

# Whats Up in the field of Erectile Dysfunction

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# Definition

- ▶ Erectile Dysfunction:
  - The inability to achieve or maintain an erection sufficient for satisfactory sexual performance

NIH Consensus Development Panel on Impotence. JAMA 270:83-90, 1993

# Epidemiology

- ▶ ED affects an estimated 2.3 million men in the UK alone
- ▶ ED affects at least 1 in every 10 men
- ▶ It is estimated that the prevalence of ED will double over the next 20 years or so

Aytac LA et al, BJU International 1999;84:50–56

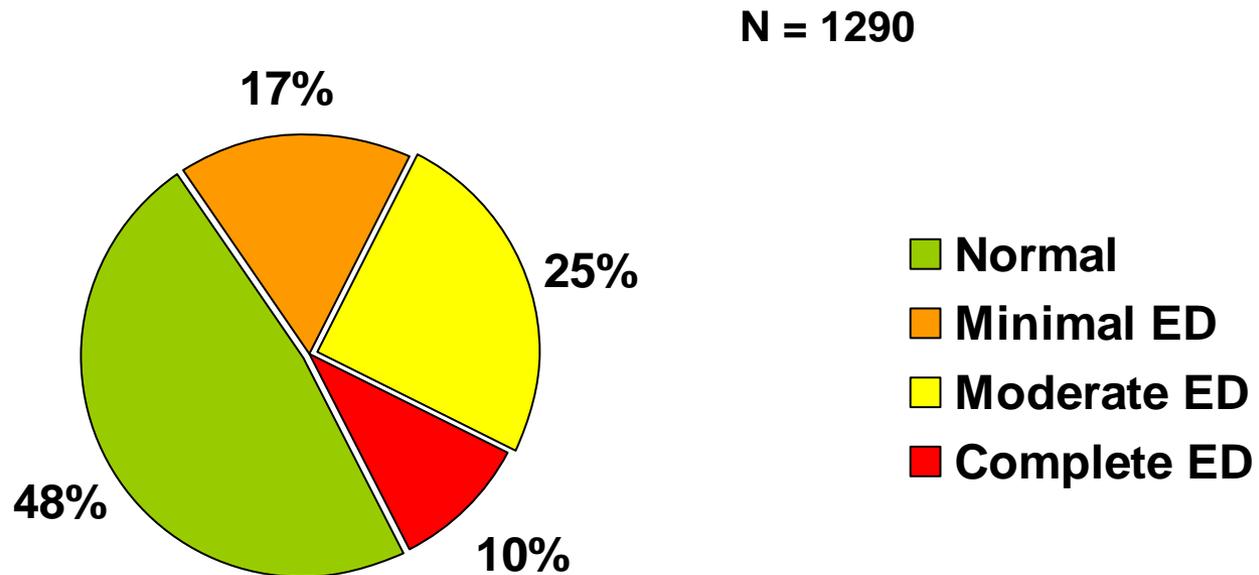
Impotence Explained. A couple's guide to Erectile Dysfunction. The Impotence Association.

