General Medical Conditions leading to Sexual Dysfunction

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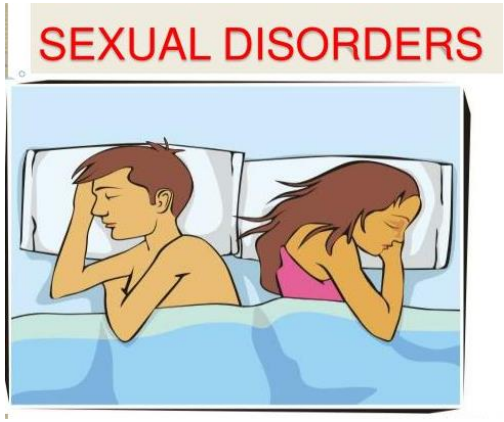
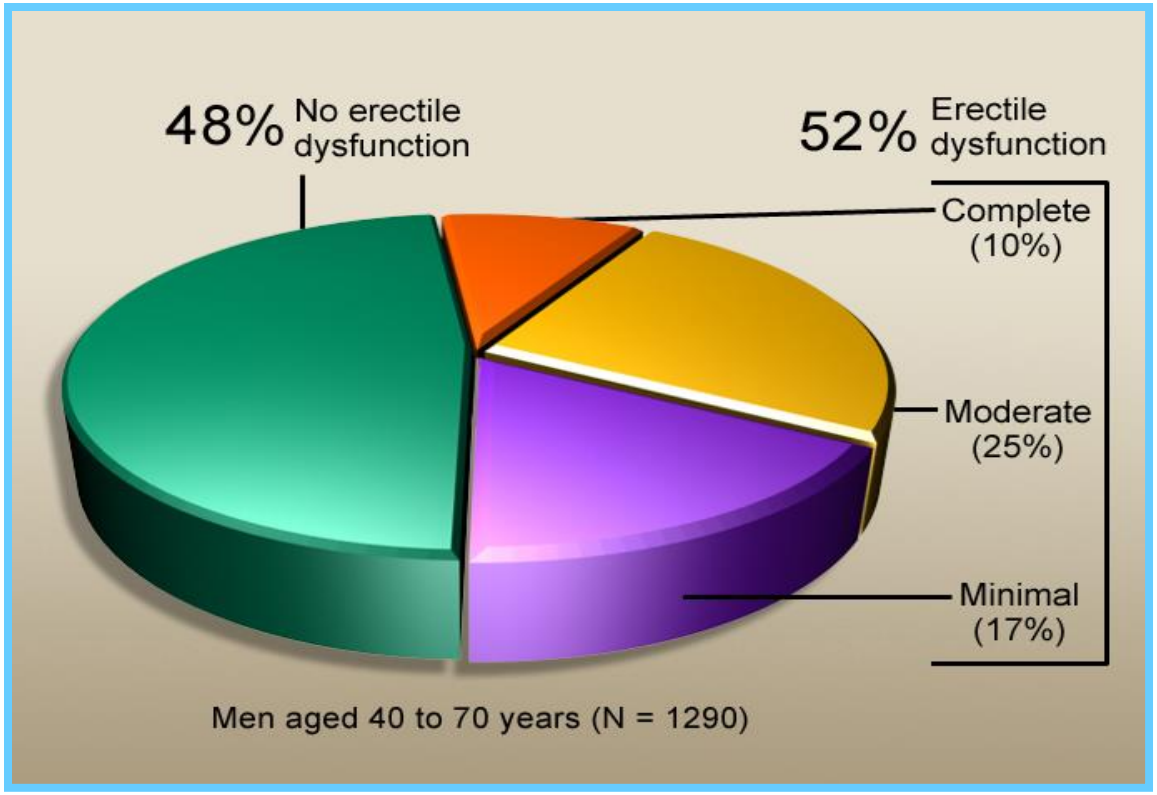
Scope of the problem

- Prevalence of sexual dysfunction in general population is very high
- 43% of women and 31% of men have some form of sexual dysfunction
- Among men, premature ejaculation is the most common male sexual dysfunction
- In women:
  - Hypoactive sexual desire disorder
  - Orgasmic and arousal disorders
  - Vaginal dryness



- Problems maybe- acquired, general or situational
- Under-diagnosed and unrecognized

Prevalence of ED
Massachusetts Male Aging Study



Feldman HA, et al. *J Urol*. 1994;151:54-61.

Differentiating features between psychogenic and organic sexual dysfunction

Characteristics	Predominantly Organic	Predominantly Psychogenic
Age	Older	Younger
Onset	Gradual (except trauma or surgery)	Acute
Circumstances	Global	Situational
Symptom course	Consistent or progressive	Intermittent
Desire	Normal to start with	Decreased
Organic risks	Present	Absent, variable
Partner problem	Usually secondary	Usually at onset
Anxiety & Fear	Usually secondary	Usually primary

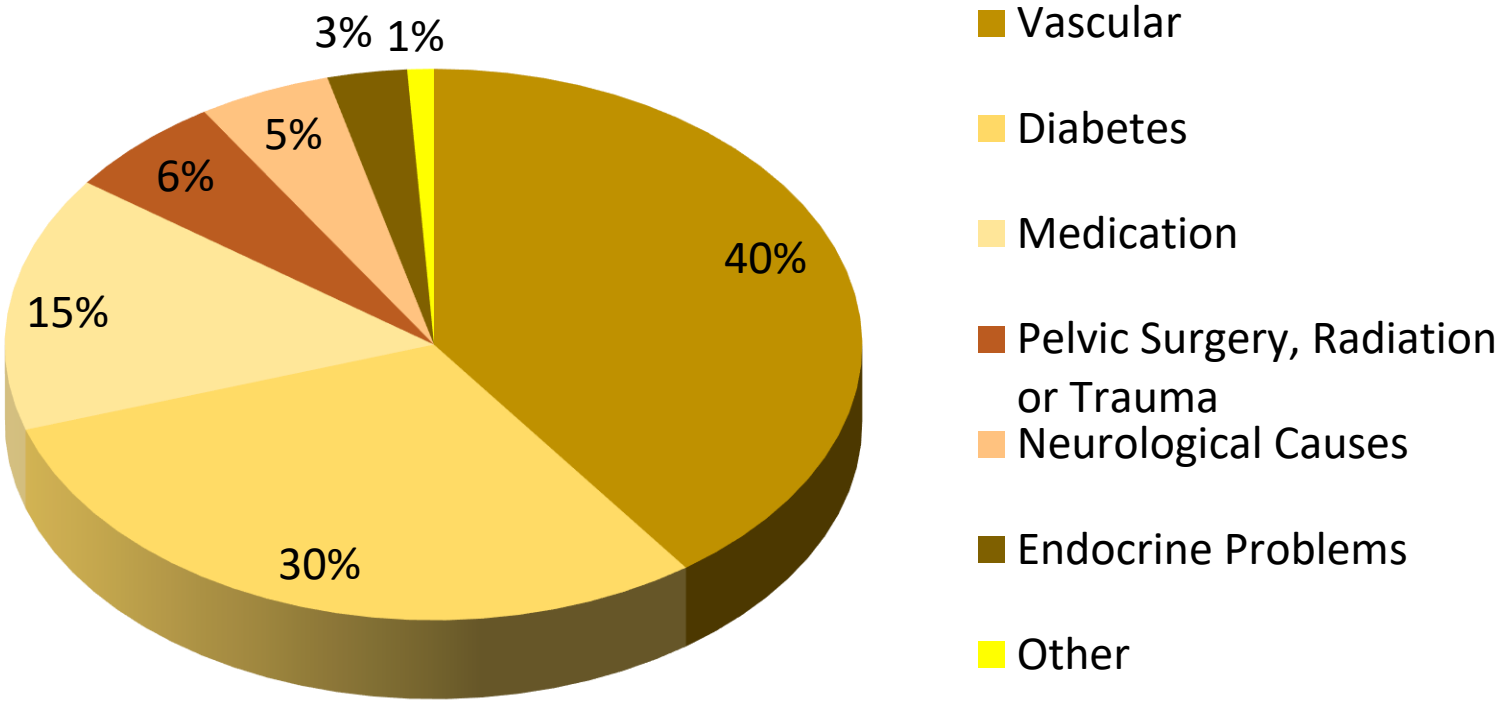
Comprehensive history for erectile dysfunction

Sexual history	Medical history
Erectile insufficiency	Exploration of co-morbid conditions
Altered patient or partner libido	Efficacy of anti-diabetic interventions
Ejaculation	Current medications/ recreational drugs, smoking
Orgasm	History of surgeries or pelvic/perineal trauma
Partner sexual function	Depressive symptoms, psycosexual disorders
Sexually induced genital pain	Evaluation for vascular risk factors

Causes of Erectile Dysfunction

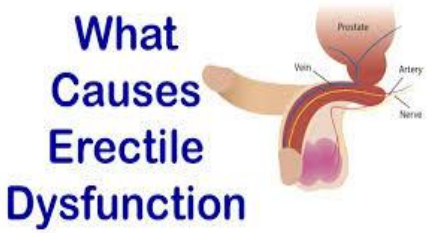
Diabetes Obesity Metabolic syndrome High cholesterol Sleep disorders Clogged blood vessels MENTAL HEALTH STRESS Alcoholism Multiple sclerosis Metabolic syndrome Parkinson's disease High blood pressure Heart disease DEPRESSION

Main Physical causes of ED



Goldstein I. Male sexual circuitry. Working Group for the study of central mechanisms in erectile dysfunction. Sci Am., Aug 2000;283(2):70-75

Causes of Erectile Dysfunction



- Heart Disease
- Severe atherosclerosis
- Dyslipidemia
- Hypertension
- Diabetes
- Obesity
- Metabolic Syndrome
- Parkinson's disease
- Multiple Sclerosis
- Peyronie's Disease (development of scar tissue inside penis)
- Spinal cord injuries
- Treatment for Ca Prostrate, enlarged prostrate
- Liver and Kidney failure

Causes of Erectile Dysfunction

- Tobacco use
- Alcoholism
- Substance Abuse
- Smoking
- Emotional or psychological stress esp with regard to relationship with partner
- History of sexual abuse
- Sleep Disorders
- Depression and Anxiety

