Female Urinary Incontinence

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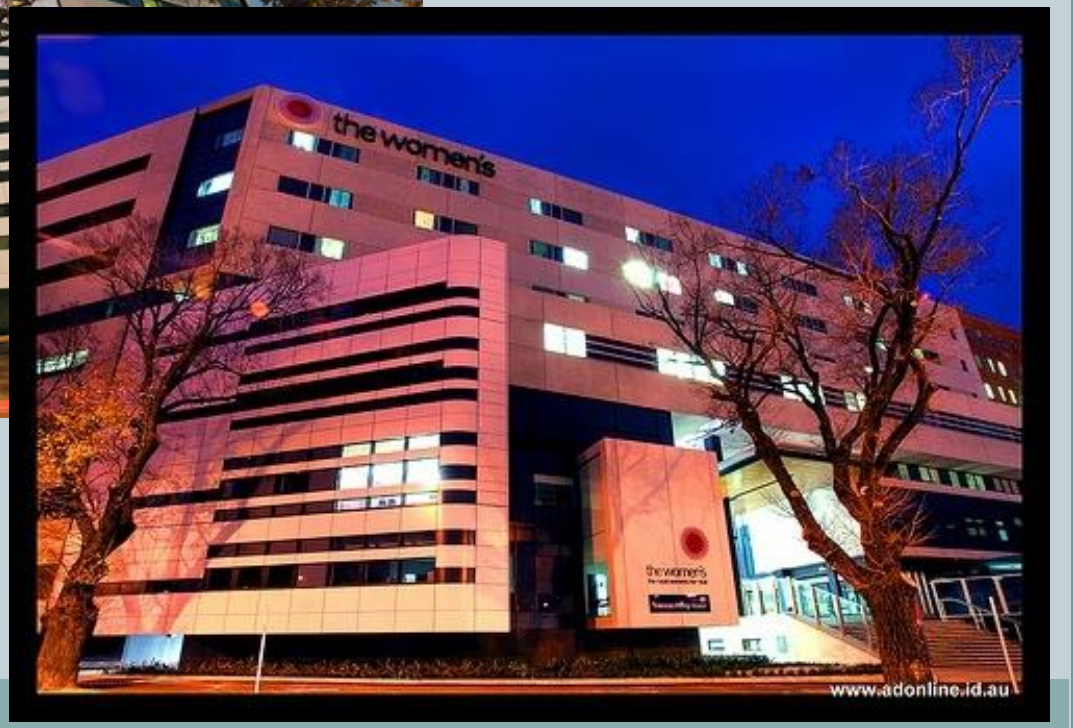
Founded 1856



Learning objectives:

- Identify the different types of female urinary incontinence.
- The pathophysiology of Bladder over activity.
- Review investigative work up for patients.
- Review the available therapies and their prospects.
- Discuss advances and pitfalls in treatment options currently available.

Prevalence

- PFD (Pelvic Floor Dysfunction) constitute both urinary and fecal incontinence as well as Pelvic organ prolapse symptoms.
- PFD affect 30% of women in the US and Europe.
- Prevalence:

25 - 35% in general population

39 - 64% in pregnant population

- Life time risk of at least one prolapse or incontinence procedure is 11.1% (Boyles et all 1997)
- Repeat surgery for recurrent prolapse or incontinence in 29.2% of patients within 4 years of primary surgery (*Olsen et al 1997*).

Background:

- Women do experience different health problems after child birth.
- At least 47% of women experience at least one or more health problems with in 3 months of delivery and persist for >6/52 (e.g. headache, backache, Hemorrhoids, depression, Bowel and Bladder symptoms).
- Many women do experience their first PFD symptoms during pregnancy.

In Australia

- Prevalence in Australia: Incontinence in women varies from 16.5% in 20-40 year olds to 31% in over 80 year olds. The prevalence increases with age; among women, it is 2 fold higher in the over 80 age group compared to 20-40 age group.

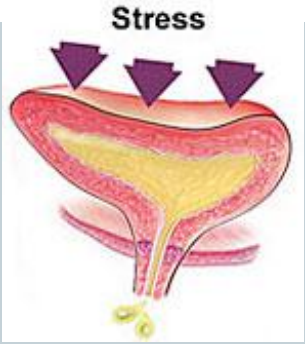
(**The prevalence of urinary incontinence within the community: A systematic review** funded by The Australian Commonwealth Department of Health and Aged Care).

- Up to 65% of those women recall that their symptoms began either during or shortly after childbirth.

In 2010, the total financial cost of incontinence in Australia was an estimated $42.9 billion.

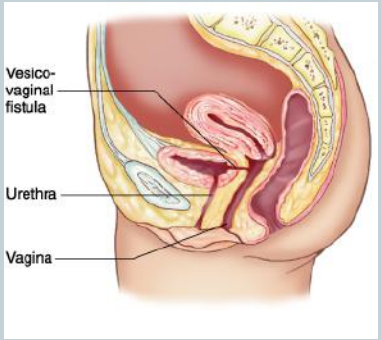
Types of Urinary Incontinence:

- Urodynamic stress incontinence.



- Detrusor over activity.
- Mixed.

- Overflow incontinence.
- Temporary (UTI).
- Functional disorder (mobility, cognitive).
- Extra urethral (ectopic ureter or Fistula).



Differential diagnosis of symptoms suggestive of overactive bladder in women

- Urinary tract infection
- Prolapse
- Urethral obstruction
- Atrophic vaginitis
- Bladder cancer
- Interstitial cystitis
- Postsurgical incontinence
- Diabetes
- Congestive heart failure
- Multiple sclerosis
- Medications/diuretics
- Neurogenic bladder
- Recent pelvic surgery
- Stress urinary incontinence

Clinical evaluation:

- Presenting Symptoms:
  - type :SI, UI, insensible leakage
  - onset, frequency, duration, severity.

- Associated Symptoms:
  - Urinary frequency, nocturia
  - Dysuria, bladder pain, haematuria
  - Voiding dysfunction
  - Bowel symptoms: constipation, AI
  - Effect on sexual function

Urge Incontinence

Components of overactive bladder

International Continence Society (ICS) definition of overactive bladder[1]

Urgency with or without urge incontinence, generally usually with increased frequency and nocturia

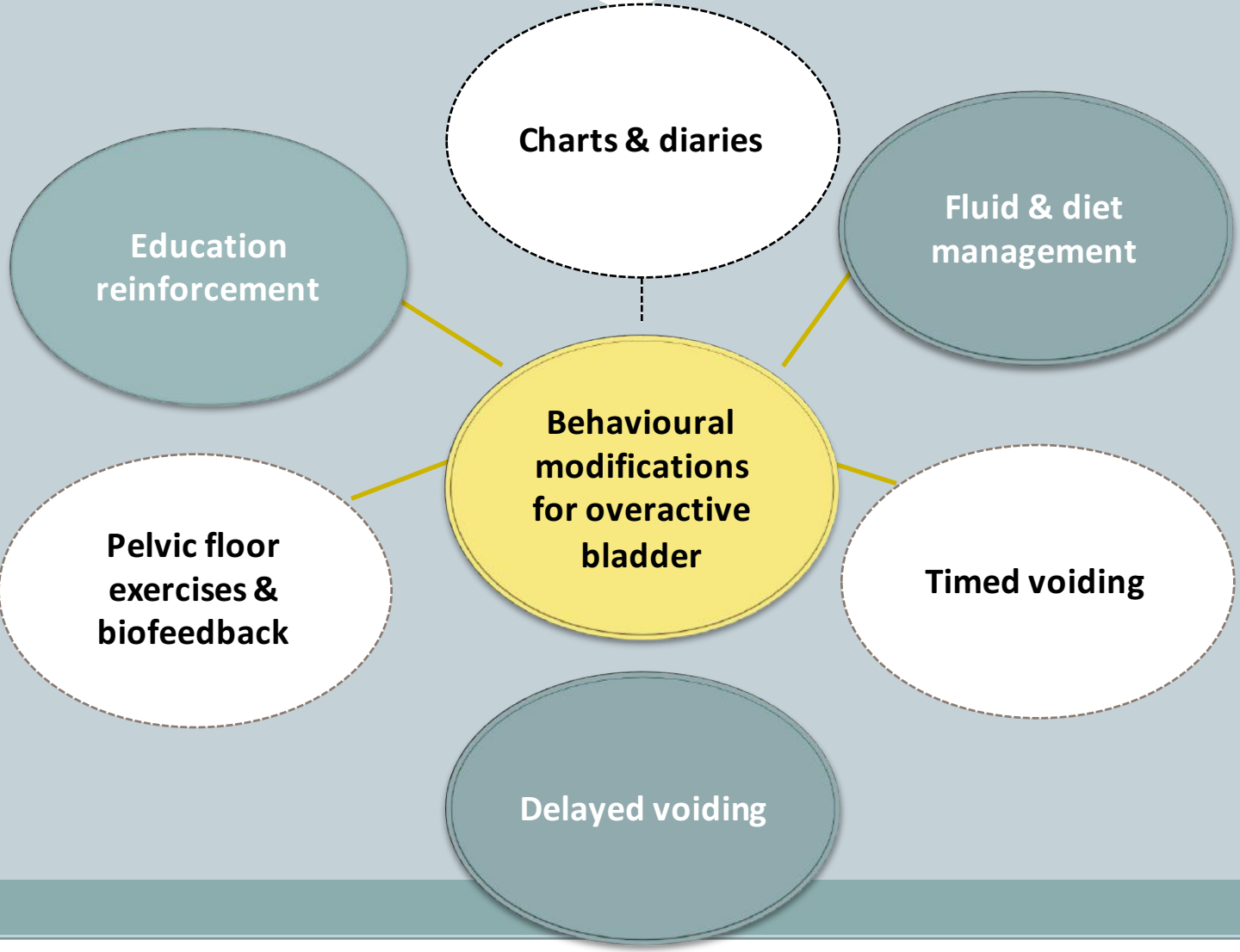
Urgency
The complaint of a sudden compelling desire to pass urine that is difficult to defer