Adapted from Consortium for Improvement In Erectile

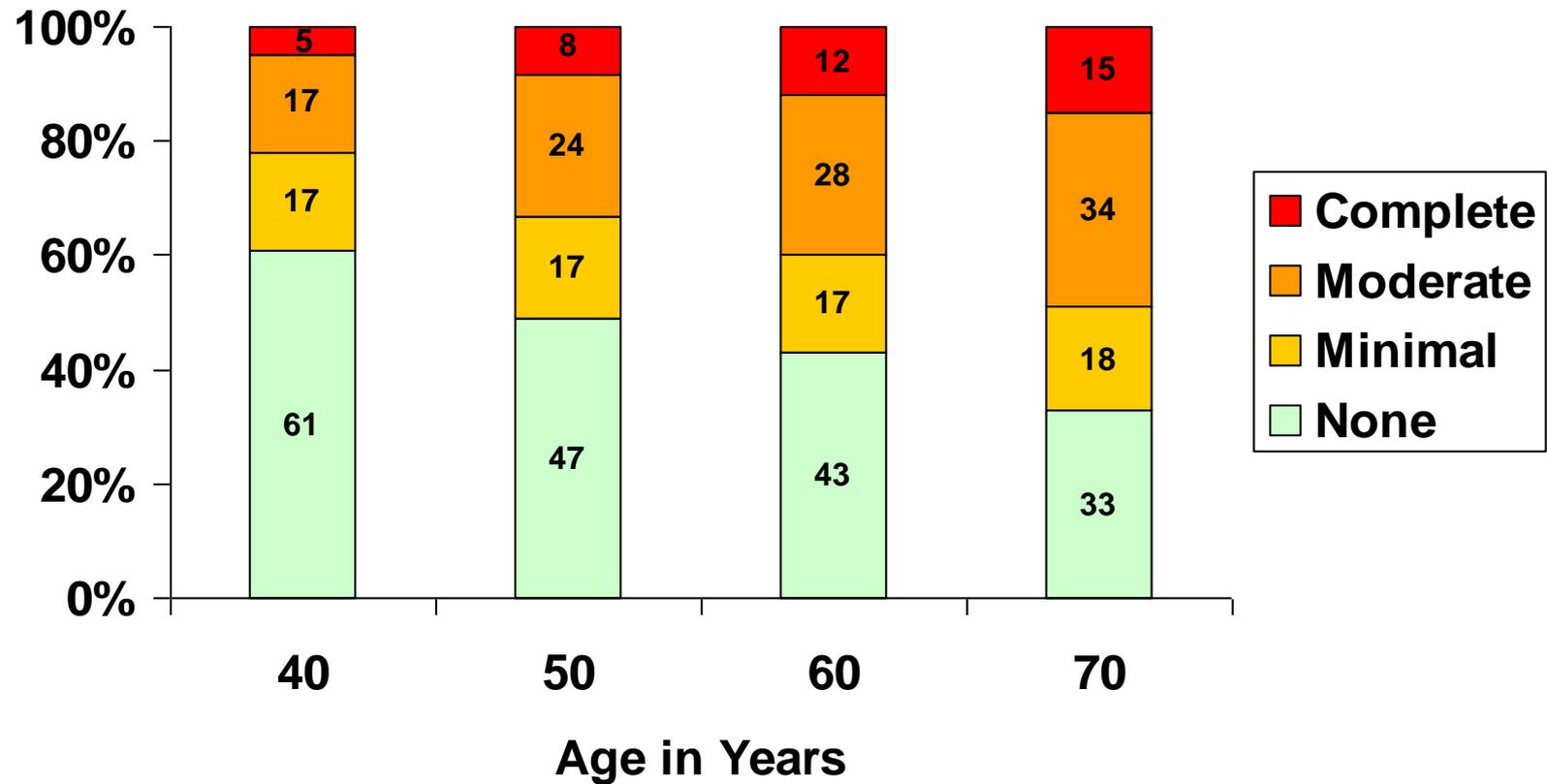
Function

# Massachusetts Male Aging Study

- ▶ The prevalence of ED by severity, according to the Massachusetts Male Aging Study (MMAS), in men 40–70 years of age

