

HERBS FOR MALE DYSFUNCTION AND OPTIMAL HEALTH

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Male Health Area to Focus

Male infertility

Testosterone & Hypogonadism

Erectile Dysfunction

The Three Prostate Conditions

- Prostate Cancer
- BPH
- Prostatitis





MALE INFERTILITY

Infertility Defined

Not being able to get pregnant despite having frequent, unprotected sex for at least one year

Between 8 and 12% of couples suffer from infertility, based on research

Male factors account for at least 50% of all infertility cases worldwide

- Sharlip ID, .Fertil steril. 2002

Male sperm production







Semen Quality and Morbidity / Mortality

A Danish cohort study of 4,712 men with long-term follow-up.

association between sperm concentration below 15 mill/mL and all-cause hospitalizations, 50% and cardiovascular disease, 40% compared to men with a concentration above 40 mill/mL.

- Latif T, et al. Am J Epidemiol. 2017 May 11.

Men with worse semen quality, and notably azoospermic men, were at higher risk of CM-related death.

- Hanson et al. Hum Reprod. 2017

MEDICATIONS ASSOCIATED WITH INFERTILITY • Ketoconazole, spironolactone, alcohol inhibit T synthesis

- Cimetidine: androgen antagonist
- Marijuana, heroin, methadone: lower T levels
- Pesticides, estrogen like activity
- Chemotherapy
- Calcium channel blockers; sulfasalazine; colchicine; allopurinol; alpha-blockers; nitrofurantoin; antipsychotics; antidepressants

Varicocele and Male Infertility

Only 20% of men with documented varicoceles have been reported to suffer fertility problems

- Diamond DA, et al. Fertil Steril. 2011;96:1294–1298.

Varicocele repair should be considered a viable choice for appropriately selected individuals and couples with otherwise unexplained infertility because varicocele repair has been shown to improve semen parameters in most men and possibly improve fertility; in addition, the risks of varicocele repair are small.

- Casey and Misseri. Clin North Am. 2015

Varicocele and Male Infertility

361 men older than 30 years who received early screening and diagnosis of varicocele (mean age 15.3 years). The investigators concluded that early screening for varicocele had no impact on paternity in adulthood.

- Bogaert G et al. J Urol. 2013 Jun. 189(6):2298-303.



Ashwagandha for Male Infertility

Double-blind, randomized, placebo-controlled parallel-group pilot study, 68 healthy men, ages 22–40 years old.

Twenty-one men in the treatment group received 225 mg of encapsulated Ashwagandha root by mouth 3 times daily for 12 weeks, while 25 men in the control group received a placebo capsule by mouth 3 times daily.

Average sperm concentration rose from 9.6 + 4.4 x 106/mL to 25.6 + 8.6 x 106/mL

53% increase in semen volume in men treated with Ashwagandha root for 90 days

- Ambiye VR et al. Evid Based Complement Alternat Med. 2013;2013:571420.

Ubiquinol and Male Infertility

Two hundred twenty-eight healthy men, ages 25–44 years old with primary, idiopathic infertility for at least 2 years were studied.

The treatment group (n=114) received 200 mg ubiquinol by mouth per day for 26 weeks, while 114 men in the control group received a placebo by mouth each day for 26 weeks.

Sperm motility and morphology increased by 18% to 30%

- Safarinejad MR, et al. J Urology. 2012 Aug; (188): 526-531.

Naturopathic Protocol

Behavioral modifications

No cellular phone in front pocketsWear loose boxer shorts

Diet: Mediterranean / Plant based pattern, de -emphasis on soy.

Antioxidants – Vitamin E (mixed tocopherols) – 400IU, Ubiqunol – 200mg / day, Lipoic acid – 400mg a day, vitamin C – 500mg bid, zinc 30mg



TESTOSTERONE & HYPOGONADISM

17β-hydroxyandrost-4-en-3-one





Testosterone Work up

Check T in the AM, at least 2x within 3 weeks apart

Check FSH & LH to identify the cause

- Normal FSH and LH testicular cause
- Low to Low Normal FSH & LH older age, obesity, pituitary / hypothalamic causes

High Prolactin may mean pituitary tumor

Increase Mortality with Low T in Men

Severe LOH has been related to an overall 5.5-fold higher risk of all-cause mortality [2-fold higher in those with testosterone ≤8 nmol/l (2.3 ng/ml), irrespective of symptoms, and 3-fold higher in those with three sexual symptoms, irrespective of testosterone concentrations].

