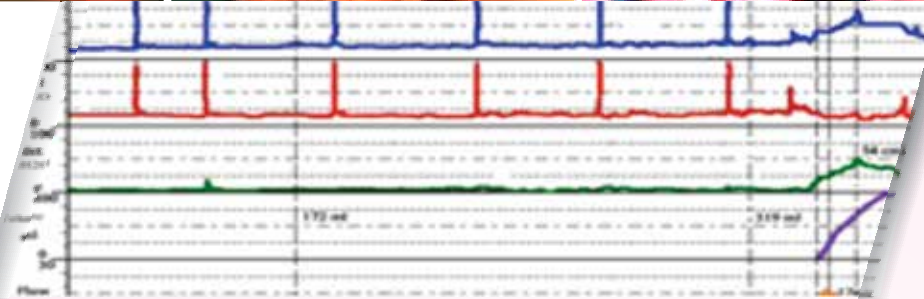




# FOGSI

# FOCUS

## UROGYNECOLOGY



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## PRESIDENT'S MESSAGE



It gives me great pleasure to present to you all, the FOGSI Focus on Urogynaecology. The aim of this FOGSI Focus is to highlight the latest evidence based guidelines, approaches to diagnosis and treatment and protocols for various urogynaecological conditions.

I hope this issue helps you to keep abreast of the latest developments in urogynaecology and give you some valuable tips and pointers which you can implement in day-to-day practice. This can be a ready reckoner for both busy practitioners and academicians to update themselves with current evidence.

The Presidential theme for my FOGSI year 2020 is "Safety first, for Indian women and for FOGSIANS". During the year, we have attempted to focus on academic, social and community health initiatives aimed at improving the profile of women in our country. Even after the challenges faced due to COVID-19 pandemic, FOGSI has been delivering online continuing medical education programmes and conferences and helping our members to perform to the best of their ability in the areas in which they practice.

This FOGSI Focus is a step forward in the academic continuum

I congratulate the editorial team for their hard work and sincere efforts in helping to write, collate, edit and publish this FOGSI Focus.

**DR. ALPESH GANDHI**  
President FOGSI

## SECRETARY GENERAL'S MESSAGE



Urogynecology is one of the most evolving sub-speciality branches. Urogynecological problems are faced by women at every stage of life which affects their personal and social relationships. Due to the recent advances in this field, awareness about the issues related to Urogynecology has now increased.

FOGSI has been forefront in inspiring and imparting knowledge in the field of Obstetrics and Gynecology. This issue of FOGSI Focus describes simplistically all the relevant topic in Urogynecology. All the contributors have done a great job in coming out with this focus especially in these unprecedented times of COVID pandemic and making this Focus very educative. This issue is an interesting read and very beneficial in treating patients.

Hope the FOGSIANS are empowered by reading this and it helps them in increasing their knowledge and practice in urogynecology.

Wishing everyone a Happy New Year 2021.

With Best Compliments  
**DR. JAYDEEP TANK**  
Secretary General FOGSI

## VICE PRESIDENT MESSAGE



It is my proud privilege to present FOGSI Focus on Urogynecology as Vice President Incharge of Urogynecology committee of FOGSI and Editor.

FOGSI has been forefront in inspiring and imparting knowledge in the field of Obstetrics and Gynecology. This FOGSI Focus is dedicated to Urogynecology which is an upcoming subspecialty.

The articles compiled describe concisely all the fundamental concepts of Urogynecology making this Focus very fruitful and educative. This issue will help the FOGSIANS in increasing their knowledge and practice in treating patients with urogynecological problems.

I congratulate Prof J B Sharma, Chairperson FOGSI Urogynaecology committee, Editor for being the main force behind this academic endeavour. He and both his co-editors, Dr Monika Gupta and Dr Rajesh Kumari have put in great efforts to bring out this ready reference on Urogynecology.

I hope it will be of great benefit to all readers.

With best wishes  
DR. RAGINI AGRAWAL  
Vice President FOGSI

## EDITOR'S DESK



I am delighted to write the Editor's desk for FOGSI Focus on Urogynaecological problems. Urogynaecology has emerged and evolved as an important subspecialty of gynaecology as women suffering from urogynaecological problems often require a dedicated and concerted attention which a general gynaecologist may not be able to offer due to time and expertise constraints.

As a chairperson of Urogynaecology committee of FOGSI and encouraged and stimulated by our dynamic President Dr. Alpesh Gandhi and Vice President incharge Dr. Ragini Agarwal, I felt the utmost need of coming out with a dedicated FOGSI focus on urogynaecological problems for the benefit of our esteemed FOGSI colleagues. I am thankful to President FOGSI Dr. Alpesh Gandhi for all the support and stimulus for it and for writing the President's message for the FOGSI Focus. I am grateful to Vice President in charge Dr. Ragini Agarwal for her inspiration, encouragement, contribution of a chapter and Vice President's message for this FOGSI focus. I am thankful to all the eminent and esteemed colleagues from all over the country who have contributed to the various chapters for this FOGSI Focus.

We have articles on "Bladder Pain Syndrome" by Vice President Dr. Ragini Agarwal and "Urinary Tract Infection" by Dr. Mangesh Narvadkar, former chairperson of Urogynaecology Committee which will be very useful to the esteemed readers. The article on "Rectus Fascial Sling" by myself which is of special significance as natural body slings are making a comeback due to short term and long term complications of artificial meshes. A special chapter on "Female Sexual Dysfunction" by Dr Rajesh Kumari from AIIMS, will be useful to the esteemed readers in their clinical practice. We have special contributions on "Basic Work-Up of a Case of Urinary Incontinence" by Dr. Amita Jain, a urogynaecologist from Medanta hospital, Gurugram "Pelvic Organ Prolapse" by Dr. Achla Batra, AOGD Urogynaecology subcommittee chairperson and "Overactive bladder- Management Update" by Dr Monika Gupta from VMMC & Safdarjung Hospital, New Delhi.

We have other chapters "Basics of Urodynamics" by Karishma Thariani and "Rectovaginal Fistula" by Dr. Anuradha Koduri for the interest and use of esteemed FOGSIANS in their clinical practice. "Vesicovaginal Fistula" is a forgotten science but it is very much relevant in developing countries as highlighted by Dr. Subhash Ch. Biswas and Dr. Avishek Bhadra from Kolkata. Drugs have a special place in management of various urogynecological problems. We have a special chapter on "Drugs in Urogynaecology" by none other than Dr. Jagdish Gandhi, Consultant Urogynaecologist, United Kingdom which will immensely benefit the readers.

We hope the esteemed FOGSIANS and readers will find this FOGSI Focus useful in their practice. We apologise for any mistakes. A special thanks to SENORA Division of Sun Pharma for their help in bringing out this dedicated FOGSI Focus in spite of COVID pandemic.

DR. JB SHARMA  
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## Basic Work-Up of Female with Urinary Incontinence

Dr. Amita Jain

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Urinary incontinence (UI) is the complaint of involuntary loss (leakage) of urine. There are two main subtypes of urinary incontinence: stress incontinence (SUI) and urgency incontinence (UUI). According to the International Urogynecological Association (IUGA) and the International Continence Society (ICS) standard definition, SUI is the complaint of urine leakage in association with coughing, sneezing or physical exertion, whereas UUI is the complaint of urine leakage associated with a sudden compelling desire to void that is difficult to defer[1].

Recently the Urological Society of India has issued guidelines on "Non-neurogenic urinary incontinence in adults", taking into consideration of Indian scenario [2] and according to this guideline, a thorough clinical evaluation should be carried out to categorize the type of UI (stress, urgency, mixed or incontinence associated with chronic retention)

Baseline clinical evaluation should include following steps:

### History

The purpose of history taking is to determine the type of urinary incontinence (UI) that is most bothersome to the patient [1, 2]. The history should include questions about the type of incontinence (eg. stress, urge, mixed), precipitating events, frequency of occurrence, severity, pad use, and effect of symptoms on activities of daily living.

Health care providers can use validated questionnaires to evaluate bother, severity, and the relative contribution of UI symptoms. Examples of Validated Urinary Incontinence Questionnaires with good test-retest reliability [3] are

- Urogenital Distress Inventory (UDI)
- Incontinence Impact Questionnaire (IIQ)

- Questionnaire for Urinary Incontinence Diagnosis (QUID)
- Incontinence-Quality of Life Questionnaire (I-QoL)
- Incontinence Severity Index (ISI)
- International Consultation on Incontinence Questionnaire (ICIQ)

A detailed medical and neurologic histories should also be obtained. Certain conditions, such as diabetes and neurologic disorders, can cause UI. In addition, a complete list of the patient's medications (including nonprescription medications) should be obtained to determine whether individual drugs may be influencing the function of the bladder or urethra [4]. Agents that can affect lower urinary tract function include diuretics, caffeine, alcohol, narcotic analgesics, anticholinergic drugs, antihistamines, psychotropic drugs, alpha-adrenergic blockers, alpha-adrenergic agonists, and calcium-channel blockers. Surgical, gynecologic, and obstetric histories should also be elicited.

### Physical Examination

This should include an abdominal examination (eg. any pelvic mass causing pressure effect on bladder, over-distended bladder), a rectal/genitourinary examination (to rule out prolapse, atrophic vaginitis or active vaginal infection etc.), an assessment of lower extremities for edema, neurological examination including assessment of cognitive impairment.

The primary purpose of the physical examination is to exclude confounding or contributing factors to the incontinence or its management. A urethral diverticulum (an out-pouching of the urethral lumen) can produce incontinence or postvoid dribbling. Occasionally, vaginal discharge can be confused with urinary inconti-

nence. Extraurethral incontinence, caused by a fistula or ectopic ureter, is rare but can be seen on examination.

Presence of pelvic organ prolapse (POP) beyond the hymen in all pelvic support compartments (anterior, posterior, and apical) should also be assessed [5, 6]. Pelvic organ prolapse can mask or reduce the severity of SUI symptoms; this is referred to as occult, potential, masked, or hidden SUI. When POP is reduced with a non-obstructing pessary or large cotton swabs, SUI may become apparent or worsen [7].

### Pelvic floor assessment

NICE states poor Inter- and intra-observer reliability of grading systems [EL = 3], however recommends routine digital assessment of pelvic floor muscle contraction before the use of supervised pelvic floor muscle training for the treatment of UI [8].

### Cough Stress Test

SUI should be objectively demonstrated before any anti-incontinence surgery is performed [9-11]. Visualization of fluid loss from the urethra simultaneous with a cough is diagnostic of SUI. Delayed fluid loss is considered a negative cough stress test result and suggests cough-induced detrusor over-activity or UUI. If urine leakage is not observed in supine position, the test needs to be repeated with the patient standing and with a full bladder (or a minimum bladder volume of 300 mL) to maximize test sensitivity.

If still no leakage is observed, physician may need to retrograde fill the bladder until the patient feels bladder fullness or is holding at least 300 mL of fluid and then repeat the cough stress test.

### Assessment of Urethral Mobility

Anti-incontinence surgery is more successful in women with urethral mobility, defined as a 30 degree or greater displacement from the horizontal when the patient is in a supine lithotomy position and straining. Lack of urethral mobility is associated with a 1.9-fold increase in the fail-

ure rate of midurethral sling treatment of SUI [12]. The cotton swab test has been the traditional assessment of urethral mobility [13], but other methods of evaluating urethral mobility include measurement of point Aa of the POP Quantification system, visualization, palpation, and ultrasonography [14-16]. Patients who lack urethral mobility may be better candidates for urethral bulking agents rather than sling or retropubic anti-incontinence procedures.

However, these tests like Q-tip, POP-Q, Bonney, Marshall and Fluid-Bridge tests are not routinely recommended by NICE for assessment of women with UI [3].

### Investigations

**Urinalysis** to rule out Urinary tract infections (UTI,) which should be treated before initiating further investigation or treatment for UI.

**Urine culture** is considered if urinalysis seems unreliable. Only one-third of positive tests are associated with bacteriologically proven UTIs.

### Postvoid Residual (PVR) Assessment

An elevated PVR in the absence of POP is uncommon and should trigger an evaluation of the bladder-emptying mechanism, usually with a pressure-flow urodynamic study.

The sensitivity and specificity of ultrasound (using a bladder scanner) in the detection of PVR, in comparison with catheterisation, is within clinically acceptable limits and former is less invasive with fewer adverse effects.

**Bladder diaries** is useful for patient education, to document baseline symptom and treatment efficacy. Encourage women to complete a minimum of 3 days of the diary covering both working and leisure days. [3]

## Other optional tests

### The pad test

The simplest method of measuring urine loss, by weighing a perineal pad before and after use, was described by Caldwell in 1974 [18]. The pad test is a diagnostic tool that assesses the degree of incontinence in patients in a semi-objective manner.

Pad tests are not recommended by NICE in the routine assessment of women with UI [3]. While EUA recommends it for quantification of UI and to measure objective treatment outcome [GR C], but also states that Home-based pad tests longer than 24 hours [19] provide no additional benefit and a weight gain > 1.3 g in a 24-hour home-based test can be used as a diagnostic threshold for UI [17].

### Multichannel Urodynamic Testing

Invasive urodynamics testing should not be performed before initiating noninvasive treatment. It may also be omitted before surgery in

women with uncomplicated stress UI. All other women should undergo urodynamics before stress UI surgery. It is also recommended in women with urgency UI before invasive therapies [2]. Latest NICE update [3] summarises that Urodynamics should be considered for following indications

- When the diagnosis remains uncertain after history and physical examination,
- When the symptoms do not correlate with physical findings
- After failed previous treatment.
- Early consideration in patients with neurogenic voiding dysfunction, prior history of radical pelvic surgery and pelvic radiation, and those at risk of upper urinary tract deterioration.

**Diagnostic cystoscopy** is not routinely recommended in the evaluation of UI in women [2].

## References

1. Haylen BT, de Ridder D, Freeman RM, Swift SE, Berghmans B, Lee J, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. International Urogynecological Association. International Continence Society. *NeuroUrol Urodyn* 2010;29:4-20.
2. Sinha, S., Agarwal, M. M., Vasudeva, P., Khattar, N., Madduri, V., Yande, S., Sarkar, K., Patel, A., Vaze, A., Raina, S., Jain, A., Gupta, M., & Mishra, N. (2019). The Urological Society of India Guidelines for the Evaluation and Management of Nonneurogenic Urinary Incontinence in Adults (Executive Summary). *Indian journal of urology : IJU : journal of the Urological Society of India*, 35(3), 185-188.
3. NICE Guidance - Urinary incontinence and pelvic organ prolapse in women: management. *BJU Int*. 2019 May;123(5):777-803.
4. Urinary incontinence in women. ACOG Practice Bulletin No. 63. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2005;105:1533-45.
5. Toozs-Hobson P, Freeman R, Barber M, Maher C, Haylen B, Athanasiou S, et al. An International Urogynecological Association (IUGA)/ International Continence Society (ICS) joint report on the terminology for reporting outcomes of surgical procedures for pelvic organ prolapse. *Int Urogynecol J* 2012;23:527-35.
6. Pelvic organ prolapse. ACOG Practice Bulletin No. 85. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2007;110:717-29.
7. Visco AG, Brubaker L, Nygaard I, Richter HE, Cundiff G, Fine P, et al. The role of preoperative urodynamic testing in stress-continent women undergoing sacrocolpopexy: the Colpopexy and Urinary Reduction Efforts (CARE) randomized surgical trial. *Pelvic Floor Disorders Network. Int Urogynecol J Pelvic Floor Dysfunct* 2008;19:607-14.
8. NICE clinical guideline 40: The management of urinary incontinence in women, developed by the National Collaborating Centre for Women's and Children's Health, Issue date: October 2006.
9. Farrell SA, Epp A, Flood C, Lajoie F, MacMillan B, Mainprize T, et al. The evaluation of stress incontinence prior to primary surgery. Urogynaecology Committee, Executive and Council of the Society of Obstetricians and Gynaecologists of Canada. *J Obstet Gynaecol Can* 2003;25:313-24.
10. Nager CW, Brubaker L, Litman HJ, Zyczynski HM, Varner RE, Amundsen C, et al. A randomized trial of urodynamic testing before stress-incontinence surgery. *Urinary Incontinence Treatment Network. N Engl J Med* 2012;366:1987-97.
11. Nager CW. The urethra is a reliable witness: simplifying the diagnosis of stress urinary incontinence. *Int Urogynecol J* 2012;23:1649-51.
12. Richter HE, Litman HJ, Lukacz ES, Sirls LT, Rickey L, Norton P, et al. Demographic and clinical predictors of treatment failure one year after midurethral sling surgery. *Urinary Incontinence Treatment Network. Obstet Gynecol* 2011;117:913-21.
13. Crystle CD, Charne LS, Copeland WE. Q-tip test in stress urinary incontinence. *Obstet Gynecol* 1971;38:313-5.
14. Mattison ME, Simsman AJ, Menefee SA. Can urethral mobility be assessed using the pelvic organ prolapse quantification system? An analysis of the correlation between point Aa and Q-tip angle in varying stages of prolapse. *Urology* 2006;68:1005-8.
15. Dalpiaz O, Curti P. Role of perineal ultrasound in the evaluation of urinary stress incontinence and pelvic organ prolapse: a systematic review. *NeuroUrol Urodyn* 2006;25:301-6; discussion 307.
16. Dietz HP, Wilson PD. The 'iris effect': how two-dimensional and three-dimensional ultrasound can help us understand anti-incontinence procedures. *Ultrasound Obstet Gynecol* 2004;23:267-71.
17. Lucas MG, Bosch JLHR, Cruz FR, et al. EUA Guidelines on Urinary Incontinence, Issue date: Feb 2012.
18. Sutherst J, Brown M, Shower M. Assessing the severity of urinary incontinence in women by weighing perineal pads. *Lancet* (1981) 1:1128-1130.
19. Al Afraa T, Mahfouz W, Campeau L, et al. Review Article, Normal lower urinary tract assessment in women: I. Uroflowmetry and post-void residual, pad tests, and bladder diaries *Int Urogynecol J* (2012) 23:681-685.