Urgency Urinary Incontinence
The complaint of involuntary loss of urine that is accompanied by or immediately preceded by urgency

Urinary Frequency
The need to void more than 8 times in a 24-hour period

Nocturia
The complaint of having to void more than once per night

Behavioural therapy for overactive bladder



Management of DOA:

- Lifestyle changes therapy.
- Physiotherapy.
- Pharmacological therapy.

Lifestyle changes:

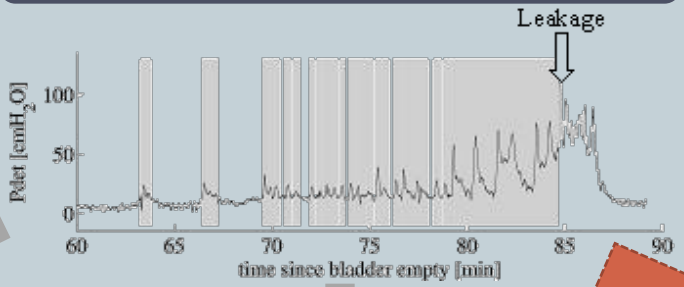
- Dietary: some foods and beverages are thought to contribute to bladder leak (not been proven it may be reasonable to see if eliminating one or all of them helps):
  - Alcohol.
  - Carbonated (+/- Caffeine).
  - Coffee and tea (+/- Caffeine).
  - Citrus juice and fruits.

Lower urinary tract symptoms may result from neurogenic or non-neurogenic causes

* **Lower urinary tract symptoms suggestive of overactive bladder**

Neurogenic
e.g. multiple sclerosis, spinal cord injury, Parkinson's disease

Idiopathic detrusor overactivity



Post-surgical detrusor overactivity

Congenital

Infective

True idiopathic

UTI:

An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction

Received: 14 February 2009 / Accepted: 27 July 2009 / Published online: 25 November 2009

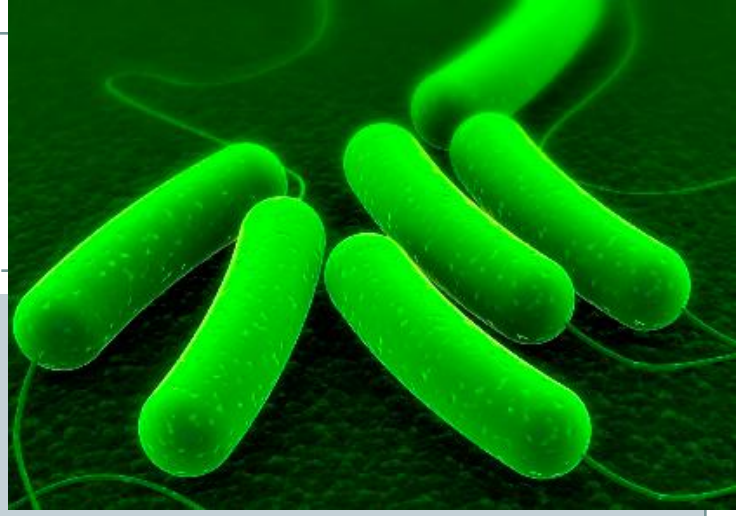
Diagnosis:

[12] Commonly suggested criteria for: (1) bacteriuria are >100,000 CFU/ml on voided specimen or >1,000 CFU/ml on catheterized specimen; (2) pyuria are >10 WBC/mm^3.

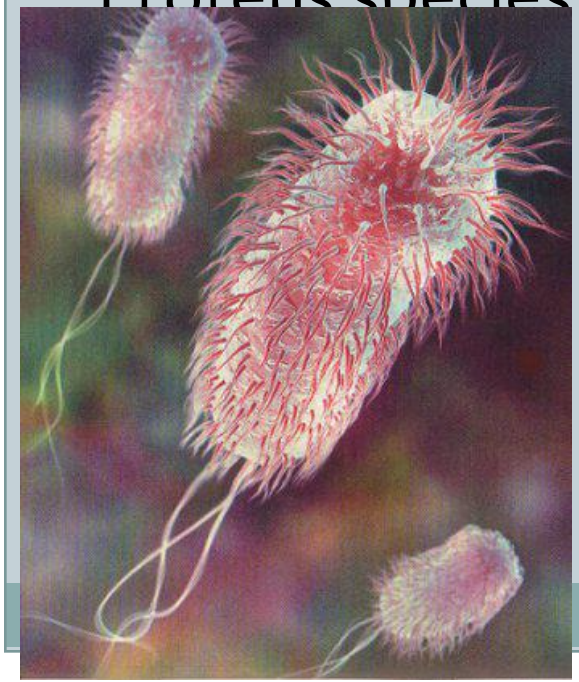
Recurrent UTI:

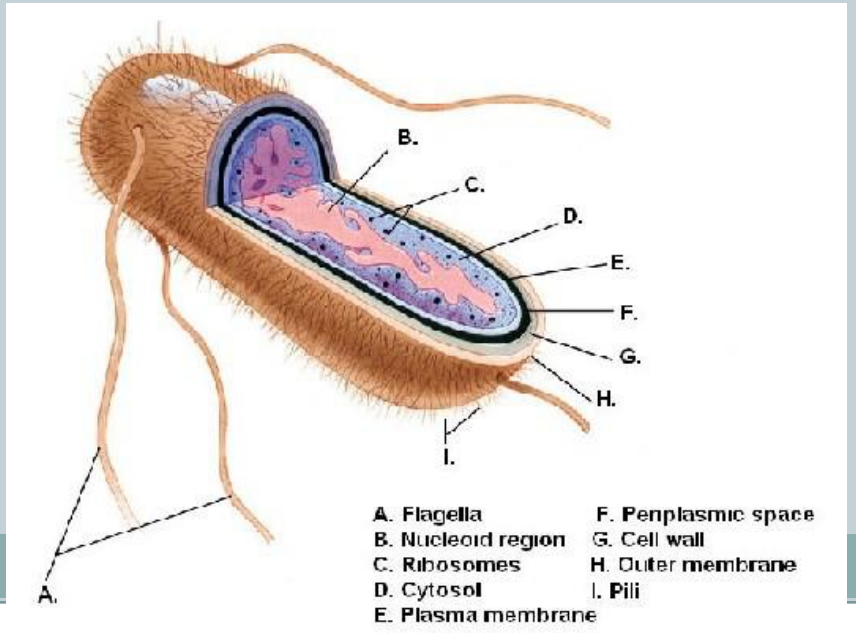
Recurrent urinary tract infections (UTIs): at least three symptomatic and medically diagnosed UTI in the previous 12 months.[13] The previous UTI(s) should have resolved prior to a further UTI being diagnosed.

UTI



- Bacteria:
- Escherichia coli 80%
- Staphylococcus saprophyticus 10%-15%
- Enterococcus, Klebsiella, Enterobacter, and Proteus species are (less common causes).