Symptoms

Males

- Decreasing Libido
- Interfering with erectile dysfunction
- Causing absent seminal emission
- Retrograde ejaculation
- Premature ejaculation

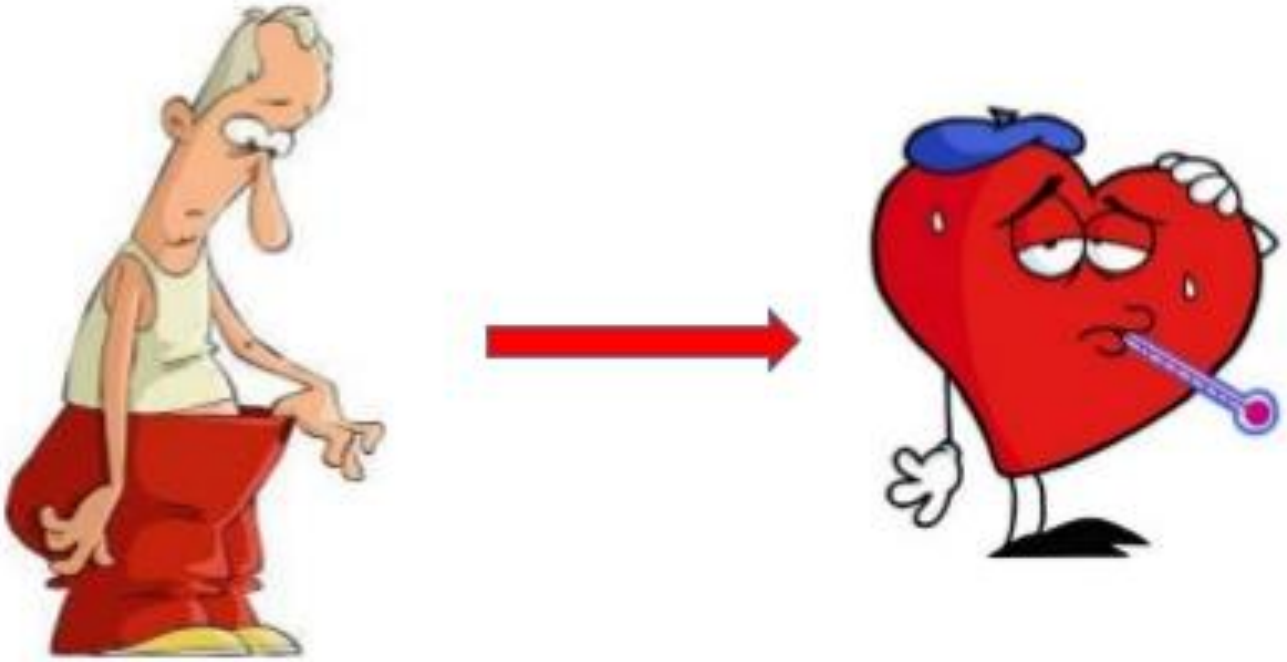
Females

- Low desire
- Lack of swelling and lubrication
- Vaginal dryness and Dyspareunia

Drugs Causing Erectile Dysfunction

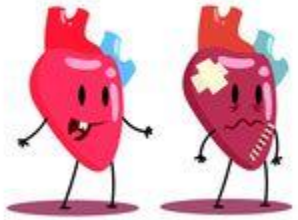
Type of drug	Generic examples
Diuretics	HTZ, Chlorthalidone, Triamterene, Furosemide
Antihypertensives	Alpha-blockers, Beta-blockers, Hydralazine, Nifedipine, Verapamil, Captopril, Enalapril, Spironolactone
Antidepressants , Anti-anxiety drugs and antiepileptics	Fluoxetine, Tranylcypromine, Sertaline, Amitriptyline, Clomipramine, Nortriptyline, Chlordiazepoxide, Diazepam, Doxepin, Imipramine, Lorazepam, Phenytoin
Antihistamines	Dimehydrinate, Diphenhydramine, Meclizine, Promethazine
NSAIDs	Naproxen, Indomethacin
Anti-Parkinson meds	Biperiden, Benztropine, Trihexphenidyl, Procyclidine, Levodopa, Bromocryptine
Antiarrythmics	Disopyramide
H2 receptor antagonists	Cimetidine, Ranitidine
Muscle relaxants, Prostrate cancer meds, Chemotherapy drugs	Cyclobenzaprine, Orphenadrine, Flutamide, Leuprolide, Busulfan, Cyclcophosphamide

Erectile dysfunction Indication of Heart Disease



Sexual activity and sexual dysfunction in patients with heart disease

- Erectile dysfunction is common
- It is an independent risk factor for cardiovascular disease, equivalent to a current moderate smoker
- Men presented with ED for 38 months on average before developing acute chest pain
- Why? The penile arteries are smaller in diameter than the coronary arteries



- ED is a helpful early warning symptom for future cardiovascular events
- Clinicians can therefore target their advice and treatment to patients to reduce their risk of future myocardial infarcts or strokes

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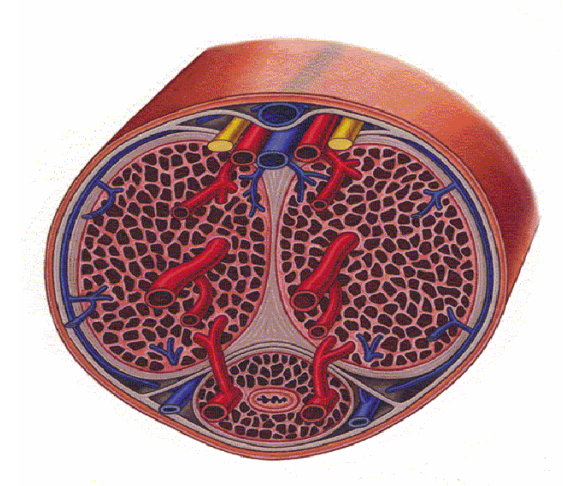
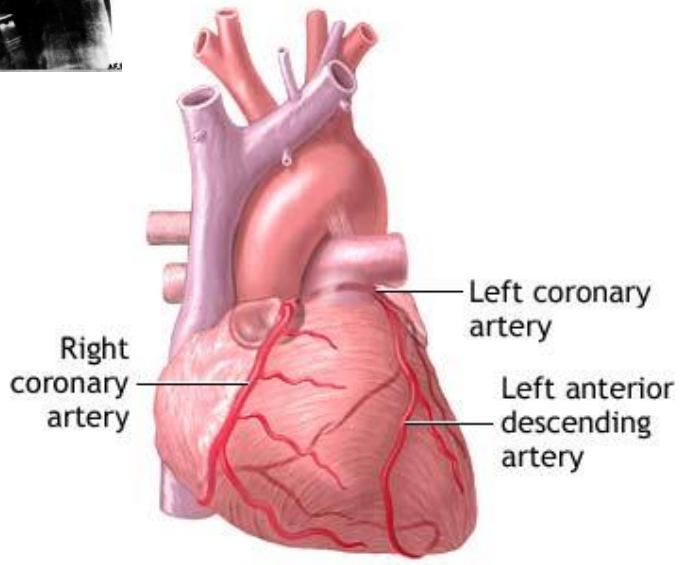
Erectile Dysfunction: A Canary in a Coal Mine

ED shares many risk factors for heart disease and warrants a cardiac risk assessment in most patients





Risks associated with heart disease

Risk of Myocardial infarction after sex

- Maximum relative risk of MI is within 2 hours after sexual activity
- Absolute increase in risk is small (< 1%)
- Many other triggers for MI viz. Psycologic stress, anger, vigorous sexual activity may cause a higher risk

Hemodynamic stress on heart of normal sexual activity

- Mean HR: can cause tachycardia upto 120 bpm
- Mean BP : can go up to approx. 160/90
- Work load (mets): approx. 3-4 mets during orgasm (1 met = 3.5ml O2 uptake/kg per min), (walking on level surface for 2-4 miles or brisk climb of 2 flights of stairs)

Modest increase in myocardial oxygen demand that lasts for brief period

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CV Risk categories of the Princeton guidelines

This risk stratification algorithm was developed by the 1st Princeton Consensus Panel to evaluate the CV risk associated with sexual activity for men with varying degrees of Cardiovascular disease

Low Risk Patient	Indeterminate Risk Patient	High-risk patient
Aymptomatic, < 3 cardiac risk factors	> 3 major cardiac risk factors	Unstable or refractory angina
Controlled Hypertension	Moderate stable angina	Uncontrolled HT
Mild, stable angina	Recent MI (> 2 ks, < 6wks)	Recent MI (< 2wks)
LV Dysfunction (NYHA class 1)	LV Dysfunction (NYHA Class II)	LV dysfunction (NYHA Gr 111-IV)
Past MI (> 6-8 wks)	Evident peripheral arterial disease	High risk arrythmias
Mild valvular disease	h/o stroke, TIA	HOCM
Post coronary revascularisations		Mod/Severe valvular disease esp AS
Pericarditis, MVP, or AF		

Place of PDE-5 inhibitors in patient with heart disease

- Use of PDE-5i showed no increase in MI or death rates
- Patients with known CAD or HF receiving PDE-5i did not exhibit worsening ischemia, coronary vasoconstriction, worsening hemodynamics on exercise testing or cardiac worsening
- PDE-5 inhibitors have a minimal effect on the QTc interval (Vardenafil is not recommended in patients on T1A antiarrhythmics, T3 antiarrhythmics congenital prolonged QT syndrome)
- PDE-5i may cause slight decrease in BP because they are mild vasodilators, but this effect is accentuated in patients with hypertension, CAD
- Contraindicated to combine with nitrates, as cyclic GMP increases causing marked hypotension
- Caution when combine with alpha blockers as there could be additive effects of vasodilatation and hypotension