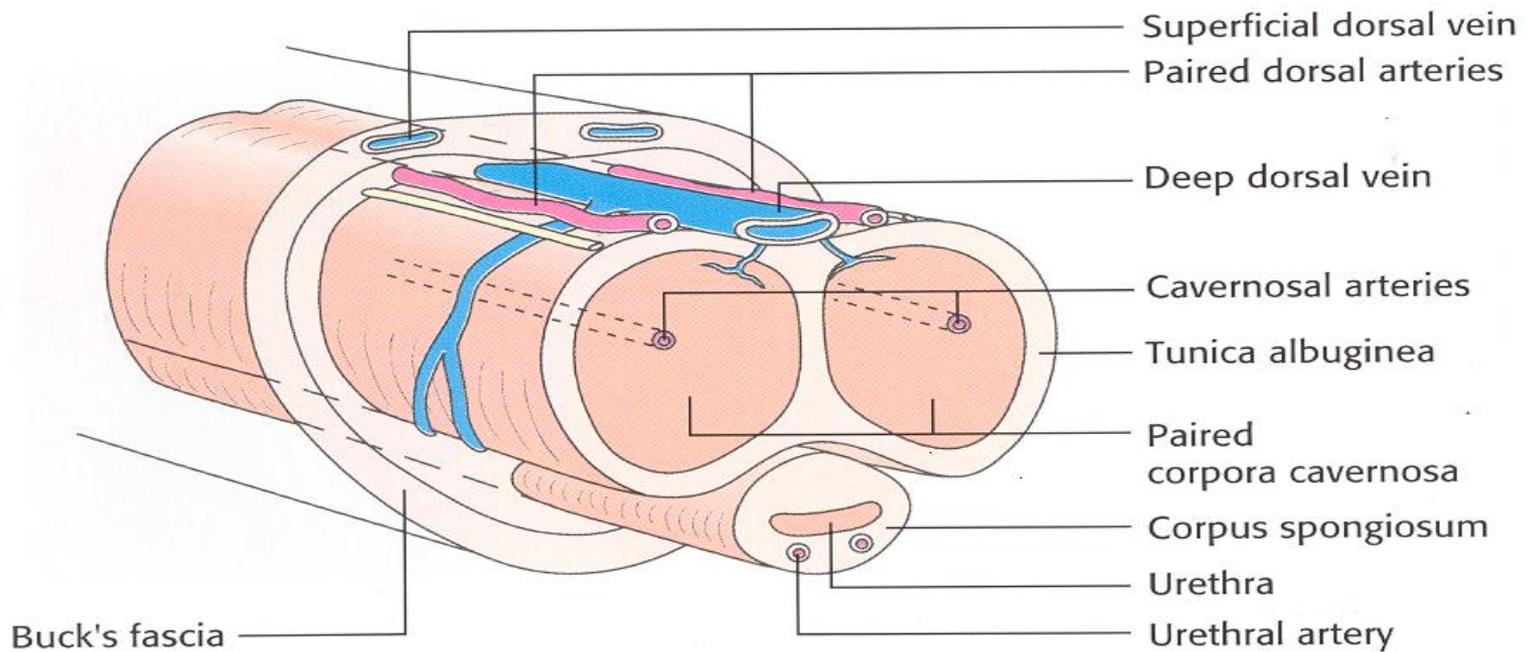


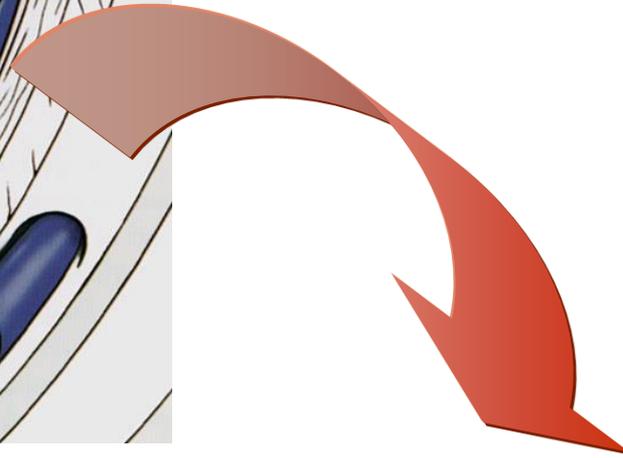
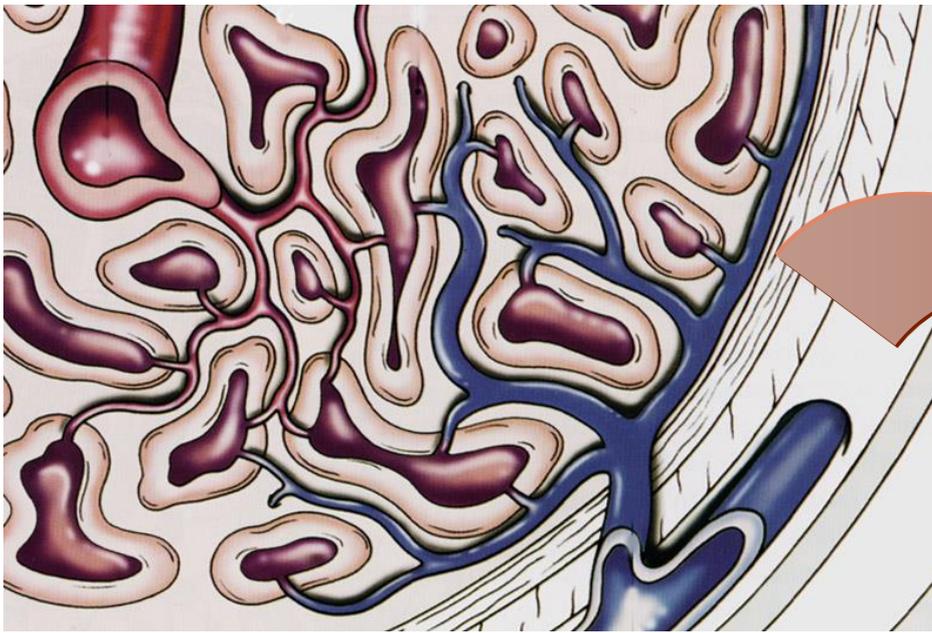
# Prevalence of ED by Age



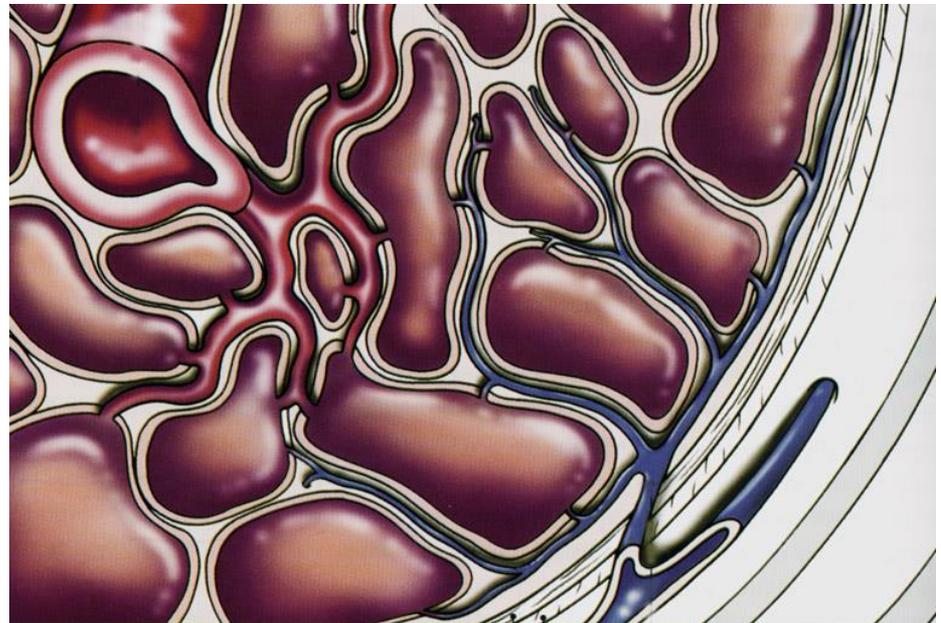
Feldman HA et al, J Urol; 1994; 151:54-61

# Anatomy of the penis





Veno-occlusive  
mechanism of  
erection



# Innervation of the Penis

## ▶ Central Control

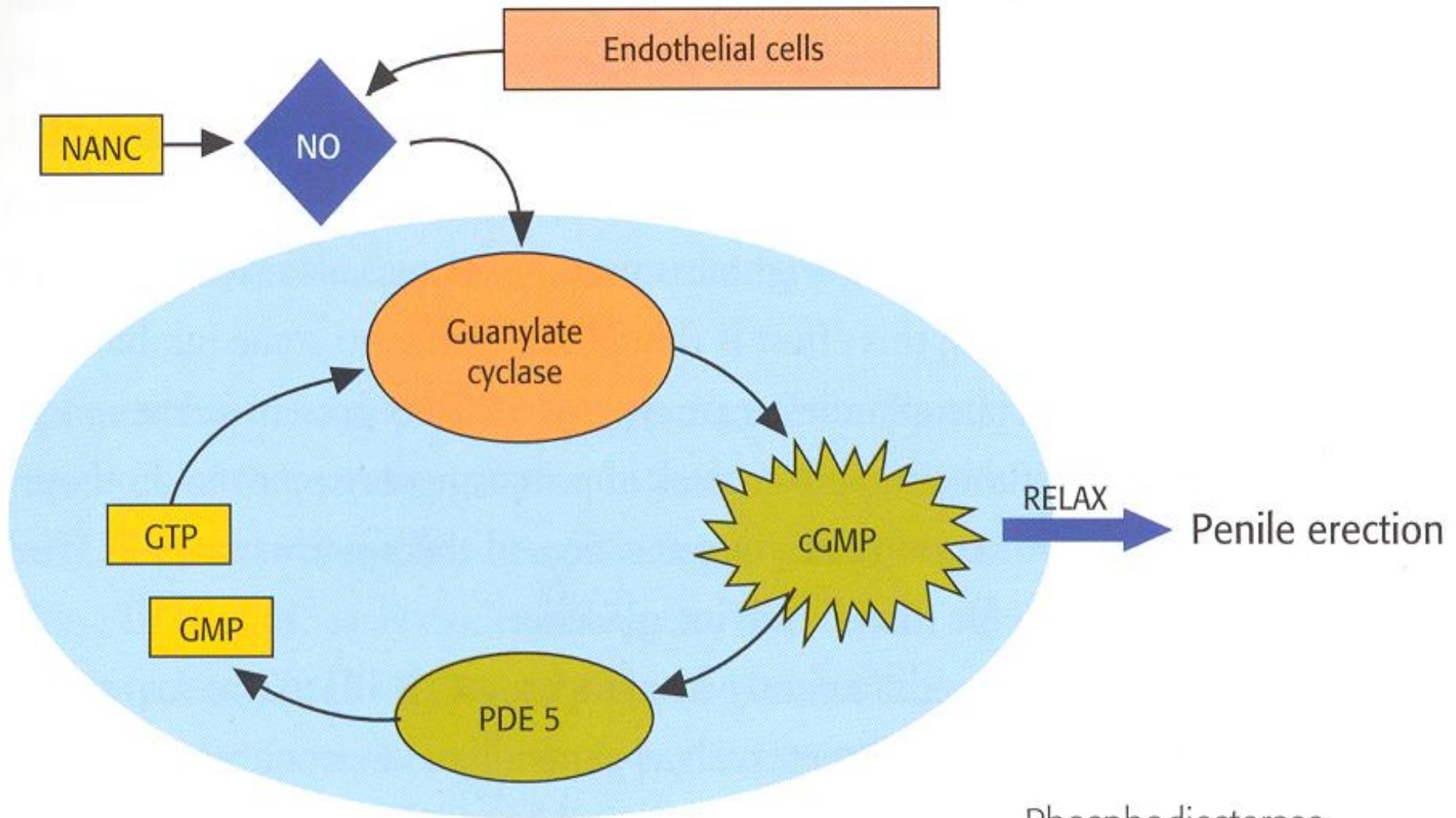
- Medial pre optic nucleus
- Paraventricular nucleus