Predisposing factors

- 1. Shorter urethra-to-anus distance.
- 2. Local pH and cervicovaginal antibody changes in the vagina
- 3. Greater adherence of uropathogenic bacteria to the uroepithelium

Risk factors:

Risk factor	*Odds ratio (95% confidence interval)*
Intercourse in the past month	
>9 times	10.3 (5.8 to 18.3)
4 to 8 times	5.8 (3.1 to 10.6)
Age at first UTI ≥ 15 years	3.9 (1.9 to 8.0)
Maternal history of UTIs	2.3 (1.5 to 3.7)
New sex partner in the past year	1.9 (1.2 to 3.2)
Spermicide use in the past year	1.8 (1.1 to 2.9)

UTI = urinary tract infection.

In Post menopausal women

- A case-control study of postmenopausal women found that mechanical and physiologic factors affecting bladder emptying (incontinence, cystocele, and postvoid- ing residual urine) were strongly associated with recurrent UTIs.
- An increased postvoid residual urinary volume is an independent risk factor for recurrent UTIs in postmenopausal women.

Table 5. Guidelines for the Management of Recurrent Complicated UTIs

A single urine specimen with a quantitative count of at least 10^5 colony-forming units per mL is consistent with a diagnosis of UTI in asymptomatic patients.
If clinically feasible, initiation of antimicrobial therapy should be delayed until urine culture results are available.
Parenteral antimicrobial therapy is indicated if patients are unable to tolerate oral therapy, have impaired gastrointestinal absorption, have hemodynamic instability, or if the infecting organism is known or suspected to be resistant to oral agents.
The duration of therapy should be seven days for patients with lower urinary tract symptoms, and 10 to 14 days for patients with upper urinary tract symptoms or sepsis syndrome.
Patients with chronic use of urologic devices should receive the shortest possible duration of therapy to limit antimicrobial pressure leading to resistance.
Whenever possible, genitourinary abnormalities should be corrected.
Prophylactic antimicrobial therapy to prevent recurrent UTIs is not recommended for patients with complicated UTIs.
Suppressive antimicrobial therapy is indicated to prevent frequent, recurrent infection for selected patients with persistent genitourinary abnormalities.
For young women with catheter-acquired UTIs, treatment of bacteriuria persisting 48 hours after catheter removal may be considered.

UTI = urinary tract infection.

Information from reference 6.

iAluRil

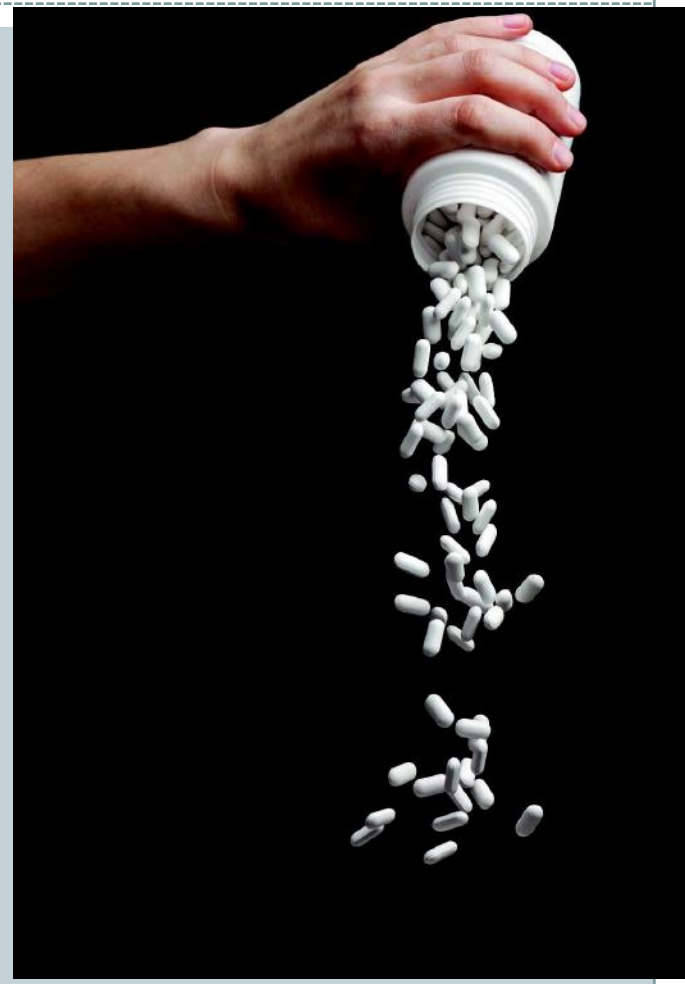
SODIUM HYALURONATE/SODIUM CHONDROITIN SULPHATE Sodium hyaluronate (1.6 % - 800 mg/50 mL); sodium chondroitin sulphate (2% - 1 g /50 mL)

iAluRil

- iAluRil Prefill is indicated to re-establish the glycosaminoglycan layers (GAGs) of the urothelial vesical tissue in cases in which their loss can cause frequent and recurring problems such as:
- Painful Bladder Syndrome (PBS),
- interstitial cystitis,
- treatment and prevention of recurrent urinary tract infection,
- cystitis as a result of Bacillus Calmette – Guerin therapy, or
- chemical and radiation therapy.

Pharmacotherapy for OAB

- **5 broad classes:**
  - Decrease detrusor contractility
    - Increase urethral resistance
      - Dual effects
    - Reduce fluid out put (Minirin)
      - Neurotoxins



Rational behind using Antimuscarinic agent in OAB

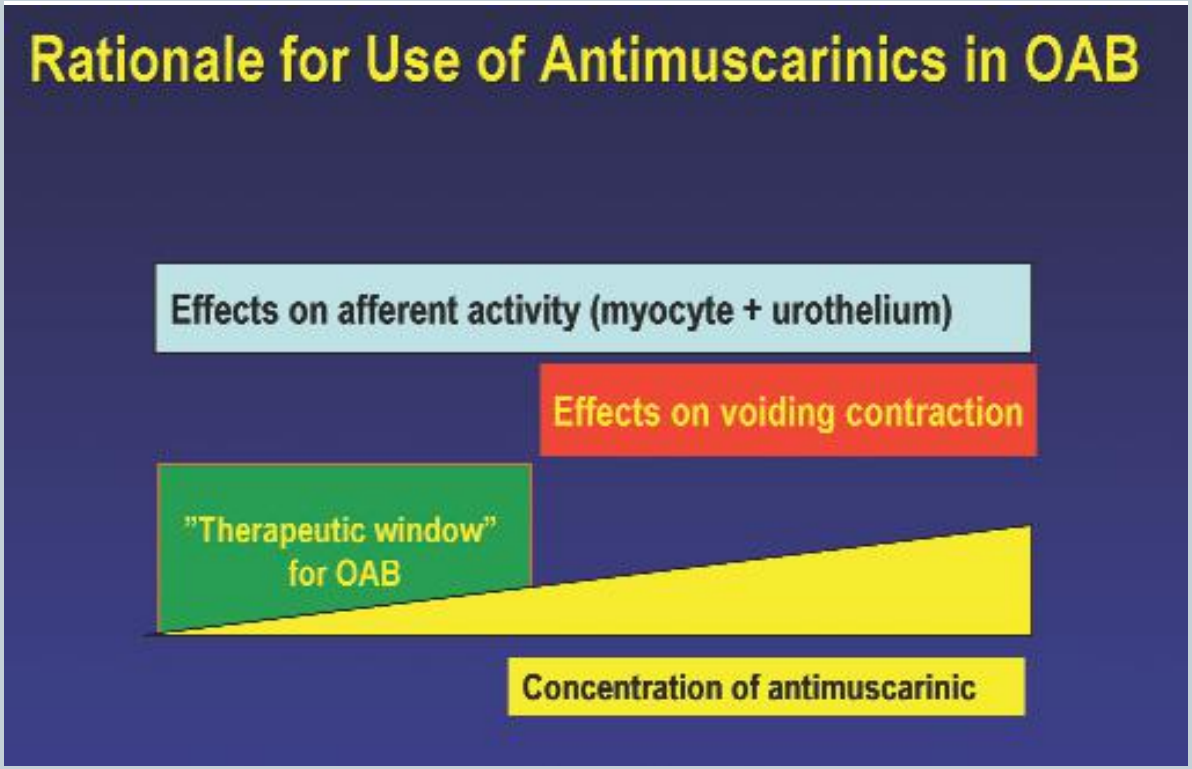


Figure 7 : Rationale for use of antimuscarinics for treatment of OAB/DO. Blockade of muscarinic receptors at both detrusor and non-detrusor sites may prevent OAB symptoms and DO without depressing the contraction during voiding