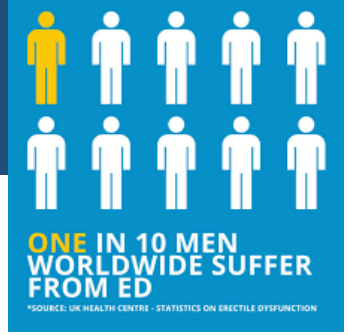

diabetes
metabolic disease
high blood sugar
insulin
liver
diabetic
hyperglycemia
glucose level
obesity
insulin pump
diabetic retinopathy
polyphagia
polyuria
gestational diabetes
pharmaceuticals
symptoms
injection
insulin pen
hormone
pancreas
type 2 diabetes
polydipsia
bloodstream
treatment
diet
hospital
sugar
type 1 diabetes
chronic disease
metabolic disease
diabetic treatment
bloodstream
hyperglycemia
gestational diabetes
diet
insulin
liver
type 2 diabetes
high blood sugar
hospital
pancreas
diabetes
diabetic retinopathy
polyphagia
insulin pump
polyuria
insulin pen
hyperglycemia
polydipsia
hormone
obesity
pharmaceuticals
chronic disease
treatment
pancreas
glucose level
symptoms
injection
type 1 diabetes
diabetic

Sexual Dysfunction in Diabetics

FEMALES

- Prevalence of symptoms is
  - 21-57% in Type 1 diabetes,
  - 30-84% in Type 2 diabetes
- Studies less conclusive due to lack of standardization of definition of sexual function in females
- Symptoms of loss of libido, problems with orgasm, lubrication and arousal, dyspareunia, lower sexual satisfaction
  - Type 1: sexual dysfunction had no co-relation to glycemic control or complications (DCCT)
  - Type 2: duration of diabetes corelated negatively with all domains of sexual function
- Depression, partner related factors and marital status had better co-relation
- No strong association with CV, Metabolic and other risk factors
- Female dysfunction in diabetes relates less to organic and more to psychological factors

Sexual Dysfunction in Diabetics



MALES

- Prevalence of symptoms is
  - UroEDIC study: T1DM- 55% had reduced libido, 34% ED, 20% orgasmic dysfunction
  - Olmsted County study- 40% had decreased sexual drive
- Significant association with ED, sexual drive, ejaculatory function, sexual problems, sexual satisfaction
- In DCCT/EDIC trial- ED was an independent predictor of health related QOL
- Most men seeks medical help only for ED
- Has co-relation with CV risk
- ED has multifactorial etiology- metabolic, neurologic, vascular, psychological
- Hyperglycemia is important and high HBA1c is associated with declining erectile function
- Pathogenesis: high AGE, glycation of elastic fibers, development of macro-, micro vascular complications

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Screen for ED in Diabetes

ED affects 34-45% of men with diabetes

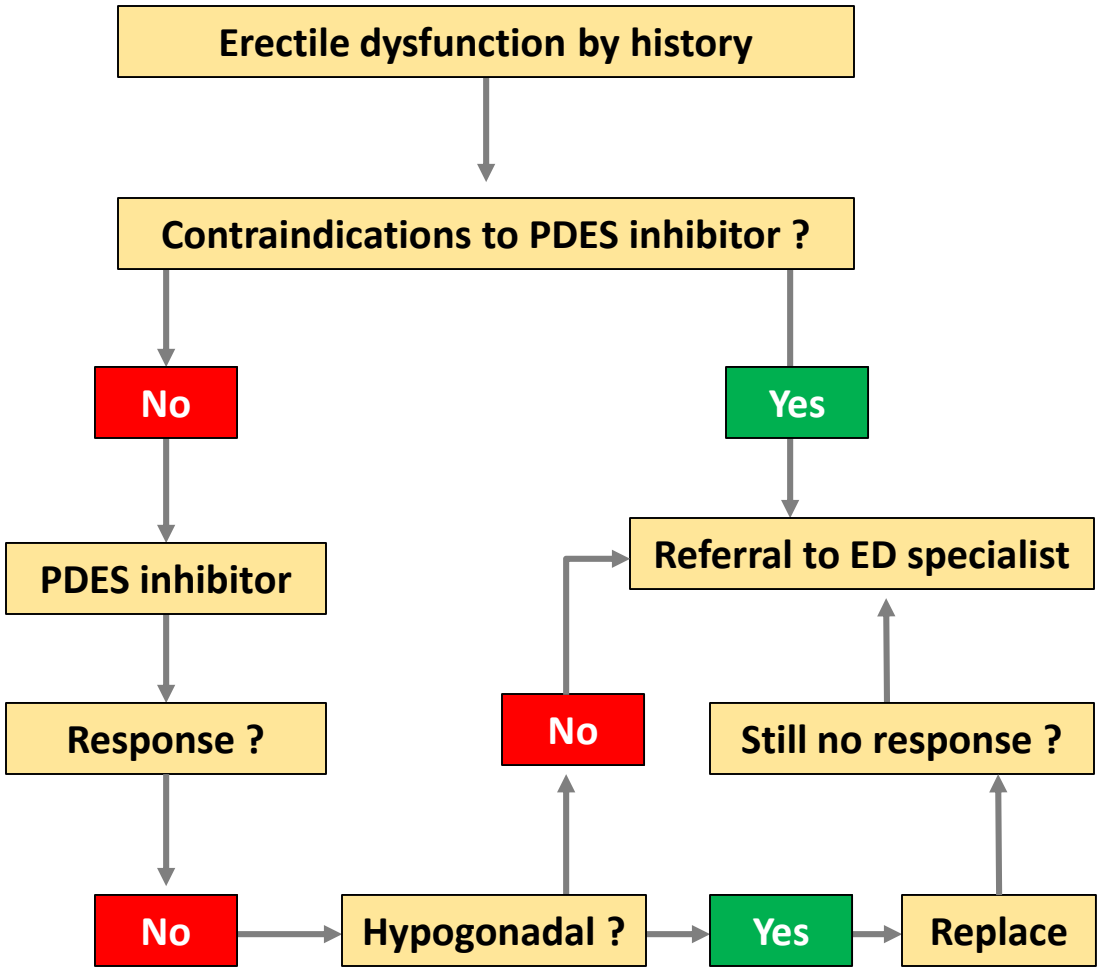
40% of men >60 years with diabetes have complete ED

ED negatively impacts quality of life

Common + Important

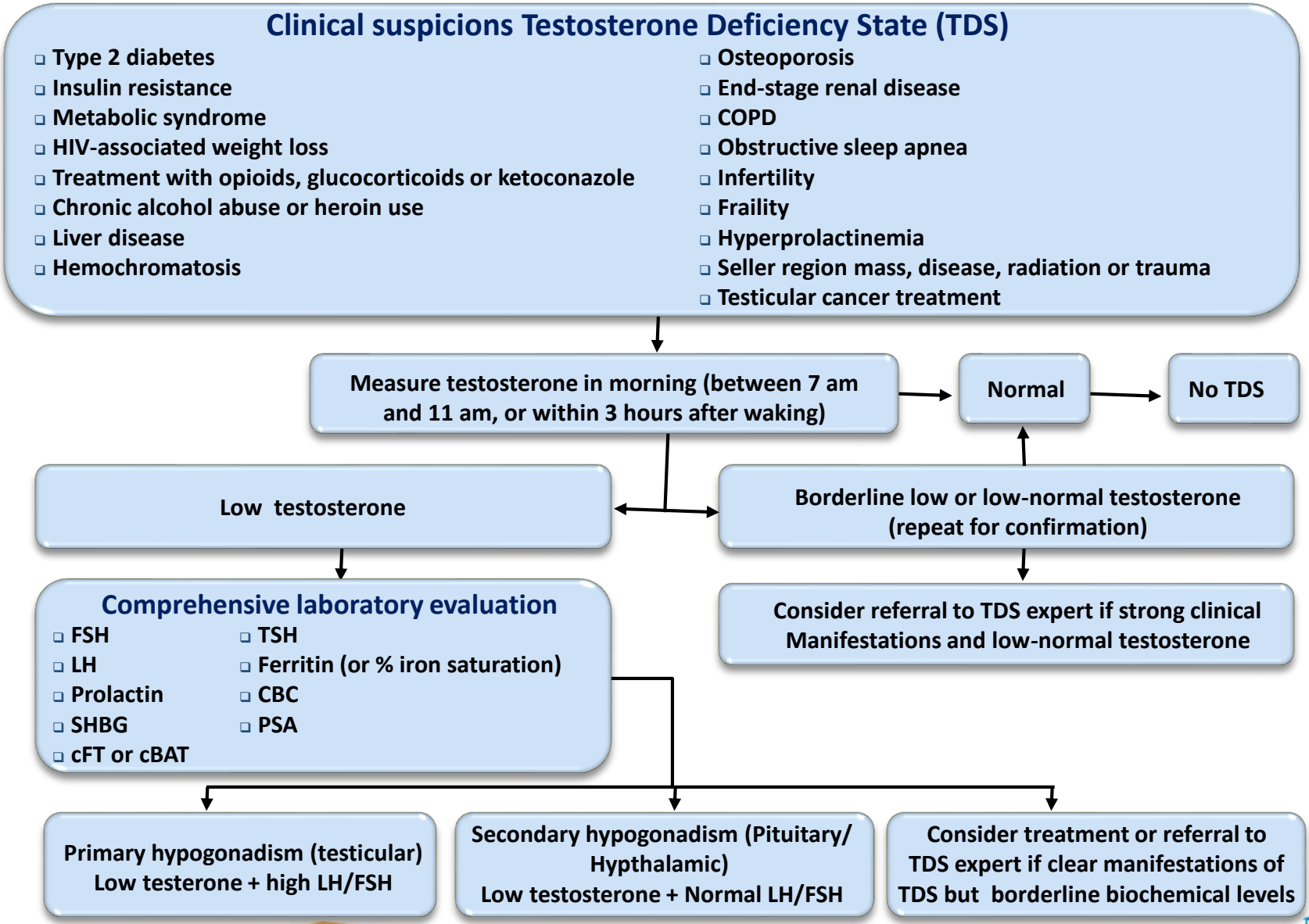
Screen all adult men with diabetes regularly as part of sexual function history

Management of ED in men with Diabetes



- Hypogonadotropic hypogonadism is common in men with T2DM with a prevalence of up to 40%
- Hypogonadal men with diabetes have a higher risk for CV mortality than eugonadal men with diabetes
- Screening for symptomatic hypogonadism in men with T2DM is recommended

Evaluation for Testosterone deficiency



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Key messages for people with Diabetes