## ▶ Sympathetic

- Adrenergic
- Inhibitory

## ▶ Parasympathetic

- Cholinergic (NOS)
- Excitatory



NO Nitric oxide  
 NANC Nonadrenergic–noncholinergic neurones  
 GTP Guanosine triphosphate

Phosphodiesterase

type 5 inhibition prevents cGMP breakdown and thereby enhances the normal erectile response.

# Drugs that may Cause ED

- ▶ Psychotropics
- ▶ Antidepressants
- ▶ Antihypertensives
- ▶ Antiandrogens
- ▶ Anti-cholinergic
- ▶ Drugs of abuse
- ▶ Others cimetidine, digoxin, metoclopramide, phenytoin & carbamazepine

# Organic Classification – approx 80%

## ▶ Endocrine

- hypogonadism
- hyperprolactinaemia
- hyperthyroidism
- hypothyroidism

## ▶ Neurogenic

- cerebral
- spinal cord
- peripheral

## ▶ Arterial

- atherosclerosis
- trauma
- iatrogenic

## ▶ Venous

## ▶ Iatrogenic

- drug
- surgery
- radiotherapy

# Erectile Dysfunction and its Risk Factors

| Population:  | All | Heart Disease | DM  | ↑BP |
|--------------|-----|---------------|-----|-----|
| Complete ED* | 10% | 39%           | 28% | 15% |

