Men's Health in 2016 Erectile Dysfunction

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"Men have four problems in life son. Women, money, booze, and prostate."

Men's Health in 2016

What should we cover?

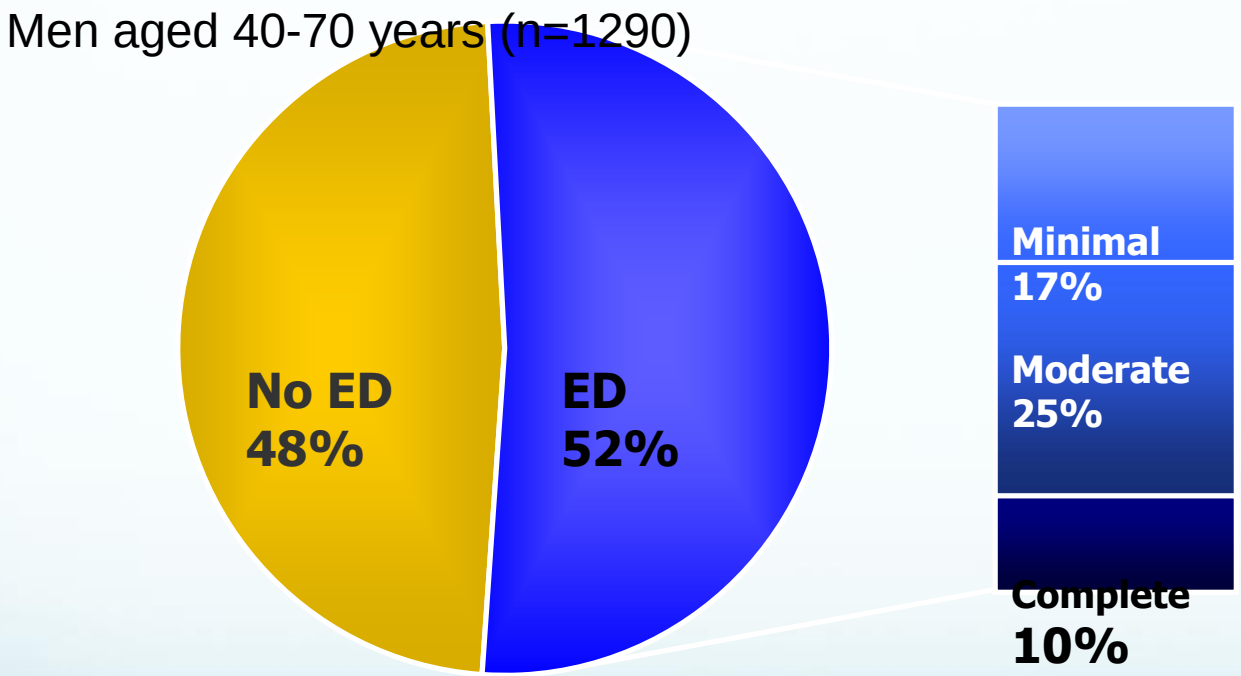
- Erectile Dysfunction
- Low Testosterone

Erectile Dysfunction

What is it?

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

Massachusetts Male Aging Study (US): Key Prevalence Study of ED



Minimal ED, "usually able to get or keep an erection."
Moderate ED, "sometimes able to get and maintain an erection."
Complete ED, "unable to get and keep an erection."

Erectile Dysfunction

- **Causes ?**
- **Physical**
- **Psychogenic**

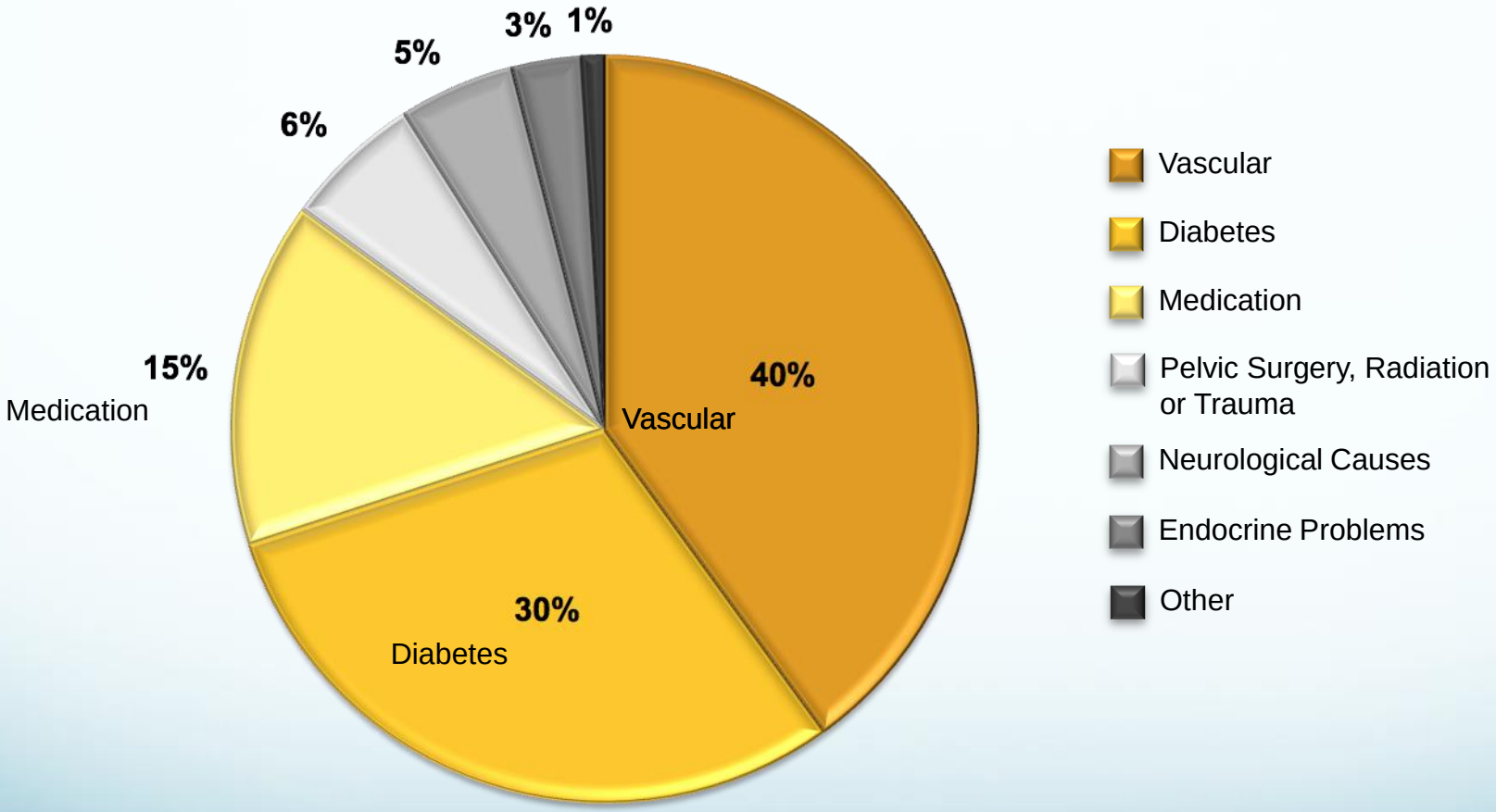
Erectile Dysfunction

- **Causes ?**

- **Physical: 90%**

- **Psychogenic: 10%**

Main Physical Causes of ED[4]



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

Do you have to live with ED?

