, double-blind, placebo-controlled study. Patients were randomly allocated to either ESWT ($n = 50$) or placebo ($n = 50$). Erectile function (EF), pain during erection, plaque size, penile curvature, and quality of life (QoL) were assessed at baseline, at 12 wk, and at 24 wk follow-up.
Intervention: Four weekly treatment sessions were administered. Each ESWT session consisted of 2000 focused shock waves. For the placebo group, a non-functioning transducer was employed.
Measurements: EF was evaluated with the shortened version of the International Index of Erectile Function (IIEF-5), pain was evaluated with a visual analog scale (VAS; 0–10), plaque size was measured in cm^2, and penile curvature was measured in degrees.
Results and limitations: After 12 wk, mean VAS score, mean IIEF-5 score, and mean QoL score ameliorated significantly in patients receiving ESWT. Mean plaque size and mean curvature degree were unchanged in the ESWT group, while a slight increase was reported in the placebo group (p-value not significant vs baseline). After 24 wk, mean IIEF-5 score and mean QoL score were stable in the ESWT group, while mean VAS score was significantly lower when compared with baseline in both groups. Interestingly, after 24 wk, mean plaque size and mean curvature degree were significantly higher in the placebo group when compared with both baseline and ESWT values. The main limitations were that the QoL questionnaire was not validated, ED was not etiologically characterized, and inclusion criteria were restricted.
Conclusions: In patients with PD, ESWT leads to pain resolution and ameliorates both EF and QoL.

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0302-2838/$ – see back matter doi:10.1016/j.eururo.2009.05.012

RCT for Peyronie's, 2012[192]

100 men with Peyronie's < 12 mos

4 weekly treatments, 2000 shock waves with or without tadalafil 5 mg po qd

12 weeks:

- Both groups decreased plaque size & curvature (not statistically significant)
- Both groups improved erections & quality of life scores
- Better erections with tadalafil

24 weeks: curvature degree further decreased in both groups. Plaque size stable in ESWT group with further, slight decrease in ESWT + tadalafil

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ORIGINAL ARTICLE

Tadalafil once daily and extracorporeal shock wave therapy in the management of patients with Peyronie's disease and erectile dysfunction: results from a prospective randomized trial

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Keywords:
extracorporeal shock wave therapy, Peyronie's disease, tadalafil

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Summary

Extracorporeal shock wave therapy improves erectile function in patients with Peyronie's disease. However, erectile dysfunction still persists in many cases. We aimed to investigate the effects of extracorporeal shock wave therapy plus tadalafil 5 mg once daily in the management of patients with Peyronie's disease and erectile dysfunction not previously treated. One hundred patients were enrolled in a prospective, randomized, controlled study. Patients were randomly allocated to receive either extracorporeal shock wave therapy alone for 4 weeks ($n = 50$) or extracorporeal shock wave therapy plus tadalafil 5 mg once daily for 4 weeks ($n = 50$). Main outcome measures were: erectile function (evaluated through the shortened version of the International Index of Erectile Function), pain during erection (evaluated through a Visual Analog Scale), plaque size, penile curvature and quality of life (evaluated through an internal questionnaire). Follow-up evaluations were performed after 12 and 24 weeks. In both groups, at 12 weeks follow-up, mean Visual Analog Scale score, mean International Index of Erectile Function score and mean quality of life score ameliorated significantly while mean plaque size and mean curvature degree were unchanged. Intergroup analysis revealed a significantly higher mean International Index of Erectile Function score and quality of life score in patients receiving the combination. After 24 weeks, intergroup analysis revealed a significantly higher mean International Index of Erectile Function score and mean quality of life score in patients that received extracorporeal shock wave therapy plus tadalafil. In conclusion extracorporeal shock wave therapy plus tadalafil 5 mg once daily may represent a valid conservative strategy for the management of patients with Peyronie's disease and erectile dysfunction.