Pye et al; J. Clin. Endocrinol. Metabol., 99 (2014),

Epidemiologic studies and meta-analyses have demonstrated higher all-cause mortality (35%) and cardiovascular mortality (25%) in men with low testosterone concentrations. - Araujo et al; J of Clinical Endocrinology and Metabolism; 2011

Statin Rx

Statins may partially operate by lowering testosterone

- Schooling et al. BMC Med. 2013



SHBG is produced in the liver where it regulates bioavailability of sex steroids , T & E.

SHBG is decreased by androgens, and hypothyroidism.

SHBG concentrations are lower in obese/overweight men because of an inhibitory effect of higher insulin concentrations on SHBG production

High levels of SHBG are associated with decreased bone mineral density and increased fracture risk in older men

liver fat, but not visceral fat or total body fat, was found to lower SHBG plasma level. A. Peter, *et al*. Diabetes 59 (2010)

Sex Binding Hormone Globulin (SHBG)

Increase concentrations

- Ageing
- Hyperthyroidism
- Hyperoestrogenaemia
- Liver disease
- HIV
- Use of anticonvulsants

Anorexia (return to normal levels after weight gain, serves as a reliable index for nutritional status in eating disorders)

Sex Binding Hormone Globulin (SHBG)

Decreased concentrations

- Obesity
- Insulin resistance and diabetes
- Hypothyroidism
- Growth-hormone excess
- Glucocorticoids
- Androgens
- Progestins
- Nephrotic syndrome

 TABLE 1. SERUM HORMONE CONCENTRATIONS IN SEVEN MEN

 GIVEN LICORICE FOR SEVEN DAYS.*

Hormonet	Day O	Day 4	Day 7	4 Days After Discon- tinuation
Testosterone (ng/dl)	740 ± 216	414±43‡	484±191‡	704±42
Androstenedione (ng/dl)	159 ± 35	140 ± 29	177 ± 30	170 ± 20
17-Hydroxyprogesterone (ng/dl)	189 ± 36	216±31	229±36‡	193±55

*Plus-minus values are means ±SD.

NEIM

1158

1999;341:

[†]To convert values for serum testosterone to nanomoles per liter, multiply by 0.0347; to convert values for serum androstenedione to nanomoles per liter, multiply by 0.0349; and to convert values for serum 17-hydroxyprogesterone to nanomoles per liter, multiply by 0.0303.

P < 0.001 for the comparison with day 0.

URDICA DIOICA ROOT (STINGING SHBG inhibitor NETTLES)

- Aromatase inhibitor
- NOT block androgen receptors
- The inhibition of human leukocyte elastase reflects anti-inflammatory activity.



- Chrubasik et al. 2007

Botanicals to Inc Testostosterone

Tribulus is an herb commonly used in dietary formulas to help increase testosterone, but it does not work to increase T. Neychev V et I. Journal of Ethnopharmacology 2000.

76 of 320 patients suffering from late-onset hypogonadism (LOH) were given 200 mg of a standardised water-soluble extract of Tongkat ali for 1 month. Tongkat ali extract appears to be useful as a supplement in overcoming the symptoms of LOH and for the management of hypogonadism - Tambi et al. Andrologia. 2012

Lepimedium meyenii (Maca)

Known as the Ginseng of Peru

3 RCT trials in men

1.Two Increased desire at
1500mg
and 3000mg / d
Gonzales et al. 2002
Stone et al. 2009

2. Improved mild ED – 2400mg /d -Zenico et al. 2009



Epimedium (Horny goat weed)

Icariin (ICA) exert PDE-5 inhibitory Effects in vitro.

Enhances eNOS expression and NO production

Low dose (ICA) improved erections in rats after nerve injury. - Shindel et al. 2010

No human studies



Rhodiola rosea

11 RCT

Improves physical performance and mental performance

Improves performance when subjects under stress

- Hung et al. 2011

Has not been studied for ED specifically



Fenugreek

2 RCT

Increased T (P<0.001) and free T (P=0.002)

Rao et al. 2016 (n=120)

Improved libido/arousal, erections, sexual activity, overall sexual function.