- Low testosterone is common in men with type 2 diabetes
- Symptoms of low testosterone can include: diminished interest in sex, erectile dysfunction, reduced lean body mass, depressed mood and lack of energy
- A decrease in sexual function may indicate your risk of cardiovascular disease is increasing
- If you are experiencing symptoms of low testosterone, you should talk with your health-care provider

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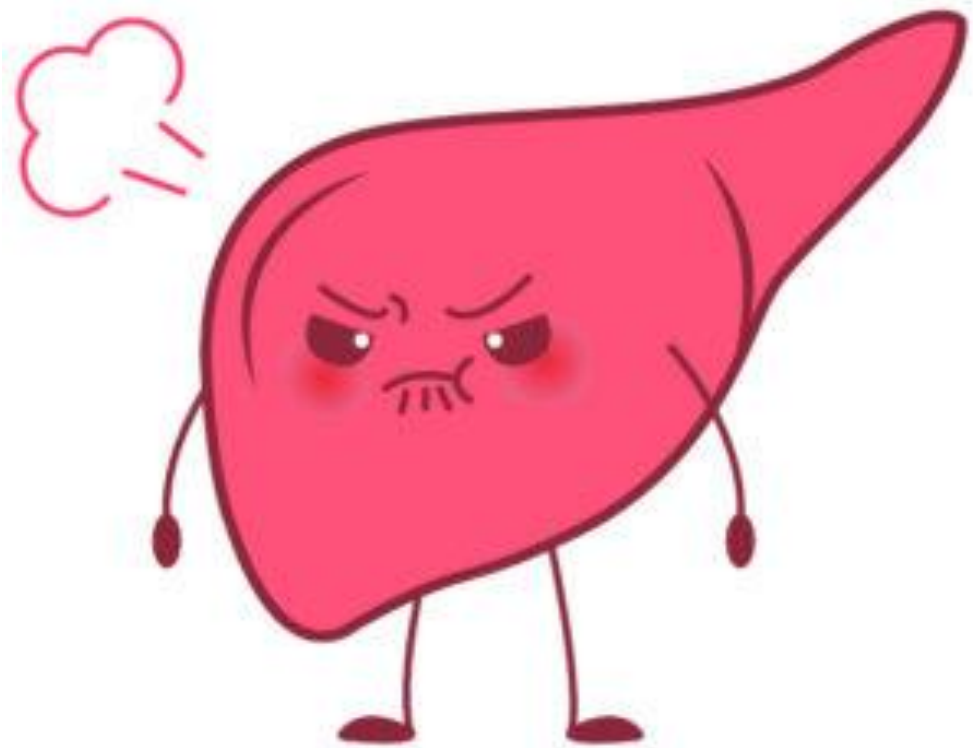
Liver and its disorders



Chronic Viral Hepatitis C

- HCV has a profound effect on HRQoL. Men with Chr HCV have marked reduction in sexual function in comparison to uninfected controls
- Plasma levels of total testosterone and free testosterone were lower in HCV +ve patients to age matched individuals
- HCV patients with ED had significantly lower testosterone levels than those with normal sexual function
- HCV itself appears to play a causative role in causing ED
- Sexual health indicators in men: low desire, ED, ejaculatory problems and overall sexual dissatisfaction are common during treatment with peg-interferon/ribavirin- decline maybe reversible partially after stopping therapy

Chronic Viral hepatitis B

- HBV male patients had lower IIEF-5 score and higher incidence of ED
- HBV patients have ED in different degrees according to severity of the disease
- In males, sex hormones can increase HBV transcription and replication, as androgen receptors can directly bind directly to HBV genome via enhancer
- In females, estrogen receptor are able to down regulate HBV gene transcription through remodeling of viral genome

Non-Alcoholic Fatty Hepatitis

- NASH is the hepatic component of metabolic syndrome
- The prevalence of low testosterone levels among men with ED and metabolic syndrome is 4 times higher than those without.
- Testosterone plays a major role affecting components of MS as androgens decrease lipoprotein lipase and upregulate β adrenargic receptors on adipocytes
- Higher serum levels of leptin was found in patients with NAFLD. Leptin levels are inversely co-related with testosterone. Excess leptin can lead to ED through androgen deficiency in males

Alcoholic Liver disease

- Heavy alcohol consumption can cause effect of erectile function through neurologic damage
- There can be primary Gonadal dysfunction resulting from:
  - Direct toxic effect of ethanol and acetaldehyde on gonads
  - Inhibition of LH binding to Leydig cells
  - Inhibition of the intratesticular activation of Vit A
- Hypothalamic-pituitary hypogonadism also results from direct toxic effect of ethanol and increased estrogen levels evident after longer periods of alcohol intake

Liver cirrhosis

- Sexual dysfunction in cirrhotic men comprises signs of hypogonadism-feminization
- Hypogonadism occurs due to—
  - Reduced production of albumin may affect ratio of FT to albumin bound testosterone as well as TT amount
  - Physical disturbance caused by protein malnutrition in cirrhotics
  - Hypothalamic-pituitary-gonadal axis affected by reducing pulsatile secretion of LH and response to GnRH
  - Estrogen/androgen ratio is usually increased. Testosterone and DHEA are reduced while estradiol levels are normal or slightly elevated
- Mechanism of feminization
  - SHBG is significantly increased in liver cirrhosis. Serum FT and T/SHBG ratio decrease,
  - Serum E2, Free E2, E2/FT ratios increase resulting in estrogen predominance

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Hepatocellular Carcinoma

- Some studies have shown both estrogens and androgens affect replication rate of hepatic cells which induce or at least promote the growth of HCC
- Patients with HCC have higher rates of sexual dysfunction due to:
  - Neuroendocrine changes due to related disease or treatment
  - Changes in body image, gynecomastia, cachexia, ascites
  - Co-morbid medical conditions that increase sexual morbidity
  - Medications – narcotics, antidepressants, anti-hypertensives etc
  - Psychological distress associated with poor prognosis
- Patients with HCC reported higher rates of sexual problems compared with general population including ED (17% vs 11%)

Before and After Liver Transplantation

- Liver transplant improves patients survival and QOL including sexual function
- Improvement of ED after transplant has been controversial as ED can be multifactorial
- Before liver transplant, sexual dysfunction and sex hormone disturbances are mainly due to abnormality in H-P-G axis or origin of liver disease

PDE-5 inhibitors in CLD

- Safe and well tolerated
- Potential use in treatment of portal hypertension


Dialysis
artificial
replace
removing
chronic
kidneys
process
excess
endocrine
measure
hemofiltration
water
previously
hemodialysis
erythropoietin
end-stage
transplant
replacement
renal disease
functions
calcitriol
acute
removal
renal
Dialysis
lost
disturbance
equilibrium
blood
formation
primarily
holding
calcium
compromised
inappropriate
hemodiafiltration
roles
maintaining
potassium
indications
performed
reversible
treatment
internal
factors
divided
primary
body's
depends
years
hyperkalemia
diffusion
red
form
patients
cells
fluid
several
latter
system
maintain
healthy
lost function
imperfect
worsening
supportive
injury
role
excreted
metabolic acidosis
magnesium
ally
intoxication
rid
stage
waste
develop
bone
production
respiration
producing
decision
kidney
progressive
body
acidic
metabolism
intestinal
chloride
phosphorus
minerals
sodium
correct
health
failure
months
function
state
plays
initiate
people
disease
contrast
involved
adidemia
via
secondary
peritoneal
end-products
ultrafiltration
treatments
regarded
sulfate
important

Chronic Kidney Disease

- Abnormalities in sexual function are common in both men and women with CKD, and become more apparent as kidney disease progresses.
- Testosterone deficiency, usually accompanied by elevation of serum gonadotropin concentrations, is present in 26 to 66% of men.
- Sexual disturbances in women include abnormalities in their menstrual cycles. Sexual dysfunction in men includes erectile dysfunction (ED).
- In both sexes, sexual abnormalities in CKD include decreased libido and infertility
- Disturbances in the hypothalamic-pituitary-gonadal axis can be detected before the need for dialysis but continue to worsen once dialytic therapy is initiated. Impaired gonadal function is prominent in uremic men, whereas central disturbances are more prominent in uremic women.

Male Sexual Dysfunction in CKD

- Prevalence of Erectile Dysfunction is estimated to be approximately 80% among CKD patients
- Possible causes of Erectile Dysfunction in Men:
  - Vascular system: Occlusive arterial diseases, Veno-occlusive diseases and venous leakage
  - Neurologic system: Impaired autonomic function due to uraemia and comorbid conditions
  - Psychologic dysfunction
  - Other factors: Zinc deficiency, Medications, Anaemia, Secondary hyperparathyroidism
  - Decreased Testosterone, Raised FSH, LH, Prolactin, Endothelial Dysfunction