## Introduction to Urodynamic

The term urodynamics means observation of the changing function of the lower urinary tract over time. Urodynamics (UDS) forms the cornerstone investigation to assess the function and dysfunction of the lower urinary tract (LUT).(1)

Although a detailed history and clinical examination are usually enough in diagnosing different types of lower urinary tract symptoms (LUTS), urodynamic testing is done with the premise to replicate the patients symptoms in clinical setting, increase the diagnostic accuracy and thereby help in planning of treatment before any invasive interventions. It is also of utility in patients in whom the initial treatments or surgery have failed to relieve the symptoms.

Urodynamics provides an insight into the physiology of bladder storage and voiding function with wide variety of outcomes, which have no meaning by themselves unless coupled with the overall history and examination (1,2). The aim of any invasive UDS test is to reproduce the patient's storage or voiding symptoms and to relate them to any synchronous urodynamic observation.

## Physiology of normal micturition

A prerequisite to performing and interpreting a urodynamic study is having a full understanding of normal lower urinary tract function. The micturition cycle comprises of 2 phases the storage phase and voiding phase (3). A normal bladder due to its property of accommodation fills with no increase in pressure or detrusor contraction. During this phase the bladder outlet is tightly closed with contraction of the extrinsic and intrinsic urethral sphincter. Whereas in the voiding phase the urethral sphincter relaxes along with contraction of

detrusor initiating the process of voiding. The urethral pressure is equal to or more than the intravesical pressure always during the filling phase of bladder. In normal anatomic position the urethral pressure increases with any rise in intraabdominal pressure to prevent leakage of urine. Any abnormality in this well-orchestrated mechanism can lead to LUTS.

## Role of Urodynamics

Before prescribing UDS in any patient the basic question that should be kept in mind is, will the result of the evaluation either alter the management plan or be able to identify a potentially life threatening condition in the patient. That is to say that the study should only be considered in situations where it helps in making the accurate diagnosis or helps in knowing the impact of a disease that has the potential to cause irreversible damage to the urinary tract. The American Urological Association (AUA) in collaboration with the Society for Urodynamics, Female Pelvic Medicine, and Urogenital Reconstruction (SUFU) summarizes the main indications for performing urodynamic studies into following categories (4):

1. To identify or rule out factors contributing to lower urinary tract dysfunction and assess their relative importance.
2. To obtain information about other aspects of lower urinary tract dysfunction.
3. To predict the consequences of lower urinary tract dysfunction on the upper tract.
4. To predict the outcome including undesirable side effects of a contemplated treatment.
5. To confirm the effects of an intervention or understand the mode of action of a particular type of treatment (especially a new one).

6. To understand the reasons for failure of previous treatments for symptoms or for lower urinary tract function in general.

## Types of Urodynamic tests

UDS comprises of a number of tests that individually or collectively can be used to gain information about lower urinary tract function. These tests are summarized below (5):

1. Uroflowmetry: It is the measurement of the rate of urine flow over time. It is also an assessment of bladder emptying and is the only non-invasive test of urodynamics. A normal uroflow is a bell-shaped curve (Figure 1). When the flow rate is reduced or the pattern is altered, this may indicate bladder underactivity or bladder outlet obstruction.

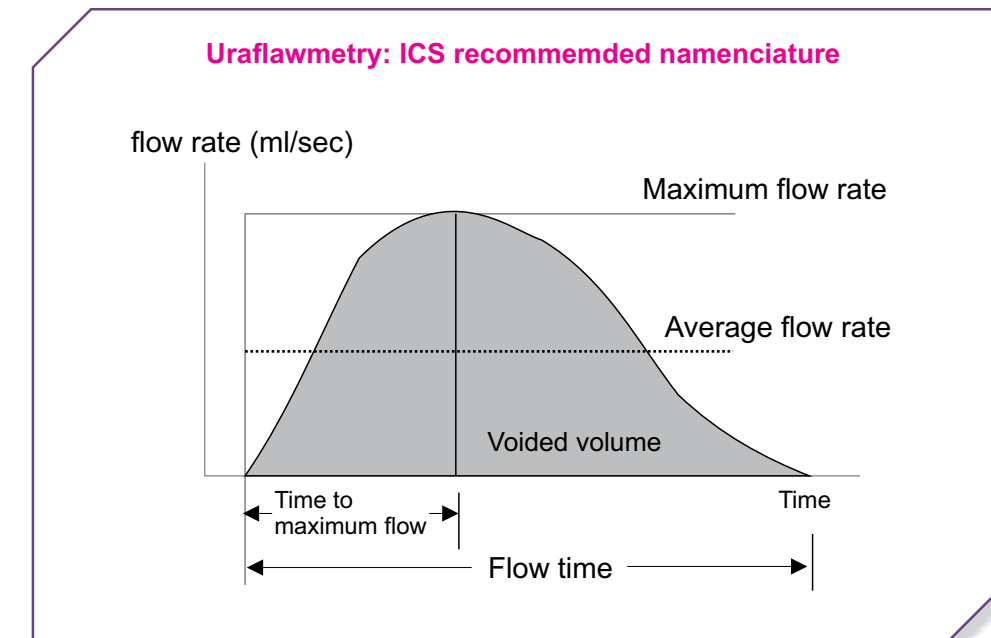


Figure 1: Bell shaped curve of normal uroflow

The 2 phases of standard invasive urodynamic testing include cystometry during the filling phase and a pressure-flow study during the voiding phase. (Figure 2)

2. **Cystometry:** Filling cystometry is the method by which the pressure/volume relationship of the bladder is measured during bladder filling. It is the dynamic measurement of detrusor pressure during the continuous filling of the bladder. It begins with the infusion of fluid into the bladder with a catheter. This can be done as a single channel or multichannel procedure. Multichannel is more reliable and usually preferred as it eliminates the changes in bladder pressure due to raised intraabdominal pressure and is also known as subtracted cystometry. Two pressure transducers are placed in the bladder and rectum to record the intraves-

ical ( $P_{ves}$ ) and intraabdominal pressures ( $P_{abd}$ ) respectively. The bladder is filled at the rate of 50 ml/min with normal saline and  $P_{ves}$  and  $P_{abd}$  are measured continuously and detrusor activity  $P_{det}$  is calculated by subtracting  $P_{abd}$  from  $P_{ves}$  ( $P_{ves} - P_{abd}$ ). It also determines the compliance and the capacity of the bladder. The competence of the sphincter also needs an assessment during any abnormal detrusor contraction that occurs as well as on increasing the intraabdominal pressure by coughing, performing Valsalva maneuver and other activity that reportedly causes incontinence in the patient. Cystometry ends with a micturition command, or "permission to void."

3. **Pressure flow study:** Also known as voiding studies and are the method by which the relationship between pressure in the

bladder and urine flow rate is measured during bladder emptying. Detrusor pressure is measured with a simultaneous measurement of flow. The voiding phase starts when permission to void is given or when uncontrollable voiding begins and ends when the patient considers voiding has finished. Following the pressure-flow study, once again, the post-void residual urinary volume is estimated, and the total cystometric bladder capacity is calculated.

**4. Urethral Pressure Profile** provides the measurement of the urethral length and its competence. It is typically performed in women to help determine the cause of stress urinary incontinence.

**5. Electromyography** records the electrical potentials generated by the pelvic floor muscle activity utilizing surface electrodes.

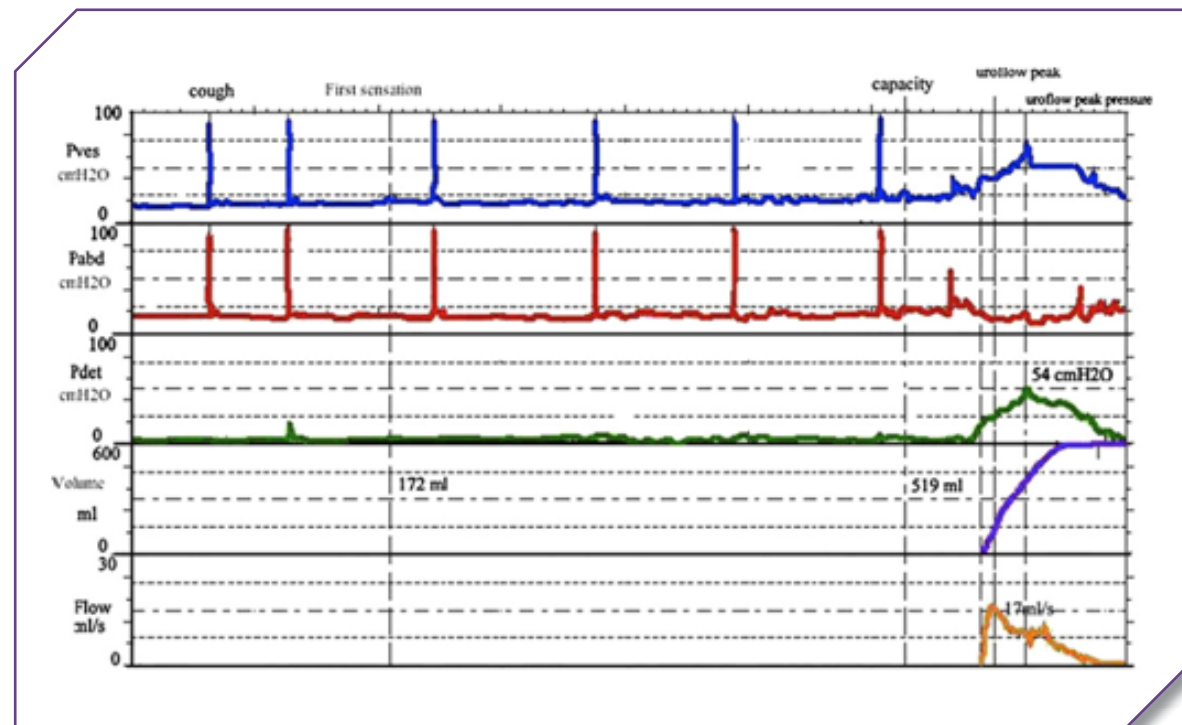


Figure 2: A normal UDS showing all phases of filling cystometry and pressure flow study

### ICS standard urodynamics protocol

Urodynamic tests should be performed with the goal of answering a specific question. "Formulating the urodynamic question" is a process of reviewing the clinical assessment already available and what potential therapy options may subsequently be appropriate, so the test can identify appropriate treatment options and potential adverse effects. Following steps should be followed before performing the invasive testing. (6)

1. Clinical history, including valid symptom and bother score(s) and medication list.
2. Relevant clinical examination (abdominal/pelvic/genital examination, and checking for possible neurological disease or oedema).
3. Three day bladder diary.
4. Representative uroflowmetry with post-void residual (PVR)

### Urodynamic Equipment

The basic requirement of a standard urodynamic system is that it can measure at least two pressures and calculate detrusor pressure (pdet) in real time, defined as the simultaneous difference between intravesical (pves) and abdominal (pabd) pressures. It can measure the flow rate of the voided volume and regulate the rate of fluid infusion. It has an on-line display of pressures and flow, with adequate scale and resolution. Systems using liquid-filled catheters and external transducers are recommended by the ICS. (7) Using ICS standard pressures based on liquid-filled systems allows comparison of data between patients and centres.

The test should ideally be performed in a quiet room with little distractions and keeping the number of observers to minimum so as to minimize patient embarrassment. It is best that the clinician who has evaluated and examined the patient initially, also does the urodynamic testing and designs the test as per the clinical questions in mind.

It is best to explain the procedure in detail to the patient beforehand, use of reading materials and leaflets is encouraged. The test may be performed preferably in sitting position

### Normal Urodynamic Parameters

Invasive UDS warrants insertion of catheters in the patient raising the probability of its non-physiological recording. Therefore these tests are best performed and evaluated by a trained clinician who understands the patient's clinical profile. Several important parameters, such as age, sex, and body mass index, affect urodynamic values, rendering it more challenging to precisely define normality from tests performed on patients (8). Table:1 shows some normal urodynamic parameters.

Urodynamic Parameter	Normal value
First Sensation (ml)	100-250
First Desire to void (ml)	200-330
Strong Desire to void (ml)	350-560
Bladder Compliance (ml/ cm H2O)	≥50
Detrusor activity	Stable
Maximum Cystometric capacity (ml)	450-550
Maximum Flow	13-25 ml/s
Detrusor pressure at maximum flow	18-30 cm H2O
Voided volume	250-600 ml
Valsalva leak point pressure	< 60 cm H2O suggestive of ISD
MUCP	< 20 CM H2O suggestive of ISD
<b>Reporting</b>	

Table 1: Normal range of values of various parameters assessed in urodynamic evaluation

A standard urodynamic report should include the details clinical assessments, along with a urodynamic diagnosis and a management recommendation. Additional details regarding the temperature and type of fluid used, the rate of filling, the size of the catheter, and patient position should also be in the report. (6)

## Complications

Risk of invasive UDS includes:

- UTI
- Urinary retention
- Dysuria
- Pain
- Hematuria

Prophylactic antibiotics reduce the risk of bacteriuria following urodynamic testing, but there is insufficient evidence to suggest it reduces rates of symptomatic urinary tract infections. (9) Therefore current advice is against giving prophylactic antibiotics for invasive urodynamic testing in all patients.

## Clinical significance of UDS

UDS is the gold standard to assess LUTS. However, it is non physiological test which may itself induce abnormal findings. Therefore, it should only be used as an accessory to the history, examination and clinical work up of the patient and not routinely in all cases.

Cochrane review demonstrated that urodynamics affects clinical decision making in women, but there is a lack of similar fitting trials for men and children.(10) Women who undergo urodynamic testing are more likely to have a change made to their management compared to those who do not undergo testing.(10) They are also more likely to receive medical management and less likely to undergo surgical intervention, following a urodynamic investigation.(10) However, the evidence does not show a difference in overall continence rates, nor an improved quality of life, following urodynamics testing.(10)

## References:

1. Wyndaele M, Abrams P. Urodynamics in Female Urology. *Eur Urol Suppl.* 2018;17(3):91-9
2. Serati M, Cattoni E, Siesto G, et al.: Urodynamic evaluation: Can it prevent the need for surgical intervention in women with apparent pure stress urinary incontinence? *BJU Int.* 2013; 112(4): E344–50.
3. Lenherr SM, Clemens JQ. Urodynamics: with a focus on appropriate indications. *Urol Clin North Am.* 2013 Nov;40(4):545-57. doi: 10.1016/j.ucl.2013.07.001. Epub 2013 Aug 8. PMID: 24182974.
4. Collins CW, Winters JC; American Urological Association; Society of Urodynamics Female Pelvic Medicine and Urogenital Reconstruction. AUA/SUFU adult urodynamics guideline: a clinical review. *Urol Clin North Am.* 2014 Aug;41(3):353-62, vii. doi: 10.1016/j.ucl.2014.04.011. PMID: 25063591.
5. Schäfer W, Abrams P, Liao L, Mattiasson A, Pesce F, Spangberg A, Sterling AM, Zinner NR, van Kerrebroeck P; International Continence Society. Good urodynamic practices: uroflowmetry, filling cystometry, and pressure-flow studies. *Neurourol Urodyn.* 2002;21(3):261-74. doi: 10.1002/nau.10066. PMID: 11948720.
6. Drake MJ, Doumouchtsis SK, Hashim H, Gammie A. Fundamentals of urodynamic practice, based on International Continence Society good urodynamic practices recommendations. *Neurourol Urodyn.* 2018 Aug;37(S6):S50-S60. doi: 10.1002/nau.23773. PMID: 30614058.
7. Rosier PFWM, Schaefer W, Lose G, Goldman HB, Guralnick M, Eustice S, Dickinson T, Hashim H. International Continence Society Good Urodynamic Practices and Terms 2016: Urodynamics, uroflowmetry, cystometry, and pressure-flow study. *Neurourol Urodyn.* 2017 Jun;36(5):1243-1260. doi: 10.1002/nau.23124. Epub 2016 Dec 5. PMID: 27917521.
8. Mahfouz W, Al Afraa T, Campeau L, Corcos J. Normal urodynamic parameters in women: part II--invasive urodynamics. *Int Urogynecol J.* 2012 Mar;23(3):269-77. doi: 10.1007/s00192-011-1585-y. Epub 2011 Oct 20. PMID: 22011933.
9. Foon R, Toozs-Hobson P, Latthe P. Prophylactic antibiotics to reduce the risk of urinary tract infections after urodynamic studies. *Cochrane Database Syst Rev.* 2012 Oct 17;10:CD008224. doi: 10.1002/14651858.CD008224.pub2. PMID: 23076941.
10. Clement KD, Lapitan MC, Omar MI, Glazener CM. Urodynamic studies for management of urinary incontinence in children and adults. *Cochrane Database Syst Rev.* 2013 Oct 29;2013(10):CD003195. doi: 10.1002/14651858.CD003195.pub3. PMID: 24166676; PMCID: PMC6599826.

# Overactive Bladder : Management Update

Dr. Monika Gupta

The term Overactive bladder (OAB) as defined by the international continence society (ICS) is “urinary urgency, usually accompanied by frequency and nocturia, with or without urgency incontinence, in the absence of urinary tract infection or other obvious pathology”.1,2,3 Basically, it is a clinical diagnosis and the absence of urgency rules out the diagnosis. OAB has got two types, it is termed as “OAB wet” when accompanied by urge incontinence, whereas without incontinence it is called “OAB dry”.4

There are various bladder related conditions interfering with the diagnosis of OAB being only slightly different from each other. One such disorder is detrusor overactivity which is more of an urodynamic observation as it is defined as the occurrence of involuntary contractions during filling cystometry on a urodynamic study.4 Another condition which needs to be appreciated is urge incontinence which is involuntary leakage of urine preceded by a strong desire to pass urine.