Introduction

Peyronie's disease (PD) is a localized disorder of the connective tissue involving the penile tunica albuginea and the surrounding areolar spaces that typically evolves in fibrotic plaques [Bivalacqua *et al.* (2000)]. Patients present with three, occasionally simultaneous, chief complaints: a palpable plaque, painful erections and a penile deformity [Palmieri *et al.* (2009)]. Moreover, PD is associated with erectile dysfunction (ED) in a percentage of patients ranging from 18 to 80% [Weidner *et al.* (1997), Levine & Latchamsetty (2002), Kadioglu *et al.* (2004), Mulhall *et al.* (2005)]. In a previous study, we demonstrated that Extracorporeal Shock Wave Therapy (ESWT) can significantly improve erectile function (EF) in patients with PD when compared to placebo [Palmieri *et al.* (2009)]. However, ED still persisted in about 50% of patients thus suggesting the need for more successful strategies [Palmieri *et al.* (2009)]. Levine L.A. demonstrated that on-demand sildenafil was an effective, safe and well tolerated first-line strategy for PD patients with ED [Levine & Latchamsetty (2002)]. Recent pre-clinical studies characterized the antifibrotic effects of chronic treatment with phosphodiesterase type 5 inhibitors

Narrative review, 2013[193]

Review of published literature on MOA of LI-ESWT & efficacy

Results:

- MOA likely neovascularization
- 60-75% of PDE5i responders could achieve erections firm enough for penetration without medication
- 72% of PDE5i non-responders become responders

ELSEVIER

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REVIEWS

Low-Intensity Extracorporeal Shock Wave Therapy in Vascular Disease and Erectile Dysfunction: Theory and Outcomes

Ilan Gruenwald MD *, †, Noam D. Kitrey MD *, †, Boaz Appel MD *, †, Yoram Vardi MD *, †

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Abstract

Introduction

Low-intensity extracorporeal shock wave therapy (LI-ESWT) to the penis has recently emerged as a new and promising modality in the treatment of erectile dysfunction (ED).

Aim

To review the published literature on the mechanism of action of LI-ESWT; and to report our clinical data on its efficacy in men with vasculogenic ED.

Methods

A Medline search using the relevant keywords on this topic has been done.

Results

From the results of numerous preclinical and animal studies that have been done to date, sufficient evidence shows that the underlying mechanism of action of LI-ESWT is probably neovascularization. Therefore, local application of LI-ESWT to the corpora cavernosa may potentially act in the same mechanism and increase corporal blood flow. We found that the application of LI-ESWT to patients who responded to oral therapy (PDE5i) eliminated their dependence on PDE5i and they were able to successfully achieve erections and vaginal penetration (60-75%). Furthermore, PDE5i non-responders became responders and capable of vaginal penetration (72%). Additionally, LI-ESWT resulted in long-term improvement of the erectile mechanism.

Conclusions

LI-ESWT has the potential to improve and permanently restore erectile function by reinstating the penile blood flow. Although these results on LI-ESWT are promising, further multi- centered studies with longer follow-up are needed to confirm these findings.

Gruenwald I, Kitrey ND, Appel B, and Vardi Y. Stem low-intensity extracorporeal shock wave

Meta-analysis, 2017[194]

14 studies, 7 RCTs 2005-2015

833 men

Improvement in ED and erectile hardness scores lasting at least 3 mos

Mild-moderate ED better effect than severe ED or comorbidities

Energy flux density, number of shock wavers, duration of treatment closely related to outcome

available at www.sciencedirect.com
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European Association of Urology

Platinum Priority – Review – Andrology
Editorial by Dimitris ?atzichristou on pp. 234–236 of this issue

Low-intensity Extracorporeal Shock Wave Treatment Improves Erectile Function: A Systematic Review and Meta-analysis

Zhihua Lu [a,b], Guiting Lin [a], Amanda Reed-Maldonado [a], Chunxi Wang [b], Yung-Chin Lee [c], Tom F. Lue [a,]*

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Clinical outcome
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Abstract