Calculated by discriminate analysis

# Diabetes Mellitus

## ▶ Neurogenic

- Autonomic neuropathy
- Peripheral neuropathy

## ▶ Arterial

- Atherosclerosis
- microangiopathy

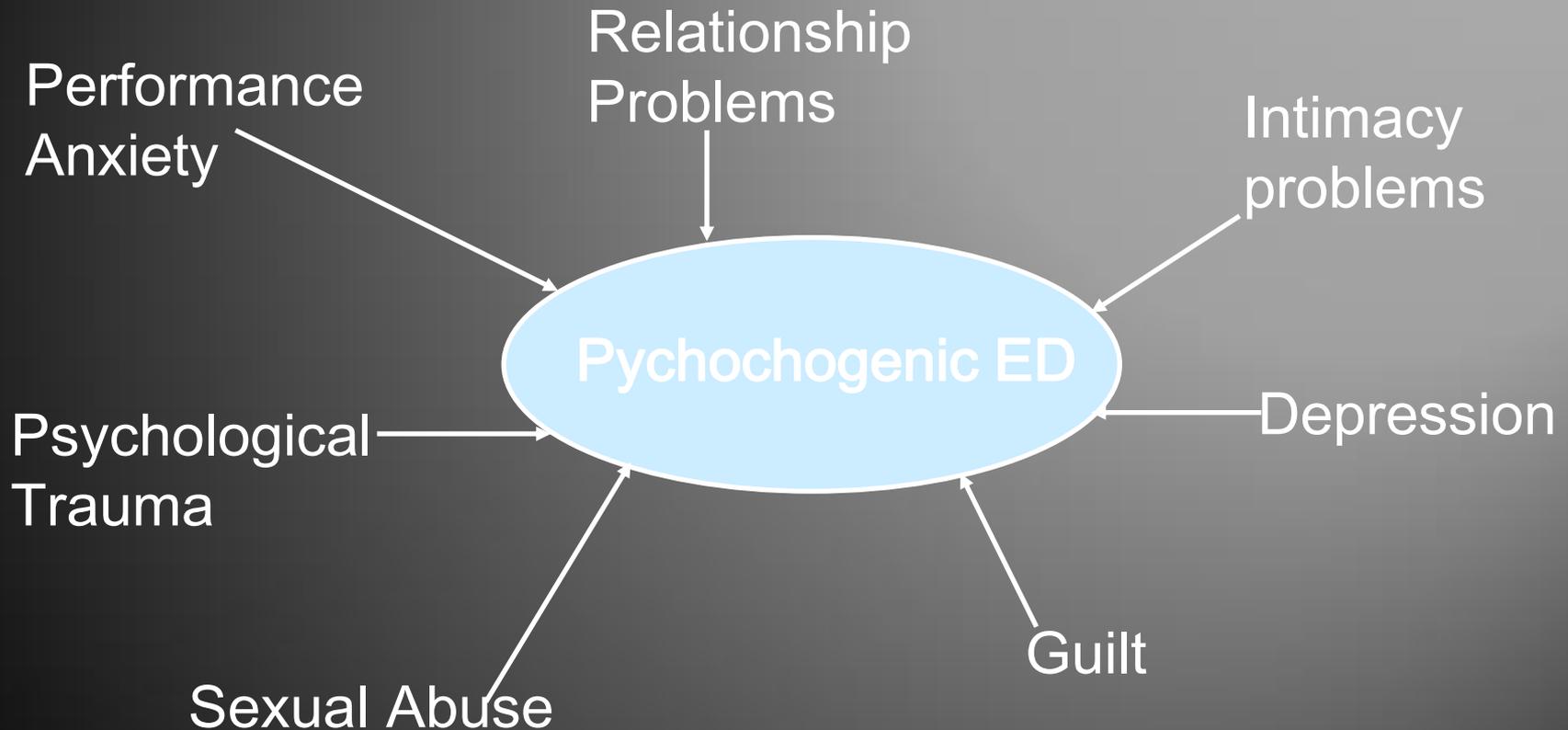
## ▶ Endothelial

- impaired endothelial-dependent smooth muscle relaxation

## ▶ Myogenic

- impaired smooth muscle function

# Psychogenic Origin



# Diagnosis and Management

- ▶ History
  - ▶ Examination
  - ▶ Special Investigations
  
  - ▶ IIEF
- 

# Recommended Diagnostic Tests

- ▶ Fasting glucose or glycated haemoglobin (HbA<sub>1C</sub>) and lipid profile
- ▶ Or dipstick urinalysis
  - If not available from the previous 12 months
- ▶ Testosterone, Prolactin, Thyroxine
  - Only if indicated

# International Index of Erectile Function

- ▶ 15 questions

- ▶ 5 domains

- Erectile function
- Orgasmic function
- Sexual desire
- Intercourse satisfaction
- Overall satisfaction

- ▶ Erectile Function Domain

- 6 questions
  - minimum score 1
  - maximum score 30
  - “normal” >25
  - “Mild” 22-25
  - “moderate” 11-21
  - “Severe” <11
- 

# Classic presentations

## Psychogenic

- ▶ Sudden onset
- ▶ Specific situation
- ▶ Normal nocturnal and early morning erection
- ▶ Relationship problems
- ▶ Problems during sexual development

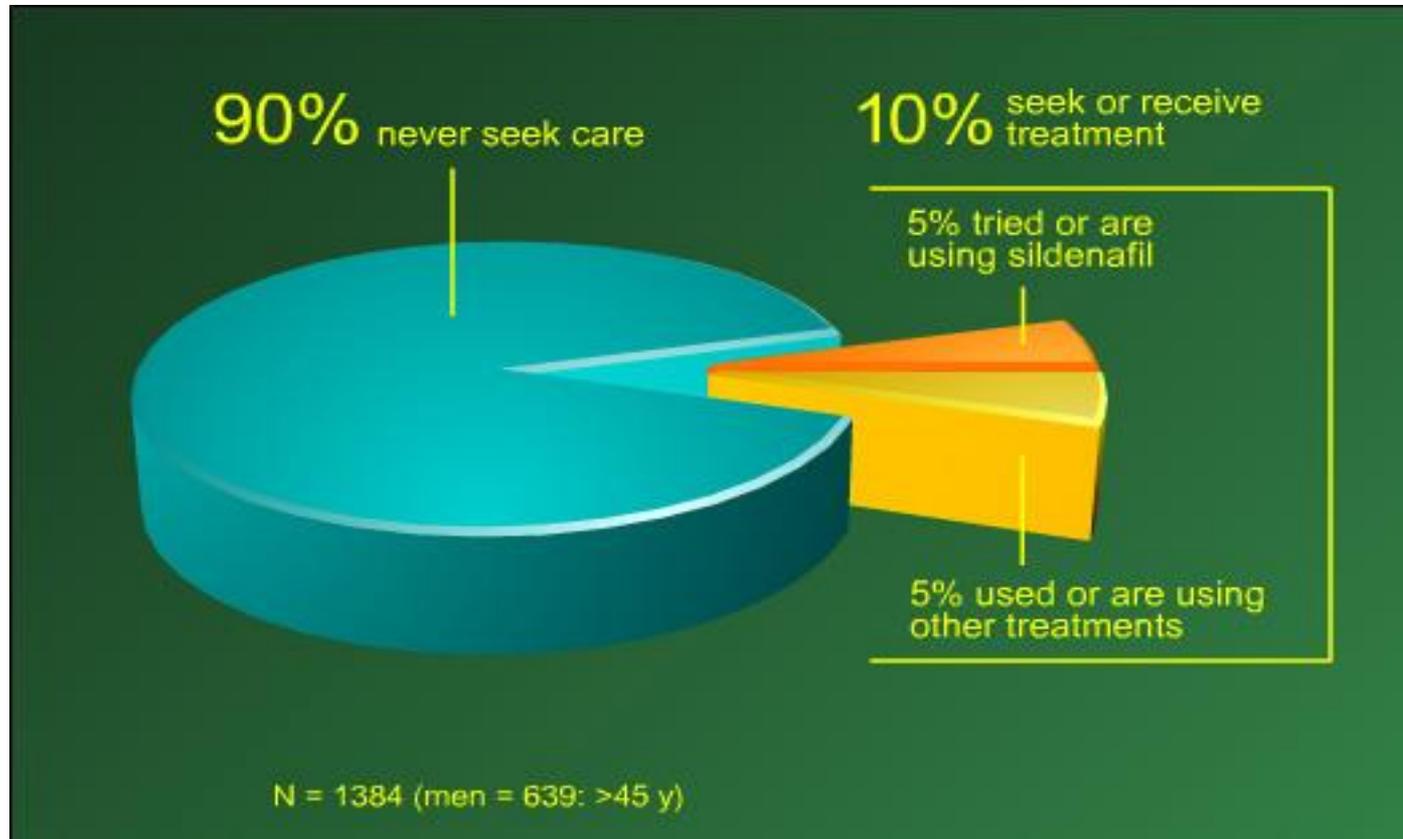
## Organic

- ▶ Gradual onset
- ▶ All circumstances
- ▶ Absent nocturnal and morning erection
- ▶ Normal libido and ejaculation
- ▶ Normal sexual development