## Prevalence

OAB is an age dependent disorder which is reflected in its overall prevalence of 12-17% in adults which further increases with age being as high as 19% in age group of 65-74 years.4 “OAB wet” is more prevalent in women and “OAB dry” is more prevalent in men. Pregnancy causes relative weakness of the bladder neck and urethral sphincter mechanism which predisposes women to higher risk of OAB wet. OAB affects quality of life with nocturia causing sleep disturbances and thus reducing work efficacy apart from negative impact on sexual life.

## Pathophysiology and Etiology

The mechanism of bladder continence involves a strong interplay between the parasympathet-

ic and sympathetic systems. The sympathetic innervation to the bladder arising from the thoraco-lumbar region of the spinal cord (T1-L2) is via the hypogastric nerve and it relaxes the detrusor muscle of the bladder via the beta-adrenergic receptors during the filling phase of the bladder.4,5,6

The parasympathetic system (S2,3,4) comes into play during micturition phase when the pelvic nerve acts via the muscarinic receptors and causes detrusor contractions to evacuate the bladder. There are 5 subtypes of muscarinic receptors in the bladder out of which M2 (80%) and M3 (20%) receptors are the pre-dominant ones.4,5,6

The understanding of these complex neuro-circuits have a role in developing pharmacotherapy for the treatment of OAB.7,8 And, due to same reason, OAB is found to be associated with various neurological disorders like Multiple sclerosis, Parkinson’s disease and cerebrovascular disorders.8,9

The most common aetiology of OAB is idiopathic which can be explained by two hypotheses, i.e., neurogenic and myogenic hypothesis. The neurogenic hypothesis explains that detrusor overactivity arises from generalized nerve mediated excitation of the detrusor muscle, while the myogenic hypothesis states that overactive detrusor contractility results from a combination of an increased spontaneous excitation potentials within detrusor muscle and enhanced propagation of contractile signals via cell to cell coupling.9,10

Various risk factors for OAB are aging, neoplasia, spinal cord injury, bladder outlet obstruction and pelvic and anti-incontinence surgery, advanced pelvic organ prolapse, psycho-somatic diseases, urine in proximal urethra, detrusor overactivity with impaired contractility, diabetes mellitus and vaginal delivery.

## OAB Management

Diagnosis of OAB is based on a careful history, physical examination and urine analysis.<sup>11</sup> The supportive investigations include post void residual urine volume and 3 day bladder diary being the most relevant ones followed by cystoscopy and urodynamic studies in case of complications. One should evaluate the impact of OAB symptoms on quality of life treatment must be aimed at improving the same.

### 1. Detailed history taking should include

- number of episodes of leaking in a day/ on the way to washroom
- usage of pads in the underwear to avoid soakage of clothes
- detailed gynaecological and past obstetric histories
- medical conditions like diabetes mellitus, closed angle glaucoma & neurological conditions
- past surgeries and radiotherapy
- intake of bladder irritants like tea, coffee, alcoholic drinks, acidic foods and drinks
- excessive intake of water/fluids
- additional information as regards POP (Pelvic organ prolapse), defecatory dysfunction and sexual dysfunction
- drug history of medications like intake of diuretics and alpha agonist

### 2. Questionnaires<sup>4</sup>

These are various validated tools for the assessment of severity of urinary incontinence and evaluation of quality of life. Health related quality of life (HRQOL), (UDI-6) Urogenital Distress Inventory and the Incontinence impact questionnaire (IIQ-7) encompasses the urinary domain component of the pelvic floor distress inventory (PFDI-20) and the pelvic floor impact questionnaire (PFIQ-7).

### 3. Bladder diary<sup>4</sup>

It is a 3 day assessment tool for the quantification and keeping record of OAB symptoms. NICE has also recommended this for the initial assessment of women with suspected bladder symptoms. It includes details about:

- Number and types of episodes of urinary incontinence
- frequency of voiding
- Exact voided volumes (recorded by a 'hat' placed in the toilet)
- Quantity of fluid intake and urine output

### 4. Physical examination<sup>8</sup>

A thorough general, physical, neurological & pelvic examination should be done and make note of:

- BMI (as obesity contributes to incontinence)
- Extremities (Evaluate for edema, which can increase nocturia, especially in elderly patients)
- Neurologic (In cases of associated neurological symptoms, test anal wink reflex, bulbocavernosus reflex, and perineal sensation)
- Abdominal (Palpate for masses or enlarged bladder to rule out any bladder outflow tract obstruction)
- Pelvic (Rule out Pelvic organ prolapse, or weakened pelvic floor, cystocele, vaginal atrophy suggesting hypoestrogenemia)

### 5. Laboratory evaluation<sup>7</sup>

- Urinalysis – to rule out urinary tract infection, haematuria, dehydration or excessive fluid intake (specific gravity normally-1.010-1.025)
- Measurement of Post Void Residual urine (PVR)
- Urodynamics (UDS)<sup>5</sup>- according to AUA (American Urological Association)/ SUFU

(Female Pelvic Medicine and Urogenital Reconstruction), urodynamics is not mandatory for those females who have a clear-cut clinical diagnosis of OAB and those without any associated neurological diseases. The management of such women is started irrespective of UDS findings. NICE guidelines advocate the use of filling and voiding cystometry in women with suspected detrusor overactivity, voiding dysfunction, anterior prolapse and in those who have had SUI surgeries. In case of diagnostic dilemma, video urodynamics can be considered, as it provides more important anatomical information about the appearance of the bladder and bladder neck (often open in women with SUI). The characteristic finding of OAB on UDS is presence of uninhibited detrusor contractions or detrusor overactivity (DO).

**Differential Diagnoses for OAB** has to be carefully ruled out viz. urinary tract infection, stress urinary incontinence, atrophic vaginitis, pelvic organ prolapse, post-surgical incontinence, neurogenic bladder, bladder diseases like bladder stone/ malignancy, diabetes mellitus, recent pelvic surgeries, female urethral stricture.

### 6. Treatment

The treatment plan can be divided into first line- conservative, second line- pharmacotherapy and third line being surgical therapy.

#### A. Conservative management<sup>5</sup>

- **Lifestyle and behavioural modifications** which are under patient's self-control along with minimal side effects. A minimum period of 3 months has to be observed for the effects to be manifested and once achieved, the effects are even longer lasting than pharmacotherapy itself.
- Weight reduction- even 5% reduction in weight decreases incontinence episodes by 50%.
- Avoidance of certain food/drinks which are bladder irritants irritate like caffeinated products, alcohol, acidic and spicy products.
- Cessation of Smoking

- Fluid restriction in patients taking excessive amount of fluids to 6-8 ounce glasses of fluid each day.
- Management of constipation
- Watch over drug intake affecting the bladder function and the continence mechanism like Anticholinergics, Antihistaminics, Beta-blockers, Calcium channel blockers, NSAIDs, Diuretics, Alpha-Blockers, Oral estrogen/Transdermal estrogen, Antipsychotics
- Electrical stimulation of Posterior Tibial Nerve
- **Pelvic Floor Muscle Training (Kegel Exercises)**

These are the first line conservative therapy for all types of Incontinence. Based on the principle of strength training, they involve periodic contractions of the pelvic floor muscles by squeezing and releasing them. These contractions voluntarily suppress the detrusor contractions by tightening the pelvic floor.

The basic regimen is set of 10 contractions 3 times per day. Improvement can be noticed after 6-12 weeks of exercise. The best way of doing Kegels exercises is during lying down but it can be performed anywhere even during sitting and watching television or talking on telephone. The correct technique can be taught to the patients by manual feedback (palpating the pelvic muscles during the exercise) and bio-feedback (using a vaginal or anal device that provides visual or audio feedback about the pelvic muscle contraction).

#### • Bladder Training

It is another appropriate first line treatment for urgency urinary incontinence. It aims at prolonging the interval between each voiding episode gradually by 2-4 hrs. The woman should be motivated to hold urine for longer periods to keep the schedule., i.e. 15-30 minutes every 1-2 weeks.

• **Combined Kegel exercises and Bladder Training** - is more effective than either modality alone.

- **Electrical and Magnetic stimu-**

**lution of Pelvic floor muscles** - a vaginal or anal electrode can be used in those women who fail to contract their pelvic floor muscles voluntarily. It can be done in two 15 minutes sessions daily for 12 weeks.

### B. Pharmacological Therapy<sup>8</sup>

It forms the second line treatment of OAB, to be added in case of no response to conservative management. But the use of drug therapy gets limited by the side effects of these drugs. There are two groups of medications that are in practice- anticholinergics and beta- adrenergic agonists. Anticholinergics have higher rates of side effects and discontinuation rates. Mirabegron – a beta-3 adrenergic agonist is the newest class of drugs to be approved by FDA in 2012 with lesser side effects.

#### Anticholinergic/ Antimuscarinic drugs

There are 5 subtypes of muscarinic receptors in the bladder of which M2 and M3 are the predominant ones. These drugs inhibit the acetylcholine mediated involuntary detrusor contractions both in the filling/storage phases, reduces the sensory input and increases the bladder capacity and thus, incontinence (Table 1). Antimuscarinic drugs are broadly classified into - Tertiary Amines and Quaternary Amines.

Tertiary Amines – are more lipophilic than Quaternary Amines and hence can pass across blood brain barrier more readily. (e.g. Oxybutynin, Tolterodine, Solifenacin, Darifenacin ). They are metabolized via cytochrome P450 enzyme system. So, risk of drug interaction is there in patients receiving other drugs which have same route of metabolism.

Quaternary Amines –cross the blood brain barrier minimally as they are less lipophilic and majority is excreted unchanged from the kidney. (e.g. Trospium chloride)

Darifenacin is the most selective M3 receptor antagonist. It has a higher degree of M3/M2 selectivity.

Antimuscarinics have been shown to be more effective than placebo in terms of mean change in the number of urgency episodes/day, number of Incontinence episodes / day, number of micturitions/day and volume voided per micturition (13-40 ml). Efficacy of all anti-muscarinics

are almost similar. Patients with more severe symptoms have on an average, greater symptom reduction experience. Extended release preparations should be used as much as possible. With typical efficacy of 40-60%, rates of achieving continence range between 5- 59%.

Duration of treatment is at least 3 months to see the complete response although improvement in symptoms could be seen after first week only. 50% of the patients discontinue taking medications by the end of 3 months because of the anticholinergic side effects like; dry mouth, pruritis, constipation, urinary retention, cognitive effects, visual impairment, increase in heart rate, etc.

If there is inadequate symptom control on using one class of antimuscarinics, then a dose modification or a different anti-muscarinic or a beta-3 adrenergic receptor agonist may be tried.

**Table 1: Various available Antimuscarinic drugs**

	Oxybutynin	Tolterodine	Solifenacin	Darifenacin	Trospium chloride
Chemical structure	Tertiary amine	Tertiary amine	Tertiary amine	Tertiary amine	Quaternary amine
Receptor selectivity	Non selective	Non selective	M3 selective	M3 selective	Non selective
Route	Oral Transdermal (patch or gel)	Oral	Oral	Oral	Oral bioavailability only 10%
Dosing	5 mg 3 times Day	1-2 mg Twice Day	5-10 mg/Day	7.5-15 mg/Day	20-60 mg/Day
Half life	2 hours patch 8 hrs ER 12 hrs	2 hours ER 9 hrs	45 -86 hours	13-19 hours	12-20 hours
Metabolism	Hepatic	Hepatic	Hepatic	Hepatic	60% Excreted unchanged in urine
Side effects	Transdermal has less side effect	•Dry mouth •Constipation •Blurred vision	Dry mouth Constipation	Dry mouth Constipation	Lower risk of CNS side effect
FDA Approval	Yes	Yes	Yes	Yes	Yes

### Beta-3 Adrenergic Agonist – Mirabegron

Beta 1, 2 and 3 adrenergic receptors are present in the human bladder urothelium and detrusor muscle, of which beta -3 is the predominant. These drugs help in bladder relaxation by activation of adeny cyclase. Mirabegron was approved by FDA in 2012 for the indication of OAB.

The usual prescribed dose is 25- 50 mg/day. The efficacy rate is similar to Antimuscarinics with a lower rate of dry mouth. It can be considered as an important replacement for antimuscarinics with better tolerability and lesser side effects profile. The only contraindication of this drug is uncontrolled hypertension of 180/110 mm Hg

A refractory patient is someone who failed a trial of symptom appropriate behavioural therapy of sufficient length (8-12 weeks) and who has failed a trial of at least one anti muscarinic medication administered for 4-8 weeks. Failure

of an anti-muscarinic medication may include either lack of efficacy and/or inability to tolerate adverse drug effects.

### C. Botulinum Toxin in OAB

It is the third line of management of OAB. The basic mechanism is the inhibition of Acetylcholine release from the presynaptic nerve terminal and thus suppression of detrusor contractions. Also, it alters urothelial sensory afferent pathway and prevents hypersensitivity responses. There are two types of botulinum toxins:

Onabotulinumtoxin Type A (BOTOX, Allergan, Inc; Irvine, CA, USA)

Abobotulinumtoxin Type A (Dysport, Ipsen. Biopharm)

Onabotulinum toxin type A is a more acceptable option for OAB as Abobotulinum causes more of urinary retention requiring self-catheterization. 100 U of Onabotulinum toxin type A is injected at average of 15-20 sites in bladder cystoscopically avoiding trigone; 5 U each sep-

arated by 1cm each. Mean duration of symptom relief is 6.3-10.6 months. There is significant reduction in urgency, frequency and urge incontinence. Complications like urinary retention, urinary tract infections and intermittent self-catheterization could be seen with botulinum use, especially with higher doses.

#### D. Surgical Neuromodulation<sup>10</sup>

The basic principle is alteration of reflex pain pathways with the use of vaginal or anal stimulators and and percutaneous stimulators of posterior tibial nerve, which shares a common nerve root with the innervation of bladder. Neuromodulation of pudendal nerve eases out the mechanism of voiding by releasing of abnormal guarding reflexes both at the level of the brainstem and the bladder. Simultaneously, there is activation of pelvic efferent hypogastric sympathetic nerves which maintains continence.

There are two types of neuromodulation:

- Implanted sacral nerve stimulator (Interstim)

This device targets S3 and includes an IPG (Implantable Pulse Generator) implanted in buttocks. It is inserted in two phases – test phase and the implantable phase. Success has been defined as 50% or greater reduction in symptoms. If test phase reports >50% symptom reduction after 3-4 weeks, then it is finally implanted with a long term battery and a neurostimulator in the buttock and lower back. Safety profile of Interstim is excellent with minimum side effects- infection and chronic pain. Success rate is 56-68%, upto 80% with p<0.001.

- Percutaneous tibial nerve stimulation<sup>10</sup>

A 34 G needle is placed 5 cm above the medial malleolus to access the posterior tibial nerve and cause stimulation of L4 to S3 nerve roots. It can be done in office setting for a period of 30 minutes every weekly for 12 weeks with subsequent monthly treatments.

#### E. Other treatments

- Intravaginal Estrogen
- Extracorporeal magnetic innervation<sup>10</sup> - used for mild incontinence
- Diversion Clam Ileocystoplasty<sup>3</sup> - augmen-

tation procedures, especially for patients with neurogenic detrusor<sup>3</sup>

#### F. Alternative Therapy-

Those who are not ready for treatment have been also shown to benefit from Acupuncture

Newer drugs currently under research are monoamine reuptake inhibitors, serotonin receptor acting agents, agents acting on NO/cyclic Guanosin Monophosphate Pathway(cGMP), PG Receptor antagonists

Treatment of OAB is basically a multimodal approach and usually, a combination of therapies will benefit the patients. The success here is defined mainly by relief of symptoms rather than cure. So, the primary aim remains management of symptoms and improvement of quality of life.

#### References

1. Haylen BT, de Ridder D, Freeman RM, et al. An International. Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. *Neurourol Urodyn.* 2010; 29(1):4-20.
2. Abrams P, Cardozo L, Griffiths D, Rosier P, Ulmsten U, et al. The standardization of terminology of lower urinary tract function:report from the Standardization Subcommittee of the International Continence Society. *Neurourol Urodyn.* 2002; 21:167-78.
3. Lucas MG, Bedretdinova D, et al. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline. *J Urol.* 2012;188:2455-63.
4. National Institute for Health and Care Excellence. Urinary incontinence: the management of urinary incontinence in women. CG171. 2013. [www.nice.org.uk/Guidance/CG171](http://www.nice.org.uk/Guidance/CG171).
5. Lucas MG, Betredinova D, Bosch JRHL, Burkhard F, Cruz F, Nambiar H, et al. Guidelines on urinary incontinence. Accessed from: [www.uroweb.org/wp-content/uploads/EUA-Guidelines-Urinary-Incontinence-2015.pdf](http://www.uroweb.org/wp-content/uploads/EUA-Guidelines-Urinary-Incontinence-2015.pdf).
6. Noblett KL. Overactive Bladder. In: A Tamisselvi; Ajay Rane. Principles and Practice of Urogynecology. Springer Pvt Ltd.
7. Hersh L, Salzman B. Clinical management of urinary incontinence in women. *Am Fam Physician.* 2013;87(9):634-40.
8. Wood LN, Anger JT. Urinary incontinence in women. *BMJ.* 2014;349:g4531. doi: 10.1136/bmj.g4531.
9. Wein AJ, Kavoussi LR, Novick AC, Partin AM, Peters CA. Urinary incontinence and pelvic prolapse: epidemiology and pathophysiology. In: Wein AJ, ed. Campbell-Walsh urology. 10th ed. Elsevier Saunders, 2012:1871-95.
10. Gormley EA, Lightner DJ, Burgio KL, Chai TC, Clemens JQ, Culin DJ, et al. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline. *J Urol* 2012;188(6 suppl):2455-63.