NO!

Nearly every man can be successfully treated.

Sexual History

- Establish exactly what the patient's symptoms are

- Be aware: some men confuse ED with disorders such as ejaculation, orgasm or desire

Focused Physical Examination

- Dose not usually need to be complete
- The most important aspects of the examination are:
- Complete genital examination
- Examination for secondary sexual characteristics
- BP

Laboratory Investigation

- EAU guidelines (2011)

- Fasting blood glucose

- Fasting lipid screen

- Serum testosterone

- ICSM (2010)

- Fasting blood glucose

- Fasting lipid screen

- Endocrine screen

Princeton Guidelines

“ The recognition of ED as a warning sign of silent vascular disease has led to the concept that a man with ED and no cardiac symptoms is a cardiac (or vascular) patient until proven otherwise”

ED predicts coronary events

ED Predicts coronary events

1400 men 40-75, with no known CAD 10yr follow up

Inman et al Mayo Clin Pr 2009;84:108-113

Age Group	ED at baseline	No baseline ED
40-49	**48.52 (1.23-269.26)**	**0.94 (0.02-5.21)**
50-59	27.15 (7.40-69.56)	5.09 (3.38-7.38)
60-69	23.97 (11.49-44.10)	10.72 (7.62-14.66)
70+	29.63 (19.37-43.75)	23.30 (17.18-30.89)
	CAD events per 1000 pt years with CI interval	Inman et al Mayo Clin Pr 2009

Who is at risk?
Metabolic Syndrome

- International Diabetic Federation (IDF)

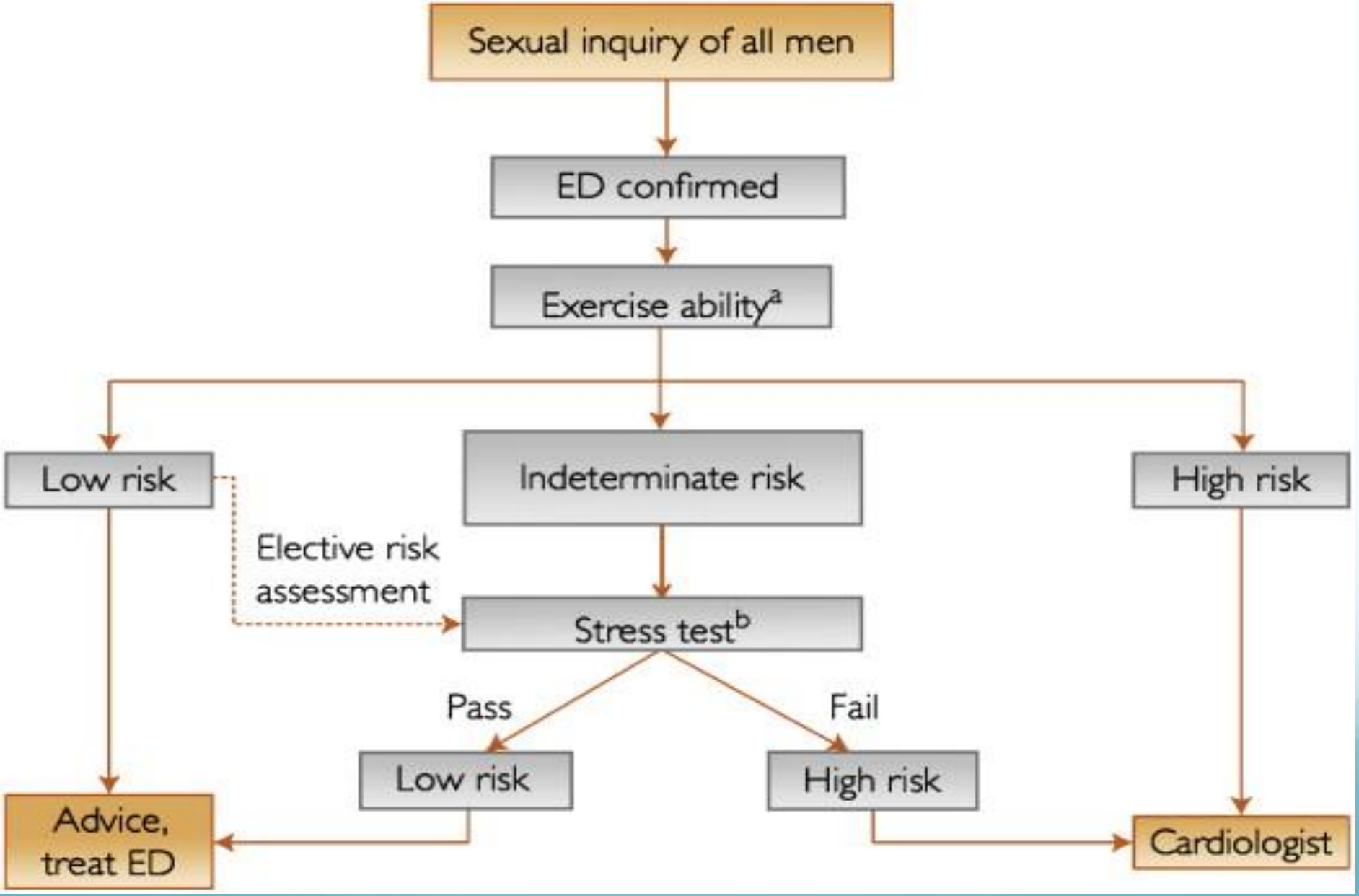
- Waist > 94cm and Two of the following:

1. Triglycerides >1.7 mmol/l
2. HDL <1.03mmol/l (men)
3. Systolic BP>130
4. Diastolic BP>85
5. Fasting glucose >5.6 mmol/l

Waist Circumference

What guidelines say?