Rao et al. 2016 (n=120), Steels et al. 2011

Effective for androgen deficiency & associated symptoms (Andropause)



Ashwagandha

Adaptogen

Reduces stress response, improves T-to-Cortisol ratio

Mahdi AA et al. 2011

Increases T and LH, normalizes PRL, FSH. Improves gluathione, SOD and reduces oxidative markers

Ahmad MK et al. 2010, Gypta et al. 2013, Wankhede et al. 2015

Improves male fertility

THE BIG THREE

- Benign Prostatic Hyperplasia
- Prostatitis
- Prostate Cancer



Prostate Anatomy



70% glandular 30% stromal m.

Berry SJ. J Urol, 1984 132:474–479

Prostate Facts

A normal size is 20 grams; 3cm in length, 4cm wide, and 2 cm depth

Location is inferior to bladder, posteriior to the pubic symphysis, anterior To the rectum, superior to the perineal membrane

Histologically divided in 3 zones – anterior, posterior and transitional

largest accessory sex gland in men

70% is glandular tissue, 30% is muscle

Berry SJ, et al. J Urol, 1984, 132:474-479

Benign Prostatic Hyperplasia



Normal Prostate

Enlarged Prostate

Benign Prostatic Hyperplasia (BPH)

Risk factors for BPH

Men w LUTS have higher HgA1C

- Rohrmann et al. Int. j. Obes. 2005

↑Obesity = ↑prostate volume - Parsons et al. J of Uro. 2013

↑Waist to Hip ratio = ↑prostate volume – Kristal et al. J. of Uro. 2007

↑CRP assoc w ↑BPH - Rohrmann et al. Prostate 2005

Bacterial and viral strains found in BPH biopsy specimens - Chughtai et al. Curr. Urol. 2011

Risk factors for BPH

Age, > 50 yo, increases about 0.6ml a year, Increase volume not necessarily associated with LUTS but it does inc the risk of LUTS

Metabolic syndrome (HTN, Hyperlipidemia, glucose intolerance, central obesity, and insulin resistance) – 3 or more components assoc w LUTS

- Gacci et al. BJU , 2015

Prostate growth is 47% in men with T2D, 17% in men with HTN and 36% in obese men, 31% in men with low HDL and 28% in men w high fasting glucose

- Hammarsten et al., Prostate Cancer Prostate Dis. 1998

SERENOA REPENS

Pharmacologic effects:

- Used in the treatment of BPH it competitively inhibits the 5α-reductase involved in the conversion of testosterone to DHT
- it also inhibits the binding of DHT to androgen receptors. It may also inhibit lipoxygenase activity.
- It has no effect on PSA levels
Serenoa repens (Saw Palmetto)

Study #1-n 155, 160 mg bid 2 yr effective -Pytel et al. 2002

Study #2 - n 219, 160 bid w Urica dioca, almost 2 yr effective -Lopatkin et al. 2007

Study #3 - n 289, 320 mg qd, 2 yr, effective - Djavan et al. 2005 Study #4 - n 154, 160 mg bid, 2 yr effective - Pierre Fabre 2002

Serenoa repens (Saw Palmetto)

Study #5 - n 225, double-blind, RCT, moderate to severe BPH, not effective.

Study #6 – n 369, double-blind, RCT, dose escalation 320 – 990mg /day did not lower LUTS in those w mild to moderate BPH using AUASI– Barry et al. 2011

Study #7 - n 591, single-arm, effective when measured Qmax, IPSS, - Giulianelli et al. 2012

Cohrane Database System Review, at double or triple doses of SP not improve BPH symptoms as a monotherapy. Tacklind et al. 2012

Curcumin and BPH

•Animal study: 4 groups (normal group, BPH group, finasteride group, curcumin group; n = 8 for each group).

•Rats in the curcumin group were treated 50 mg/kg, administered orally for 4 weeks.

•They reported that after 4 weeks of treatment with curcumin, the treated arm had significantly lower prostate volumes and decreased expression of growth factors such as VEGF, TGF-β1, and IGF1

Kim SK, et al.. BMC Complement Altern Med. 2015;15:380.

Pygeum Africanum

•18 clinical trials, 1562 men studied total.