## Stress Urinary Incontinence: Surgical Management

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Surgical management for SUI can be offered to women for (a) uncomplicated SUI when conservative management has failed or (b) predominant stress-component of mixed urinary incontinence (after appropriate treatment of the urge component).

In women with mixed urinary incontinence, consider an initial trial of medication for Urge Urinary Incontinence (UUI) regardless of the dominant symptom. Inform women with MUI about the unpredictable long- term resolution of urgency symptoms, even after surgical management. The decision for the choice of surgery is made after evaluating the following:-

- Relative degree of Urethral Hypermobility and ISD (intrinsic sphincter deficiency)
- Previous trial of conservative treatment
- Need for concomitant surgeries like genital prolapse, hysterectomy or fistula repair
- Patient's life style: Sedentary/heavy physical activity
- Age and overall medical condition of patient
- Previous pelvic or retropubic surgery
- Previous abdominal surgery or mesh hernia repair
- Previous fractured pelvis or road traffic accident or problems with hip abduction.

Discuss the potential for failed correction, intra-operative injury, postoperative retention, erosion, infection or voiding dysfunction. Women should be advised regarding risks and prognosis of different procedures so that an informed decision can be made.

Various options of surgical procedures include the following:

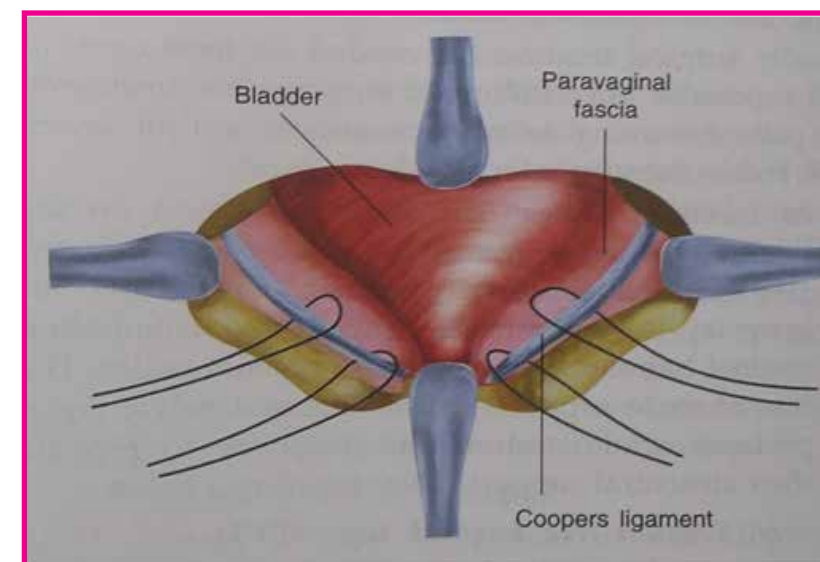
- Retropubic colposuspension
- Burch (Open/ Laparoscopic/ Robotic)
- Marshall- Marchetti- Krantz procedure
- Paravaginal defect repair
- Tension-free mid-urethral slings (MUS) / synthetic tapes (TVT, TVT-O, Mini Arc sling)
- Biological bladder neck (autologous) slings Anterior colporrhaphy with Kelly's stitch, needle suspensions (Pereyra, Stamey), paravaginal defect repair and the Marshall-Marchetti-Krantz procedure for the treatment of SUI are no longer offered as per latest recommendations.

**Retropubic Colposuspension** aims to suspend and stabilize the anterior vaginal wall, and thus the bladder neck and proximal urethra in a retropubic position. This prevents their descent during raised intra abdominal pressure and allows urethral compression against a stable suburethral layer. Selection of a retropubic approach (versus vaginal approach) depends on many factors, such as the need for laparotomy, or laparoscopy for other pelvic prolapsed or disease, the amount of pelvic organ prolapsed, status of intrinsic urethral sphincter mechanism, age and health status of the patient, history of previous sling or mesh complications, desire for future fertility, preference or expertise of the surgeon and preferences of the informed patient.

Type of procedure	Transfixation site
Marshall- Marchetti- Krantz (1949)	Periosteum of the pubic symphysis
Burch colposuspension (1961) (Gold standard)	Ileo-pectineal (Cooper ligament)ligament
Paravaginal (White, 1909)	Arcus tendinus fascia pelvis
Vaginal obturator shelf (Turner- Warwick 1986)	Obturator internus fascia

**Burch colposuspension** In this procedure, after the retropubic space is entered, the urethra and anterior vaginal wall are depressed. The surgeon's non-dominant hand is placed in the vagina, palm facing upward, with the index and middle fingers on each side of the proximal urethra. Using non-absorbable sutures (Prolene no. 1), two sutures are placed bilaterally, at the level of the bladder neck and lateral to the proximal third of the urethra. When placing the sutures, one should take full-thickness of vaginal wall, with the needle parallel to the urethra. All the four sutures are now passed

through the Cooper's ligament so that all four suture ends exit above the ligament. When tying the sutures, one does not have to be concerned about whether the vaginal wall meets the Cooper's ligament, as the cure mainly depends upon the fibrosis and scarring of peri-urethral and vaginal tissues over the obturator internus and levator fascia than on the suture material itself.



Diagrammatic representation of Burch's colposuspension

The Cochrane review from 2012 concluded that continence rates at 1 year are 85%- 90%, and at 5 years are about 70%. This was earlier considered as the gold standard treatment for SUI. Conditions that decrease the chance of cure of incontinence after retropubic colposuspension are greater baseline urge incontinence, hypoestrogenic state, obesity, prior hysterectomy, prior procedures to correct SUI, more advanced prolapse and intrinsic sphincter deficiency. Complications include voiding difficulty (10.3%), de novo detrusor overactivity (17%), and genitourinary prolapse (enterocele, cystocele, or rectocele; 13.6%)

**Laparoscopic retropubic colposuspension** is not recommended for routine surgical treatment of SUI. However, it can be considered in women who need a concomitant laparoscopic surgery in hands of experienced laparoscopic surgeons. On comparing laparoscopic versus open Burch, it has been observed that there were no significant differences in objective and subjective measures of cure and in patient satisfaction at 6 months, 24 months, or 3-5 years of follow up. Also, laparoscopic colposuspension took longer time to perform (87 versus 42 minutes) but was associated with less blood loss, less pain and quicker return to normal activities. **Synthetic Mid-Urethral Tapes** have gained widespread acceptance as the procedure is minimally invasive, cost effective with success rates similar to Burch, associated with

decreased morbidity, shorter hospital stay and early return to work.

**Tension free vaginal tape (TVT)**- Retropubic MUS are of two types namely bottom-up (TVT Exact, RetroArc) or top-down (SPARC) techniques depending upon the direction of trocar passage. A 2-3 cm mid urethral vertical incision is made on the vagina. Small tunnels are created to the inferior pubic ramus. A polypropylene tape attached to two 5 mm sharp curved trocars is passed on each side of the urethra through retropubic space to two exit locations in the suprapubic area of the anterior abdominal wall. Cystoscopy is done to rule out bladder injury. Plastic sheaths covering the mesh matrix are removed and tension of the mesh is rechecked. Finally, the vaginal incision is closed. This procedure has almost 87% success rate.

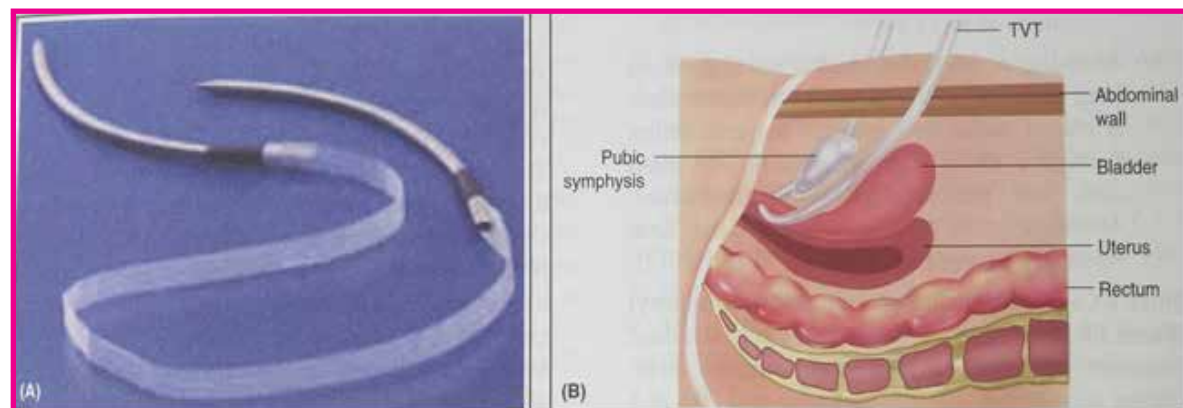


Fig. (A) TVT; (B) Diagrammatic representation of TVT in a patient

**Transobturator tape (TVT-O)**- This transobturator approach (described by DeLorme) almost eliminates any potential for bladder or bowel perforation and major vascular injury (which are reported to be approximately 3%- 5% in TVT technique due to blind passage of trocars). Here, specially designed needles are passed either from the inner groin into the vaginal incision (outside-in technique, e.g. American Medical Systems) or from the vaginal incision into the inner groin (inside-out, e.g. Gynecare, Sommerville). The decision regarding which approach to use depends on the preference and experience of the surgeon. The trocar tip

is inserted into the previously dissected vaginal incision and advanced gently while rotating the trocar handle, hugging the pubic rami to finally emerge at the exit site marked previously at the level of the clitoris. Vaginal sulcus is inspected to ensure that no perforation has occurred. Cystourethroscopy is then done and if normal, the vaginal incision is sutured after appropriate tensioning of the sling. It's success rate varies from 73%- 92%.

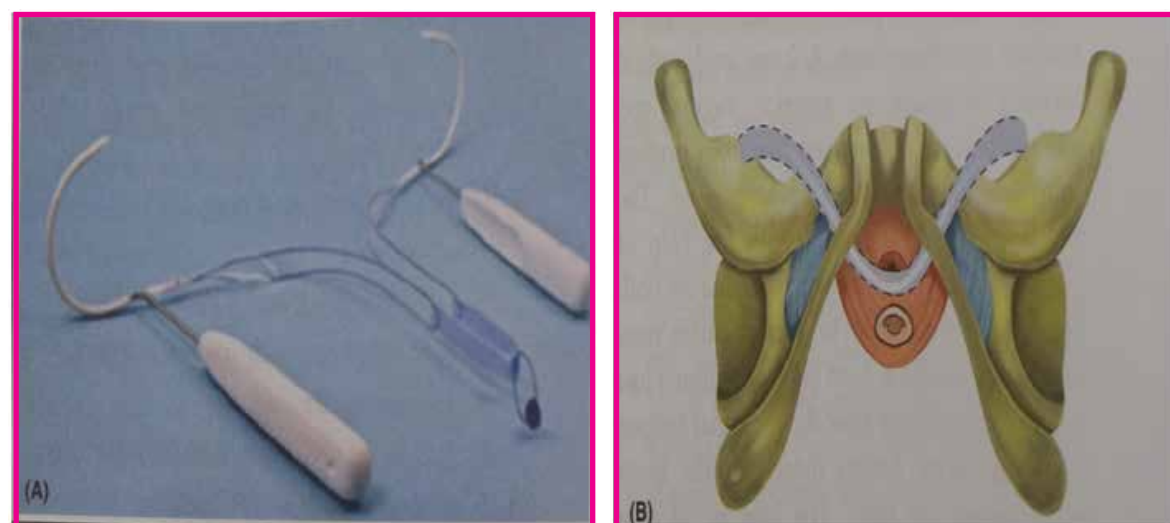


Fig. (A) Transobturator tape (TVT-O); (B) Diagrammatic representation of TVT-O in a patient

In case of an inadvertent bladder perforation, the patient may still proceed with postoperative voiding trial without the need of an indwelling catheter as the perforation is usually small and situated in a high, non-dependant portion of the bladder. If excessive hematuria is present or if base/ trigone of the bladder is perforated, indwelling catheter is advisable for a few days. If urethral injury is noted, the procedure is preferably abandoned until complete healing has occurred to reduce the likelihood of erosion of mesh into the urethra.

Offer mid-urethral sling to women with uncomplicated SUI as the preferred surgical intervention whenever available. For uncomplicated and less severe SUI, TOT (Transobturator tape) is preferred over TVT (retropubic route) due to lesser postop voiding dysfunction and lesser risk of bladder perforation. TVT are preferred in patients with more severe or recurrent SUI or ISD. Synthetic slings have generally low rate of complications, high efficacy and safety but small possibility of irreversible tape related adverse events. Women who are being offered a single-incision sling (MiniArc) should be informed that it's long-term efficacy remains uncertain. The mesh implant does not penetrate the obturator membrane and is permanent but, if removal is needed because of complications, the anchoring system can make the device very difficult to remove.

**Autologous Fascial Sling (AFS)** Pubovaginal sling is meant to be placed at the proximal urethra and bladder neck. It achieves continence by producing a direct compressive force on the urethra or by re-establishing a re-enforcing platform or hammock against which the urethra is compressed during increased abdominal pressure. A 10cm Pfannenstiel incision is made 3-5 cm above the pubic bone and dissection is carried till the level of rectus fascia. A fascial segment at least 8 cm long and 2 cm wide is harvested after delineating with a surgical marking pen. Permanent suture (polypropylene no. 1) is affixed to each end of the sling. Vaginal dissection proceeds with a midline incision followed by raising flaps. Dissection is carried until endopelvic fascia is encountered. Long clamps are passed from the open abdominal wound posterior to the pubic bone, (approximately 4 cm apart) under finger guidance through the vaginal incision. Cystoscopy is mandatory to rule out accidental bladder in-

jury. The free ends of sutures affixed to the sling are grasped with clamp and each suture pulled upto anterior abdominal wall through the retropubic space. The sutures are then tied across the midline while holding a right angle clamp between the sling material and posterior urethral surface. The abdominal and vaginal incisions are then closed. A drain is advised to be placed in the subcutaneous tissue space after copious wound irrigation since hematomas are not uncommon otherwise. An indwelling bladder catheter is removed after 24 hours. If patient is unable to void, bladder catheter is left for 1 week.

AFS is indicated as a primary therapy of SUI (both for ISD and urethral hypermobility), recurrent SUI, as an adjunct for bladder and urethral reconstruction, in patients who decline to have a synthetic material implanted or who have had a complication after a synthetic sling placement (vaginal erosion), past history of radiotherapy, repair of urethral injuries/ urethrovaginal fistulae/ diverticulum. AFS is an effective treatment for SUI that has longevity and may be more effective than other biological and synthetic slings. The porcine dermal graft appears to lose tensile strength over time and is associated with a decreased cure rate compared to AFS and MUS. But, this modality has a high risk of voiding difficulty than MUS and the women opting for this procedure need to be informed about the requirement of clean intermittent self-catheterization (incidence reported between 1.5% and 7.8%) which typically resolves by 2-4 weeks..

**Bulking Agents** Most above operations work best for SUI due to urethral hypermobility and not very well for ISD. For ISD, periurethral injections of synthetic bulking agents (silicone, carbon-coated zirconium beads or hyaluronic acid/dextran copolymer) are administered in the submucosa of proximal and midurethra under cystourethroscopy. This increases urethral coaptation. Major disadvantages are multiple sessions and poor long-term efficacy. Also, these are currently not available in India.

**Artificial Urinary Sphincter (AUS)** This consists of an inflatable cuff, a balloon to control pressure and a pump. There is lack of good quality evidence for efficacy of AUS. Patients need to be counselled about the cumbersome procedure of installation and need for life long



follow up because of involved risk of malignancy.

### Surgical management in Special Clinical situations

- SUI and a fixed, immobile urethra (often referred to as 'ISD') : offer pubovaginal slings/ Bladder neck slings, retropubic MUS, urethral bulking agents, or AUS.
- Inadvertent injury to urethra in a planned MUS procedure: Avoid mesh sling
- Patients undergoing concomitant urethral diverticulectomy, repair of urethrovaginal fistula, or urethral mesh excision and SUI surgery: synthetic MUS contraindicated
- Patients at risk for poor wound healing (e.g. following radiation therapy, presence of significant scarring, poor tissue quality): mesh sling contraindicated
- Patients undergoing concomitant surgery for pelvic prolapse repair and SUI: any of the anti-incontinence procedures (e.g., MUS, pubovaginal sling, Burchcolposuspension) but surgery for prolapse should be performed first so as to avoid displacement of sling, if done afterwards.
- Patients with SUI and concomitant neurologic disease affecting lower urinary tract function (neurogenic bladder): surgical treatment of SUI after appropriate evaluation and counselling have been performed.

### Postoperative Assessment

First follow up should be offered within the early postoperative period to assess if patients are having any significant voiding problems, pain, or other unanticipated events. Early intervention is required to avoid potential complication. Asymptomatic patients should be seen and examined within six months post-operatively. Patients should be asked about residual incontinence, ease of voiding/force of stream, recent UTI, pain, sexual function and new onset or worsened OAB symptoms.

Most physicians suggest that the patient finish childbearing before surgical correction of stress incontinence is attempted. An elective caesarean delivery would be an acceptable

option for patients who become pregnant , if desired after careful review of the pertinent risks and benefits.