- All men with ED should undergo a thorough medical assessment
- Patients should be stratified to their risk of future cardiovascular events
- Those at high risk of cardiovascular disease should be evaluated by stress testing with selective use of computed tomography (CT) or coronary angiography


Sexual inquiry of all men
ED confirmed
Exercise ability[a]
Low risk
Indeterminate risk
High risk
Elective risk assessment
Stress test[b]
Pass
Fail
Low risk
High risk
Advice, treat ED
Cardiologist

Management

- Lifestyle management in ED with concomitant risk factors

Some Risk factors can be modified

- Men who began exercising in midlife had a 70% reduced risk for ED compared to sedentary men (MMAS)

- A multicentre, randomised study in obese men with moderate ED showed significant improvement in erectile functions when they lost weight and increase physical activities

Management

CURE

- Hormonal Causes
- Post-traumatic arteriogenic ED in young patients
- Psychosexual counseling and therapy

ED Treatment Options

- Oral Medication
- Vacuum Pump Device
- Intracorporeal Injections
- Urethral Suppository – MUSE
- Cream – Vitaros
- Penile Implants

Development of Sildenafil, the first PDE 5 inhibitor

- Developed in 1988 in Sandwich, Kent, as compound :

  UK-92,480

- Anti-hypertensive and later anti –angina

- Wales: 1992 toleration study

First-line therapy

- PDE 5 Inhibitors

- Sildenafil—1998 (25mgs, 50mgs and 100mgs)

- Tadalafil—2003 (5mgs,10mgs and 20 mgs)

- Vardenafil—2003 (10mgs and 20mgs)

- Avanafil – 2013 (50mgs,100mgs, 200mgs)

PDE 5 Inhibitor

- What is your first choice and why?

PDE 5 Inhibitor

- What is your first choice and why?
- SILDENAFIL CITRATE
- Cost Effective
- Has been studied for more than 15 years in more than 136 completed and ongoing clinical trials involving more than 23,000 men with ED (Viagra)

PDE 5 Inhibitors Cautions ?

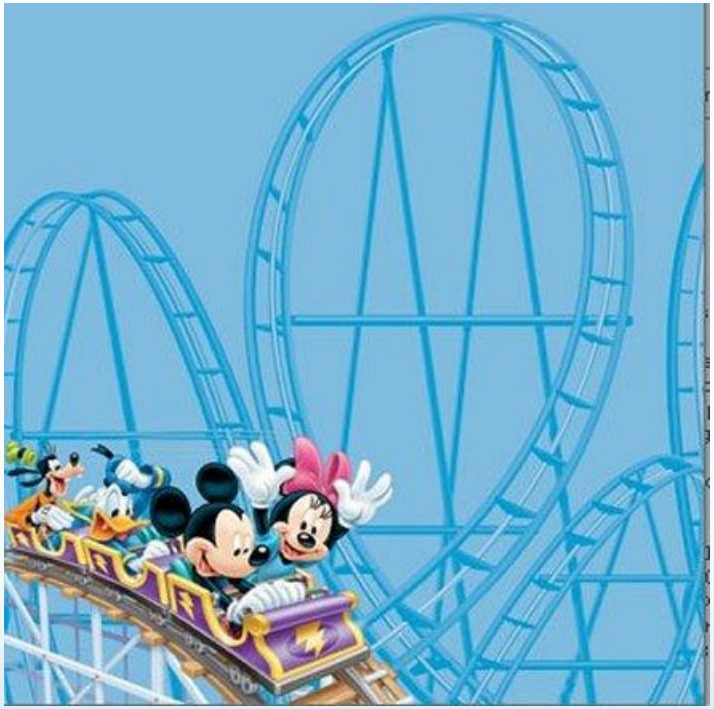
- What will you ask the patient about medical history before starting PDE 5 Inhibitors ?

PDE 5 Inhibitors Cautions

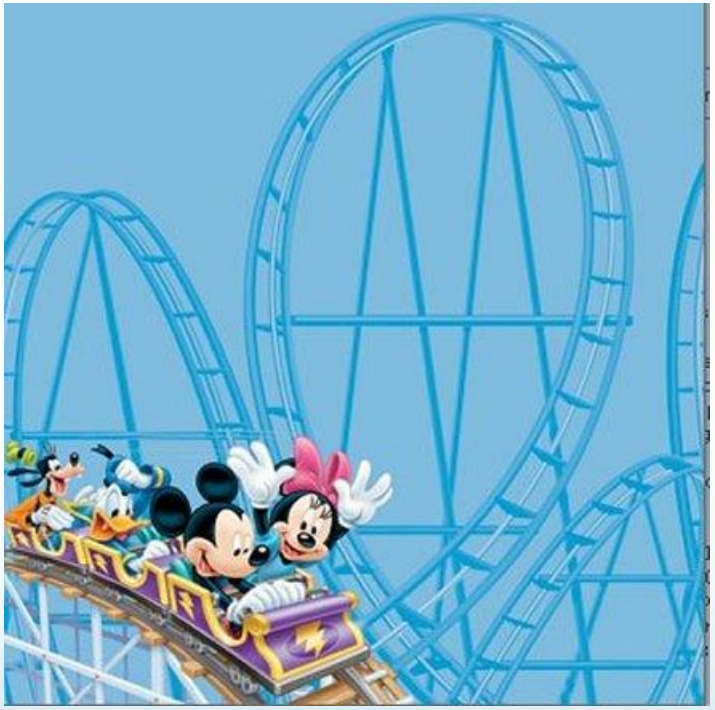
- NITRATES – Patients with Angina

- Alpha Blockers

Why is on-demand PDE5 inhibitors like Disneyland?



Why is on-demand PDE5 inhibitors like Disneyland?



There's a one-hour wait for a two-minute ride …

Management of non-responders to PDE5 inhibitors

- **Check** : that the patient has been using a licensed medication

- 4 sexual attempts after taking PDE5 inhibitors

- The medication has been properly prescribed and correctly used :