Doses ranged from 75 mg/day to
200 mg/day.



•Significant results of the analysis included that P. africanum decreased PVR by 24% in a total of 264 men in two studies –

 increased Qmax compared to placebo by 23% in 363 men over four studies

•Overall the results point to a modest benefit for the use of P. africanum over placebo. — Ishani et al. 2000

Pygeum Africanum

Endangered Species – Dr. Eric Yarnell

I do not use.

Cranberry (Vaccinium)



RCT – 160 women electing gynecological surgery involving catheterization, 2 caps bid UTI was lower in the cranberry treatment group compared with the placebo group(P = .008) – Foxman et al. 2015 Pilot study – 22 patients, effective and safety from cranberry extract in the prevention of R-UTI. - Ledda et al. 2015

RCT – 41 men in men post EBRT. The incidence of cystitis was lower in men taking cranberry capsules (65%)) (p = 0.058); severe cystitis was seen in 30% in placebo arm

-Hamilton et al. 2015

RCT – 780 women in long-term facility center, 1 capsule bid. Reduction the incidence of clinically defined UTI. – Caljouw et al. 2014

BETA-SITOSTEROL STUDIES

Agent	Number of Patients	Daily Dose	IPSS	Qmax (ml/sec)	PVR (ml) Reference	
Beta- sitosterol	177	130 mg	- 5.4	+ 4.5	- 33.5	Klippel, et al.⁵
Beta- sitosterol	200	60 mg	- 5.3	+ 5.3	- 35.4	Berges, et al. ³
Beta- sitosterol	519	not stated	- 4.9	+ 3.91	- 28.62	Wilt, et al. ⁷

Reishi mushroom (Ganoderma lucidum)



RCT – 88 men with BPH, G. lucidum was well improved IPSS scores. (P < 0.0001)No changes were observed with respect to quality of life scores, peak urinary flow, mean urinary flow, residual urine, prostate volume, serum prostate-specific antigen or testosterone levels. - Noguchi et al. 2008

BPH: Summary of Tx Plan

Diet: Low CHO, anti-inflammatory. Should focus on metabolic syndrome, obesity, Poor blood sugar regulation.

Nutrients: Selenium , vitamin D, zinc – should focus on protecting against oxidative stress

Phytotherapy-Spasmotylitic herbs: Scutellaria, Mellisa, Piscidia piscipula, Gelsimium, Hyoscyamus niger, etc. Hormone regulatory herbs: S. repens, epimedium. Anti-inflammatory herbs: Curcumin, boswellia, quercetin, etc.

Other: Cranberry extract, lycopene, beta-sitosterol, rye pollen extract, reishi mushroom

Lyme Dz protocol: Herbal Abx: oregano, garlic, olive leaf, etc.



PROSTATITIS

CLASSIFICATION OF PROSTATITIS

- Category I
 - Acute Bacterial Prostatitis –pathogenic infection with fever, chills and hypotension
- Category II
 - Chronic Bacterial Prostatitis Mostly voiding disfxn problem or chronic UTI. E.coli up to 80% of times
- Category III
 - Chronic Pelvic Pain Syndrome 90 to 95% most common
- Category IV
 - Asymptomatic Inflammation incidental finding from biopsy or infertility work-up

•Affects up to 15% of men, 2 million medical visits a year

- Pelvic pain for 3 or the previous 6 months
- Involves urinary sx's, painful ejaculation
- No uropathogen identified
- It is considered a syndrome Prostatitis Syndrome
- No physical findings or diagnostic tests
- •NIH CPSI questionnaire excellent for clinical eval.