### References:

1. Kobashi KC, et al. Surgical Treatment of Female Stress Urinary Incontinence: AUA/SUFU Guideline. J Urol. 2017 Oct;198(4):875-883.
2. JB Sharma. Urinary problems. Textbook of Gynecology.2018; 1: 392-429.
3. Alyaa Mostafa et al. Single-Incision Mini-Slings Versus Standard Midurethral Slings in Surgical Management of Female Stress Urinary Incontinence: An Updated Systematic Review and Meta-analysis of Effectiveness and Complications. European Urology. February 2014; 65: 402-427
4. Richter HE, Albo ME, Zyczynski HM, Kenton K, Norton PA, Sirls LT, et al. Retropubic versus Transobturator. Midurethral Slings for Stress Incontinence. N Engl J Med 2010; 362: 2066-76.
5. Stanford EJ, Paraiso MFR. A comprehensive review of suburethral sling procedure complications. J Min Invas Gynecol. 2008; 15: 132-45.
6. JB Sharma et al. A comparative study of autologous rectus fascia pubovaginal sling surgery and synthetic transobturator vaginal tape procedure in treatment of women with urodynamic stress urinary incontinence. European Journal of Obstetrics & Gynecology and Reproductive Biology 2020; 252: 349-354.

# Rectus Fascia Sling Surgery

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## Introduction

Stress urinary incontinence (SUI) is common in the adult females. Surgical treatment options for SUI are synthetic mid-urethral sling (MUS), autologous sling, bulking agents, and Burch colposuspension. The autologous pubovaginal sling (PVS) like Rectus fascia sling surgery has re-emerged in due to complications of synthetic MUSs and FDA communications regarding the use of vaginal mesh<sup>1</sup>.

The use of the **autologous sling** in treatment of female SUI is known since the beginning of the last century. Synthetic MUS emerged in the **early 1990s** and now is the most commonly used procedure for female SUI<sup>1,2</sup>. This has increasingly been associated with **sling-related complications, malpractice litigations, and associated patients' concerns**. This has forced many synthetic sling manufacturers to withdraw their products off the market. Therefore many pelvic surgeons have reduced the utilization of synthetic and increased the utilization of autologous slings<sup>3,4</sup>.

**Aldridge popularized the use of the rectus fascia sling in 19425. In 1978, McGuire and Lyton popularized the ARFS procedure for type III-SUI**<sup>6</sup>(a severe form of SUI secondary to ISD). This was further modified by **Ghoneim in 1989**<sup>7</sup>. In **1991, Blaivas and Jacobs** reported on the use of ARFS in patients with complicated SUI<sup>8</sup>.

## Mechanism Of Continence of Autologous Rectus Fascia Sling

The **primary mechanism of continence of ARFS is by increasing outlet resistance**. One of the proposed mechanism of action of ARFS is to restore the normal urethrovesical junction support and mechanical compression of proximal urethra during stress. This increas-

es bladder outlet resistance during increased intra-abdominal pressure and hence, prevents SUI<sup>9</sup>.

During increased intraabdominal pressure, the rectus muscle contracts pulling the sling anteriorly. This forward sling move leads to rotation of the bladder base posteroinferiorly causing kinking at the posterior urethra and increasing the bladder outlet pressure which prevents SUI. This means **applying overly tension on the sling during sling positioning is unnecessary and should be discouraged**<sup>9,10</sup>.

## Indications of autologous rectus fascia sling surgery<sup>11-13</sup>

- Although ARFS was reserved for **complicated cases of SUI**
- Can also be used as primary treatment option for women with **uncomplicated SUI**
- **Synthetic MUS is less preferred or contraindicated.**
- **Violation of the urethral mucosa** (periurethral excision of urethral diverticulum)
- Closure of **urethra-vaginal fistula**
- **Eroded synthetic sub-urethral sling**
- Prior **pelvic irradiation,**
- Women on **chronic steroid therapy,**
- **Extensive tissue fibrosis and scarring**
- women with **chronic pelvic pain & dyspareunia.**

## Technique Of Autologous Rectus Fascia Sling Surgery

The technique has been previously described by McGuire<sup>6</sup>.

Patient in the modified dorsal lithotomy position (under anesthesia). Foleys catheter is inserted.

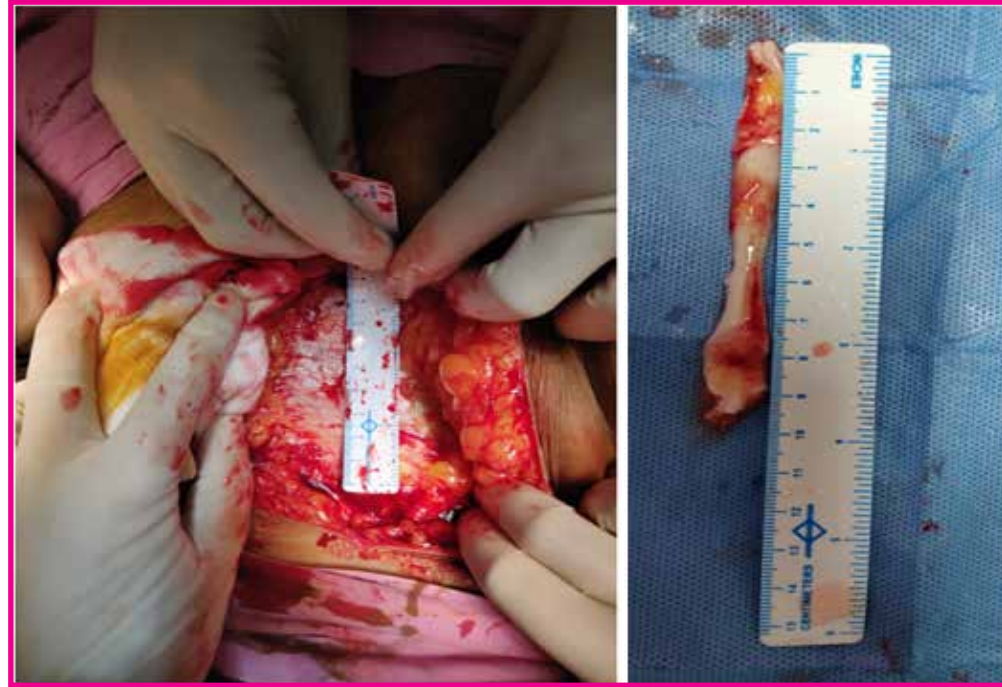


Fig 1. Harvesting Rectus Fascia

A linear midline or inverted U-vaginal incision is made at the level of the mid urethra and up to the bladder neck level. The vaginal epithelium is then dissected from the periurethral and pubocervical fascia till the inferior border of the pubic rami are clearly palpated on each side. At this point, enough space is created to reach

the retropubic space. Kellys clamp are passed from the suprapubic space down into the vaginal incision. The sling sutures are then inserted into the tip of the clamp on each side and the sutures are delivered in an inside-out fashion delivering the sutures to the suprapubic region.

A Pfannenstiel suprapubic incision is made and the rectus fascia is reached. The fascia is freed from the covering subcutaneous fat. The sling outline is made by a marking pen. The sling dimensions are of 8 long and 2 cm wide. The marked fascial strip is then freed off circumferentially from the rectus fascia. The ends of the sling are suspended with 0 polypropylene (Prolene) or polydioxanone (PDS) sutures, one on each side.

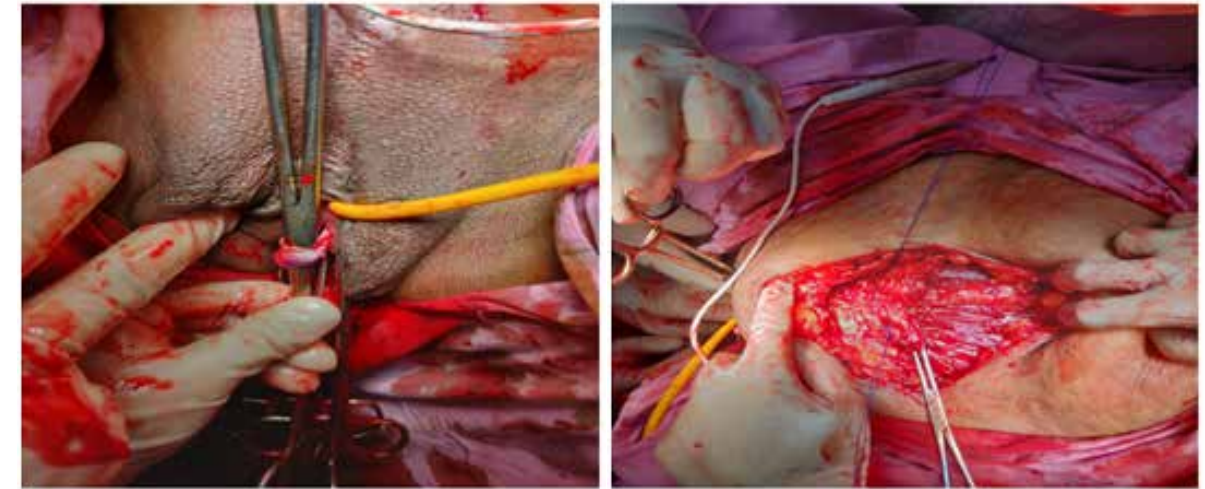


Fig 2. ARFS Application Vaginally and Through Retropubic Space and Closure

The rectus fascial defect is closed with continuous 00\_PDS suture. Sling tension is adjusted in a way that the assistant ties the Prolene sutures to each other in the midline over clamp or artery forceps. During the suture ligature on vaginal side the surgeon observes for the sling tension and location making sure the sling sits loose underneath the mid-urethra. The sling is then secured to the periurethral fascia using 3/0 absorbable sutures. We then close the vaginal and abdominal incisions. Cystoscopy is performed. A vaginal packing and the Foley catheter are left in place. Patient is kept for overnight observation. Both the vaginal packing and the Foleys catheter are removed in postoperative Day 1 and a trial of void is performed same day. Patient is then discharged.

## Outcome And Complications Of Rectus Fascia Sling Surgery

The overall success rate of the ARFS ranged between 31% and 100%<sup>14,15,16</sup>.

The most common two important complications related to the ARFS are **de novo urgency and bladder outlet obstruction**<sup>17,18</sup>.

De novo urgency after AFRS is reported in 15-20% of patients. De novo urgency after AFRS could be secondary to increased bladder outlet pressure<sup>19,20,21</sup> and disruption of the bladder autonomic nerve supply during dissection<sup>22</sup>.

Other complications are- **voiding dysfunction**

**and urinary retention** with reported **urine retention rate between 5% and 20%** and **voiding difficulty rate between 1.5% and 7.8%**<sup>23,24</sup>.

For Voiding dysfunction preoperatively urodynamic evidence of hypocontractile or acontractile detrusor muscle are reported risk factors<sup>25</sup>. The risk for long-term urinary retention is particularly high in patients who tend to strain to void. During straining, angulation of the vesico-urethral angle creates bladder outlet obstruction that can worsen voiding dysfunction<sup>25</sup>.

Pelvic examination and post-void residual urine volume assessment may help with the diagnosis.

## Management Of Complication

Most complications of Autologous Rectus Fascia Sling surgery can be managed conservatively. observation in case of urinary retention after ARFS for up to 3 months while patient is kept on regular CIC. The sling tension tends to be spontaneously relieved over time probably secondary to gradual loosening of the sling. If urinary retention persists, sling incision with or without urethrolisis can be performed<sup>27,28,29</sup>.

## Conclusion

ARFS is a reasonable primary treatment option for uncomplicated female SUI. This proce-

dure can also be used after removal of synthetic MUS. Concomitant ARFS at the time of synthetic sling excision, poor tissue quality patient. ARFS should be considered as a primary option of treatment for female SUI in cases of urethral perforation, following repair of urethrovaginal fistula, in irradiated urethra, and following excision of urethral diverticulum. ARFS is preferred over synthetic MUSs in female SUI associated with chronic pelvic pain. ARFS procedure needs specific level of surgical skills and surgeons who pursue this procedure should obtain sufficient training before performing this surgery

### References

1. Wu JM, Gandhi MP, Shah AD, et al. Trends in inpatient urinary incontinence surgery in the USA, 1998–2007. *Int Urogynecol J*.
2. Deng DY. Urinary incontinence in women. *Med Clin North Am*. 2011;95:101–109.
3. Albo ME, Litman HJ, Richter HE, et al. Treatment success of retro-pubic and transobturator mid urethral slings at 24 months. *J Urol*. 2012;188:2281–2287.
4. Rac G, Younger A, Clemens JQ, et al. Stress urinary incontinence surgery trends in academic female pelvic medicine and reconstructive surgery urology practice in the setting of the food and drug administration public health notifications. *Neurourol Urodyn*. 2017;36:1155–1160.
5. Aldridge A. Transplantation of fascia for the relief of urinary stress incontinence. *Am J Obstet Gynecol*. 1942;44:398–411. 7.
6. McGuire EJ, Lytton B. Pubovaginal sling procedure for stress incontinence. *J Urol*. 1978;119:82–84.
7. Ghoniem G. Modified pubovaginal sling for treatment of complicated stress urinary incontinence in females. *AUA Today*. 1991;4:5–5. 10.
8. Blaivas JG, Jacobs BZ. Pubovaginal fascial sling for the treatment of complicated stress urinary incontinence. *J Urol*. 1991;145: 1214–1218
9. Ghoniem GaS A. Sub-urethral slings for treatment of stress urinary incontinence. *Int Urogynecol J*. 1994;5:228–239.
10. Ghoniem GM, Rizk DEE. Renaissance of the autologous pubovaginal sling. *Int Urogynecol J*. 2018;29:177–178.
11. Sarver R, Govier FE. Pubovaginal slings: past, present and future. *Int Urogynecol J Pelvic Floor Dysfunct*. 1997;8:358–368.
12. Kobashi KC, Albo ME, Dmochowski RR, et al. Surgical treatment of female stress urinary incontinence: AUA/SUFU guideline. *J Urol*. 2017;198:875–883.
13. Enemchukwu E, Lai C, Reynolds WS, Kaufman M, Dmochowski R. Autologous pubovaginal sling for the treatment of concomitant female urethral diverticula and stress urinary incontinence. *Urology*. 2015;85:1300–1303.
14. McGuire EJ, O'Connell HE. Surgical treatment of intrinsic urethral dysfunction. *Slings*. *Urol Clin North Am*. 1995;22:657–664.
15. Chaikin DC, Rosenthal J, Blaivas JG. Pubovaginal fascial sling for all types of stress urinary incontinence: long-term analysis. *J Urol*. 1998;160:1312–1316.
16. Morgan TO, Jr., Westney OL, McGuire EJ. Pubovaginal sling: 4- YEAR outcome analysis and quality of life assessment. *J Urol*. 2000;163:1845–1848.

17. Athanasopoulos A, Gyftopoulos K, McGuire EJ. Efficacy and preoperative prognostic factors of autologous fascia rectus sling for treatment of female stress urinary incontinence. *Urology*. 2011;78:1034–1038
18. Richter HE, Varner RE, Sanders E, et al. Effects of pubovaginal sling procedure on patients with urethral hypermobility and intrinsic sphincteric deficiency: would they do it again? *Am J Obstet Gynecol*. 2001;184:14–19.
19. Beck RP, Grove D, Arnusch D, Harvey J. Recurrent urinary stress incontinence treated by the fascia lata sling procedure. *Am J Obstet Gynecol*. 1974;120:613–621.
20. Summitt RL, Jr BA, Ostergard DR, et al. Suburethral sling procedure for genuine stress incontinence and low urethral closure pressure: a continued experience. *Int Urogynecol J Pelvic Floor Dysfunct*. 1992;3:18–21.
21. Speakman MJ, Sethia KK, Fellows GJ, Smith JC. A study of the pathogenesis, urodynamic assessment and outcome of detrusor instability associated with bladder outflow obstruction. *Br J Urol*. 1987;59:40–44.
22. Mitsui T, Tanaka H, Moriya K, Kakizaki H, Nonomura K. Clinical and urodynamic outcomes of pubovaginal sling procedure with autologous rectus fascia for stress urinary incontinence. *Int J Urol*. 2007;14:1076–1079.
23. Chaikin DC, Rosenthal J, Blaivas JG. Pubovaginal fascial sling for all types of stress urinary incontinence: long-term analysis. *J Urol*. 1998;160:1312–1316.
24. McGuire EJ, Letson W, Wang S. Transvaginal urethrolysis after obstructive urethral suspension procedures. *J Urol*. 1989;142: 1037–1038; discussion 38–39.
25. Webster GD, Kreder KJ. Voiding dysfunction following cystourethropy: its evaluation and management. *J Urol*. 1990;144: 670–673.
26. Beck RP, Grove D, Arnusch D, Harvey J. Recurrent urinary stress incontinence treated by the fascia lata sling procedure. *Am J Obstet Gynecol*. 1974;120:613–621
27. Foster HE, McGuire EJ. Management of urethral obstruction with transvaginal urethrolysis. *J Urol*. 1993;150:1448–1451.
28. McGuire EJ, Letson W, Wang S. Transvaginal urethrolysis after obstructive urethral suspension procedures. *J Urol*. 1989;142: 1037–1038; discussion 38–39.
29. Nitti VW, Raz S. Obstruction following anti-incontinence procedures: diagnosis and treatment with transvaginal urethrolysis. *J Urol*. 1994;152:93–98

## Pelvic Organ Prolapse

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Pelvic organ prolapse can be defined as downward descent of pelvic organs including uterus, bladder or bowel resulting in herniation of these organs into or through the vagina. The World Health Organization has reported a global prevalence range of pelvic organ prolapse of 2–20% among women below age 45 years (1,2). In India, a prevalence of uterine prolapse ranging from 1–18% has been reported.(3)

### Pelvic supports

Pelvic organs are supported by connective tissue, its condensation as ligaments attached to bony pelvis and by pelvic floor muscles. According to Delancey, pelvic organs are suspended by the pelvic ligament and supported by the levator ani muscle at three levels(4)

Level I (suspension): The upper part of the vagina and the cervix are suspended from above.. This comprises of the uterosacral and cardinal ligaments at level1

Level II (attachment): In the middle portion of the vagina support consists of pelvic connective tissue attached medially to the vaginal wall and laterally to the pelvic side walls through arcus tendinous fascia pelvis and arcus tendinous levator ani. Anteriorly pubocervical fascia is present between pubic bone and vagina, posteriorly rectovaginal fascia is present between posterior vaginal wall and rectum

Level III (fusion): Towards its distal margin the vagina is fused with, laterally to urogenital diaphragm and posteriorly to the perineal body whereas anteriorly it blends with the urethra

.Urogenital diaphragm is composed of levator ani muscles which has a an inverted u shaped opening for passage of urethra, vagina and rectum. Uterus and vagina lies horizontally over the levator ani muscles due to resting tone of levator ani which keeps the hiatus closed and prevents herniation of pelvic organs.