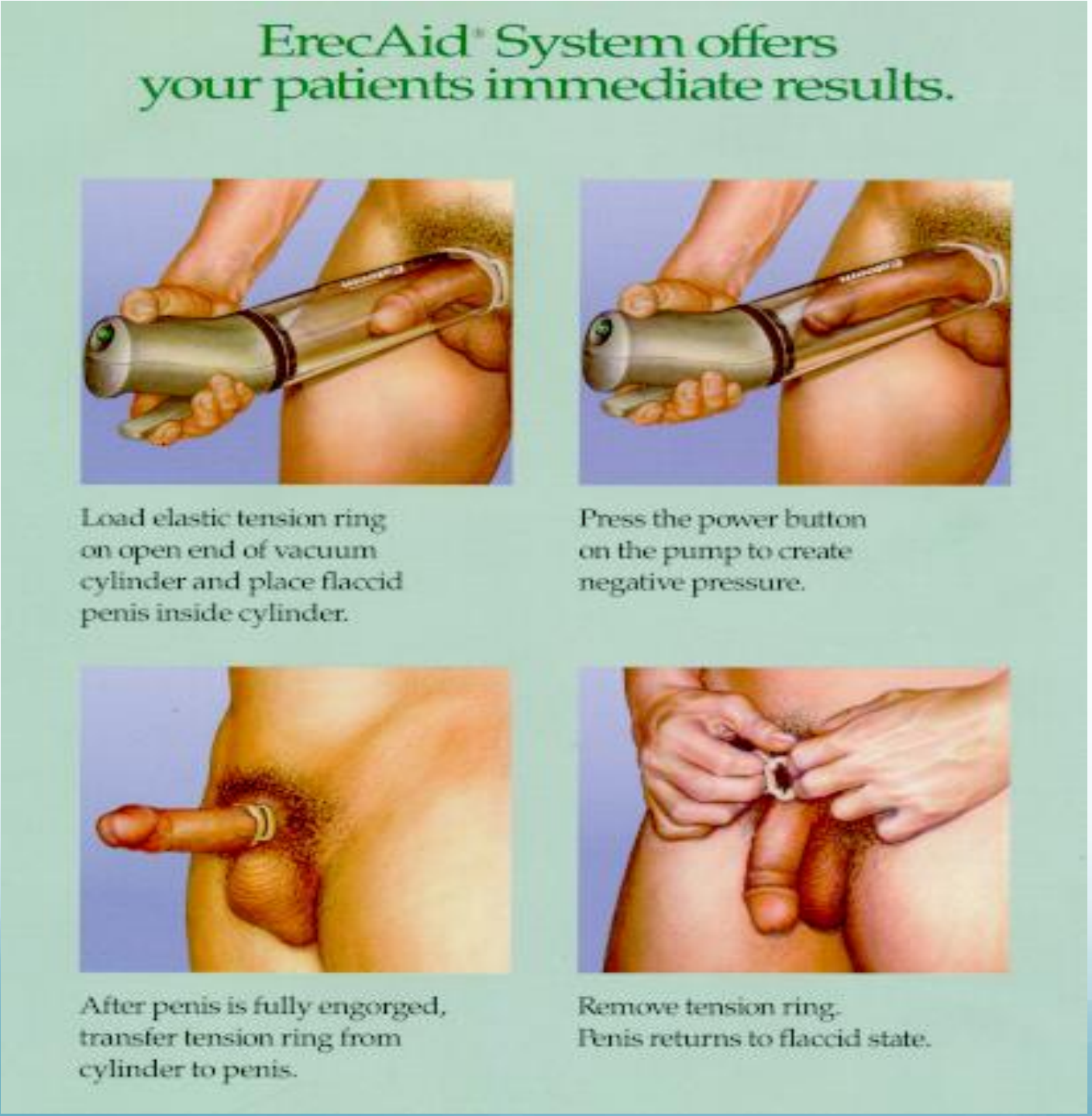
-meals

-alcohol

-concomitant medication

Management of non-responders to PDE5 inhibitors

- Adequate sexual stimulation
- Adequate dose
- Adequate time between taking the medication and intercourse attempt
- Treatment of associated hypogonadism
- Regular dosing of PDE5 inhibitors