Context: As a novel therapeutic method for erectile dysfunction (ED), low-intensity extracorporeal shock wave treatment (LI-ESWT) has been applied recently in the clinical setting. We feel that a summary of the current literature and a systematic review to evaluate the therapeutic efficacy of LI-ESWT for ED would be helpful for physicians who are interested in using this modality to treat patients with ED.
Objective: A systematic review of the evidence regarding LI-ESWT for patients with ED was undertaken with a meta-analysis to identify the efficacy of the treatment modality.
Evidence acquisition: A comprehensive search of the PubMed and Embase databases to November 2015 was performed. Studies reporting on patients with ED treated with LI-ESWT were included. The International Index of Erectile Function (IIEF) and the Erection Hardness Score (EHS) were the most commonly used tools to evaluate the therapeutic efficacy of LI-ESWT.
Evidence synthesis: There were 14 studies including 833 patients from 2005 to 2015. Seven studies were randomized controlled trials (RCTs); however, in these studies, the setup parameters of LI-ESWT and the protocols of treatment were variable. The meta-analysis revealed that LI-ESWT could significantly improve IIEF (mean difference: 2.00; 95% confidence interval [CI], 0.99–3.00; $p < 0.0001$) and EHS (risk difference: 0.16; 95% CI, 0.04–0.29; $p = 0.01$). Therapeutic efficacy could last at least 3 mo. The patients with mild-moderate ED had better therapeutic efficacy after treatment than patients with more severe ED or comorbidities. Energy flux density, number of shock waves per treatment, and duration of LI-ESWT treatment were closely related to clinical outcome, especially regarding IIEF improvement.
Conclusions: The number of studies of LI-ESWT for ED have increased dramatically in recent years. Most of these studies presented encouraging results, regardless of variation in LI-ESWT setup parameters or treatment protocols. These studies suggest that LI-ESWT could significantly improve the IIEF and EHS of ED patients. The publication of robust evidence from additional RCTs and longer-term follow-up would provide more confidence regarding use of LI-ESWT for ED patients.
Patient summary: We reviewed 14 studies of men who received low-intensity extracorporeal shock wave treatment (LI-ESWT) for erectile dysfunction (ED). There was evidence that these men experienced improvements in their ED following LI-ESWT.

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Meta-analysis, 2018[195]

7 RCTs that used IIEF-EF score

602 men, ave age 60.7 yrs

Ave f/u 19.8 weeks

Statistically significant improvement

Significant between-group differences for total treatment shocks per patient

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SEXUAL MEDICINE

REVIEW PAPERS

Effects of Low-Intensity Extracorporeal Shockwave Therapy on Erectile Dysfunction: A Systematic Review and Meta-Analysis

Raul I. Clavijo, MD,[1,*] Taylor P. Kohn, MD,[2,*] Jaden R. Kohn, BS,[2] and Ranjith Ramasamy, MD[3]

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Main Outcome Measures: Change in IIEF-EF score after treatment with Li-ESWT in patients treated with active treatment vs sham Li-ESWT probes.

Results: Data were extracted from seven trials involving 602 participants. The average age was 60.7 years and the average follow-up was 19.8 weeks. There was a statistically significant improvement in pooled change in IIEF-EF score from baseline to follow-up in men undergoing Li-ESWT vs those undergoing sham therapy (6.40 points; 95% CI = 1.78−11.02; I^2 = 98.7%; $P < .0001$ vs 1.65 points; 95% CI = 0.92−2.39; $I^2 = 64.6\%$; $P < .0001$; between-group difference, $P = .047$). Significant between-group differences were found for total treatment shocks received by patients ($P < .0001$).

Conclusion: In this meta-analysis of seven randomized controlled trials, treatment of ED with Li-ESWT resulted in a significant increase in IIEF-EF scores.

J Sex Med 2017;14:27−35.

Key Words: Erectile Dysfunction; Shock Waves; Randomized Controlled Trial; Meta-Analysis

INTRODUCTION

Erectile dysfunction (ED) is when a man is unable to achieve or maintain an erection for satisfactory sexual performance. ED is estimated to affect one in every five men and, given the aging male population and increasing prevalence of comorbid conditions, it is likely to become even more prevalent.[1] Phosphodiesterase type 5 inhibitors (PDE5is) are often effective in treating patients with ED and are associated with few side effects; however, a significant proportion of men do not respond to therapy.[2] In men who do not respond to PDE5is or cannot tolerate them because of side effects, options such as medicated urethral suppositories for erection, intracorporal injections, and penile prostheses are available.[3] Although these treatment options can be effective, long-term usage rates are hindered by side effects and potential complications.[4] Furthermore, these treatments attempt to improve erectile function without treating the underlying pathophysiology of ED.[5]