Defect at different levels will give rise to prolapse of a certain type, and management will require correction of the support at that particular level. (table 1)

Level1	Level1	Level2	Level3
Function	Suspends uterus and upper vagina	Suspends bladder rectum and mid vagina	Perineal membrane and perineal body
Effect of damage	<ul style="list-style-type: none"> <li>• Uterine prolapse</li> <li>• Vault prolapse</li> <li>• Enterocele</li> </ul>	<ul style="list-style-type: none"> <li>• Cystocele</li> <li>• Urethrocele</li> <li>• Rectocele</li> </ul>	<ul style="list-style-type: none"> <li>• Perineal descent,</li> <li>• perineal hypermobility</li> <li>• urethrocele</li> <li>• SUI</li> </ul>

## Pathophysiology:

There are various risk factors for POP, they can be grouped as predisposing, inciting, promoting, or decompensating events (5).

- Predisposing factors:** Patient's genetic factors and female gender. Genetic mutations in type I collagen and alteration in ratios of type I to type III collagen increase the predisposition to pelvic floor disorders. Other connective tissue disorders such as Ehler Danlos and Marfans increase the chances of prolapse at a younger age.
- Inciting factors:** Factors that cause damage to the pelvic floor such as pregnancy, delivery, hysterectomy or nerve injuries.
- Promoting factors:** factors that put a constant strain on the pelvic floor leading to its weakness. These are obesity, smoking, chronic cough, constipation and occupational activities like prolonged standing, lifting heavy weights etc.
- Decompensating factors:** Factors such as age, menopause, debilitation or medications.

Depending on a combination of these risk factors a patient may or may not develop prolapse in her lifetime.

Anatomically site of prolapse is divided into three compartments, anterior of bladder and urethra, middle of uterus or vaginal vault and posterior of rectum and pouch of Douglas.

Prolapse of the anterior vaginal wall, is the most common form of POP, detected twice as often as posterior vaginal prolapse, and is three times more common than apical prolapse (6,7) However in most symptomatic women with POP, prolapse of multiple segments are noted.

## Symptomatology

Pelvic organ prolapse may be asymptomatic in early stages in some women while in others it may cause a lot of bother affecting her quality of life. Symptoms of prolapse depend upon the compartment and level of support affected.

Symptoms that are common to all forms of prolapse:

Sense of fullness in the vagina associated with dragging discomfort, visible protrusion of the cervix and vaginal walls, sacral backache which is usually relieved on lying.

**Anterior compartment:**

Difficulty in passing urine, double voiding, recurrent infection, SUI.

**Posterior compartment:**

Straining at stools and need for digitations because of rectocele and perineal damage results in wide introitus, loose vagina, sexual dysfunction.

**Central compartment**

Descent of cervix can cause discharge and ulceration as well as dyspareunia.

## Clinical evaluation of prolapse

A detailed history is important for evaluation of symptoms and quality of life affected. There are various questionnaires available to assess pelvic floor dysfunction and quality of life. Clinical evaluation of prolapse is made to define the extent of prolapse and the compartment affected. Assessment is made in resting and maximum straining in both supine and standing position to observe the descent of all the three compartments in reference to hymen. Up to now, there is no consensus on clinical methods for evaluation of prolapse. There have been many classification systems used to describe the descent.

The International Continence Society recommends use of pelvic organ quantification system (POPQ) for objective assessment of POP (8).

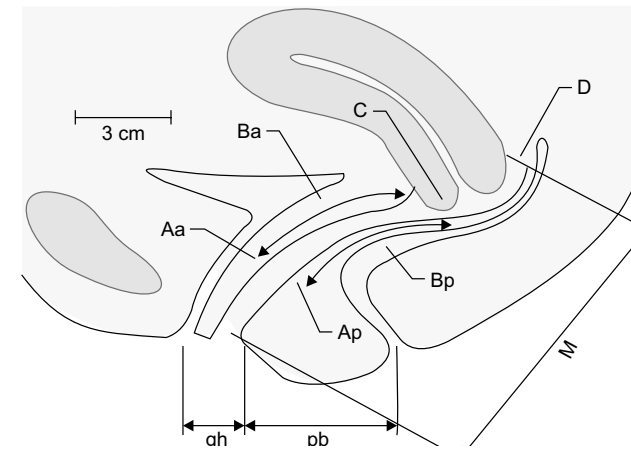


Figure 1: The nine points which are measured in the Pelvic organ Quantification system to assess the stage of prolapse.

Women may need further evaluation depending on symptoms. If complicated SUI is present urodynamic study may be needed and defecation proctography or pelvic MRI may be needed if symptoms of obstructed defecation do not correlate with degree of prolapse.

## Management

Most women with early stage of POP are asymptomatic and do not seek treatment but are diagnosed on routine examination. These women should not be offered surgical treatment.

In early stages of prolapse with symptoms, conservative treatment in form of decrease in weight, diet modification and PFMT should be offered. Although evidence of its effectiveness is very limited as there are no universally accepted exercise protocols and sustained patient compliance is also poor. (9)

Vaginal pessaries are an effective option for conservative treatment of prolapse. Pessaries prevent the pelvic organs from bulging beyond the vagina. They provide immediate relief and can be used for long term. Now various models of silicon pessaries are available (figure 2). Ring pessaries are the best option if introitus is not too wide (2 finger wide in horizontal axis). For wide introitus, space occupying pessaries such as gelhorn or cube pessaries are more suitable. (10,11)



Figure 2: Different types of pessaries.

## Surgical Treatment

The primary objective of surgical treatment is restoration of anatomy and relief of symptoms..

Most women with higher stage prolapse have multicompartiment defect and require combination of surgery for apical ,anterior and posterior compartment and resuspension along with uterosacral approximation.

### Anterior compartment prolapse

The defect in anterior compartment can be central, lateral or apical. Central defect is from loss of pubocervical fascia, lateral defect as a result of detachment of pelvic connective tissue from arcus tendinous fascia pelvis (ATFP) and apical from loss of level 1 supports. The repair of central defect can be done by plication of pubocervical fascia in the centre.

For paravaginal repair pelvic fascia is attached to ATFP. These can be combined with attachment of fascia to uterosacral and mackenrods ligament. The use of mesh for anterior repair is not recommended because of side effects and may be used only in cases of recurrence (12). The repair is done by vaginal route but if abdominal surgery has to done for any indication repair can also be done abdominally.

### Posterior compartment prolapse

Posterior compartment prolapse can be of rectal ampulla, pouch of Douglas(enterocele) or perineum(perineal hypermobility or disruption ). The surgery depends on the site of defect . If there is central defect plication of fascia in mid-line is the treatment of choice . Levatoroplasty is not recommended as it leads to dyspareunia(13). Apical suspension of fascia is done when attachment of rectovaginal fascia to level 1 supports is disrupted. . Perineorrhaphy is done for perineal defect. Higher defect in posterior compartment can be corrected both vaginally and abdominally but perineal defects have to be repaired vaginally only.

Enterocele repair is done by dissecting the sac and its contents and closing the peritoneum and plicating uterosacral . The procedure can be done abdominally as well as vaginally.

### Apical prolapse

Prolapse can be of uterus or vaginal vault post hysterectomy, though the uterus descends but as such there is no defect in uterus only attenuation of apical supporting ligaments is there ,therefore the option for uterine prolapse are hysterectomy with vault suspension procedure or uterus sparing surgery with or without use of grafts for suspension. The choice of surgery depends on age of women, desire for fertility or conservation of uterus.

Younger women mostly have prolapse because of inherent weakness of pelvic connective tissue with central compartment prolapse. These women require an exogenous support which may be autologous or synthetic . Various sling operations have been described . Purandere's cervicopexy using rectus sheath, Shirodkar's Sling, Jhoshi's Sling, Sonawala's sling and Khanna's sling using synthetic material . Virkud,s sling using combination of rectus sheath and synthetic material(5,14,15).

The other vault suspension procedures sparing the uterus are sacrospinous hysteropexy, high uterosacral suspension, and Manchester operations.. Manchester operation was found to be an effective procedure in terms of anatomical outcomes as compared with VH for uterine prolapse caused by true cervical elongation (16)

The traditional treatment for older women with apical prolapse is Vaginal hysterectomy with vault suspension.

The surgery for those desiring uterine conservation can be done through abdominal or vaginal route .Abdominally open or laparoscopic Sacro hysteropexy and high utero sacral suspension can be done. Sacrospinous hysteropexy or high uterosacral suspension are the surgeries through vaginal route,

Uterus preserving surgery should be avoided in women with fibroids or adenomyosis, suspicion of malignancy and history of familial cancer involving uterus or ovary.

A randomised controlled trial comparing vaginal hysterectomy and vault suspension with abdominal Sacro hysteropexy demonstrated that score on urogenital distress were higher after abdominal surgery(17). Laparoscopic Sacro hysteropexy has been shown to have

superior apical support and vaginal length in a pilot RCT compared to abdominal(18) It has also been seen to be a safe and effective treatment with low rate of apical recurrence .(19)

High uterosacral suspension can be done transvaginal or laparoscopically. There is a slightly higher rate of complications like ureteric injury, bowel injury, pelvic cellulitis and atonic bladder symptoms (20) with vaginal route. laparoscopic uterosacral ligament suspension is associated with high anatomic and clinical cure rates and patient satisfaction. (21)

Sacrospinous hysteropexy when compared with vaginal hysterectomy was not found non-inferior to vaginal hysterectomy (22), At five year follow-up significantly less anatomical recurrences of the apical compartment with bothersome bulge symptoms or repeat surgery were found after sacrospinous hysteropexy compared with vaginal hysterectomy with uterosacral ligament suspension.(23)

A recent Cochrane review concluded that no definite conclusions could be drawn about superiority of vaginal hysterectomy versus uterus conserving surgery for uterine prolapse .(24)

In women who are very old and sexual function is not desired there is option of colpocleisis , which is an obliterative procedure in which anterior and posterior wall of vagina are stitched together after denuding them . Success rate from case series is 100%.(25) The vaginal epithelium has to be healthy and endometrial &cervical pathology has to be ruled out before colpocleisis.

### Vault Prolapse

Vaginal sacrospinous fixation, abdominal or laparoscopic colposacropepy ,high uterosacral suspension or colpocleisis are the procedures done for vault prolapse. Sacro colpopepy is superior to sacrospinous fixation. A fully powered RCT showed clinical equivalence of open and laparoscopic colposacropepy but lesser blood loss and shorter postoperative recovery in laparoscopic group.(26)Colpocleisis is reserved for women who are very old and do not desire sexual function

### Prevention of prolapse

Primary prevention is feasible through mod-

ification of obstetric management the main modifiable risk factor for pelvic floor trauma and later pelvic organ prolapse is forceps For secondary prevention PFMT has shown a small but significant and clinically important decrease in prolapse symptoms(27)

## References

1. World Health Organization. Measuring reproductive morbidity. Report of technical working group WHO/MCH/90.4. Division of Family Planning, Geneva. Aug. 30–Sept. 1, 1989;1–39.
2. Shah B. Correction of utero-vaginal prolapse by Shirodkar's sling operation. The J Obstet Gynecol India 1993;43:123–5.
3. Omran AR, Standlay CC. Family formation pattern and health: an international collaborative study in Columbia, Egypt, Pakistan and Syrian Arab Republic. Geneva: WHO 1981;217–302.
4. DeLancey JO. The anatomy of the pelvic floor. Curr Opin Obstet Gynecol. 1994 Aug;6(4):313–6.
5. Virkud A. Conservative Operations in Genital Prolapse. J Obstet Gynaecol India.2016Jun;66(3):144–8. 6
6. Hendrix, S. L., Clark, A., Nygaard, I., Aragaki, A., Barnabei, V., & McTier-nan, A. (2002). Pelvic organ prolapse in the women's health initiative: Gravity and gravidity. American Journal of Obstetrics and Gynecology, 186(6), 1160–1166. doi:10.1067/mob.2002.123819
7. Handa, V. L., Garrett, E., Hendrix, S., Gold, E. B., & Robbins, J. A. (2004). Progression and remission of pelvic organ prolapse: A longitudinal study of menopausal women. American Journal of Obstetrics and Gynecology, 190(1),27-2.https://doi.org/10.1016/j.ajog.2003.07.017
8. BumpRC,MattiassonA,BøK,etal.The standardization of terminology of female pelvic organ prolapsed and pelvic floor dysfunction.AmJObstetGynecol1996;175:10-7.doi:10.1016/S0002-9378(96)70243-0pmid:869403
9. Hagen S, Stark D. Conservative prevention and management of pelvic organ prolapse in women. Cochrane Database of Systematic Reviews 2011, Issue 12. Art. No.: CD003882. DOI: 10.1002/14651858.CD003882.pub4
10. Lamers BH, Broekman BM, Milani AL. Pessary treatment for pelvic organ prolapse and health-related quality of life: a review. Int Urogynecol J. 2011;22(6):637–644.
11. Clemons JL, Aguilar VC, Tillinghast TA, Jackson ND, Myers DL. Patient satisfaction and changes in prolapse and urinary symptoms in women who were fitted successfully with a pessary for
12. Ugianskiene, A., Davila, G. W., & Su, T. (2019).FIGO review of statements on use of synthetic mesh for pelvic organ prolapse and stress urinary incontinence. International Journal of Gynecology & Obstetrics. doi:10.1002/ijgo.12932pelvic organ prolapse. Am J Obstet Gynecol 2004;190:1025–9.
13. Karram M, Maher C. Surgery for posterior vaginal wall prolapse. Int Urogynecol J 2013;24:1835–41.
14. Dastur B, Gurubaxani G,Shirodkar sling operation in the treatment of genital prolapse,J. Obstet. Gynaec. Brit. Cwlth. Feb. 1967. Vol. 74. pp. 125-128
15. Rameshkumar R, Kamat L, Tungal S, Moni S. Modified purandare's cervicopexy-a conservative surgery for genital prolapse: a retrospective study. Int J Reprod Contracept Obstet Gynecol 2017;6:1777-81
16. Park YJ, Kong KM , Lee J, Kim FH, and Bai SW .Manchester Operation: An Effective Treatment for Uterine Prolapse Caused by True Cervical Elongation .Yonsei Med J. 2019 Nov 1; 60(11): 1074–1080. . doi: 10.3349/ymj.2019.60.11.1074
17. Roovers JP,van der Vaart CH, van der Bom JG, van Leeuwen JHS, Scholten PC, Heintz AP. A randomised controlled trial comparing abdominal and vaginal prolapse surgery: effects on urogenital function. BJOG 2004;111:50–6.

18. Rahmanou P, Price N, Jackson SR. Laparoscopic hysteropexy versus vaginal hysterectomy for the treatment of uterovaginal prolapse: a prospective randomized pilot study. *Int Urogynecol J Pelvic Floor Dysfunct* 2015;26:1687-94.

19. Rahmanou P, White B, Price N, Jackson S. Laparoscopic hysteropexy: 1- to 4-year follow-up of women postoperatively. *Int Urogynecol J Pelvic Floor Dysfunct* 2014;25:131-8.

20. Romanzi LJ, Tyagi R. Hysteropexy compared to hysterectomy for uterine prolapse surgery: does durability differ? *Int Urogynecology J*. 2012 May;23(5):625-31.

21. Haj-Yahya R, Chill HH, Levin G, Reuveni-Salzman A, Shveiky D. Laparoscopic Uterosacral Ligament Hysteropexy vs. Total Vaginal Hysterectomy with Uterosacral Ligament Suspension for Anterior and Apical Prolapse: Surgical Outcome and Patient Satisfaction. *J Minim Invasive Gynecol*. 2019 Feb 22. pii: S1553-4650(19)30101-3. doi: 10.1016/j.jmig.2019.02.012

22. Detollenaere R J, den Boon Jan, Stekelenburg J, Int'Hout Joanna, Vierhout Mark E, Kluivers Kirsten B et al. Sacrospinous hysteropexy versus vaginal hysterectomy with suspension of the uterosacral ligaments in women with uterine prolapse stage 2 or higher: multicentre randomised non-inferiority trial *BMJ* 2015; 351 :h3717

23. Schulten, Sascha F M Detollenaere, RJ Stekelenburg, J, Int'Hout J, Kluivers K B van Eijndhoven, Hugo W F Sacrospinous hysteropexy versus vaginal hysterectomy with uterosacral ligament suspension in women with uterine prolapse stage 2 or higher: observational follow-up of a multicentre randomised trial *BMJ* 2019; 366 :i5149

24. Maher C, Feiner B, Baessler K, Christmann-Schmid C, Haya N, Brown J. Surgery for women with apical vaginal prolapse. *Cochrane Database Syst Rev* 2016;10:CD012376

25. FitzGerald MP, Richter HE, Siddique S, Thompson P, Zyczynski H, Ann Weber for the Pelvic Floor Disorders Network. Colpoceleisis: a review. *Int Urogynecol J* 2006;17:261-71.

26. Freeman RM, Pantazis K, Thomson A, et al. A randomised controlled trial of abdominal versus laparoscopic sacrocolpopexy for the treatment of post-hysterectomy vaginal vault prolapse: LAS study. *Int Urogynecol J Pelvic Floor Dysfunct* 2013;24:377-84.

27. Hagen S, Glazener C, McClurg D et al. Pelvic floor muscle training for secondary prevention of pelvic organ prolapse (PREVPROL): a multicentre randomised controlled trial. *Lancet*. 2017;389(10067):393-402.