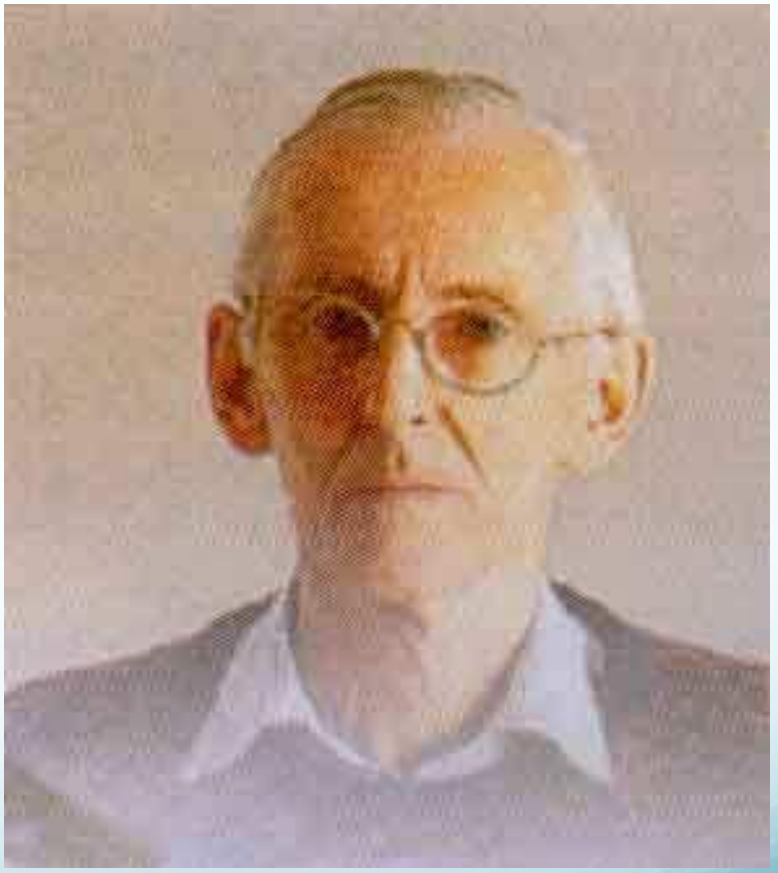


Vacuum constriction devices

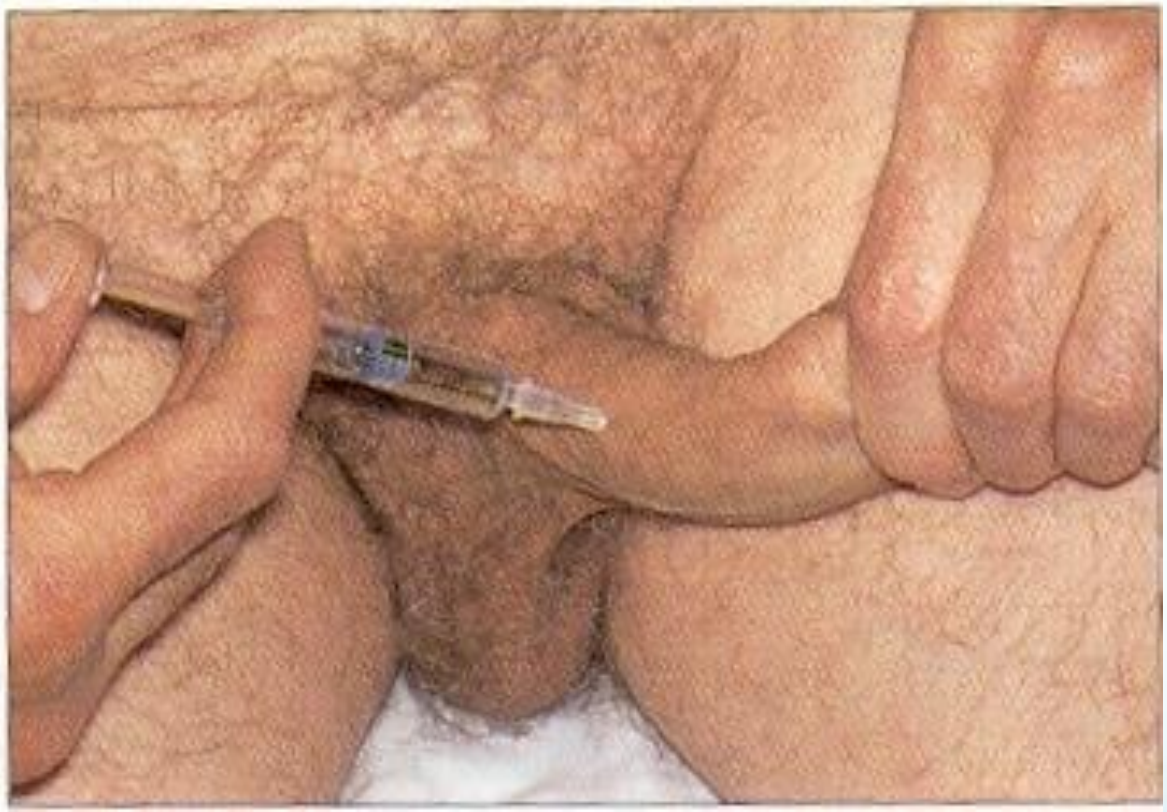
Satisfaction rate 27-94%

At 2 years only 50-64% men continue to use

- 1983 a British physiologist Giles Brindley, Ph.D. dropped his trousers and demonstrated to a shocked AUA audience his phentolamine-induced erection