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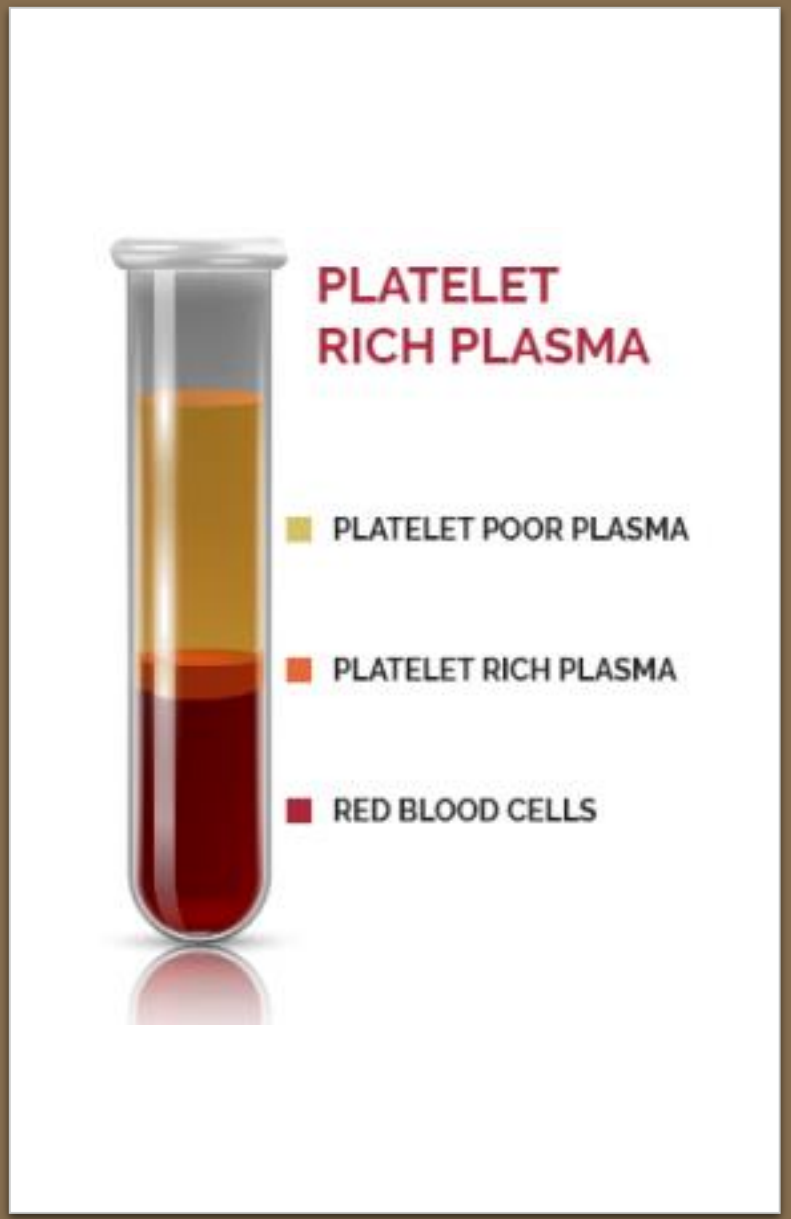
PRP & stem cell

Theory

Animal studies

Limited human pilot trials

No human RCTs



PRP

Platelets from anticoagulated blood spun in centrifuge—concentrated 3-5 x

Contain more than 300 bioactive proteins/growth factors[196,197]

- PDGF, TGF-β, VEGF, EGF, IGF-1, FGF, chemokines, immune mediators
- Also contains fibrin, fibronectin, vitronectin, & thrombospondin—adhesion proteins

Concentrated platelets may be activated by calcium chloride or combined with remaining blood before injected