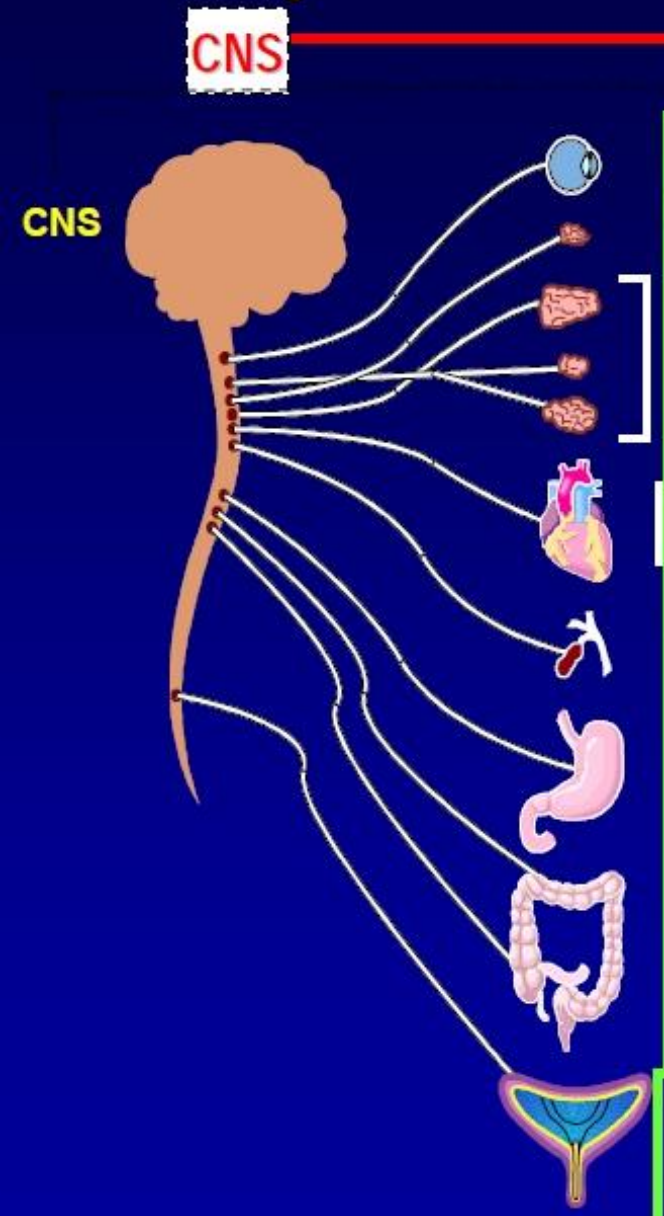
ICI 4th edition 2009

The role of muscarinic receptors in bladder function

- M2 and M3 receptors are located in the bladder
  - M2 receptors are thought to be indirectly involved with detrusor contraction. They may also play a predominant role in cardiac function
  - Although less prevalent, M3 receptors are thought to be predominantly responsible for the direct contraction of the detrusor

Organ system	Receptors
Bladder (detrusor muscle)	**M2, M3**
Salivary glands	M1, M3, M4
Cardiac tissue	M2
Eye (ciliary muscle, iris)	M3, M5
Gastrointestinal tract	M1, M2, M3
Central nervous system, Brain (cortex and hippocampus)	M1, M2, M3, M4, M5

Important Sites of Action for Antimuscarinics



Iris/ciliary body

Lacrimal gland

Salivary glands

Heart

Gallbladder

Stomach

Colon

Bladder (detrusor muscle)

Safety and tolerability

Reduce involuntary bladder contractions

↓

Reduce OAB symptoms including:

↓

Micturition Frequency
Nocturia

↓

Urgency
Urinary incontinence

Quality of life

Available anticholinergic agents and their predominant receptor affinity

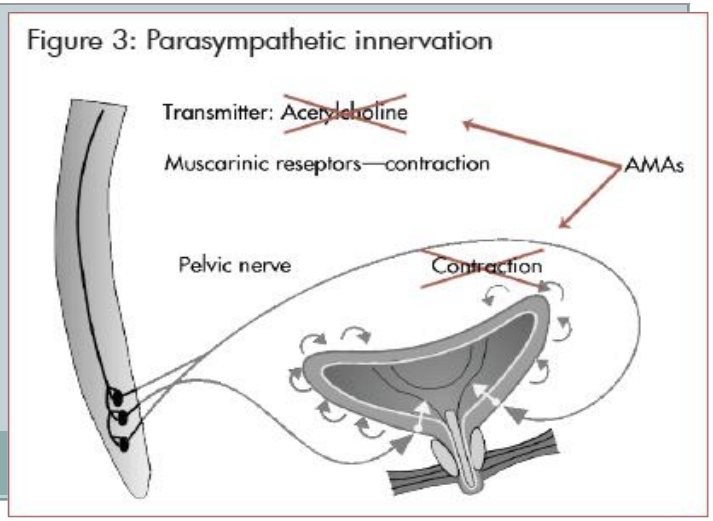
Medication	Predominant receptor affinity*	Metabolism
Oxybutynin	M1, M2, M3, M4	Hepatic
Tolterodine	M1, M2, M3, M4, M5	Hepatic
Solifenacin	M3	Hepatic
Darifenacin	M3	Hepatic

*NOTE: muscarinic activity may vary with assay and procedures.
In vitro and animal data do not necessarily predict human clinical effects.

Evidence in the use of Antimuscarinic agents in OAB

Table 2. Drugs used in the treatment of OAB/ DO. Assessments according to the Oxford system (modified)

	Level of evidence	Grade of recommendation
Antimuscarinic drugs		
Tolterodine	1	A
Trospium	1	A
Solifenacin	1	A
Darifenacin	1	A
Fesoterodine	1	A
Propantheline	2	B
Atropine, hyoscyamine	3	C



Evidence:

- *Oral oxybutynin (IR and ER) – 28-44% dry*
- *Oxytrol – 66% dry*
-
  - Pharmacology
    - Half-Life: 2-3 hr (immediate-release); 12-13 hr (controlled-release)
    - Onset: 30-60 min
    - Duration: 6-10 hr
    - Bioavailability: 6% (~1.5-2x higher for controlled release)
    - Peak plasma time: <1 hr (immediate-release); 12 hr (controlled-release)
    - Metabolism
      - hepatic and gut CYP3A4
      - converted to an active metabolite, N-desethyloxybutynin (N-DEO) by GI metabolic pathways, which are bypassed in transdermal delivery, resulting in lower N-DEO ratio
    - Metabolites: N-desethyloxybutynin (N-DEO)
    - Excretion: feces, urine

Oxybutynin


OXYTROL
Oxybutynin Transdermal System
3.9 mg/day
NDC 52544-920-08
OXYTROL®
Oxybutynin Transdermal System
3.9 mg/day
Contains
8
transdermal
systems
Rx Only
WATSON PHARMA
See patient package insert for application instructions.


clear backing
drug reservoir
drug-release membrane
contact adhesive

Evidence

- *Pharmacology of Oxytrol*
  - *same MOA as IR formulation*
  - ***transdermal system**, is designed to deliver oxybutynin continuously and consistently over a 3- to 4-day interval after application to intact skin*
  - ***delivers 3.9mg/day***
  - ***matrix-type transdermal system composed of three layers***
    - *Layer 1 (Backing Film)*
      - *thin flexible polyester/ethylene-vinyl acetate film that provides the matrix system with occlusivity and physical integrity and protects the adhesive/drug layer.*

Evidence

- *Layer 2 (Adhesive/Drug Layer)*
  - *cast film of acrylic adhesive containing oxybutynin and triacetin, USP*
- *Layer 3 (Release Liner)*
  - *two overlapped siliconized polyester strips that are peeled off and discarded by the patient prior to applying the matrix system*
- ***Transdermal administration of oxybutynin bypasses the first-pass gastrointestinal and hepatic metabolism → reduced formation of the N-desethyl metabolite***
  - ***Only small amounts of CYP3A4 are found in skin, limiting pre-systemic metabolism during transdermal absorption***
  - *The resulting plasma concentration AUC ratio of N-desethyl metabolite to parent compound following multiple Oxytrol applications was **1.3:1***

Adverse events:

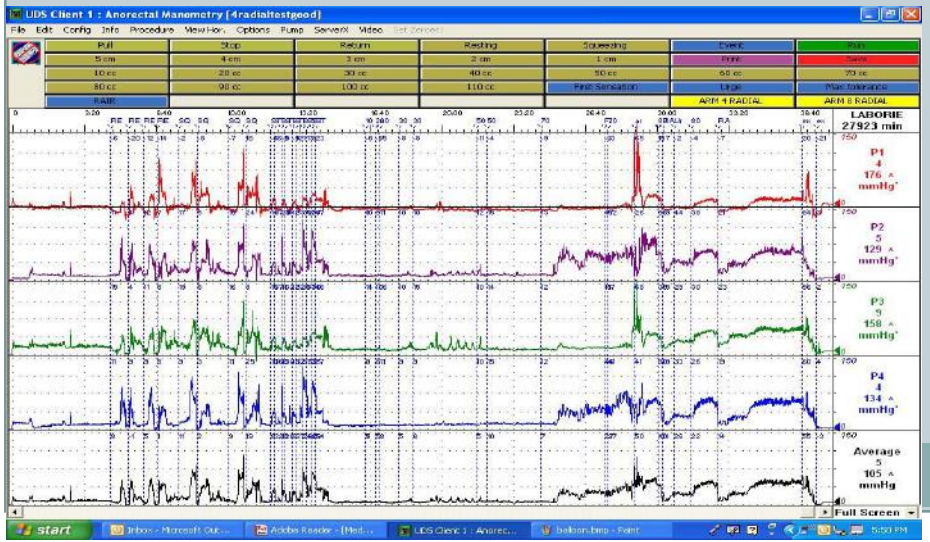
Adverse event	Oxybutynin IR	Oxybutynin ER	Oxytrol
Dry mouth	60-80%	60%	5-10%
Constipation	10-20%	13%	10%
Blurred vision	10%	5-8%	2.5%
Application site pruritis	-	-	17%
Application site erythema	-	-	7%
Application site vesicles/macules	-	-	3%
Dizziness and somnolence	14-17%	12%	<1%

When to refer?
And “Who” do you refer to?

- Failed conservative Management.
- Pain, Haematuria or recurrent UTIs (>or=3 in 6/12)
- Voiding difficulty.
- Suspected fistula.
- Neuropathic bladder.
- Significant pelvic organ prolapse.
- Uncertain diagnosis.

Indications for Urodynamics:

1. Failed to respond to empirical treatment.
2. Previous continence surgery.
3. Prior to definitive continence procedure.
4. Prior to prolapse repair accompanying stress incontinence.
5. Symptoms suggesting of voiding difficulty.
6. Presence of neurological disease.

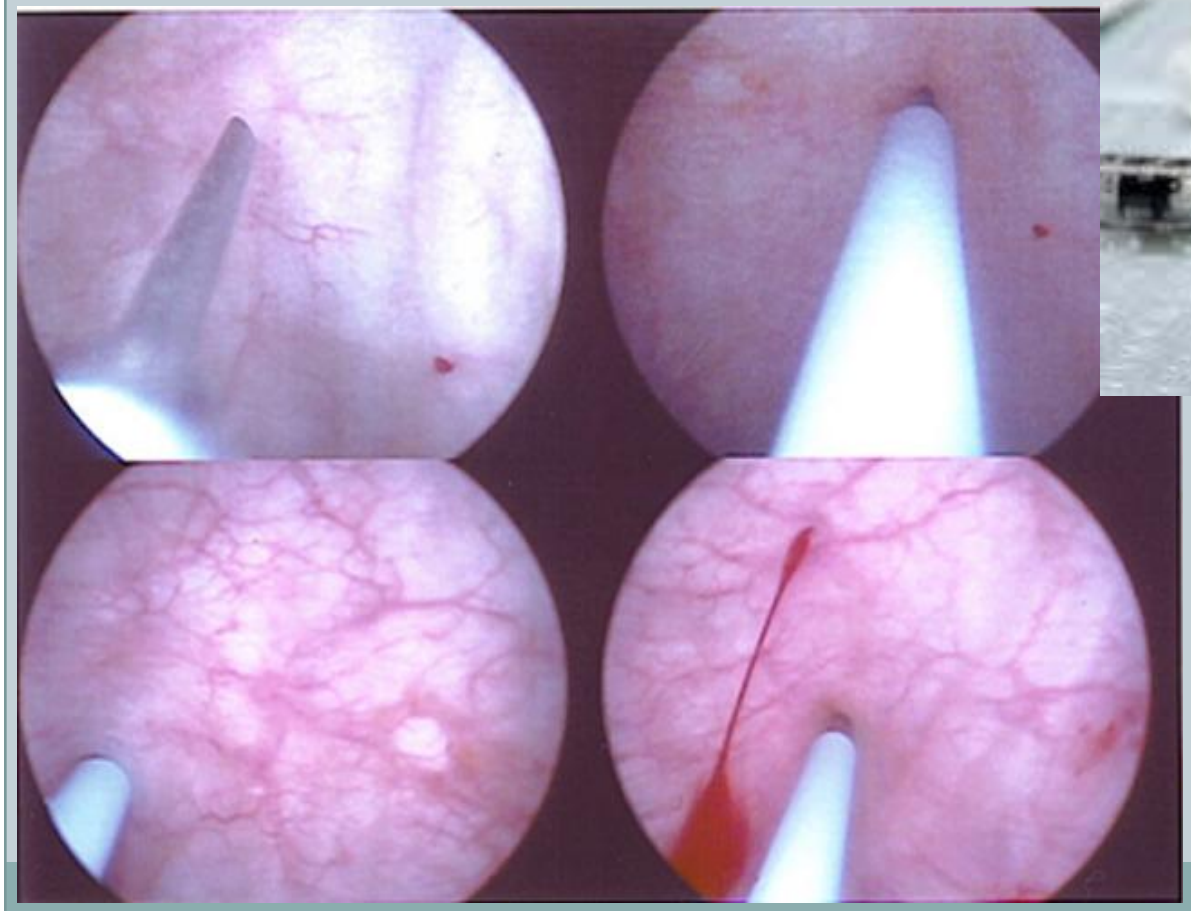


Aim of Uds:

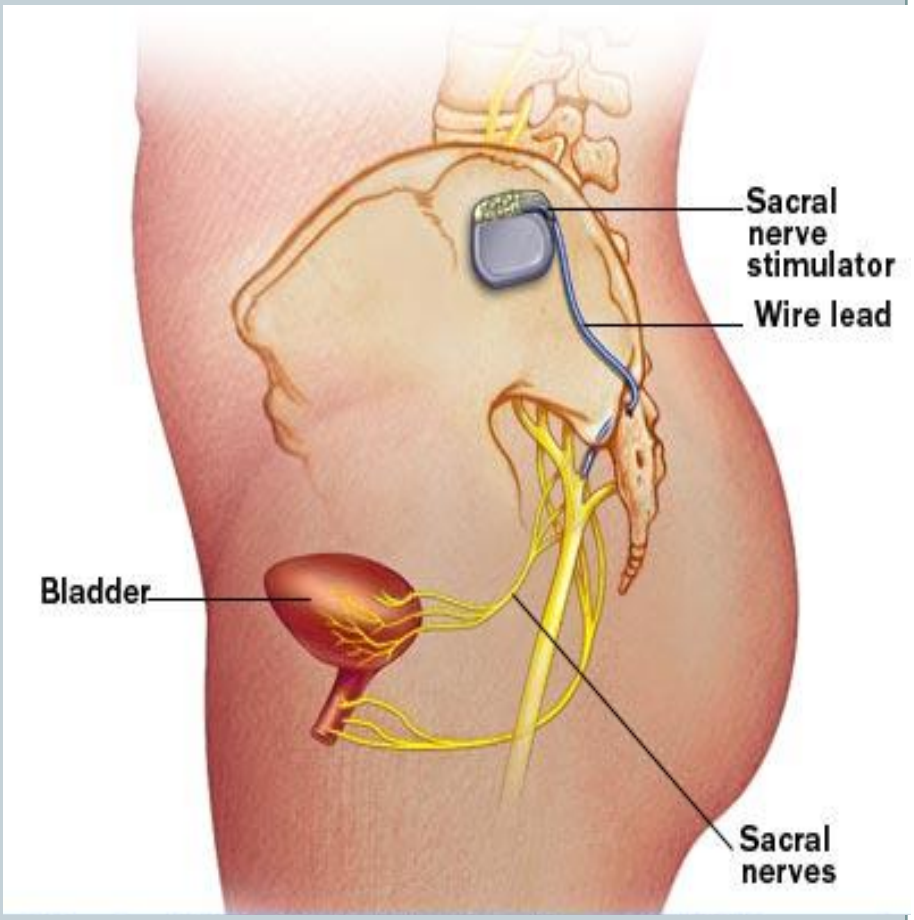
- 1. Identify / eliminate detrusor overactivity (it influence treatment options).
- 2. Identify / eliminate voiding difficulty (complicate treatment outcome)
- 3. Confirm the presence of SI.
- 4. Identify the presence of prolapse and relation to the bladder dysfunction (Boney's test)
- 5. Assess severity (help triage patients).