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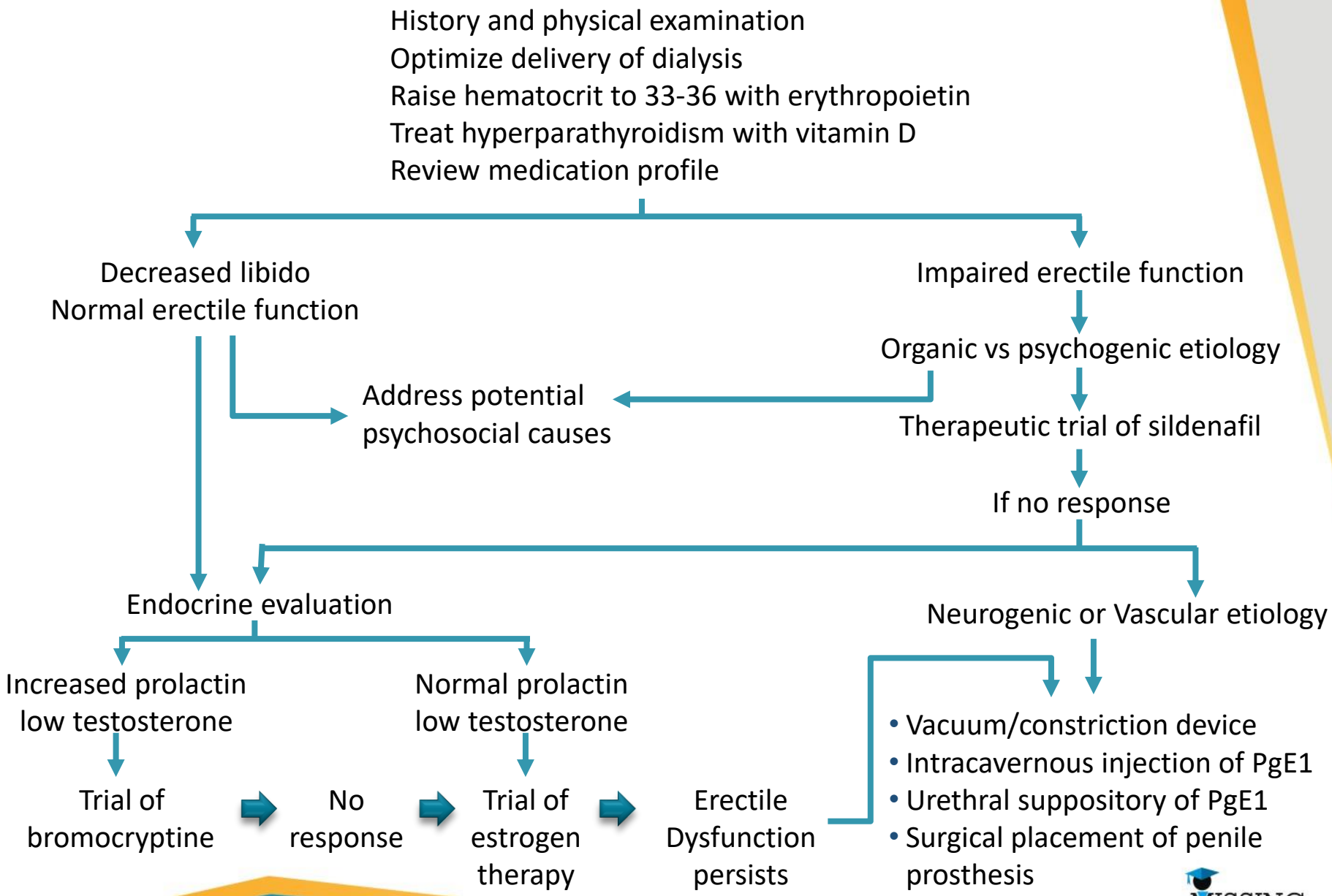
Approach to sexual dysfunction in Uremic Men



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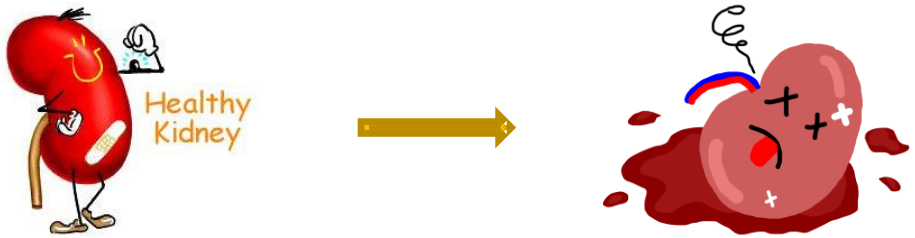
Treatment of Sexual Dysfunction in Men with CKD

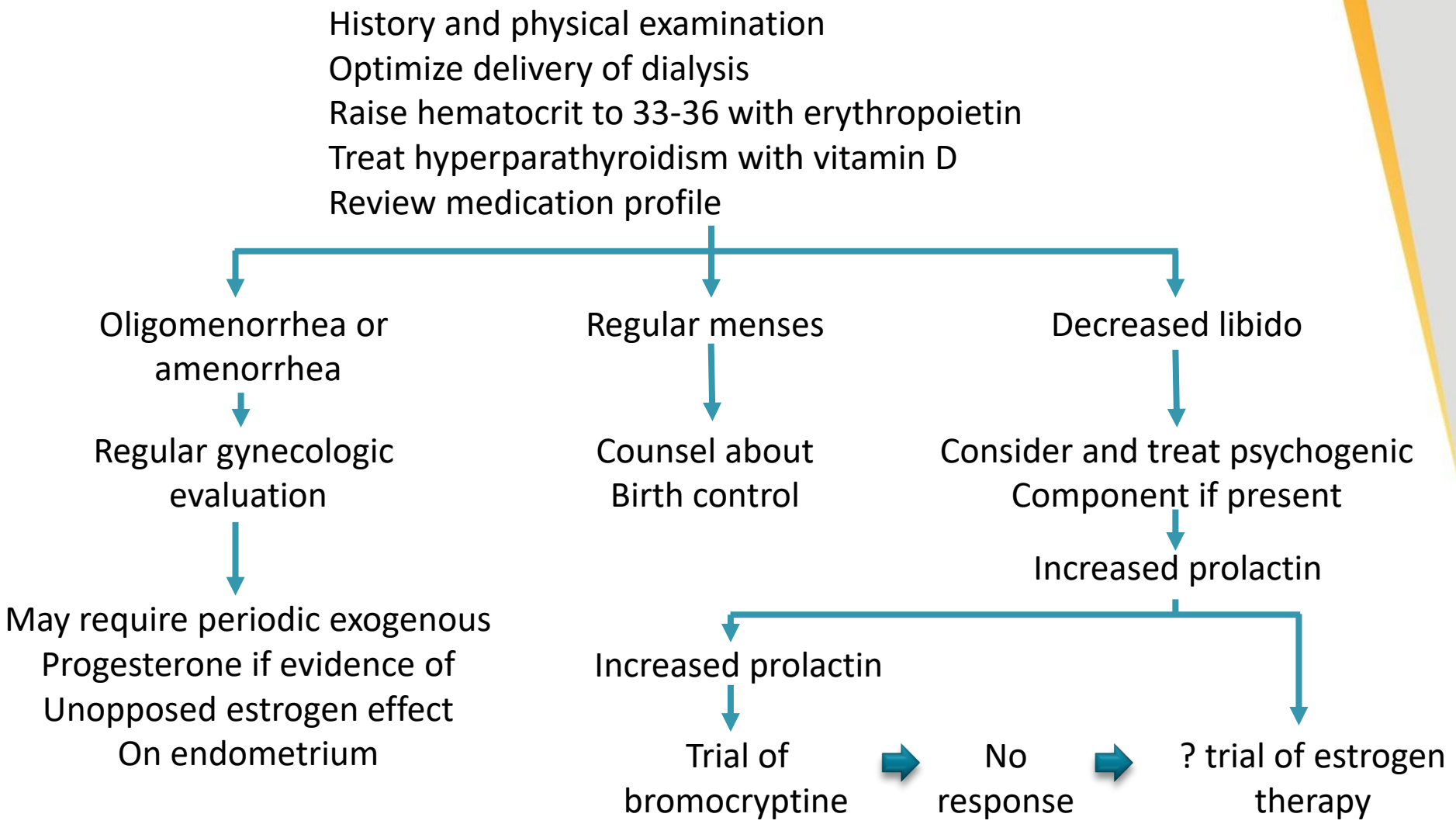
- PDE5 Inhibitors - It may be safer to start with half the dose (25 mg) and subsequently increase it up to 100 mg, depending on the patients' responses
- Testosterone replacement - combination therapy of testosterone and PDE5Is may be more effective than treatment with either testosterone or PDE5Is alone.
- Erythropoiesis stimulating agent (ESA) therapy, anti-estrogens, dopamine agonists, vitamins, essential trace elements, and chorionic gonadotropin
- Renal Transplantation: Erectile function was reportedly better in renal transplant recipients as compared to patients on Dialysis
- Injecting prostaglandin E1 into the shaft of the penis, vacuum constriction devices and constriction bands, and penile prostheses.

Female Sexual Dysfunction in CKD

- Disturbances in menstruation and fertility are commonly encountered in women with chronic renal failure, usually leading to amenorrhea by the time the patient reaches end-stage renal disease.
- Several hormones have been implicated in hypothalamic–pituitary–gonadal dysfunction, including leptin, prolactin and endorphins.
- Hyperprolactinemia: Elevated prolactin levels may impair hypothalamic-pituitary function and contribute to sexual dysfunction and galactorrhoea in these patients.



Approach to sexual dysfunction in Uremic Men



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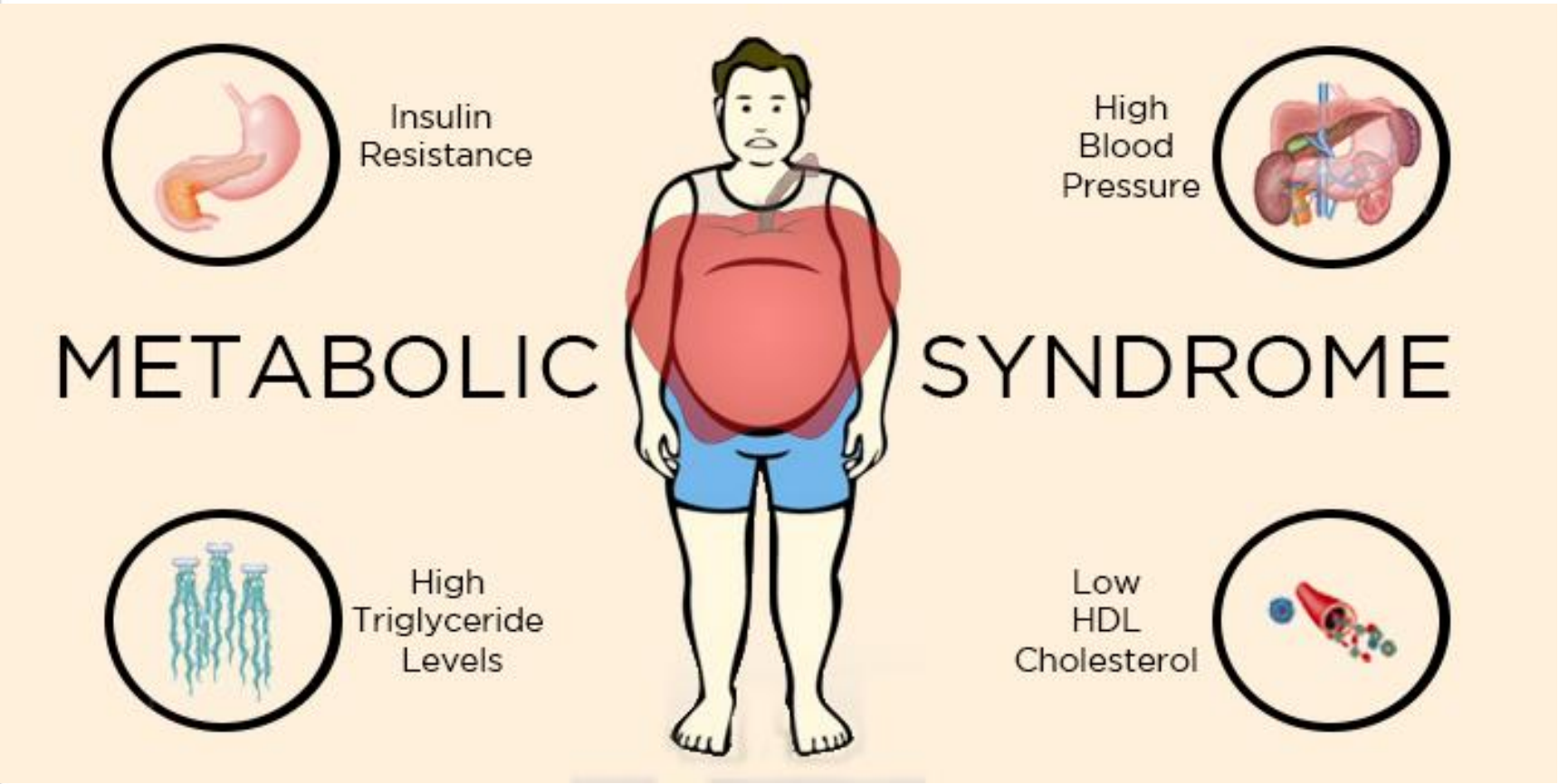
Treatment of Sexual Dysfunction in CKD Women