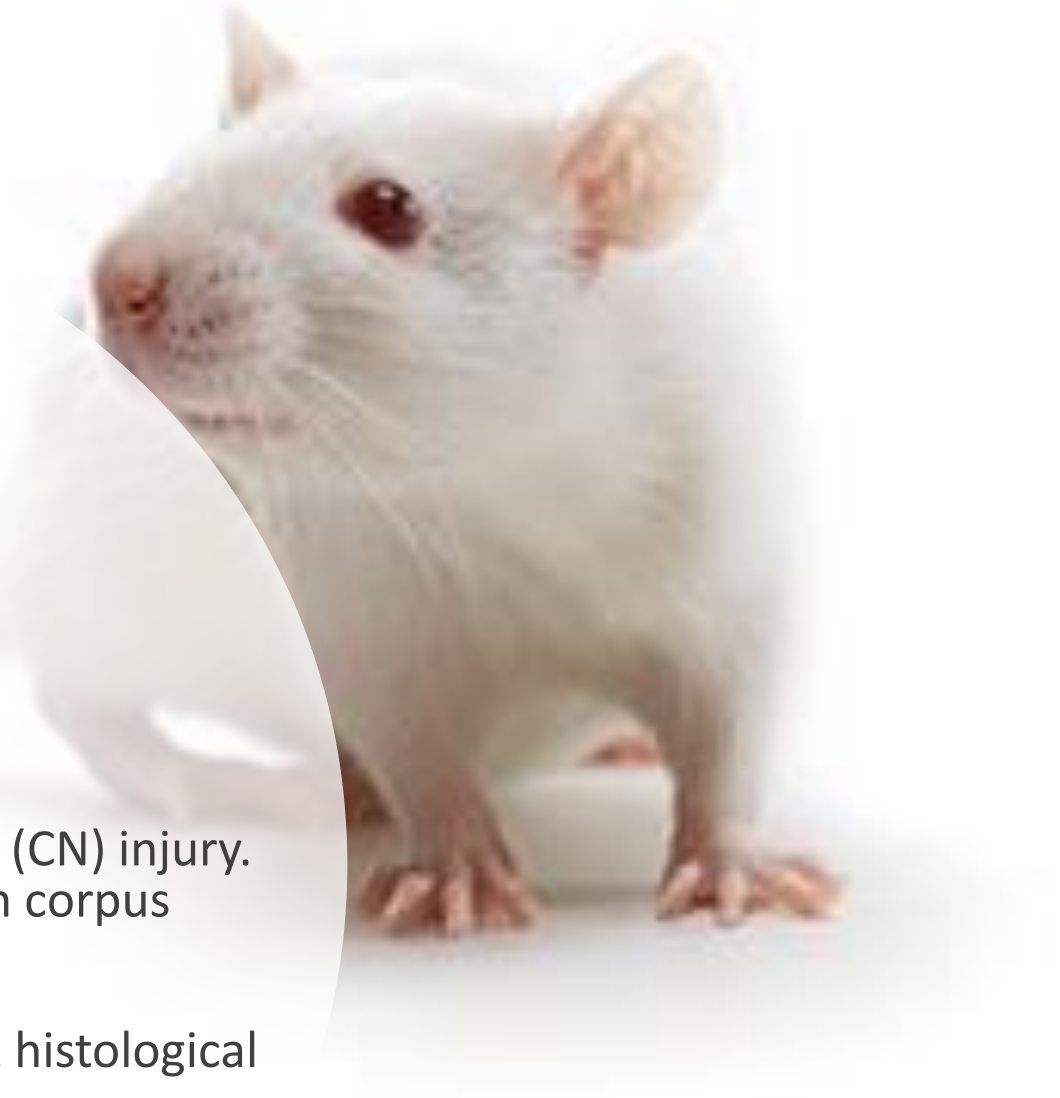
May improve tissue healing, nerve & blood vessel regeneration[198,199]

Success based on platelet concentration, volume of PRP delivered, extent of tissue damage/dysfunction, overall condition of patient

Penile vasculature—most endothelial-rich region of the body

Blood flow in flaccid penis slower compared to systemic circulation, allowing for better retention

Nerve repair



Group I: sham operation

Groups 2 & 3: bilat cavernous nerve (CN) injury. Received PRP or N saline injection in corpus cavernosum

4 weeks, electrostimulation of CN & histological exam of CN & penis

PRP increased number of myelinated axons & improved erectile function[200]

Humans, PRP ED & PD[201]

17 men, urology department, Wake Forest Baptist Medical Center, NC from 2012-2017

- 4 ED
- 11 PD
- 1 PD & ED4 PD
- 1 female w/SUI

PRP activated with calcium chloride, 4-9 mL PRP per treatment

PD patients, erection induced with alprostadil & injection directly into plaques

ED improved (IIEF-5 score ave +4.14 points)

PD: 80% improved degree of curvature

Adverse effects: mild bruising and pain, no complications at f/u (mean 15.5 mos)

Human trial, PRP in PD[202]