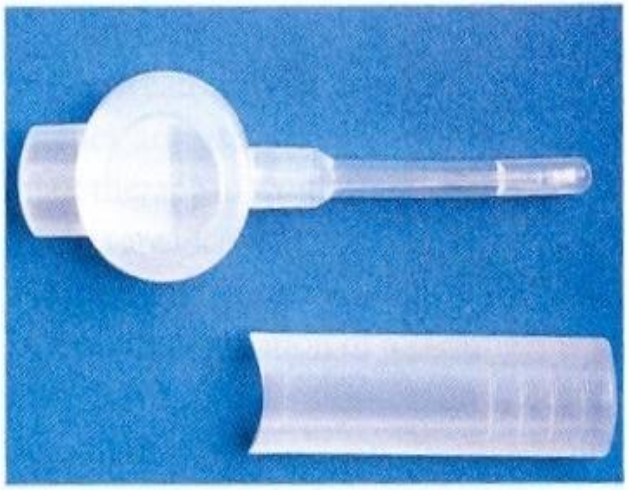
Intracavernous injections

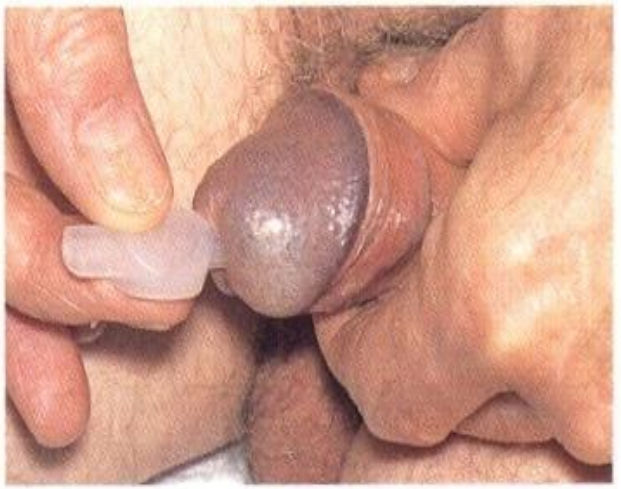


Efficacy rates: 70%

- Drop out rate: 41%-68%

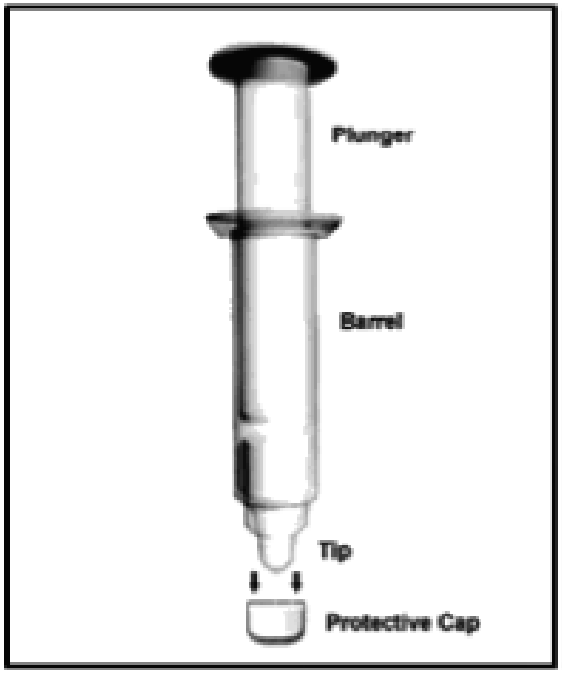
Intraurethral alprostadil *(MUSE)*

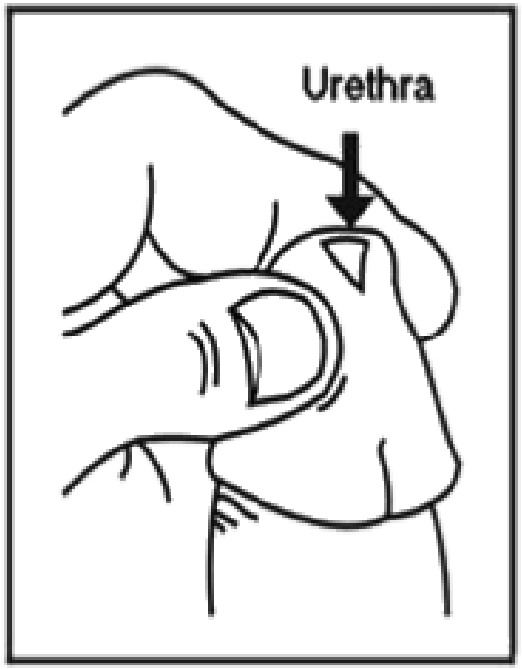


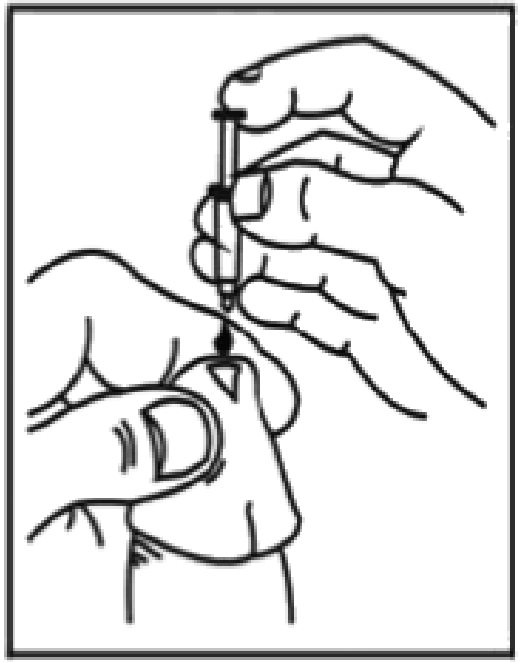


Efficacy Rate: 30-66%

VITAROS



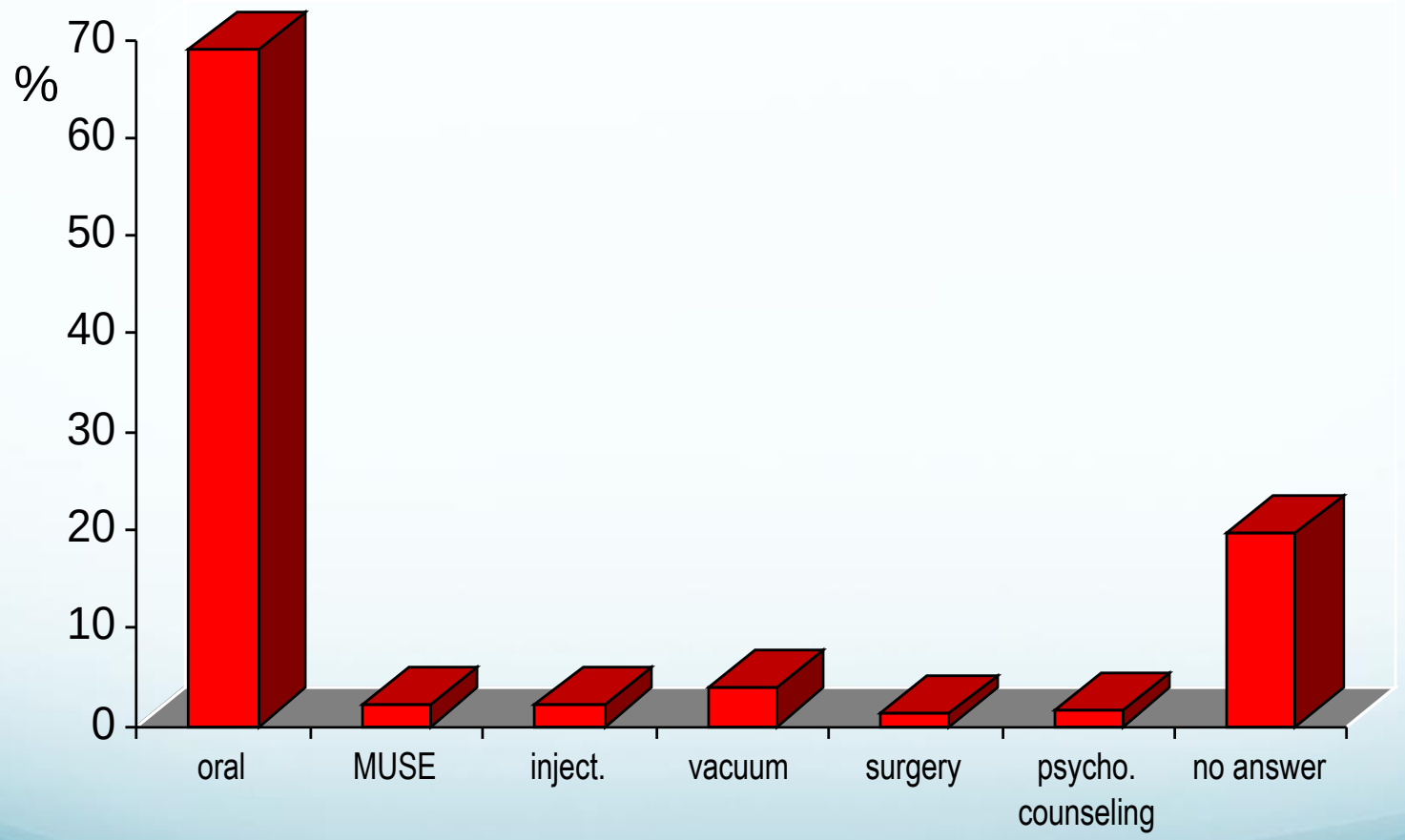




Penile Prostheses

Satisfaction Rate: 70-87%
Mechanical failure rate: 5%
Life: up to 10 years

Therapeutic Options
Patient Preferences



Cologne survey of 8,000 men

Role of Clinicians

- The early diagnosis and management of some cardiovascular and endocrine conditions e.g., diabetes and dyslipidemia are fundamental to the clinician' s role (2002 General Medical Services (GMS) contract)

- Men do not readily visit their clinicians with medical problems and a consultation for ED may represent an important opportunity for health intervention.

- It is clinician's responsibility to ask about any erectile dysfunction

Summary

- Clinician should make an effort to routinely ask their patients about erectile dysfunction

- The ultimate goal must be not only to treat the ED but also to diagnose and adequately treat any cardiac risk factors found

- ED may be the 'Tip of the Iceberg' of a systemic vascular disorder.

  Montorsi 2003


PREMATURE EJACULATORS ANONYMOUS
.... LOOKS LIKE I CAME TOO SOON!
HumorBomb.com

Low Testosterone

(Male Hypogonadism)

Testosterone is produced by

- Testis
- Adrenals

Testosterone is produced by

- Testis: 90%
- Adrenals: 10%

Low Testosterone (Low T)

What is it?

- Low testosterone (sometimes called “hypogonadism” or “low T”) occurs when a man’s body produces less testosterone than is normal

How many men are estimated to have Low T?

- Approximately 4 in 10 men over age 45 may have low testosterone
- The percentage rises as men get older
- Low testosterone is more common in men who are obese, type-2 diabetic, have high cholesterol or have high blood pressure than in men without these conditions

Mulligan T et al. *Int J Clin Pract*. 2006;60(7):762-769.

TESTOSTERONE DEFICIENCY SYNDROME (TDS)

An often unrecognised problem

TDS may be:

- Primary (a testicular problem)
- Secondary (a problem with the hypothalamus or pituitary) (1,2)

The two forms of hypogonadism have to be differentiated, as this has implications for patient evaluation and treatment and makes it possible to identify patients with associated health problems and infertility [2]

TDS is often unrecognised by patients and physicians due to the subtle onset of symptoms (3,4)

1. Wang et al. *J Andrology* 2009; 30:1-9
2. Dohle GR et al, Guidelines on Male Hypogonadism. *EAU* 2012 (last accessed on 10/04/15)
3. Behre M. *European Urology Supplements* 2005:10-5
4. Katz D et al. *BJU* 2011; 110:573-78

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Want are Some of the Signs and Symptoms of Low Testosterone?