- Pharmacologic therapy with estrogen/progesterone and androgens.
- Correction of anaemia.
- Treatment of underlying depression.
- Changes in lifestyle, such as smoking cessation, increased physical activity, and aerobic exercise, as well as enhanced body image may have a positive impact on sexuality
- Renal Transplantation
- Bromocriptine therapy for hyperprolactinemia and its effects on restoring Sexual function is still under studies


Insulin Resistance
High Blood Pressure
METABOLIC SYNDROME
High Triglyceride Levels
Low HDL Cholesterol

Declining androgen levels associated with components of the Metabolic Syndrome

Obesity	Inverse correlation between plasma T levels and BMI, WC, WHR and amount of visceral fats
Dyslipidemia	Positive correlation between plasma T levels and HDL-C; inverse correlation with triglycerides, total cholesterol and LDL-C
Hypertension	Inverse correlation between T levels and SBP/DBP; ↑hypogonadal men with history of hypertension in HIM study
Impaired Glucose tolerance	Low T is associated with insulin resistance; diabetic men have low T levels

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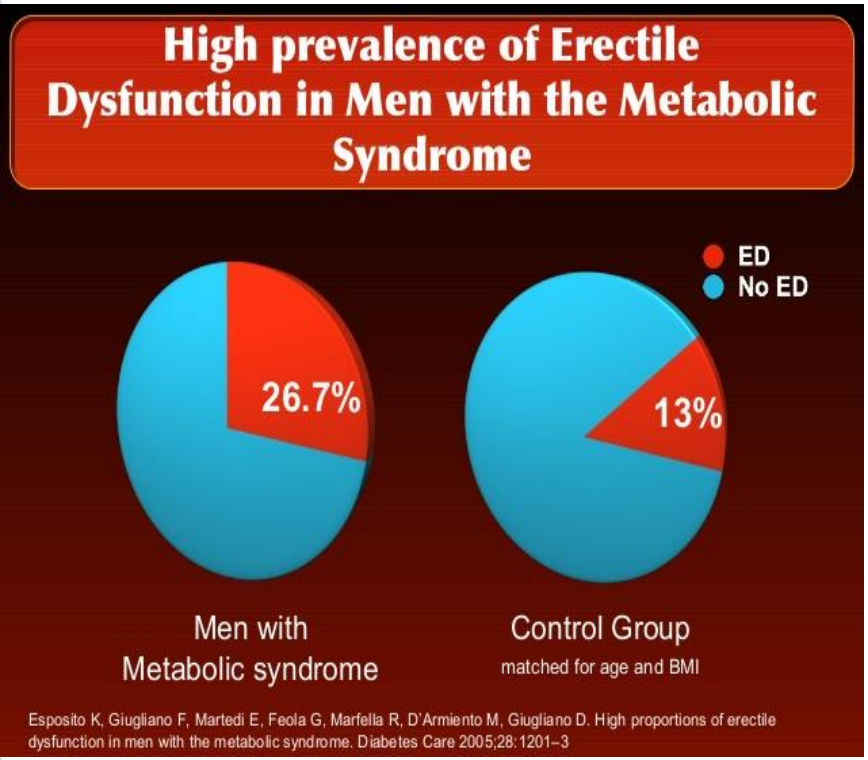
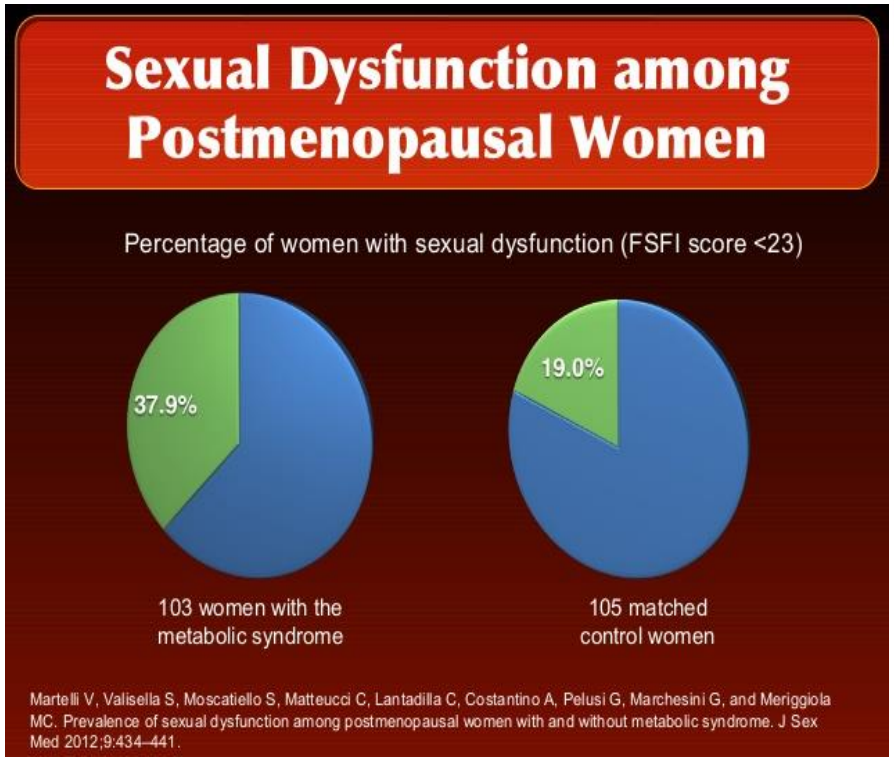
Prevalence of Sexual Dysfunction