13 men, ave age 57.5 y

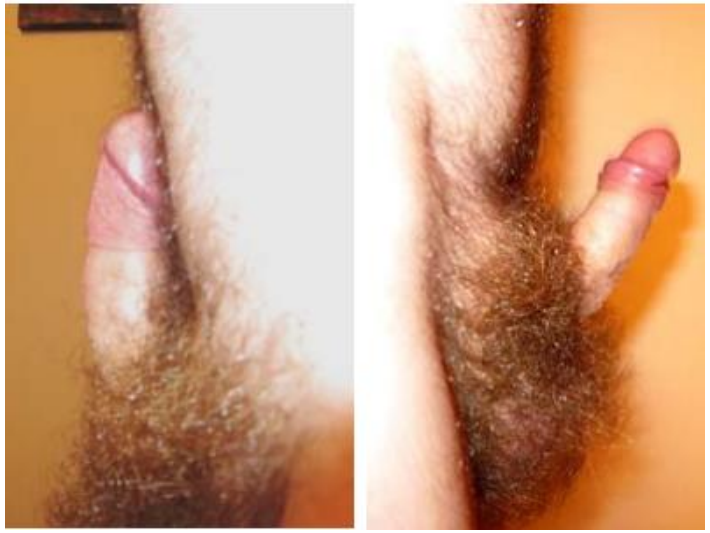
8 had curvature angles >50°

4 injections PRP + hyaluronic acid over 2 mos

F/U 9.3 mos average, 77% (10/13) improved with mean 30 ° decrease in curvature

53% decreased plaque density

Adverse effects: one hematoma, resolved



Human trial ED[203]

9 men, 34-66 yo, ave age 56

12 mos 2015-2016 Midwest Urological Group in Italy

PRP tx added to medication & vacuum therapy

IIEF 15.6 to 19.9
(mild/moderate ED to mild ED)

No side effects

Bone marrow mononuclear cells

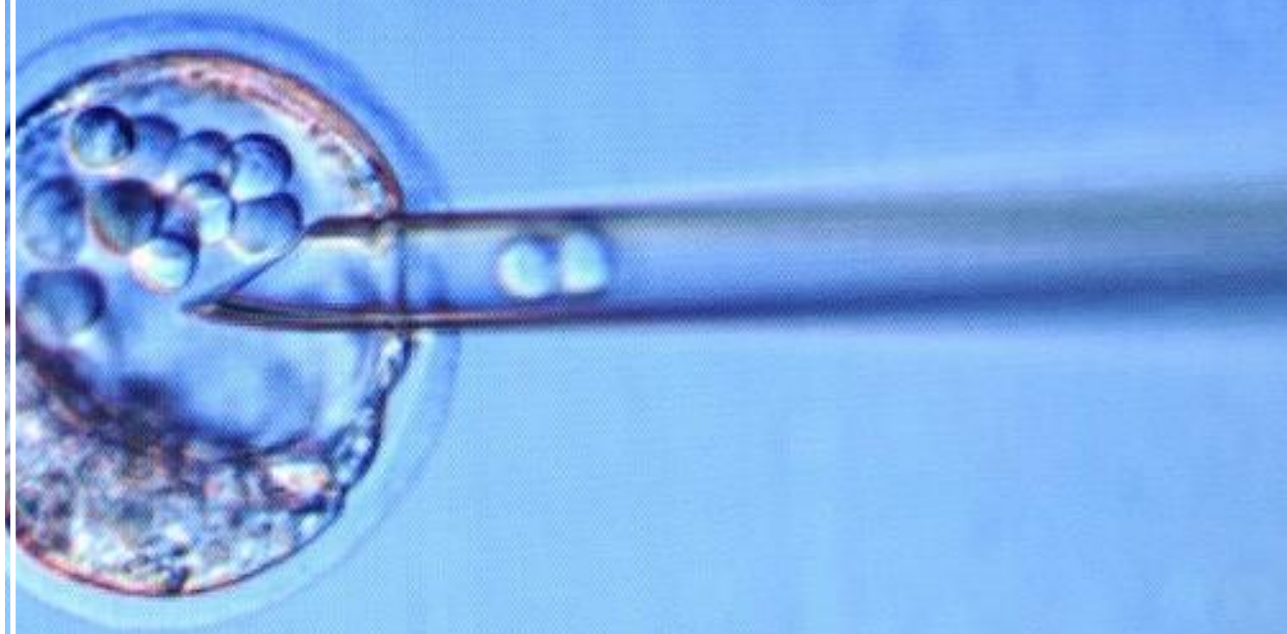
Includes hematopoietic cells such as lymphocytes, monocytes, stem cells, progenitor cells, & mesenchymal stromal cells

Chemotactic factors in injured tissue (SDF-1α, VEGF, granulocyte colony-stimulating factor, stem cell factor) mobilize EPC from bone marrow for angiogenesis[204]

Testosterone/androgens stimulate angiogenesis via VEGF & EPO production. Also improve EPC function[205,206]

EPCs decreased with chronic inflammation—DM, hypercholesterolemia, obesity, CVD, smokers all have decreased EPCs[207]