SIGNS AND SYMPTOMS OF LOW TESTOSTERONE		
PHYSICAL	**MENTAL or EMOTIONAL**	**SEXUAL**
• Fatigue and loss of energy • Decreased muscle mass and strength • Increased body fat • Loss of body hair or reduced need to shave* • Decreased physical or work performance • Hot flushes, sweats*	• Feeling sad or blue • Less motivation or drive to do things • Less self-confidence, enthusiasm or "feeling like myself" • Poor concentration and memory	• Reduced sex drive (libido)* • Erectile dysfunction (ED)*

** More specific signs and symptoms of low testosterone*

DIAGNOSIS AND TESTING

Measuring testosterone levels

To calculate free testosterone level, **total testosterone serum levels, serum sex hormone-binding globulin (SHBG) and free testosterone levels** need to be measured. [1-3]

The EAU Guidelines recommend[3] :

1. Diagnosis of testosterone deficiency should be restricted to men with persistent symptoms suggesting hypogonadism
2. Total testosterone assessment should be repeated on two occasions
3. Questionnaires are not reliable as case-finding tools
4. Testosterone assessment is recommended in men with a disease or treatment in which testosterone deficiency is common
5. LH serum levels should be analysed to differentiate between primary, secondary and late-onset hypogonadism

1. Wang C, et al. J Andrology 2009; **30**: 1-9.
2. AACE. Endocr Pract. 2002; **8**:439-56
3. Dohle GR et al, Guidelines on Male Hypogonadism. *EAU* 2012 (last accessed on 10/04/15)

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TESTOSTERONE REPLACEMENT THERAPY

Various forms of testosterone replacement therapies exist:

- Intramuscular injections
- Oral
- Buccal
- Transdermal patches
- Transdermal gels

TRT may improve[1-7]:

- Mood
- Libido
- Erection & Ejaculation
- Muscle Mass & Strength
- Body Composition (reduced BMI & waist size)
- Bone Mineral Density
- Cognition
- Improved glycaemic control & lipid profile

1. Dohle GR et al, Guidelines on Male Hypogonadism. *EAU* 2012 (last accessed on 10/04/15)
2. Surampudi PN et al. *Int J Endocrinol*. 2012. doi: 10.1155/2012/625434.

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TESTOSTERONE REPLACEMENT THERAPY (TRT)

Testosterone Formulations Comparison of Advantages[1,2]

Gels

Daily application

- Steady-state T without fluctuation
- Easy to apply
- Readily absorbed into skin
- Flexible-dose modifications
- T levels maintained in normal range

Injections

One injection every 2-3 weeks or 10-14 week preparations

- Short-acting preparation allows drug withdrawal in case of onset of side effects
- Relatively low cost
- T levels maintained in normal range

Buccal tablets

2 doses per day

- Rapid absorption
- Achievement of physiological serum level of testosterone
- Provides sustained release of T

Patches

Daily application

- Steady-state T without fluctuation
- Mimics circadian rhythm
- Simple administration

Implant

Every 5-7 months

- Steady-state T without fluctuation
- Inserted every 16-24 weeks

Oral capsules

2-6 cps every 6 hours

- Absorbed via the lymphatic system, with consequent reduction of liver involvement

1. Dohle GR et al, Guidelines on Male Hypogonadism. *EAU* 2012 (last accessed on 10/04/15)
2. Surampudi PN et al. *Int J Endocrinol*. 2012. doi: 10.1155/2012/625434.

Abbreviation: T = Testosterone

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TESTOSTERONE REPLACEMENT THERAPY (TRT)

Testosterone Formulations **Comparison of Disadvantages**[1,2]

Gels

Daily application

- Skin irritation at the site of application
- Interpersonal transfer – contact with children and women should be avoided

Injections

One injection every 2-3 weeks or 10-14 week preparations

- Possible fluctuation of T levels
- Cannot allow drug withdrawal in case of side effects
- Pain at injection site
- High risk of polycythemia

Buccal tablets

2 doses per day

- Irritation
- Pain/tenderness at application site
- Unpleasant taste
- Can stick to gums
- Headache

Patches

Daily application

- Skin irritation at application site
- Interpersonal transfer
- Occasional allergic contact dermatitis

Implant

Every 5-7 months

- Invasive procedure
- Risk of infection
- Extrusion of the implants

Oral capsules

2-6 cps every 6 hours

- Variable levels of T above and below mid-range
- Need for several doses per day with intake of fatty food.

1. Dohle GR et al, Guidelines on Male Hypogonadism. *EAU* 2012 (last accessed on 10/04/15)
2. Surampudi PN et al. *Int J Endocrinol*. 2012. doi: 10.1155/2012/625434.

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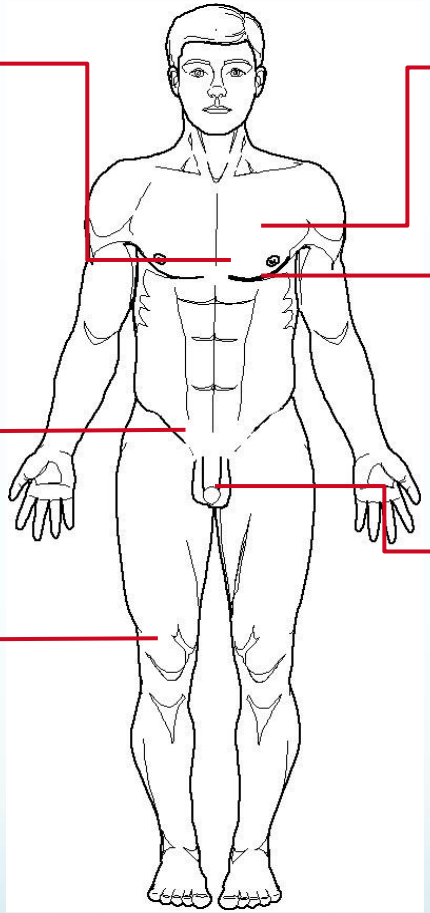
TESTOSTERONE REPLACEMENT THERAPY

What are the risks?[1,2]



Cardiovascular system

- Leg oedema and fluid retention
- Polycythemia (abnormally high) level of red blood cells)
- Adverse effects on plasma lipids (controversial)

Liver

- Hepatic toxicity (oral preparations)

Skin

- Oiliness, acne and associated problems

Respiratory

- Obstructive sleep apnoea (no consistent evidence)

Male Breast Cancer

- Male breast cancer is a rare disease
- TRT and the development of Breast Cancer is not supported by strong evidence

Prostate Cancer

- Prostate cancer growth may be influenced by testosterone
- Pre-existing cancer growth stimulation