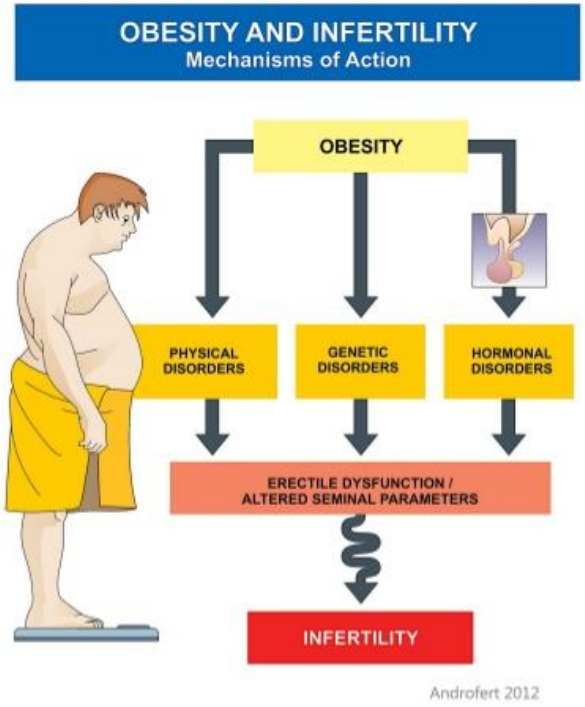


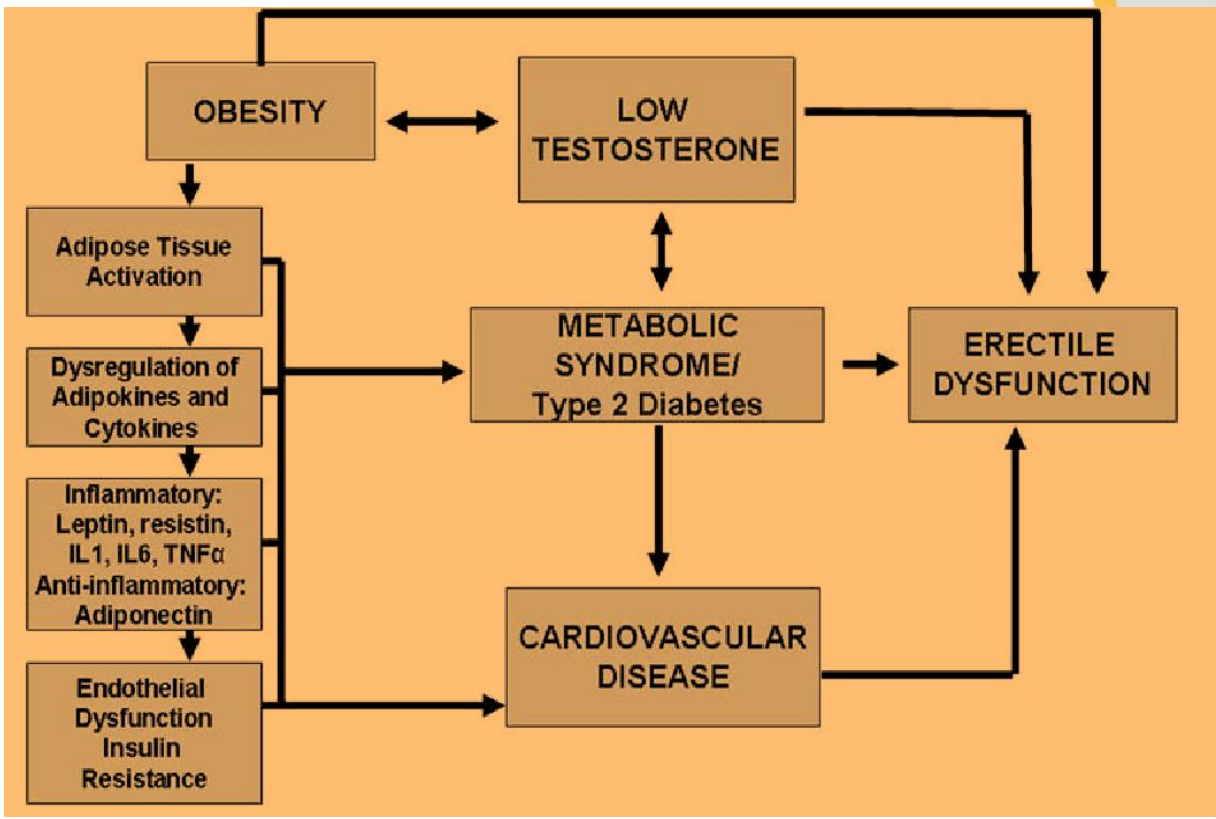

stomach
big
obese
anxiety
female
examination
medicine
male
concept
large
belly
gut
healthcare
woman
hospital
beauty
clinic
fat
waist
sick
overweight
patient
eating
measure
overeating
human
waistline
loss
unhealthy
condition
pressure
fitness
diet
nutrition
care
obesity
physician
heart
exercise
medical
lifestyle
disease
figure
health
metabolic
abdomen
adult
shape
diabetes
healthy
food
potbelly
diagnosis
weight
person
danger
treatment
suffer
dieting
serious
excess
body

Obesity and Sexual Dysfunction

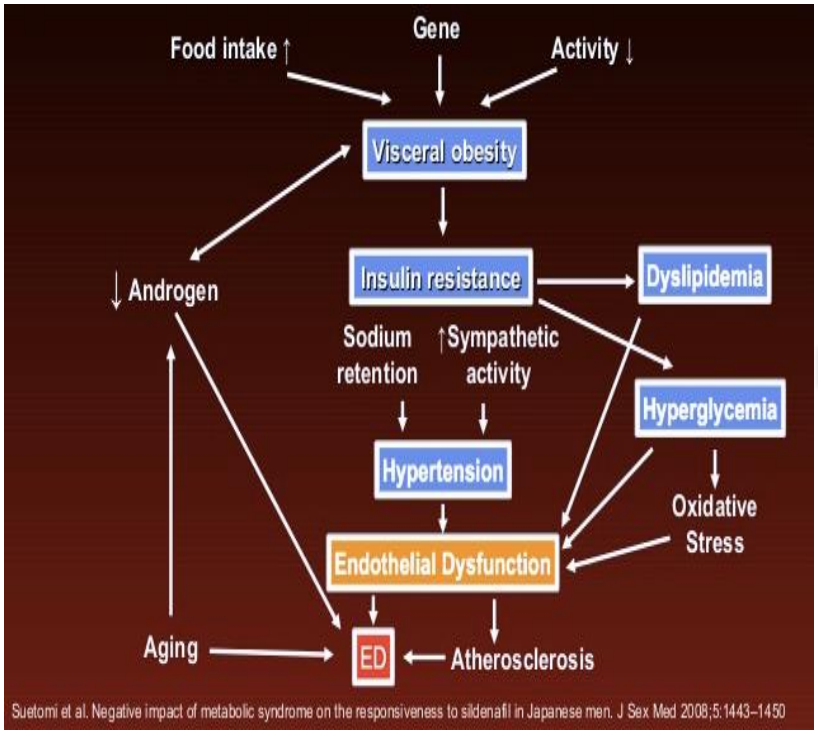
- Obesity may be a risk factor for sexual dysfunction in both sexes
- Plasma testosterone levels are reduced in obesity, further contributing to an increased risk of vascular pathology in obesity.
- Obesity is associated with low serum T levels as well as reduced SHBG (sex hormone-binding globulin) levels
- Studies suggest that one-third of obese men with ED can regain their sexual activity after 2 y of adopting health behaviours, mainly regular exercise and reducing weight

Overview of Obesity, Low testosterone and Erectile Dysfunction

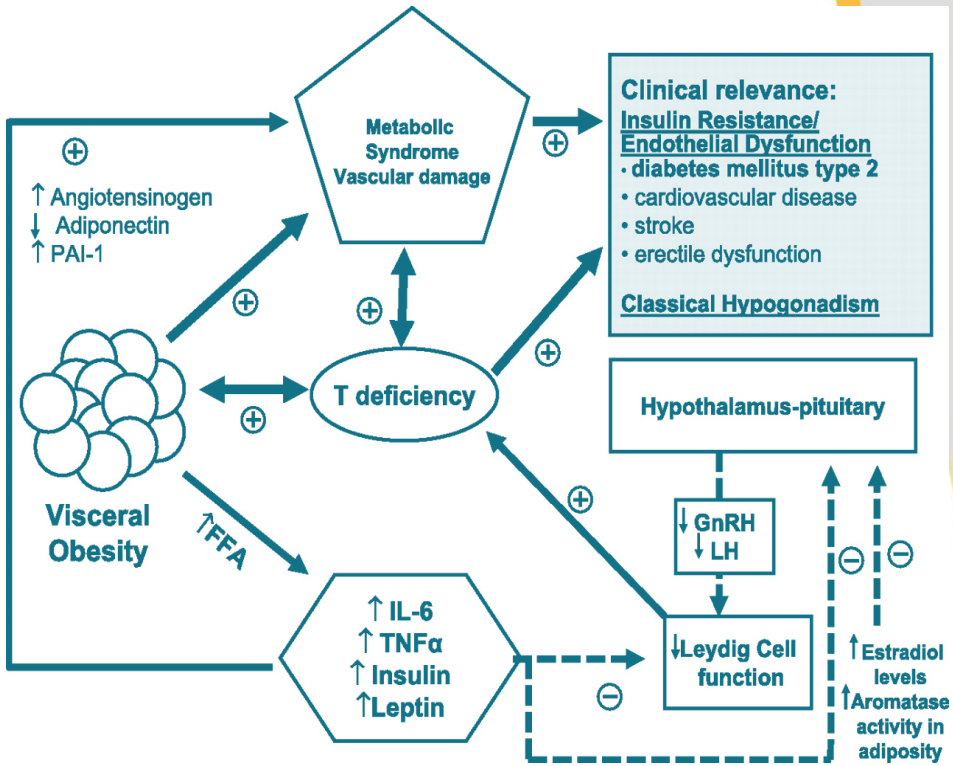




Pathogenesis of ED in Metabolic Syndrome

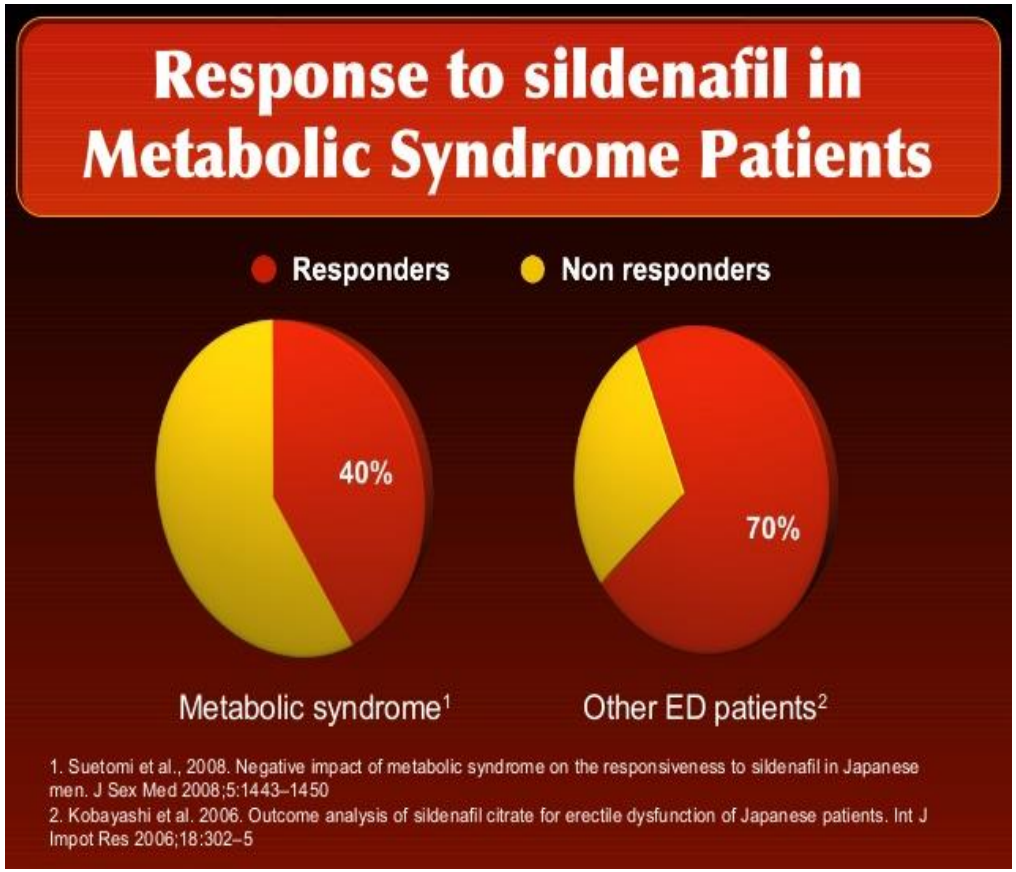


Suetomi et al. Negative impact of metabolic syndrome on the responsiveness to sildenafil in Japanese men. J Sex Med 2008;5:1443–1450