ED assoc with deficiency in circulating EPC[208]



Meta-analysis, diabetic rats[209]

10 studies, 302 diabetic rats

Smooth muscle, smooth muscle to collagen ratio, & endothelium content greater than controls

Increase in endothelial nitric oxide synthase (eNOS), neuronal nitric oxide synthase (nNOS), & VEGF

Beneficial effect of stem cell therapy in improving erectile function

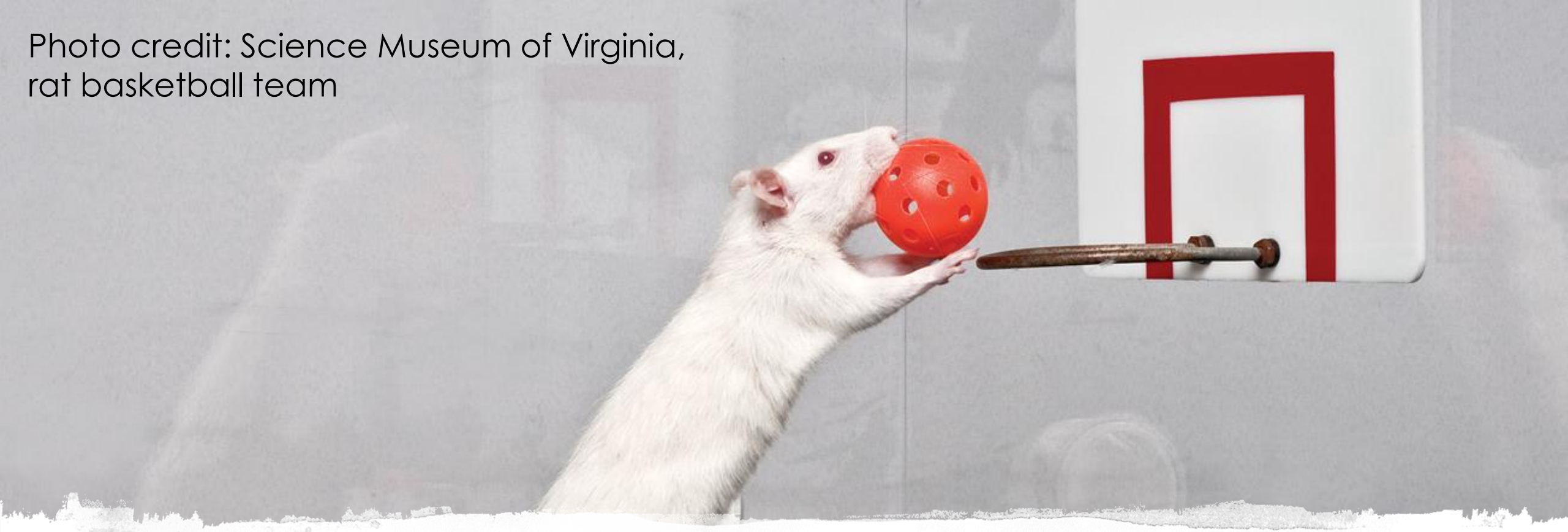


Photo credit: Science Museum of Virginia, rat basketball team

Stem Cell Rat Studies[210]

16 rat studies

Stem cells (bone marrow, adipose tissue, skeletal muscle)

Endothelial, smooth muscle, & CN improved

Intracavernously injected SCs rapidly escaped penis & homed into bone marrow

Injected SCs have systemic antidiabetic effects & prolonged anti-ED effects

Human pilot study[211]

7 men, DM2, PDE5i non-responders, mean age 69.5 yrs

Human umbilical cord blood stem cells (1.5 x 10(7))

Morning erections regained in 3 men at 1 mo, 6 men by 3rd mo

2/7 erections firm enough for penetration with PDE5i, maintained >6 mos

BG decreased by 2 weeks, HbA1c improved for up to 4 mos

No adverse effects (despite no immunosuppression)

Human pilot study[212]

12 men, ED post-radical prostatectomy (6 -18 mos prior)