Careful monitoring required

1. Dohle GR et al, Guidelines on Male Hypogonadism. *EAU* 2012 (last accessed on 10/04/15)
2. Wald et al. J Andrology 2006; **27**(2):126-32

Consult summary of product characteristics for product specific information

Prescribing Information can be found on the final slide

TESTOSTERONE REPLACEMENT THERAPY

Contraindications

Contraindications[1,2]

- Breast cancer
- Prostate cancer
- PSA > 4ng/mL
- Severe sleep apnoea
- History of liver tumours
- Hypercalcaemia
- Male infertility
- Haematocrit > 50%
- Severe lower urinary tract symptoms due to benign prostatic hyperplasia

Cautions[1]

- Cardiac impairment
- Elderly
- Ischaemic heart disease
- Hypertension
- Epilepsy
- sleep apnoea
- Migraine
- Diabetes mellitus
- Tumours or skeletal metastases—risk of hypercalcaemia or hypercalciuria
- Monitor prostate and PSA in men over 45 years pre-pubertal boys

1. BNF. Available at: https://www.medicinescomplete.com/mc/bnf/current/PHP4512-testosterone-and-esters.htm. (Last accessed on 10/04/2015)
2. Dohle GR et al, Guidelines on Male Hypogonadism. *EAU* 2012 (last accessed on 10/04/15)

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European Association of Urology (EAU) Guidelines

EAU Guidelines recommend that **short-acting testosterone preparations may be preferred** to long acting depot administration in the initial treatment phase, so that any adverse events that may develop can be observed and treatment can be discontinued if needed.

Several preparations are available, which differ in route of administration and pharmacokinetics, and the selection should be a joint decision by both the patient and the physician.

TRT is recommended in patients with:

1. A decline in muscle mass and strength
2. Reduced bone mineral density at the lumbar spine
3. Decreased libido and erection

1. Dohle GR et al, Guidelines on Male Hypogonadism. *EAU* 2012 (last accessed on 10/04/15)

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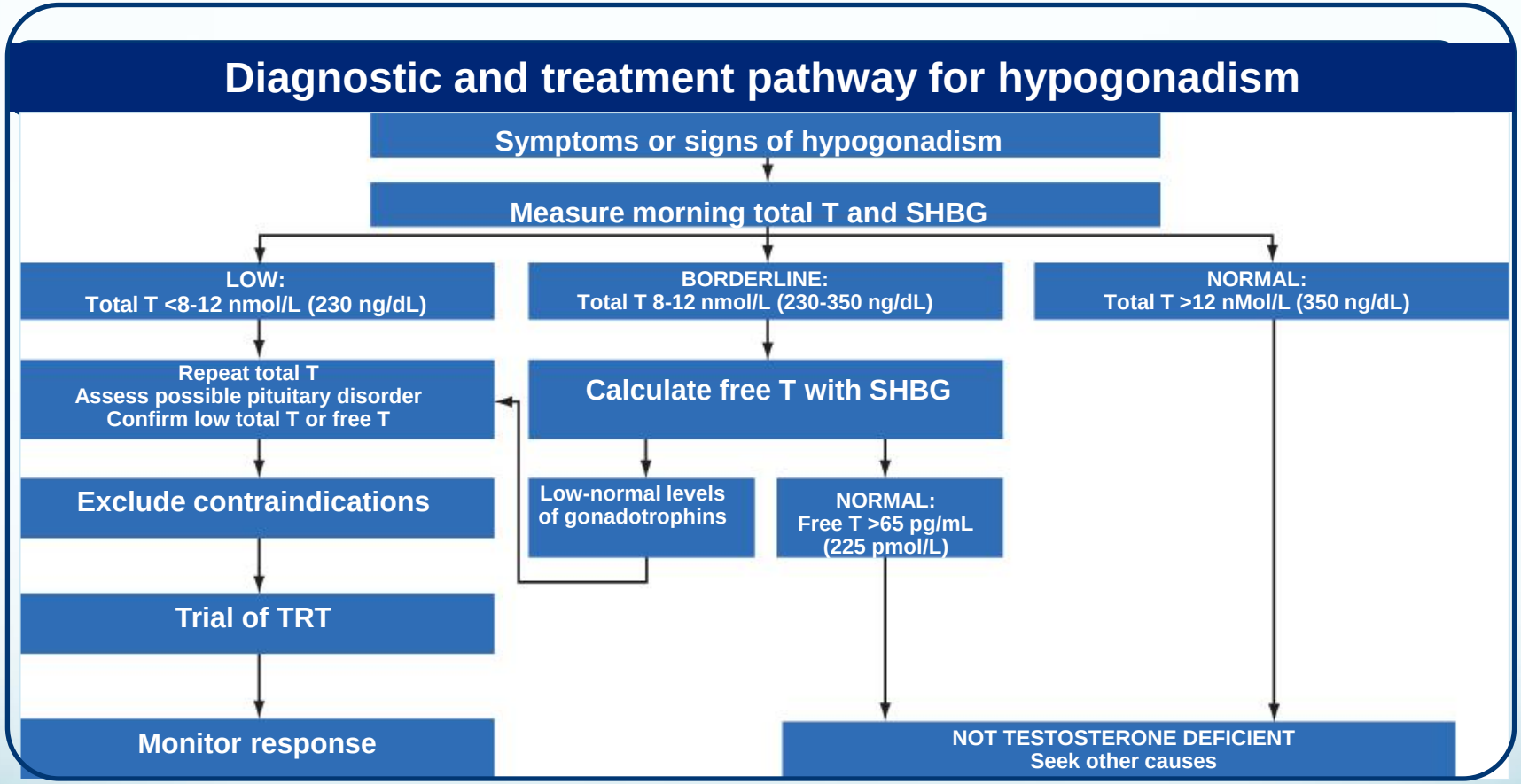
DIAGNOSIS AND TESTING

Measuring testosterone levels



1. ISA, ISSAM and EAU recommendations. Adapted from Nieschlag E, et al. *Eur Urol* 2005;**48**:1-4.
2. T thresholds amended according to Wang C, et al. *J Andrology* 2009; **30**:1-9
3. Zitzmann M, Nieschlag E. J Resproduktionsmed. *Endokrinol* 2006; **3**(2) 109-116
4. Dohle GR et al, Guidelines on Male Hypogonadism. *EAU* 2012 (last accessed on 10/04/15)

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Key principle in ED management

- Optimal management of associated conditions
- PDE5 I are effective in 75%
- Testosterone is vital both: for normal sexual function and effectiveness of PDE5 I
- MUST not to ignore the partner and relationship

Assessment Conclusions

- Assessment problem orientated – extensive investigation is unnecessary in most men
- Be certain that the problem is erectile dysfunction
- Look for treatable cause
- Look for cardiovascular risk factors