NIH - CPSI

ndex Domains

		N	H-Chroni	c F	Prostatitis S	ympt	om Index (NIH-CPSI)
1.	Pain or Discomfort In the last week, have you experienced any pain or discomfort in the following areas?						How often have you had to urinate again less than two hours after you finished urinating, over the last week?
							🗅 Notatall
				es	No		Less than 1 time in 5
	a.	Area between rectum and		1			D ₂ Less than half the time
		testicles (perineum)					D ₃ About half the time
	b.	Testicles	-	1			Image: A start of the start
	D.	resucies		-1			□ ₅ Almost always
	c.	Tip of the penis (not related to urination)		1			
						7.	Impact of Symptoms How much have your symptoms kept you from doing
	d.	Below your waist, in your		I ₁		1.	the kinds of things you would usually do, over the
		pubic or bladder area					last week?
2.	in th	he last week, have you experienced					D None
		, ,					□ ₁ Only a little
			Y	es	No		
	a.	Pain or burning during urination?		ונ			🖂 A lot
	b.	Pain or discomfort during or after sexual climax (ejaculation)?		ים		8.	How much did you think about your symptoms, over the last week?
							D ₀ None
3.	Hov	w often have you had pain or discom	fort in any o	ŧ			D1 Only a little
•.	these areas over the last week?				□ ₂ Some		
							D ₃ A lot
		Never					
		Rarely					
	۵	Sometimes					Quality of Life
	•3	Often				9.	
		Usually Always					symptoms just the way they have been during the last week, how would you feel about that?
							□ ₀ Delighted
4.					-		□ ₁ Pleased
	disc	comfort on the days that you had it,	over the last	we	CK f		D2 Mostly satisfied
							Image: A marked and a marked a mar
0		1 2 3 4 5 6	7 8	9	10		□ ₄ Mostly dissatisfied
N	-				PAIN AS		□ ₅ Unhappy
PA	IN				BAD AS You can Imagine		D ₆ Terrible
5.		<u>nation</u>	not omnihin			-	
J .	5. How often have you had a sensation of not emptying your bladder completely after you finished urinating, over the last week?					Sco	oring the NIH-Chronic Prostatitis Symptom Index Do
		Not at all				Pai	m: Total of items 1a, 1b, 1c,1d, 2a, 2b, 3, and 4
	D ₁	Less than 1 time in 5		Un	nary Symptoms: Total of items 5 and 6		
□ ₂ Less than half the time						Qu	ality of Life Impact. Total of items 7, 8, and 9
	□ ₃ About half the time □ ₄ More than half the time						
	5	Almost always					

Nine question survey

Covers the three domains of:
Pain (location, frequency and severity),
Urinary symptoms
Quality of life

Six point improvement score is clinically significant

QUERCETIN FOR CPPS/CP

- Studied in a non-randomized trial 500 mg bid, 59% of participants improved
 - Shokes DA , 1999
- Randomized trial, symptoms improved in 67% of the treatment group at 500 mg bid

- Shokes et al, 2001

Spasmolytic Herbs

Piper methysticum (kava) root, Zingiber officinale, Piscidia piscipula, Gelsimium, Hyoscyamus niger (strong genitourinary affinity

– Yarnell, 2011)

Minimal AE: including sleepiness is rare

Unlike Alpha Blocker Drugs - No AE retrograde ejaculation, hypotension, asthenia

69 yo with LUTS, urinary frequency and urgency. Zyziphus spinosa 20ml Scutellaria latiflora 20ml Virbunum opulus 20 ml Crataeva nurvala 40 ml, 100ml total, Rx: 8 ml with water bid

- Bone K, Mills S; Priniciples and Practices of Phytotherapy, 2nd Edition

Anxiolytic Herbs

Skullcap (genus *Scutellaria*), Hops (*Humulus lupulus*), Passion flower (genus *Passiflora*), Chamomile (*Matricaria recutita*), and lemon balm (*Melissa officinalis*) are great.

Lemon balm increases synaptic GABA and reduced cortisol

Skullcap components, bacalin and bacalein, are GABA receptor agonists and promote GABA activity

Piper methysticum - kavalactones that bind to GABA receptors, dopamine receptors and opiate receptors and work to uncouple the sodium potassium channels thereby reducing impulses to muscles and serves as a muscle relaxant

FLOWER POLLEN EXTRACT

- An extract of flower pollen derived primarily from rye, may improve symptoms of chronic prostatitis and prostadynia
- 2 tablet bid, for 18 mths, non-randomized, improvement of symptoms
 - Buck et al 1989
- Larger study showed improvement
 - Rugendorff et al 1993
- Randomized trial, 60 patients total, treatment group did much better (p<0.0001) - Elist, 2006