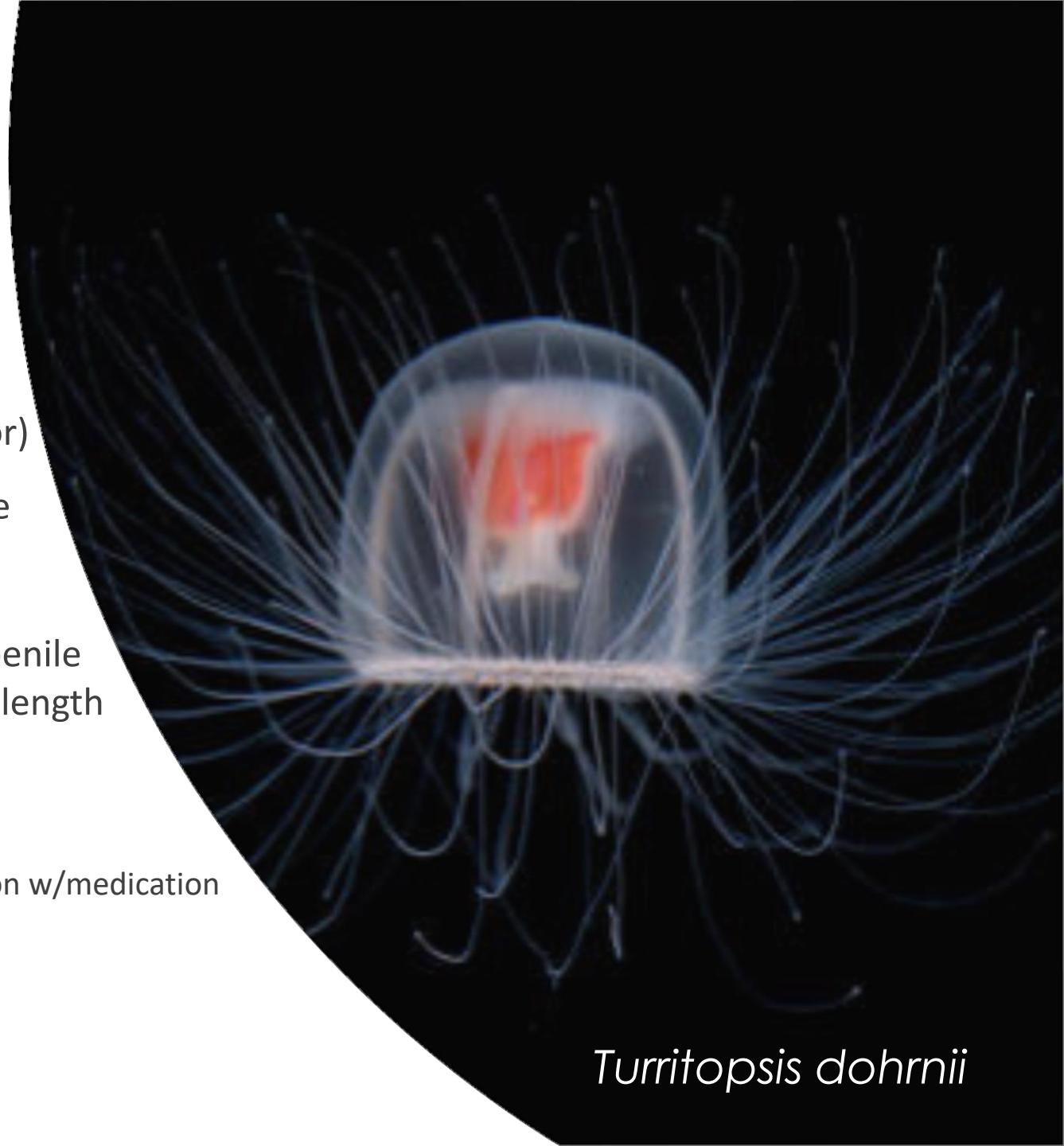
ED despite alprostadil injections, PDE5i, vacuum device

4 groups, single injection, escalating doses BM-MNC

Primary objective safety; secondary: sexual function, penile vascularization, endothelial function, change in penile length

Results:

- 6 mo f/u: improved ED & satisfaction
- 9/12 men achieved erections firm enough for penetration w/medication
- Spontaneous erections > with higher doses
- Benefit sustained at 1 yr
- No side effects



Turritopsis dohrnii

Sexual dysfunction

Identify type

- Desire
- Orgasm
- ED

Diagnosis & monitoring

- History (include pornography use)
- Lab work
- PE
- Questionnaires (SHIM, IIEF)

Treat cause(s) & the whole person

- Psychological
- Physical

THANK YOU

REFERENCES

Photo credit: Greg Lecoeur, National Geographc

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