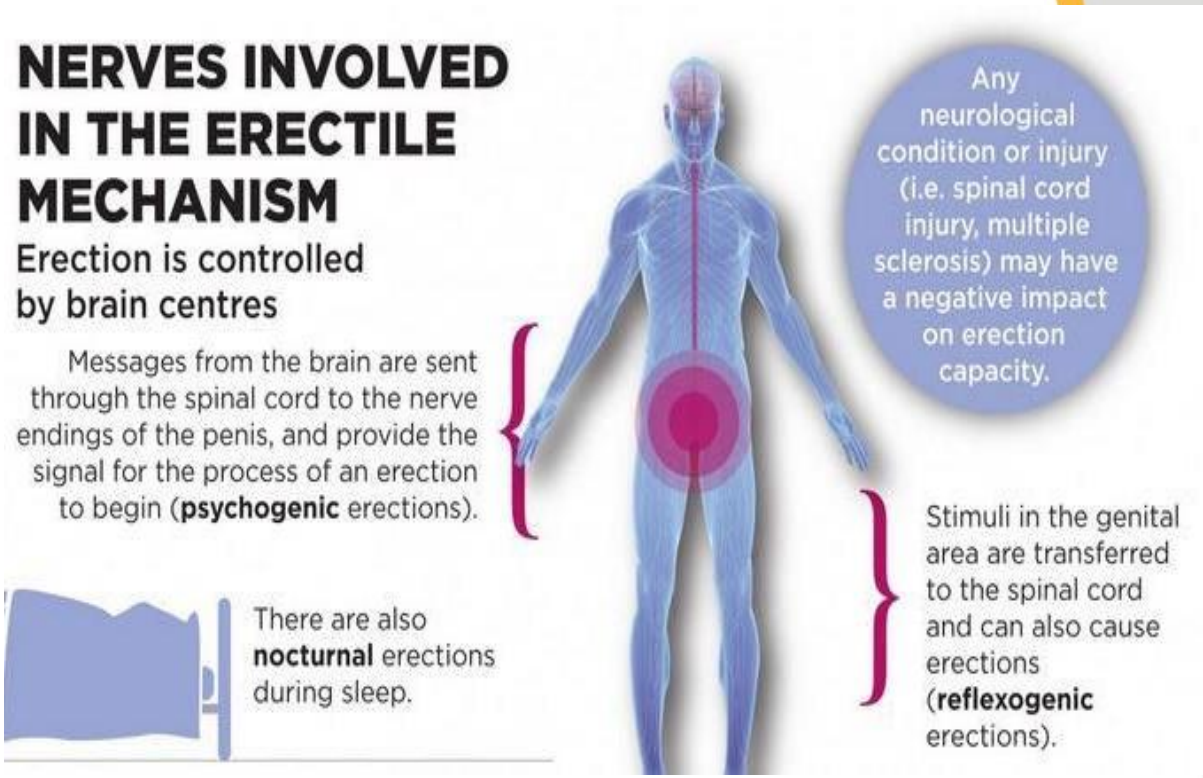
Screening and Treatment

- No recommendation to screen men with symptoms of T deficiency for metabolic syndrome
- No recommendation to screen men with metabolic syndrome for T deficiency



Sexual Dysfunction and Neurology

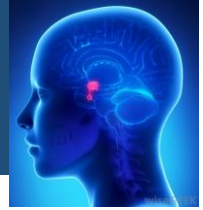
- Two major pathways are involved in initiating penile erection: psychogenic and reflexogenic.
- Psychogenic erections involve visual or auditory inputs that interface with the cortical organizing regions of the brain
- Reflexogenic erections involve genital sensory stimulation through a spinal cord reflex



Neurogenic Sexual Dysfunction

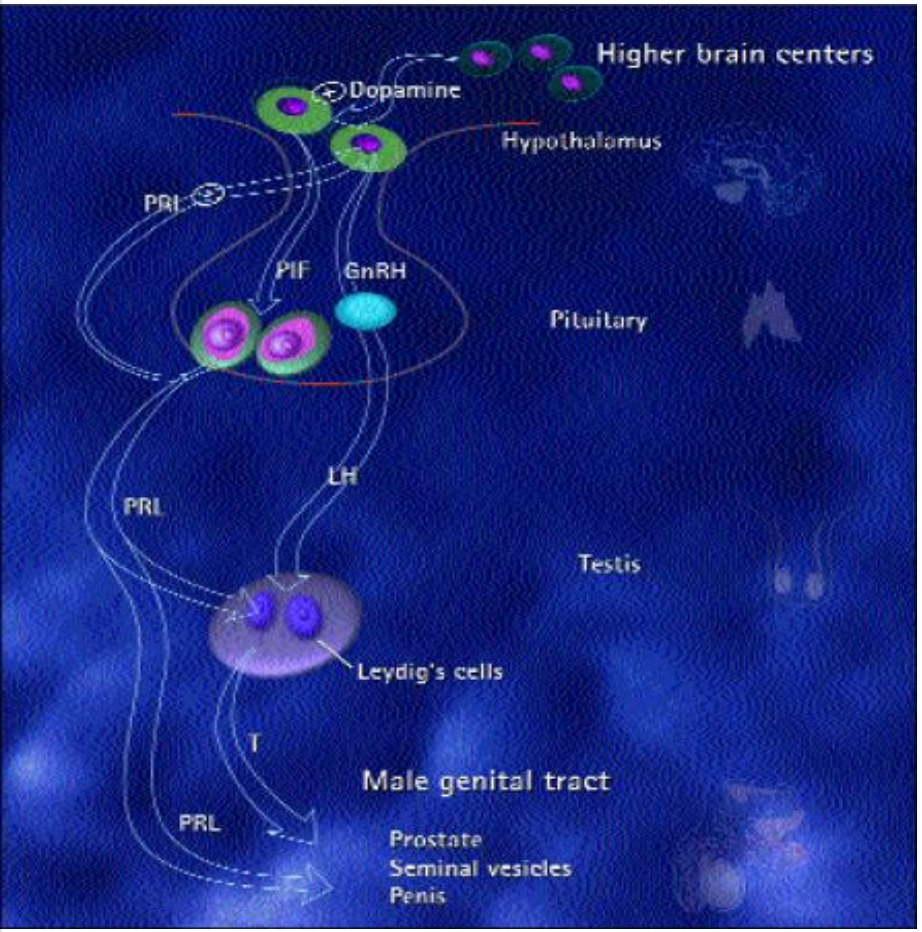
- Neurologic ED can result from complications of chronic disease, trauma, surgical injury, or iatrogenic causes, autonomic neuropathy
- **Work Up:**
  - Nocturnal penile tumescence studies to assess psychogenic erectile dysfunction
  - An endocrinological work-up to determine levels of hormones such as prolactin, luteinizing hormone, and testosterone
  - Doppler ultrasonography to measure hemodynamic in response to injected erection-inducing drugs and exposure to visual sexual stimulation.
  - Dermal punch biopsies and measurement of nerve densities can be used to diagnose diabetic peripheral neuropathy
- **Treatment:**
  - PDE 5I - Sildenafil citrate
  - Vacuum constriction devices, Intraurethral and Intracavernosal therapies and penile implants.

Hyperprolactinemia and Sexual Dysfunction



- In the evaluation of patients with erectile dysfunction, an endocrinopathy is the rarest of causes.
- However, when an endocrinopathy does affect erectile function, it is almost always caused by hypogonadism.
- Obtaining a serum testosterone (T) level is the most cost-effective way of screening for an endocrinopathy as the cause of erectile dysfunction.
- If the serum T level is abnormally low, then additional evaluation should include obtaining
- serum luteinizing hormone, free T, and prolactin levels.
- If the serum T is elevated, then a thyroid evaluation may be indicated

Hormonal regulatory Pathway



- Dopamine from higher brain centers stimulates release of prolactin inhibitory factor (PIF), and prolactin (PRL) from the pituitary inhibits gonadotropin-releasing hormone (GnRH) secretion.
- Bromocriptine, a dopamine agonist, works to further increase production of PIF to decrease PRL production.

LH, Luteinizing hormone.

Signs, Symptoms and Treatment

- **Signs and Symptoms of Hyperprolactinemia**
  - Decreased libido
  - Erectile dysfunction
  - Galactorrhea
  - Gynecomastia
  - Headache
  - Visual-field defects
- **Treatment**:
  - Surgery
  - Bromocriptine

- **Main Points**
  - The prolactin level should be measured in men presenting with a complaint of erectile dysfunction who have a low serum testosterone level.
  - Hypogonadism is almost always the cause of an endocrinopathy that affects erectile function.
  - In hyperprolactinemia, which induces hypogonadism, the excess prolactin interferes with secretion of gonadotropin-releasing hormone, resulting in decreased testosterone and erectile dysfunction.
  - Hyperprolactinemia caused by a pituitary tumor can be managed with surgery and/or a dopamine agonist.

Thyroid Disorder and Sexual Dysfunction

- ED is extremely common in males with dysthyroidism.
- Treatment of the latter restores erectile function.
- Screening for thyroid dysfunction in men presenting with ED is recommended
- Whereas specific treatment for ED should be postponed in such patients for at least 6 months after achieving euthyroidism because the latter might be responsible for ED.

Effect of Thyroid Hormones

Effect on Reproductive System

Females	Males
T3 induced modulation ▪ Estrogen metabolism ▪ Sexual maturation ▪ Menstrual function ▪ Ovulation & Fertility ▪ Develop full term infants ▪ Stimulates production of SHBG	**TH receptors in Sertoli cells** ▪ Male reproductive tract development ▪ Maturation of testes (in pre-natal and post-natal) ▪ Maturation of sperm

(Based on research work by National Institute of Environmental Health Science by US Govt)

Sexual Function:

- In men, lack of thyroid hormone is likely to cause loss of libido
- Great excesses of the hormone, sometimes cause impotence
- In women, lack of thyroid hormone often causes menorrhagia, polymenorrhea, irregular periods, amenorrhea, decreased libido
- Hyperthyroid woman, oligomenorrhea, amenorrhea