Other treatment for OAB:

Botulinum neurotoxin



Sacral nerve Modulation
(for refractory Bladder over activity)



Other Treatment options:

- Electro-magnetic: No evidence that it has more effect compared to placebo.

*** A double-blind randomized controlled trial of electromagnetic stimulation of the pelvic floor vs sham therapy in the treatment of women with stress urinary incontinence.** BJU Int. 2009 May;103(10):1386-90. Gilling PJ, Wilson LC, Westenberg AM, McAllister WJ, Kennett KM, Frampton CM, Bell DF, Wrigley PM, Fraundorfer MR.

Other Treatment options: Laser

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Urinary Incontinence

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Urinary Incontinence - Laser Treatment

The laser used is an Erbium Yag 2940nm. This has been widely used for facial skin resurfacing in the last 10-15 years and has been proven to be safe and effective.

How it works :

A special laser introducer is inserted into the vagina after the area has been sterilized with an antiseptic. A laser applicator is inserted into the introducer which lasers the front wall of the vagina. A different laser head is then used to laser the rest of the vagina. New collagen growth occurs over 1-3 months resulting in contraction of the vagina by 20-30%. This contraction results in the elevation and tightening of the pelvic floor reducing incontinence.

Office Hours

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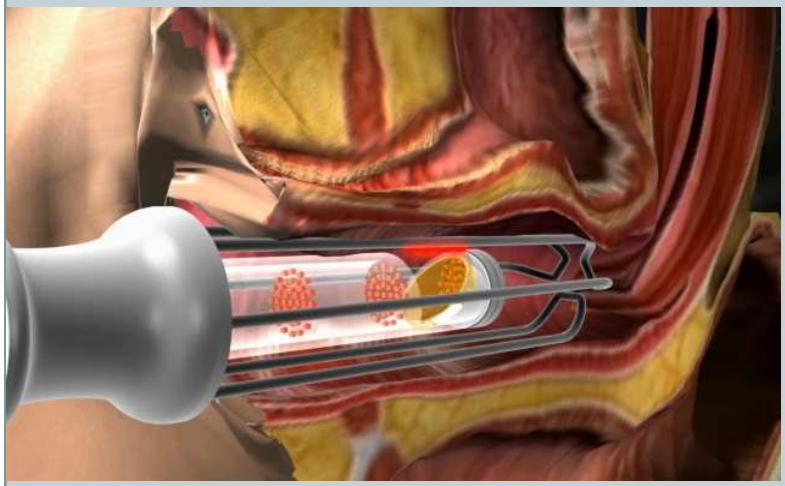
Other Treatment options: Laser

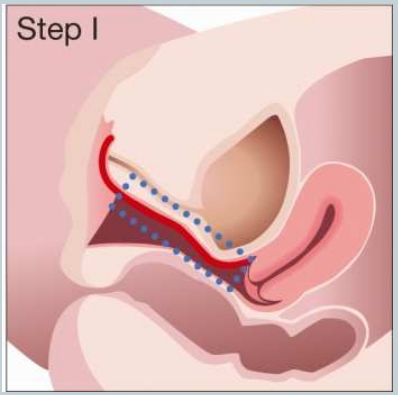
ISSN 1855-9913

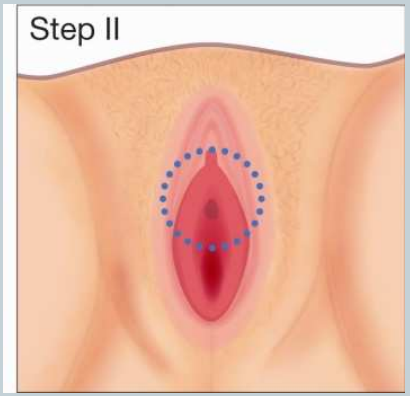
Journal of the Laser and Health Academy
Vol. 2012, No.1; www.laserandhealth.com

Minimally invasive laser procedure for early stages of stress urinary incontinence (SUI)

Fistonić Ivan[1], Findri-Guštek Štefica[2], Fistonić Nikola[3]
[1]Gynecology clinic, Zagreb, Croatia
[2]Ob/Gyn Office, Zagreb, Croatia
[3]Health Community Center, Zagreb, Croatia







Surgery for UI

- Augmentation cystoplasty

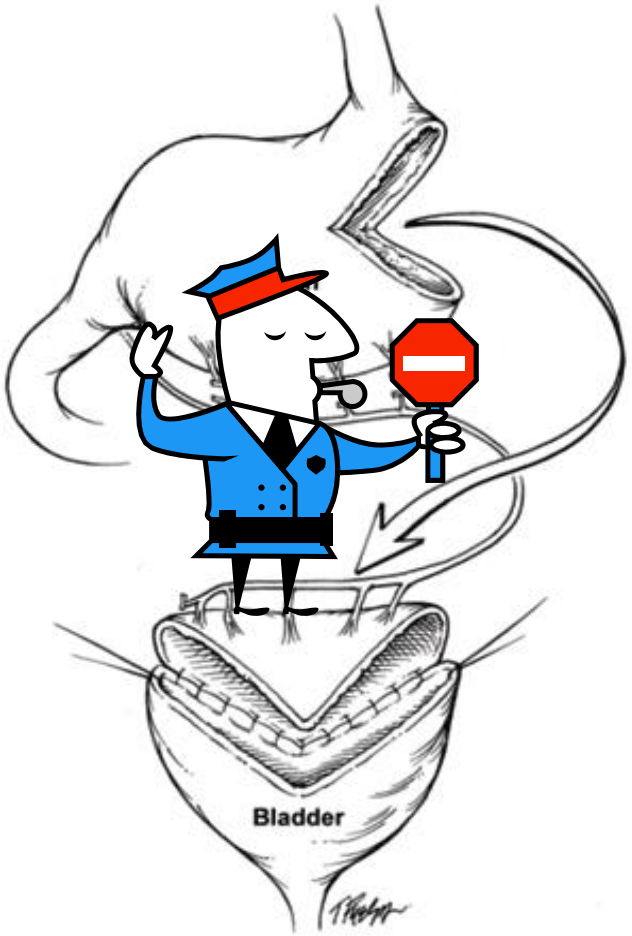


***Figure 2** – The wedge-shaped gastric flap is brought with its blood supply close to the bladder, taking care to avoid twisting of the pedicle (note that all clips are facing the left side of the gastric pedicle).*

Urinary Stress incontinence

- Incontinence of urine when the intra-vesical pressure exceeds the maximum urethral pressure in the absence of detrusor activity.
- Presents as: involuntary leakage on effort or exertion, or on sneezing or coughing.
- During Urodynamics: the involuntary leakage of urine during increased abdominal pressure, in the absence of a detrusor contraction.