Anti-Inflammatory Herbs

Boswellia 200 to 500 mg bid

Curcumin 400 to 800 mg bid

Ginger 200 to 400 mg bid

Quercetin 500mg bid

PROSTATITIS: SUMMARY OF TX PLAN

- Dx: NIH CPSI, DRE, Urine culture, UA
- Tx: Short term: Tx Sx's, Physical medicine, Trigger point release, Acupuncture, Physical Therapy
- Herbs Boswellia, Corydalis, Melissa, Piper methysticum, Rye pollen extract
- Nutrients Magnesium, Theanine, Omega 3s
- Long term: TREAT THE GUT: probiotics, glutamine, food intolerance elimination. Psychotherapy, ketogenic diet may work for pain



PROST



PROSTATE CANCER

 The most common type of cancer in men and second most frequent cause of cancer-related death in men

• One in 6 men will develop prostate cancer (PC) during his lifetime.

 An estimated 217,730 men diagnosed and, 32,050 deaths in the United States in 2010

The CaPLESS Method What's the Dose? Movement

Goals:

Manage Insulin Sensitivity
Promote Detoxification
Low Body fat
Decrease IGF-1
Increase IGFBP-1 (protective)

Men 65yo 70% reduction in dx of advanced prostate cancer – 3 hours vigourous activity a week. - Kenfield et al., J Clin Oncol 2011

Men on ADT: >3 hours a week of moderate intensity, aerobic and weight resistance exercise morbidity: abdominal fat, less cardiovasc disease, less fatigue, bone density loss compared to control. - Cormie et al. BJU Int. 2014

Grape Seed Extract Protects

VITAL Study – 35,000 subjects – GSE was associated with 41% CaP reduction. No associations for use of chondroitin, co-enzyme Q10, fish oil, garlic, ginkgo biloba, ginseng, glucosamine, or saw palmetto.



- Brasky et al. 2011

Reishi mushroom (Ganoderma lucidum)



Inhibits nuclear factor kappa B (NF-kappaB) and AP-1. Suppressed cell adhesion and cell migration of highly invasive breast and prostate cancer cells, suggesting its potency to reduce tumor invasiveness.

Demonstrates anticancer activity in experiments with cancer cells and has possible therapeutic potential as a dietary supplement for an alternative therapy for breast and prostate cancer. - Silva, Dan 2003

CaP: Summary of Tx Plan

Diet: CaPLESS Nutrition: Mediterranean / Plant based

Nutrients: Selenium, vitamin D, zinc, vitamin C, Mixed tocopherols (gamma) – should focus on protecting against oxidative stress

Phytotherapy-Curcumin, boswellia, quercetin, Modified Citrus Pectin, Grape seed extract, Milk Thistle, etc.

Other: Reishi mushroom

Physical Activity: 4 hours a week with moderate intensity



ERECTILE DYSFUNCTION

ERECTILE DYSFUNCTION

The inability to maintain an erection firm enough to have sexual intercourse.



Anatomy





THE DEADLY QUARTET (HIGH RISK ED) METABOLIC SYNDROME



Beware of Over-the-Counter Supplements













L-Citrulline

Produces L-Arginine in the body

L-Arg produces NO with the NOS. 5 g / d beneficial for mild to moderate ED in RCT.

- Chen et al. 1999

L-Cit recycles the production of L-Arg. Improves Hardness factor in men with mild to moderate ED.

- Cormio et al. 2011



Epimedium (Horny goat weed)

Icariin (ICA) exert PDE-5 inhibitory Effects in vitro.

Enhances eNOS expression and NO production

Low dose (ICA) improved erections in rats after nerve injury. - Shindel et al. 2010

No human studies



Pomegranate

Potent anti-oxidant (anthocyanins)

Enhance NO levels

Reduces atherosclerotic lesions

Decreases LDL cholesterol

RCT – n=53, Overall increased erectile function but not statistically significant (P=0.058) – Forest et al. 2007



Lepimedium meyenii (Maca)

Known as the Ginseng of Peru

3 RCT trials in men

1.Two Increased desire at 1500mg and 3000mg / d

- Gonzales et al. 2002
- Stone et al. 2009



2. Improved mild ED – 2400mg /d -Zenico et al. 2009



7 RCT 1800 to 3000mg / d 1000 tid best (p=0.00003)

AE= Headache, Insomia

- Jang et al. 2008

Questions



Stay in Touch!

DRGEO

Insights on Holistic Urology and Men's Health



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