# Treatment of ED

- ▶ Alter modifiable risk factors or causes
- ▶ Direct therapies

# Under treatment of ED



Adapted with permission from McKinlay JB. *Int J Impot Res.* 2000;12 (suppl 4):S6-S11.  
Based on data from the American Association of Retired Persons. *Modern Maturity Magazine*, Washington DC, 1999.

# Alter Modifiable Risk Factors or Causes

- ▶ Prescription or nonprescription drug use
  - Antihypertensives, antidepressants, antipsychotics, antiarrhythmics, antiandrogens, etc.
- ▶ Hormone replacement therapy (eg, hypogonadism, hyperprolactinemia)

# Life Style Modification

- ▶ Smoking Reduction
  - 85% of smokers have abnormal penile vasculature
- ▶ Obesity and Exercise
  - BMI  $>28.7$  gives 30% higher risk of ED than a BMI 25 or less
- ▶ Pelvic floor exercises
  - Some evidence that these may improve ED in men
- ▶ Regular Intercourse
  - Intercourse once a week may preserve vascular function “Use it or loose it”.

# Therapeutic Options

- ▶ Non-invasive Therapy
    - Oral medications
    - Intraurethral agent – MUSE
  - ▶ Intracorporal Injection Therapy
    - Caverject
  - ▶ Vacuum devices
  - ▶ Surgery
    - Prostheses
    - Vascular surgery
  
  - ▶ Androgen Replacement
    - for Hypogonadism
- 

# Hypogonadism

- ▶ Primary
  - Genetic (Klinefelters)
- ▶ Secondary
  - Age
  - Diabetes
  - Metabolic syndrome
  - Testicular Trauma
  - Infections : mumps, orchitis, HIV, STIs
  - Hormonal causes : Prolactinoma, steroids, Cannabis, Ketoconazole
  - Chemotherapy and Radiotherapy to the pelvis

# Tests for Hypogonadism

- ▶ Testosterone: morning sample x2
  - ▶ Sex hormone binding globulin
  - ▶ FBC
  - ▶ Fasting Lipids
  - ▶ Fasting Glucose
  - ▶ Thyroid
  
  - ▶ **PSA**
- 

# Treatment of Hypogonadism

- ▶ Testosterone replacement
- ▶ Oral
  - Tablet QDS
- ▶ Buccal
- ▶ Intramuscular
  - Nebido 1g 3monthly, Sustanon 1ml every 2–3 weeks
- ▶ Implant
  - 4–6monthly
- ▶ Transdermal
  - Gels, 5mg daily

# Symptoms

- ▶ Fatigue
- ▶ Loss of libido, Sex drive
- ▶ Loss of Morning erection
- ▶ PDE5 Failure
- ▶ Loss of muscle mass
- ▶ Increased central visceral fat
- ▶ Decreased mood or Depression

## Later symptoms

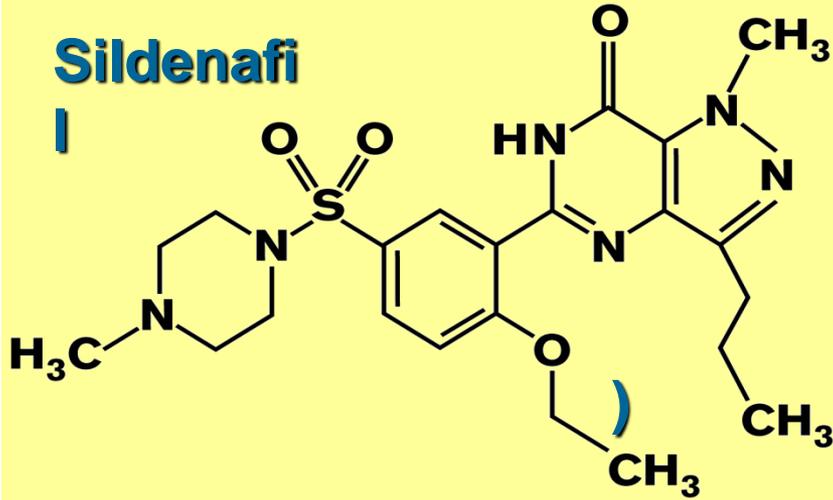
- ▶ Testicular atrophy
- ▶ Reduced body hair
- ▶ Gynaecomastia
- ▶ Osteopenia