NOT A SOLUTION

Surgical treatment SI

1. **Retro pubic urethropexy (Burch)**

* **2. Suburethrtal slings (Advantage tape, TVT-O et al)**

* **3. Retropubic Rectus sheath sling (Pubovaginal Sling).**

* **4. Periurethral Injection**

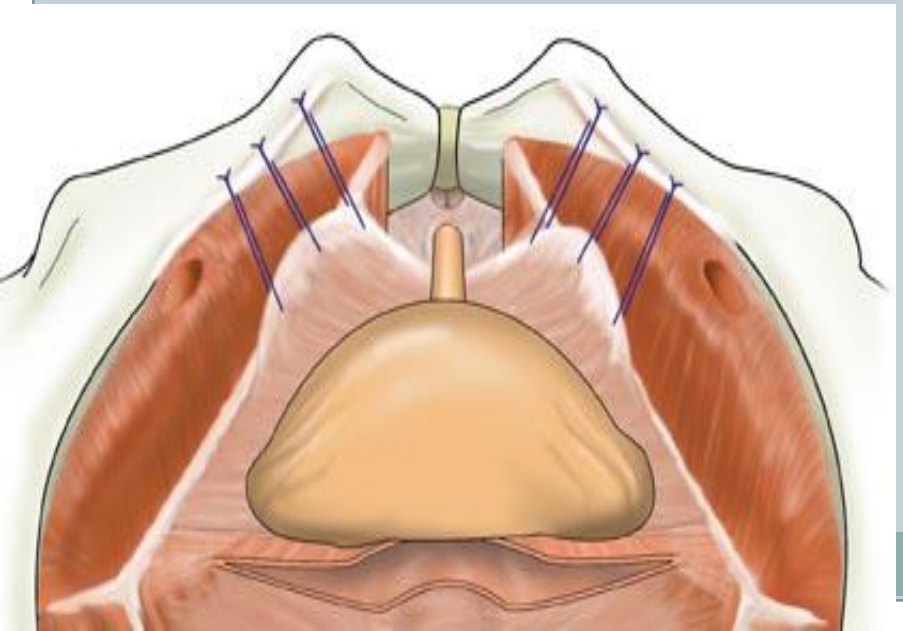
Burch colposuspension

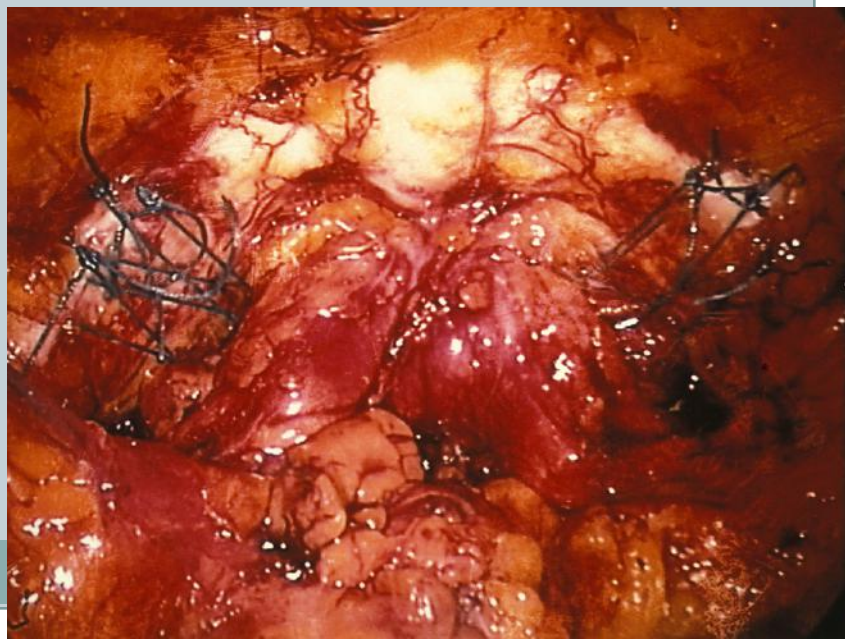
- Gold standard for many years (not now)!

Laparoscopic colposuspension:

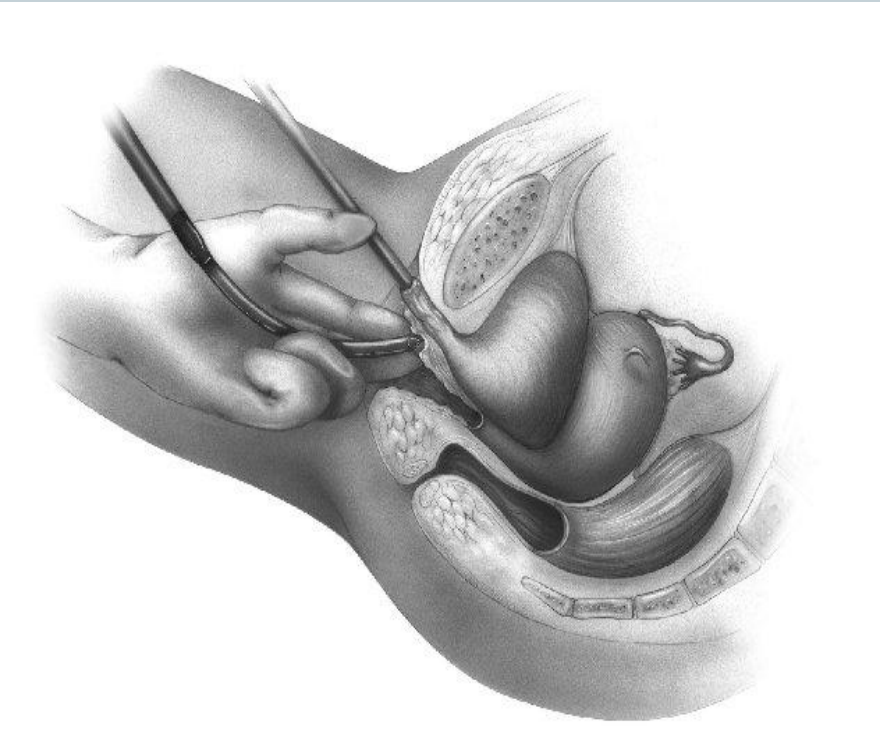
Long learning curve: 35-50 cases
No standardized technique
Suture type, placement and number identical to open
Expensive procedure

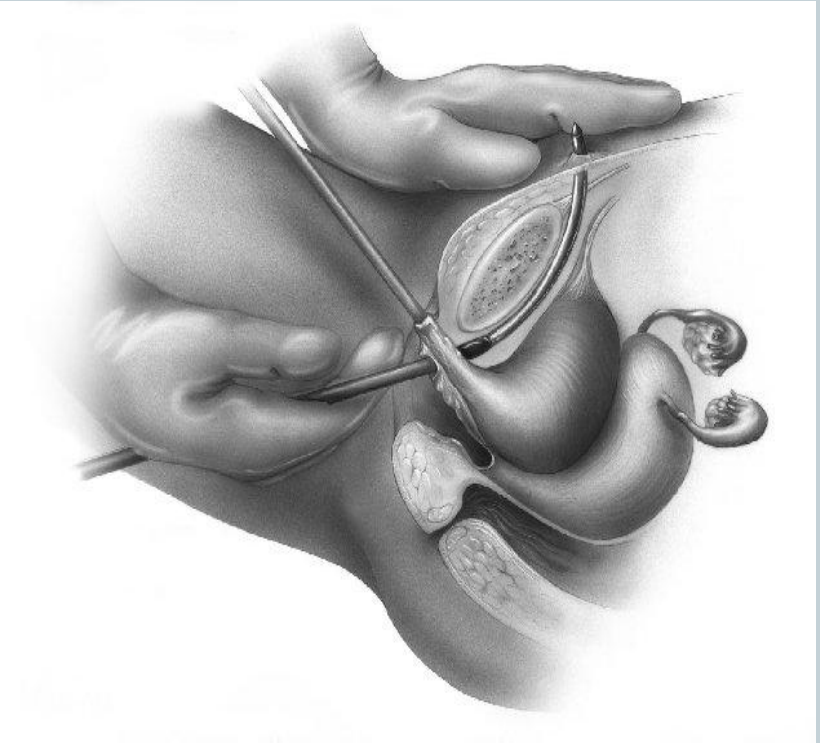
RCT's : LB to be as effective as OB for USI