## Urinary Tract Infection- How to diagnose ? when and how to treat?

**Dr. Mangesh Narwadkar**  
**Dr. Rajashree Dasarwar**

Urinary tract infections are among the most common bacterial infections in adults and may involve the lower or upper urinary tract or both. 15% of all outpatient prescriptions are written for treatment of UTI. The burden from UTIs on both the clinical and financial aspects of health care is immense.

As the prevalence is high among menopausal women, pregnant women, women in nursing homes, patients with incontinence or voiding dysfunction, and patients undergoing procedures that require instrumentation of the genitourinary tract, gynaecologists need to be well versed in the diagnosis and management **UTI**.

50% of women experience a urinary tract infection during their lifetime, with approximately 5% experiencing frequent infections.

Due to short female urethra, which puts the urinary tract in close proximity to the flora of the vagina and rectum, UTI is more prevalent among women (ratio of 20:1). The prevalence increases with age.

### Risk factors

Significant risk factors among younger women are sexual activity and pregnancy. Important risk factors in older women are vaginal atrophy, pelvic floor relaxation, systemic illness, and hospitalization.

### Classification

1. Cystitis (symptomatic disease of the bladder)- infection is limited to the lower urinary tract and occurs with symptoms of dysuria and frequent and urgent urination and, occasionally, suprapubic tenderness.

2. Pyelonephritis (symptomatic disease of the kidney)- infection of the renal parenchyma and pelviccaliceal system accompanied by significant bacteriuria, usually occurring with fever and flank pain.

3. Asymptomatic bacteriuria (ABU)- considerable bacteriuria in a woman with no symptoms.

4. Uncomplicated UTI - acute disease in non-pregnant outpatient women without anatomic abnormalities or instrumentation of the urinary tract;

5. Complicated UTI – urinary infection occurring in a patient of structural or functional abnormality of the genitourinary tract.

### Microbiology

Urinary tract infections result from interactions between host biologic and behavioral factors and microorganism virulence.

Gram-negative bacilli are mainly responsible for 90% of UTIs. *Escherichia coli* is the single most important organism and accounts for 80% to 90% of uncomplicated infections. *Staphylococcus saprophyticus* is the second most common cause of cystitis and causes approximately 10% of infections in sexually active females. Other common pathogens are *Klebsiella*, *Enterobacter*, *Serratia*, *Proteus*, *Pseudomonas*, *Providencia*, and *Morganella* species.

*Pseudomonas aeruginosa* - almost always results from urinary tract instrumentation. *Staphylococcus epidermidis* - nosocomial pathogen in patients with indwelling catheters. *Staphylococcus aureus* is less commonly isolated and is often caused by hematogenous renal infection. Other gram-positive organisms such as enterococci and *Streptococcus agalactiae* cause about 3% of episodes of cystitis.

Candida albicans and other fungal organisms can cause lower urinary tract infections in patients with Diabetes mellitus, with indwelling urinary catheters, or immunocompromised state.

## Clinical Presentation

Cystitis

- Usually causes dysuria
- May also cause frequency, urgency, nocturia, and suprapubic discomfort.
- Occasionally, mild incontinence and hematuria
- Gross hematuria is rare.

Upper tract infections

- Commonly present with fever, chills, malaise, flank pain, costovertebral angle tenderness, and occasionally nausea and vomiting.
- These patients may not have signs of acute cystitis.

## Diagnostic Criteria for Urinary Tract Infection

Presumptive diagnosis of UTI is made by history, clinical examination, and analysis of urine to assess the presence of bacteria, white blood cells and red blood cells which is confirmed by urine culture. Still blood test and other investigations may be required in some cases for diagnosis and management.

## Urine Collection Methods

One should take a clean catch specimen or a catheterized specimen. However, up to one-third of clean catch specimens are contaminated. To minimize contamination, spread the labia, wipe the periurethral area from front to back with a clean, moistened gauze sponge, and collect a midstream urine sample holding the labia apart.

## Diagnostic Testing

One can confirm UTI by doing Office urine dipstick, microscopic urinalysis, and urine culture. A positive urine dipstick and/or microscopic urinalysis in a symptomatic patient are generally considered sufficient evidence to support empiric treatment. Urine cultures should be sent when diagnosis of cystitis is questionable or in whom complicating factors are present

Regardless of the urine testing method used, the urine specimen should be sent to the lab immediately, because bacteria will continue to proliferate if the specimen is kept at room temperature. If there is delay for some reason you should store the specimen at 4 °C to stop bacterial growth.

## Urine Dipstick

This is a simple screening tool, which detects urine nitrites and leukocyte esterase. Gram-negative bacteria convert nitrates to nitrites. Leukocyte esterase corresponds to pyuria and indicates a host immune or inflammatory response. As per Turner et al. (2010) treatment based on urine dipstick results is the most cost-effective management strategy for acute uncomplicated cystitis. False positives can occur when the urine is contaminated. False negatives can occur in early infection and with gram-positive infections that do not produce nitrites. A sensitivity of 75% and specificity of 82% in patients with  $\geq 100,000$  CFU/mL. Clinical judgment and/or additional diagnostic testing to make a final decision regarding treatment

## Microscopic Urinalysis

Detect the presence of significant bacteria, leukocytes, and red blood cells. Pyuria is defined as  $\geq 10$  leukocytes/mL or  $\geq 3$  leukocytes per HPF of unspun urine. In the absence of pyuria, the diagnosis of urinary tract infection should be questioned. Neither microscopic hematuria nor bacteriuria is a particularly sensitive finding.

## Sterile pyuria

Presence of white blood cells in the urine in the absence of infection. Typically the presence of more than 5-8 leukocytes per high power field of microscopy, in the absence of positive urine culture would be classified as sterile pyuria. Due to tuberculosis, renal or bladder calculi, mesh or sutures in the bladder, glomerulonephritis, interstitial cystitis, and chlamydial or Ureaplasma urethritis, Urinalysis after initiating antimicrobial therapy.

## Urine Culture

This is considered the reference standard for diagnosis of a urinary tract infection. Cultures should be submitted if Suspected complicated urinary tract infection, A negative dipstick in a symptomatic patient, Poor response to initial therapy, and Recurrent symptoms <1 month after treatment for a previous urinary tract infection for which no culture was performed. Infections with an immunocompromised host, a genitourinary structural or functional abnormality (e.g., urolithiasis, renal insufficiency), pregnancy, and recent antibiotics or genitourinary tract instrumentation culture is must.

A culture result of  $\geq 100,000$  CFU/mL has historically been considered a required diagnostic criterion. Some feel that  $\geq 100$  CFU/mL should suffice in a patient who has symptoms consistent with urinary tract infection and pyuria.

## Symptom-Based Diagnosis

This is advocated by some because of the false-negative results with urine dipsticks and the expense and time delay associated with microscopic urinalyses and culture but there is a risk of overtreatment and inappropriate antibiotic use also delay the diagnosis of other causes of urinary tract symptoms.

## Additional Studies

Renal usg should be considered when

- Poor response to appropriate antimicrobial therapy,
- Infections caused by usual organisms such as Proteus,

- A history of calculi, potential ureteral obstruction,
- Recurrent pyelonephritis,
- Suspected urethral diverticula, and
- A history of many UTIs during childhood.

## CT Scan

A non-contrast CT is the current reference standard for radiographic diagnosis of calculi.

## Indications for cystourethroscopy

- Inadequate response,
- Gross hematuria,
- Suspected urethral diverticulum, and
- Suspected mesh or
- Nonabsorbable suture material in the bladder or urethra

## Management

**A) Acute Uncomplicated Cystitis-** superficial infection of the bladder mucosa that rarely invades the lamina propria or results in severe disease.

Selection of antimicrobial agents depends upon bacterial sensitivity, cost of the agent, anticipated incidence and severity of adverse effects, and dosing interval. 7 to 10-day therapy used historically for treatment but multiple studies demonstrate the efficacy of a shorter course with certain antibiotics. Shorter treatments offer the advantage of increased compliance, decreased cost, and reduced adverse effect rates.

- **First-line therapy**
- Fosfomycin (3-g sachet in a single dose).
- Nitrofurantoin 100 mg twice daily for 5 days,
- Trimethoprim-sulfamethoxazole 160/180mg twice daily for 3 days

### 1. Fosfomycin

- Largely underused single-dose regimen
- Diarrhea, nausea, and headache.

### 2. Nitrofurantoin

- Less tissue penetration and fewer systemic side effects,.
- Nausea and headache.
- Contraindicated in patients with renal insufficiency,
- long-term exposure can result in pneumonitis or peripheral neuropathy.

### 3. Trimethoprim-sulfamethoxazole

- Avoided in areas where resistance exceeds 20%.
- Risk of rash, urticaria, nausea, and hematologic side effects.

### 4. Fluoroquinolones - good tissue penetration

- Ciprofloxacin (250 mg twice daily for 3 days) and
- Levofloxacin (250-500 mg once daily for 3 days)
- Have a higher risk of systemic effects and should not be considered first-line treatment.

### 5. Beta-lactam agents

- Amoxicillin-clavulanate - less efficacy and more systemic effects, so they should be used sparingly for cystitis
- Although they may be used based on culture-sensitivity

### B) Pyelonephritis

Most episodes of acute uncomplicated pyelonephritis are now treated in the outpatient setting. A urine culture and susceptibility test should be performed to guide treatment. Women should be admitted if pyelonephritis is se-

vere, if there is hemodynamic instability or any complicating factor (e.g., diabetes, renal stone, or pregnancy), if oral medications are not tolerated, or if there is concern regarding potential nonadherence to treatment. Empirical treatment should have broad-spectrum in vitro activity against likely uropathogens and be started quickly to minimize progression. Fluoroquinolones are the only oral antimicrobials recommended for the outpatient empirical treatment of acute uncomplicated pyelonephritis. When there is concern about antimicrobial resistance or tolerance of oral medications, one or more doses of a broad-spectrum parenteral antimicrobial are recommended until in vitro activity can be assured.

### Recurrent or Relapsing UTI

One of the most common problem faced by the gynecologist treating his patients. The pathogenesis involves bacterial reinfection or bacterial persistence, with the former being much more common

#### Recurrent

- Two or more infections in 6 months period or 3 or more in a year.
- Must be separated at least 2 weeks or involve documented success of the first infection

#### Relapse

- Recurrent infection with the same bacteria within 2 weeks of treatment of the original infection

#### Risk factors- Recurrent

- Most recurrent infections are caused by ascent of rectal and vaginal flora into the urinary tract
- Intercourse is one of the strongest risk factors
- Postmenopausal women –Alteration of the vaginal flora can also predispose
- Genetic factors
- Incomplete bladder emptying, cystocele, urinary incontinence, and mesh or sutures in the bladder

### Antibiotic prophylaxis –Recurrent

Considered in women with particularly bothersome recurrent UTIs, although it should be used with caution in women with a history of drug-resistant infections.

#### Continuous prophylaxis

- Can decrease the risk of recurrent infection by up to 95%, but it puts the patient at risk of antibiotic-related side effects and colonization with anti-biotic-resistant organisms.
- Regimens include one tablet of trimethoprim-sulfamethoxazole or nitrofurantoin nightly, or fosfomycin every 10 days.
- There is no definitive evidence indicating the proper duration of treatment, but most authorities advocate treatment for 6 months or longer.

#### Postcoital prophylaxis

- A single dose after intercourse should be considered in women whose symptoms seem temporally related to intercourse, because it typically decreases over all antibiotic exposure
- It should be taken within 2 hrs.

#### Self-treatment

- Self-treatment of symptomatic urinary tract infections is an alternative to prophylaxis, because studies show women are over 80% accurate in self-diagnosis.
- This approach may result in more symptomatic infections than routine prophylaxis, although it will likely reduce over-all antibiotic exposure and reduce the duration of symptoms.

#### Topical estrogen

- Topical estrogen should be considered for urinary tract infection prevention in postmenopausal women with recurrent urinary tract infection
- Vaginal estrogen normalizes the vaginal flora, increases the prevalence of lactobacilli, decreases vaginal E. coli colonization, and may even positively regulate GAG layer thickness over time

#### Preventive measures

- Probiotics for prevention are inconclusive

- Use of cranberry use and cranberry extract clinical studies do not consistently demonstrate efficacy in prevention

- These have not been well studied, although they may reduce the risk of infection and put the patient at minimal risk.

⇒ voiding after intercourse,

⇒ increasing fluid intake, and

⇒ wiping perineally front to back

### Catheter-Associated UTI

- Can prolong hospital stay and cause bacteremia, joint infections, and death
- 70% of catheter-associated UTI arise from the biofilm that grows on the outside of the catheter in the urethra and bladder;
- Remaining infections generally arise from a contaminated collecting system (catheter, bag or tubing)
- Collecting urine from from the end of the catheter is acceptable.
- The bag is virtually always colonized with bacteria and should not be used for specimen collection.
- Avoid screening asymptomatic catheterized patients for bacteriuria, because they do not merit treatment.
- Antibiotic prophylaxis during catheterization should be avoided, but may be considered after catheter removal in selected surgical patients
- Treatment requires 7 to 14 days of antibiotics.
- A shorter course (3 days) can be considered in young women if the infection arises after catheter removal.
- Catheter-associated UTI respond more rapidly to treatment if the existing catheter is removed at the time of diagnosis

### References

1. Uncomplicated Urinary Tract Infection Thomas M. Hooton, M.D. N Engl J Med 2012;366:1028-37.
2. Urogynecology and Reconstructive Pelvic Surgery by Mark D. Walters and Mickey M. Karram
3. Uptodate
4. FOGSI FOCUS - Urinary Tract Infection



First line Empirical Therapy In Uncomplicated UTI

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- ✓ Broad spectrum<sup>5</sup>
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- ✓ Effective on Bio film<sup>6</sup>
- ✓ No Cross Resistance<sup>5</sup>
- ✓ Pregnancy category B<sup>7</sup>

Ref.

1. Concia E et al. Journal of Chemotherapy, 29:sup1,19-28  
2. Choe HS et al. Int J Urol.2018 Mar;25(3):175-185  
3. José Antonio Ortega Martel et al Ther Adv Urol 2019, Vol. 11: 29 –40 DOI: 10.117  
4. Wayan Phillips et al. Pregnancy outcome after first – trimester exposure to Fosfomycin for the treatment of urinary, infection journal Feb – 2020

5. Zhanel GC. Et al. Can J Infect Dis Med Microbiol.2016;1-10.London: Public Health England;2017  
6. G.C. Schito. Int J Antimicrob Agents 2003 Oct 2003; 22 suppl 2:79-83  
7. Novofos [ Prescribing I formation], Sun Pharmaceutical Lab Ltd;2016

\*IDSA: Infectious Diseases Society of America



## Fosfomycin In Management Of Urinary Tract Infections

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### Introduction

Urinary tract infection (UTI) is the infection in the any part of urinary system which includes kidney, bladder, ureters and urethra. It is one of the most frequent health problem encountered during clinical practice. The rate of UTI is higher amongst women as compared to men. The estimated global incidence rate of UTI is approximately 18 episodes per 1000 per-son-years (1).

UTI can be classified as either uncomplicated or complicated based on the anatomical site of infection, causative agent and presence of associated risk factor in the host. Complicated UTI often occurs in elderly diabetic women, renal transplant patients, patients with anomalous urinary tracts, patients with urinary catheters or impaired renal function. Complicated UTI is associated with isolation of the bacteria other than E.coli and treatment is often associated with longer treatment duration, resistance to antibiotic therapy, inadequate treatment, treatment failure, recurrences, relapse and other complications. Hence it is essential to differentiate between uncomplicated and complicated UTI.

### Causative Organisms

The most common pathogen associated with complicated UTI is E.coli. Other gram negative pathogens which may be associated with complicated UTI include Klebsiella, Enterobacter cloacae, Serratia marcescens, Proteus and Pseudomonas aeruginosa. Gram positive bacteria such as enterococci, staphylococcus and candida are also frequently isolated. The conventional therapy to treat UTI involves use of first line antibiotics such as  $\beta$ -lactams and fluoroquinolones. With indiscriminatory use of antibiotics in recent years, the susceptibility has changed and antibiotic resistance to penicillin and fluoroquinolones has emerged. Due to the increase in extended-spectrum  $\beta$ -lactamase

(ESBL)-producing and AmpC-producing microorganisms, the treatment has become challenging. Recently, the role of Fosfomycin in UTI has gained importance.

### Fosfomycin

Fosfomycin was initially isolated in 1969 from cultures of Streptomyces (2). It is a bactericidal agent acting through inhibition of the UDP-N-acetylglucosamine-3-0-enolpyruvyl transferase (MurA) enzyme in the bacterial cell wall (3). It also reduces the adherence of bacteria to urinary epithelium and also shown to have an immunomodulatory effect by suppressing the production of tubular necrosis factor- $\beta$  and interleukins (4).