# Oral Therapy Options

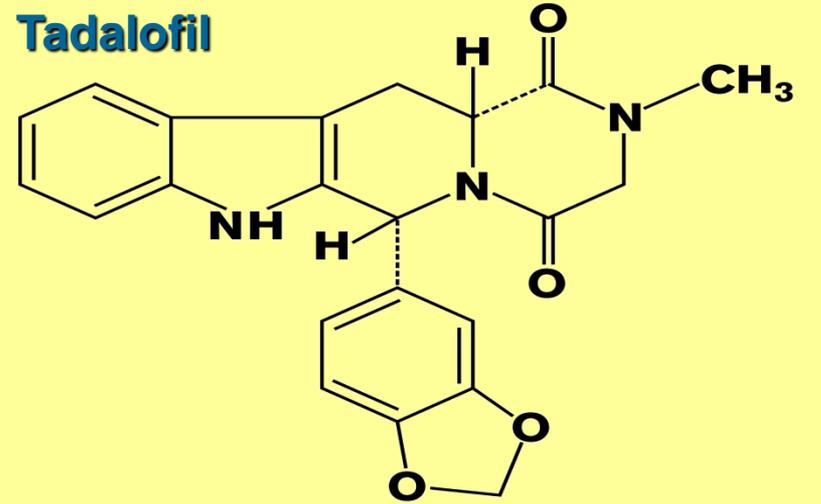
- ▶ PDE 5 Inhibitors
- ▶ On demand or Once daily preparation
  - Viagra
    - Well know and used
    - Onset of action 30–60 mins
    - Avoid alcohol and fatty food prior to taking medication
  - Cialis
    - Efficacy for 24 hours.
    - No limitations to food intake prior to taking dose
  - Levitra
    - Similar mode of action to Viagra

# PDE5 Inhibitors

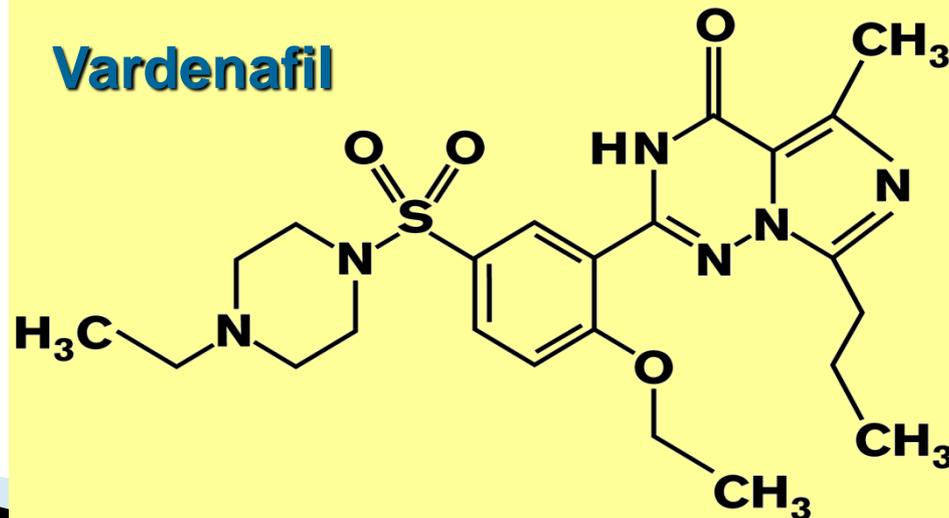
**Sildenafil**



**Tadalafil**



**Vardenafil**



# Oral therapies

- ▶ Dopamine antagonists
  - Apomorphine
    - Sublingual administration.
    - Quicker onset of action – 20mins
    - Can be used with nitrates but with caution

# Oral Therapies – Efficacy

|                            | <b>Improved<br/>Erection</b> | <b>Successful<br/>intercourse</b> |
|----------------------------|------------------------------|-----------------------------------|
| <b>Viagra 100mg</b>        | <b>86%</b>                   | <b>75%</b>                        |
| <b>Cialis 20mg</b>         | <b>81%</b>                   | <b>75%</b>                        |
| <b>Vardenafil<br/>20mg</b> | <b>85%</b>                   | <b>72%</b>                        |
| <b>Uprima 3mg</b>          |                              | <b>50%</b>                        |

# Oral therapies – Side effects

|                       | Headache | Flushing | Dyspepsia | Nasal congestion<br>Rinitis | Back pain | Myalgia |
|-----------------------|----------|----------|-----------|-----------------------------|-----------|---------|
| Viagra<br>Sildenafil  | 16%      | 10%      | 7%        | 4%                          |           |         |
| Cialis<br>Tadalafil   | 14%      |          | 12%       |                             | 6.5%      | 6%      |
| Levitra<br>Vardenafil | 13%      | 10%      | 6%        | 5%                          |           |         |

# Cardiac Risk

- ▶ Nitrates are contraindicated with all PDE5 inhibitors.
  - ▶ Is the patient “Fit for Sex”
  - ▶ Blood pressure should be stable
  - ▶ At least 3 months post MI or CVA
- 

# Cardiac Risk with PDE5 inhibitor

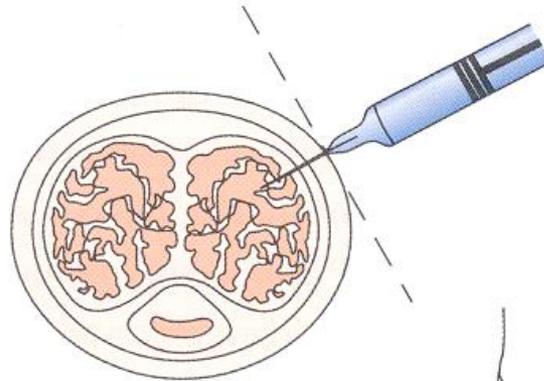
- ▶ Low Risk –
  - Controlled hypertension
  - Mild valve disease, mild stable angina,
  - post re-vascularisation
- ▶ Moderate Risk –
  - Recent MI or CVA
  - Congestive heart failure
  - Moderate stable angina
- ▶ High Risk
  - Uncontrolled angina
  - Uncontrolled hyper / hypotension
  - Recent MI / CVA
  - High risk arrhythmia, Hypertrophic cardiomyopathy.