Retropubic sling : technique





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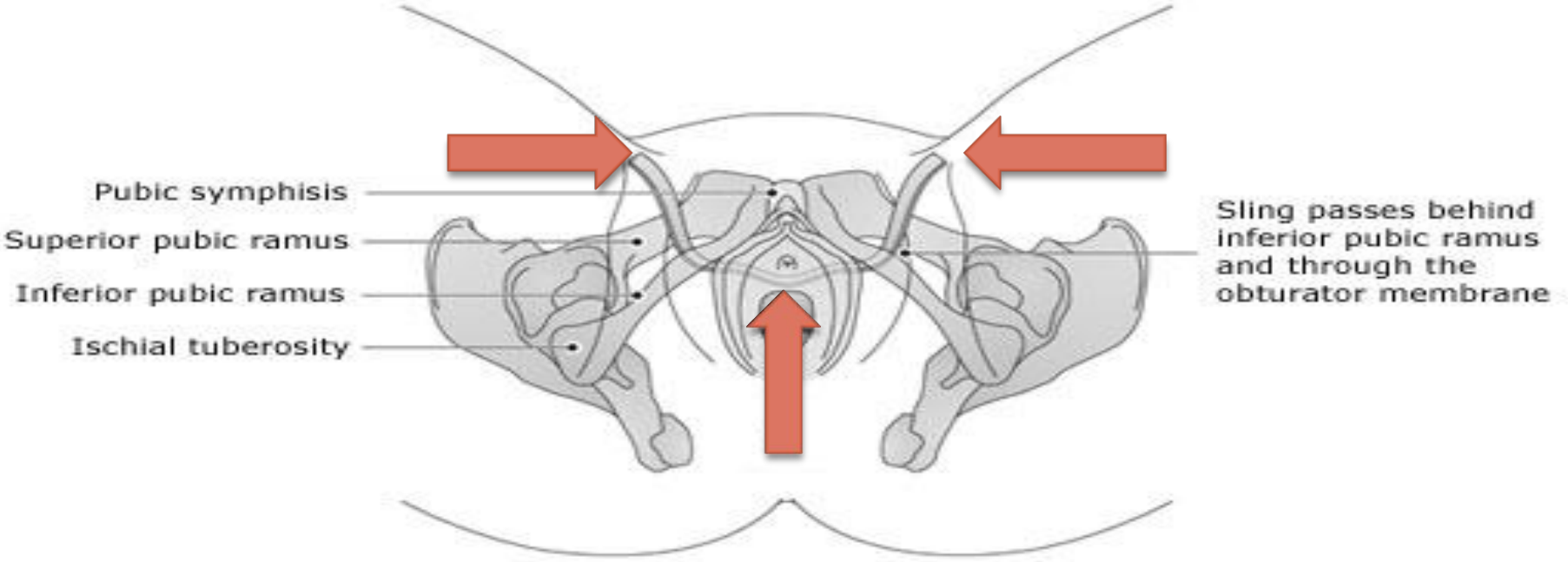
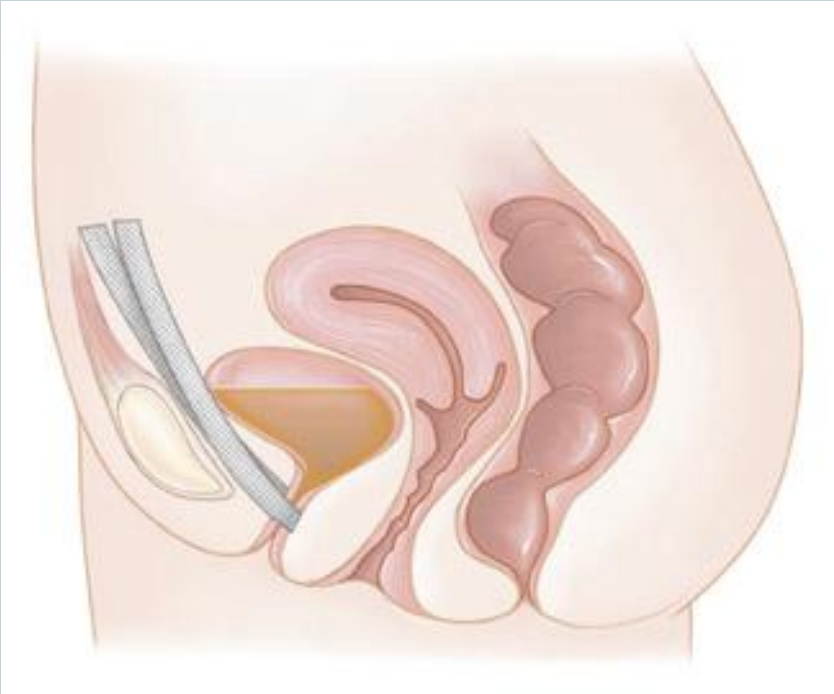
- **3. Retropubic Rectus sheath sling (Pubovaginal Sling).**
- **4. Periurethral Injection**

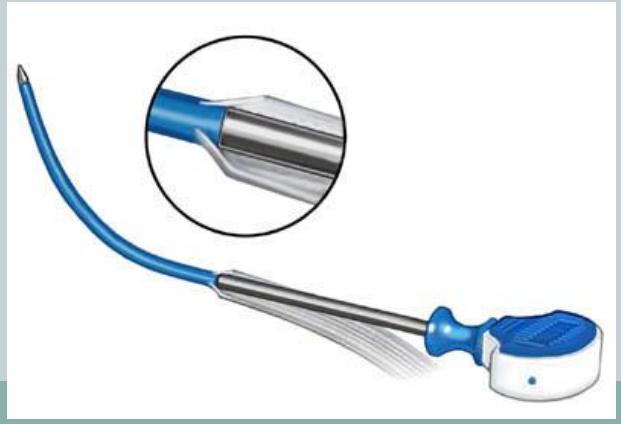
Mid-Urethral Sling



Mid-Urethral sling

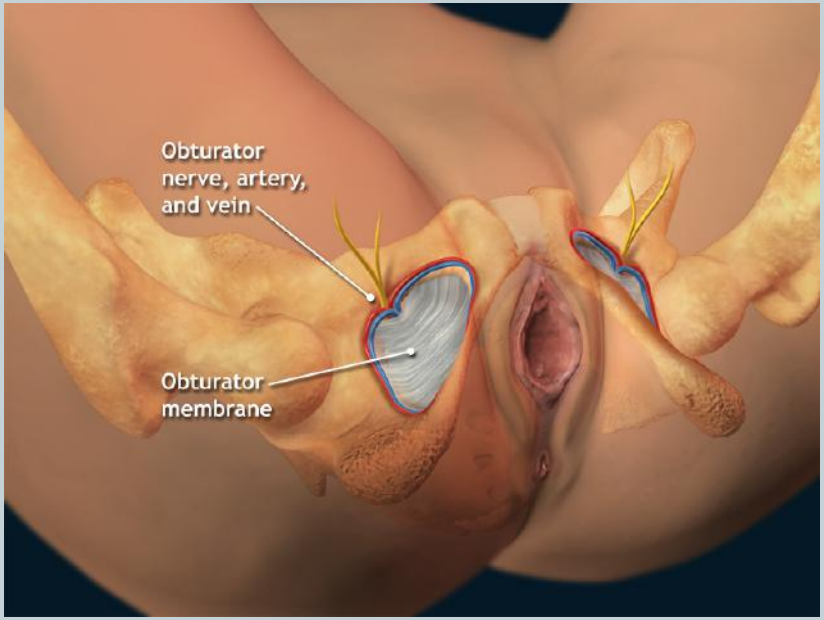


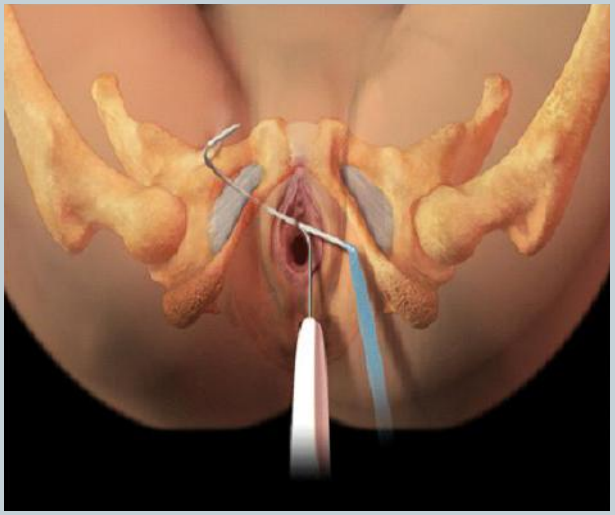
Advantage Tape Fit



Boston Scientific

Transobturator tapes





AUGS statement 2013:

- **Statement of The American Urogynecologic Society and**
- **The Society of Urodynamics, Female Pelvic Medicine and**
- **Urogenital Reconstruction**
- **Position Statement on Mesh Midurethral Slings for Stress Urinary Incontinence**
- ***The polypropylene mesh midurethral sling is the recognized***
- ***worldwide standard of care for the surgical treatment of***
- ***stress urinary incontinence. The procedure is safe, effective, and***
- ***has improved the quality of life for millions of women.***
- .. This procedure is probably the most important advancement in the treatment of stress urinary incontinence in the last 50 years and has the full support of our organizations which are dedicated to improving the lives of women with urinary incontinence.

IUGA Statement June 2014:

- Surgery is generally a more effective treatment than PFMT.[2]
- The FDA publications clearly state that MUS were not the subject of their safety communication.
- There is robust evidence[9-11] to support the use of MUS from over 2,000 publications making this treatment the most extensively reviewed and evaluated procedure for female stress urinary incontinence now in use.
- the results of a recent large multicentre trial[13] have again confirmed the excellent outcomes and low risks of complications to be expected after treatment with MUS. Additionally, long term effectiveness OF UP TO 80% has been demonstrated in studies following patients for up to 17 years.[14-15]

IUGA Statement June 2014:

- In conclusion:
- IUGA supports the use of monofilament polypropylene mid-urethral slings for the surgical treatment of female stress urinary incontinence.

Pregnancy after continence surgery

- There is no consensus on management of pregnancy and delivery in women who have undergone a surgical procedure for treatment of SUI.

- While many patients and clinicians assume that cesarean delivery is the only delivery option in these cases, this has not been established.

In Summery:

- OAB is a rather common health and quality of life problem that faces medical practitioners every day.
- Starts with a question and work up, as it is paving the way towards different options of management.
- It is a multidisciplinary team of health professionals required in managing women with BOA.
- Although there are different treatment modalities with some are less effective than others, it is essential to set the expectation to improve the patients' QOL.

Thank you..