# Injection therapy

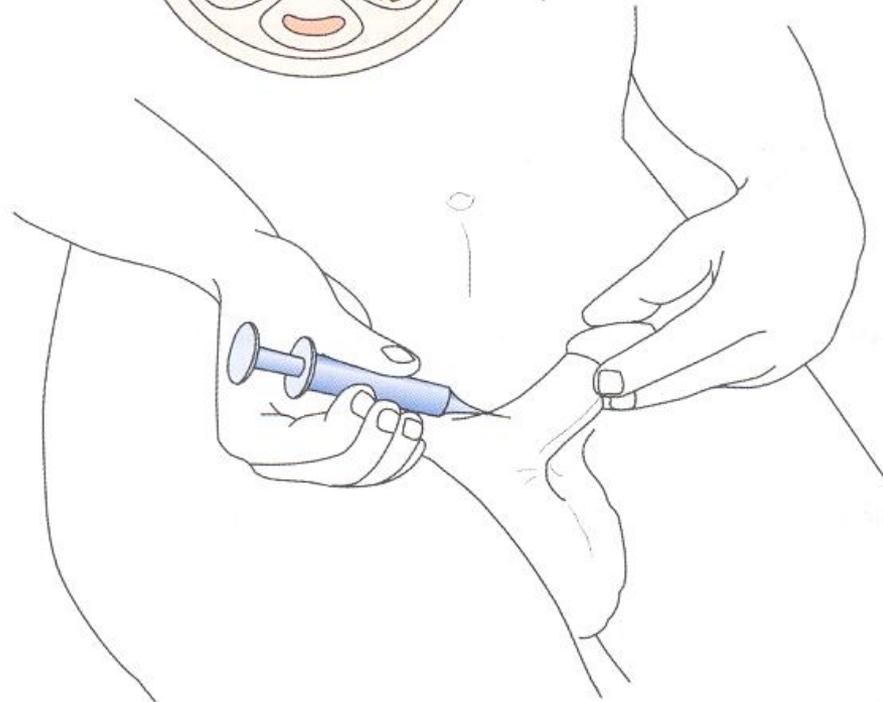
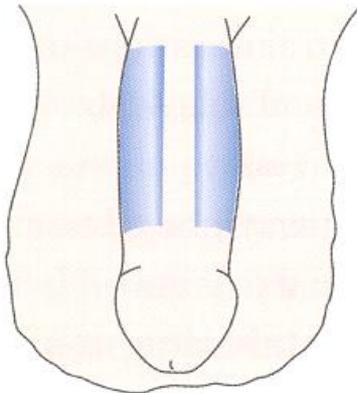
- ▶ Alprostadil
  - Caverject
  - Viridal Duo
- ▶ Vip & Phentolamine
- ▶ Dose is titrated upwards to achieve an adequate response. Max 60 micrograms.
- ▶ Studies demonstrate excellent efficacy with injection therapy

# Injection therapy

Cross-section showing injection sites and angle of needle insertion



Injection sites along the side of the penis

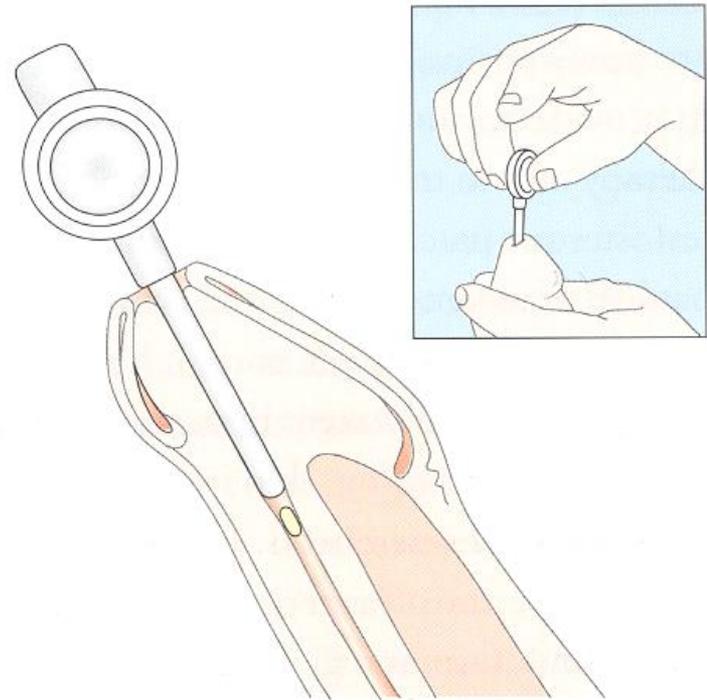


# Injection therapy – Side effects

|                       | Alprostadil % | VIP & Phentolamine % |
|-----------------------|---------------|----------------------|
| Priapism              | 0.5-1.3       | < 0.5                |
| Pain on Injection     | 17 -50        | 1                    |
| Heamatoma             | 3             | 3                    |
| Systemic side effects | 1             | 10-50                |

# Intraurethral therapy – MUSE

- ▶ 125 –1000 mcgs
- ▶ Easy to use
- ▶ Efficacy 20–80% !
- ▶ Pain
  - Penile
  - Urethral
  - Testicular
- ▶ Vaginal discomfort 6%
- ▶ Priapism 0.4%
- ▶ Up to 123mcgs of alprostadil found in semen.
- ▶ 10 minutes to onset of erection



Intraurethral administration of alprostadil using the MUSE® system.

# Intraurethral therapy – MUSE

- ▶ Alprostadil pellet inserted into the urethra
- ▶ Once inserted takes approx 10 minutes to be absorbed. 125 – 1000 mcgs
- ▶ Early reports – 66% efficacy. Subsequent reports show a much reduced efficacy.
- ▶ Side effects
  - Pain 7%
  - Urethral Trauma 1%
  - Partner vaginal discomfort
  - Up to 123mcgs of alprostadil in seaman.

# Surgical Implants

- ▶ Last resort treatment as surgery involves dilatation of erectile tissue
- ▶ High incidence of infection and mechanical failure
- ▶ Patient selection
- ▶ High satisfaction for some patients when all other treatments have failed



# Conclusions

- ▶ ED is highly prevalent
  - ▶ ED incidence is age-related
  - ▶ ED is associated with significant co-morbidities
  - ▶ ED is currently significantly undertreated
  - ▶ ED can be effectively managed
- 

# Any Questions?