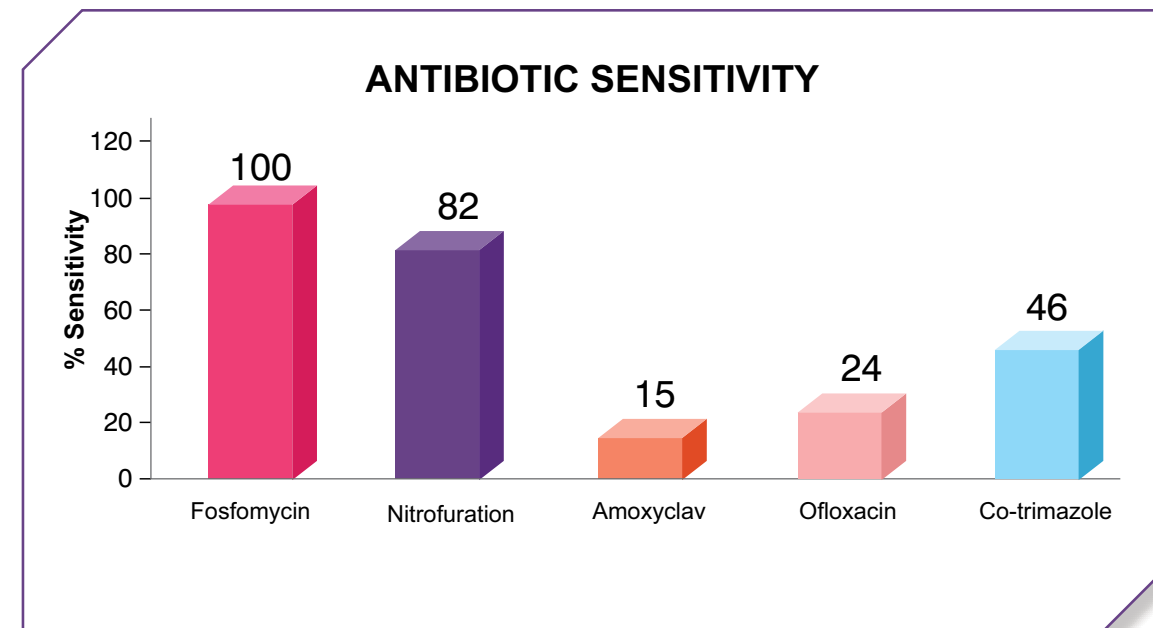
### Spectrum of Activity of Fosfomycin against urinary pathogens

This antibiotic is considered active against a broad spectrum of Gram-positive and Gram-negative microorganisms. It has considerable activity against E. coli, Klebsiella, Enterobacter, Proteus mirabilis, Shigella, Serratia, Citrobacter and Salmonella. Fosfomycin is also active against multidrug-resistant enterobacteria, extended spectrum beta-lactamase/carbapenemase-producing enterobacteria, Listeria monocytogenes, Neisseria gonorrhoeae, Aerococcus urinae, Helicobacter pylori and bacteria resistant to quinolones and cotrimoxazole suggesting that it can be highly useful in UTI patients with multidrug resistance. Morganella morganii, Staphylococcus capitis and Staphylococcus saprophyticus are fosfomycin-resistant. Amongst anaerobic infections, fosfomycin has shown efficacy against Peptococcus and Peptostreptococcus but not against Bacteroides.

There are comparative Indian studies of Fosfomycin activity with other antimicrobial agents

against E.coli isolates from UTI and it was observed that Fosfomycin shows higher and better sensitivity compared to other antibiotics like Nitrofurantoin, Cotrimoxazole, Amoxicillin-Clavunate and Ofloxacin (5,6). Sardar. A et al conducted a prospective study in South India with 564 urine samples with 170 E.coli isolates to evaluate Fosfomycin activity against E.coli isolates and compared its activity with other

antimicrobial agents. The author concluded that E.coli isolates showed 100% sensitivity to Fosfomycin as compared to other commonly used antibiotics like Amoxyclav and Fluoroquinolones. (7)



### Pharmacokinetics

Oral Fosfomycin is mainly absorbed in the small bowel with bioavailability of almost 34-58% (8). It barely binds to the plasma proteins. Majority of the drug, almost 93-99%, is excreted unaltered in urine. The peak plasma concentration is reached after 2 hours of intake. The half-life is 3-8hours and may be prolonged up to 50 hours if renal function is impaired. The trometamol formulation is better than calcium formulation as the latter is hydrolysed readily by the gastric acid and bio-availability is decreased.

### Clinical Experience

Fosfomycin is available in two formulations:

1. Fosfomycin trometamol (2 or 3 gram pack-age)- oral preparation
2. Fosfomycin disodium (1 g to 8 g)- intravenous preparation

### Various Recommendations

A single oral 3-g dose of Fosfomycin trometamol is recommended as one of the first-line treatments for uncomplicated UTI, especially in women and for infections caused by E. coli. The recommendations by various guidelines are as follow:

1. Various textbooks state that Fosfomycin shows anti-microbial activity against more than 90% of isolates causing uncomplicated cystitis and is also recommended as first line treatment for uncomplicated UTI (9-12).
2. Latin American Guideline (2019) (13)

Fosfomycin is recommended in Acute cystitis & antibiotic prophylaxis with good compliance, fewer side effects and low impact on peri-urethral, vaginal & rectal Flora

### 3. Spanish Guidelines (2019) (14)

- a. Single 3-g dose of Fosfomycin trometamol is recommended as one of the first-line treatments for uncomplicated UTI, especially in women and for infections caused by E. coli
- b. 80% microbiological eradication in cystitis in treated patients, with clinical healing that exceeded 90%, even for those infections caused by ESBL strains

c. Fosfomycin is the empiric treatment of choice for acute cystitis, immunocompetent patients and patients with renal transplants

### Other International Guidelines recommending Fosfomycin as first line treatment for Uncomplicated UTI (15,16)

SR.NO	Year	Guidelines
1	2019	Infectious Diseases society of America
2	2018	The Deutsch Interdisciplinary Society updated
3	2017	European Association of Urology
4	2017	Public Health England Guide lines
5	2017	Urological Association of Asia Guideline
6	2016	Societe de Pathologie Infectieuse de Langue Francaise guidelines (French guidelines) <sup>1</sup>
7	2015	Italian Society of Urology <sup>1</sup>

**Indications:** Acute uncomplicated cystitis, Acute cystitis by E.coli, E.faecalis, Multidrug resistant UTI

**Contraindications:** Hypersensitivity, Hepatic dysfunction

### Side-effects:

The drug is generally considered safe. The most common side-effects noted include diarrhoea, epigastric discomfort, headache, nausea or vomiting. Very rarely patients can complain of dizziness, drowsiness or fatigue. It is considered FDA category B drug and can be prescribed during pregnancy. However, not recommended during lactation as it is excreted in the breast milk.

### Fosfomycin Use During Pregnancy:

Philipps et al conducted a study to assess pregnancy outcome after first trimester exposure to Fosfomycin and concluded that there is no increased risk of adverse pregnancy outcome after Fosfomycin exposure during early pregnancy and no risk of congenital abnormalities (17). A meta-analysis compared single dose Fosfomycin and other antibiotics for lower UTI in women and asymptomatic bacteriuria in pregnant women and suggested that Fosfomycin is clinically effective & safe in pregnancy women (18). As per European Association of Urology & Canadian Guideline recommendations, Fosfomycin is a suitable antibiotic for treatment of cystitis during pregnancy and is found to be safe and well tolerated in antenatal women (19,20). Moreover, Fosfomycin is safe for development of fetus (21).

To conclude, role of fosfomycin has become an important alternative therapy in current era of multidrug resistant gram positive and gram negative microorganisms and should be considered as a first line therapy in UTI. It can be safely used during pregnancy.

#### References:

1. Laupland KB, Ross T, Pitout JDD, Church DL, Gregson DB. Community-onset Urinary Tract Infections: A Population-based Assessment. *Infection*. 2007;35(3):150-3. DOI: 10.1007/s15010-007-6180-2.
2. Hendlin D, Stapley EO, Jackson M, Wallick H, Miller AK, Wolf FJ, et al. Fosfonomycin, a New Antibiotic Produced by Strains of Streptomyces. *Science*. 1969;166(3901):122-3. PMID: 5809587.
3. Skarzynski T, Mistry A, Wonacott A, Hutchinson SE, Kelly VA, Duncan K. Structure of UDP-N-acetylglucosamine enolpyruvyl transferase, an enzyme essential for the synthesis of bacterial peptidoglycan, complexed with substrate UDP-N-acetylglucosamine and the drug fosfomycin. *Structure*. 1996;4(12):1465-74.
4. Falagas ME, Vouloumanou EK, Samonis G, Vardakas KZ, Matthew E. Fosfomycin. *Clin Microbiol Rev*. 2016;29(2):321-47. 10.1128/CMR.00068-15).
5. Patwardhan V, Singh S. Fosfomycin for the treatment of drug-resistant urinary tract infections: potential of an old drug not explored fully. *Int Urol Nephrol*. 2017 Sep;49(9):1637-1643.
6. Lawhale MA, Naikwade R. Recent pattern of drug sensitivity of most commonly isolated uropathogens from Central India. *Int J Res Med Sci* 2017;5:3631-6.
7. Sardar A, Basireddy SR, Navaz A, Singh M, Kabra V. Comparative Evaluation of Fosfomycin Activity with other Antimicrobial Agents against E. coli Isolates from Urinary Tract Infections. *J Clin Diagn Res*. 2017; 11(2): DC26-DC29.
8. Patel S, Balfour J, Bryson H. Fosfomycin Tromethamine. *Drugs*. 1997;53(4):637-56. DOI: 10.2165/00003495-199753040-00007.
9. Jameson et al 20th edition Harrison's Principles of Internal Medicine. Chapter 130 Urinary Tract Infections pg 973.
10. David Schlossberg, Clinical Infectious Disease 2015, Clinical Syndrome: Genitourinary tract.65, Urinary Tract Infection (pp.737).Cambridge University Press
11. John E. Bennett et al Chapter 36: Urinary Tract Agents; Principles and Practice of Infectious diseases; 2015; Eight Edition volume.1
12. Carlos Franco -Pardes Core Concepts of Clinical Infectious Diseases Chapter 9 Genitourinary Infections pg. 90.
13. Ortega Martell JA, Naber KG, Milhem Haddad J, Tirán Saucedo J, Domínguez Burgos JA. Prevention of recurrent urinary tract infections: bridging the gap between clinical practice and guidelines in Latin America. *Ther Adv Urol*. 2019 May 2;11:1756287218824089.
14. Candel FJ, Matesanz David M, Barberán J. New perspectives for reassessing fosfomycin: applicability in current clinical practice. *Rev Esp Quimioter*. 2019 May;32 Suppl 1(Suppl 1):1-7.
15. Concia E, Azzini AM. Aetiology and antibiotic resistance issues regarding urological procedures. *J Chemother*. 2014 Oct;26 Suppl 1:S14-23.
16. Choe HS, Lee SJ, Yang SS, Hamasuna R, Yamamoto S, Cho YH, Matsumoto T; Committee for Development of the UAA-AAUS Guidelines for UTI and STI. Summary of the UAA-AAUS guidelines for urinary tract infections. *Int J Urol*. 2018 Mar;25(3):175-185.

17. Philipps W, Fietz AK, Meixner K, Bluhmki T, Meister R, Schaefer C, Padberg S. Pregnancy outcome after first-trimester exposure to fosfomycin for the treatment of urinary tract infection: an observational cohort study. *Infection*. 2020 Feb;48(1):57-64.
18. Wang T, Wu G, Wang J, Cui Y, Ma J, Zhu Z, Qiu J, Wu J. Comparison of single-dose fosfomycin tromethamine and other antibiotics for lower uncomplicated urinary tract infection in women and asymptomatic bacteriuria in pregnant women: A systematic review and meta-analysis. *Int J Antimicrob Agents*. 2020 Jul;56(1):106018.
19. Grabe M et al. Guidelines on Urological Infections, European Association of Urology 2015
20. Moore A et al. Recommendations on screening for asymptomatic bacteriuria in pregnancy. *CMAJ* 2018 July 9; 190:E823-30.
21. Souza et al. Bacterial sensitivity to fosfomycin in pregnant women with urinary infection. *Braz J Infect Dis*.2015;19(3):319-323.

## Interstitial Cystitis / Bladder Pain Syndrome

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Dr. Raman Tanwar

Interstitial Cystitis / Bladder Pain Syndrome is a condition characterized by symptoms like lower abdominal pain, difficulty in passing urine, and lower urinary tract symptoms like urgency, feeling to pass urine multiple times and getting up at night to pass urine. These symptoms are severe enough to impair the quality of life. In this chapter a very practical approach to this disease will be discussed with focus on sensitization of the gynaecologist to this condition and broad overview of the management of this condition. It is recommended that the condition be managed by a urogynaecologist or a gynaecologist in close association with a urologist. The ideal definition of IC/BPS as endorsed by the Indian Society (GIBS) is pain or discomfort in lower abdomen or the urogenital regions which is more than 3 months old and associated with increase on being full bladder, associated frequency, urgency or nocturia and with no other explainable pathology or disease. It may or may not be associated with stigmata on cystoscopy.

### Pathophysiology of IC/BPS

It is difficult to certainly state that IC/BPS is a separate disease. In the opinion of the author and many other experts IC/BPS is a terminal stage of constant irritability of the bladder. This can initiate following a UTI, allergy, intervention, defective urothelium, dietary irritants, exposure to urinary toxins or surrounding inflammation. The established pathogenesis revolves around breach of the epithelial layer of the bladder leading to exposure of the interstitium to urine. The leakage of potassium into these layers causes activation of C Fibres and mast cells and release of Substance P and histamine. Further inflammation causes more damage to the epithelium and interstitial inflammation. The continuous exposure of the interstitium to irritants leads to creation of the neural circuit which becomes the harder part to manage. Even when the irritation reduces the neural circuit constantly searches for pain

signals and keeps the disease active. This non inflammatory IC/BPS results from neuroplasticity, cross sensitization, stress and pelvic floor dysfunction.

### How to Diagnose IC/BPS ?

We have all seen patients who present with so called recurrent UTI. A subset of these patients have never had a culture positive urinary tract infection or have occasionally had a positive culture. While these patients describe their agony we do understand that the

severity of their symptoms is much more than that of cystitis. When a patient presents with a vague pain in the urinary passage or the lower abdomen that is partially relieved on passing urine and forces the patient to keep emptying the bladder to make the patient comfortable, we may be looking at a patient of interstitial cystitis / Bladder pain syndrome.

There is a close similarity in symptoms of overactive bladder and Interstitial Cystitis/Bladder pain syndrome. Unlike overactive bladder the patient will not feel that they will leak if they don't pass urine. Frequency nocturia and urgency will be there but never urge incontinence. The patient will want to pass urine often just to reduce the discomfort and not to prevent leakage.

### Differential Diagnosis of IC/BPS

Urinary tract infection is the most common differential of IC/BPS. This also includes infections like Tuberculosis which are not picked up on culture and are known causes of sterile pyuria. Based on the symptomatic closeness overactive bladder remains one of the other most common differentials of Interstitial Cystitis. This is further complicated by the fact that

overactive bladder may co-exist with IC/BPS. Endometriosis also closely mimics symptoms of IC/BPS but the relationship with menses may provide a differentiation.

Vulvodynia, vaginitis, neurogenic bladder, urethral syndrome, urethral diverticula, Bladder outlet obstruction, climacteric disturbances, gynaecological cancers and prolapse are other common differentials which should be kept in mind when diagnosing IC/BPS. Careful and exhaustive history and examination are important for accurate diagnosis.

### Evaluation of IC/BPS

The diagnosis of Interstitial Cystitis is presently one of exclusion. The diagnosis is made when all other conditions which may cause these symptoms like UTI, Stone, Foreign Body, Cancer, Tuberculosis, Diverticula, Sinuses and Fistulae have been excluded. There are many signs that point to a diagnosis of Interstitial Cystitis with certainty. These Include:

- High Levels of Antiproliferative-Factor
- Hunner's Ulcer (Seen on Cystoscopy in about 10% patients with IC/BPS1)
- Glomerulations (Seen on Cystoscopy)

Supportive evidence may be acquired by tests like

- Urine culture
- Uroflowmetry

- Micturition diary
- Ultrasonography of the lower abdomen and pelvis
- MRI of the pelvis and urethra
- Cystoscopy with hydrodistension
- Bladder biopsy
- Pelvic floor muscle evaluation
- Urine for AFB (3 samples)
- Urine Culture for Tuberculosis
- Urodynamics

The mandatory initial screening tests are urinalysis, frequency volume chart and ultrasonography. They are complemented by a thorough history and examination.

Cystoscopy has an important role to both confirm the diagnosis as well as to categorize the disease into ulcerative vs non ulcerative IC/BPS. According to the criteria of the NIDDK, HD must take place under anesthesia, at a pressure of 80 to 100 cmH<sub>2</sub>O, lasting 1 to 2 minutes and up to 2 times<sup>2</sup>. According to Nordling et al<sup>3</sup>, the bladder should be filled with glycine with the bottle kept at a height of 80cms from the pubic symphysis. Once the irrigation stops on its own one should wait for 3 minutes to observe the tell tale signs of IC/BPS. Cystoscopy with hydrodistension has a key role in identification of patients with BPS/IC (3C subtype vs. other subtypes)<sup>4</sup>.

### ESSIC Classification based on Cystoscopy with hydrodistension

Cystoscopy	not done	normal	glomerulation	Hunner's lesion
Biopsy				
Not done	XX	1X	2X	3X
Normal	XA	1A	2A	3A
Inconclusive	XB	1B	2B	3B
Positive*	XC	1C	2C	3C

### Management Guidelines

Management of IC/BPS revolves around correct diagnosis and a multidisciplinary approach starting from lifestyle changes and medication to rarely removal of the bladder itself. Advice should also cover sensitive areas like sexuality as there is a close connect between IC/BPS and sexuality<sup>5</sup> and sexual distances will be usually helpful. As a gynaecologist, if you suspect the possibility of IC/BPS in your patient dietary modifications and lifestyle modifications must immediately be instituted. A comprehensive list of medications and various forms of treatment are also advised in this section. All therapies should however be preceded by counselling that this disease is associated

with flares, and medications can only alleviate symptoms to an extent but not necessarily cure the disease.

### Dietary Changes:

Elimination diet is the best way to reduce flares in IC/BPS. There are certain foods which are known to cause a flare or sudden worsening in the symptoms.

Item type	Most Bothersome	Least Bothersome
Beverages	Regular and Decaf Cofee, Cola, Non- Colas, Diet and Caffeine Free, Beer, Red Wine, White Wine, Champagne	Water/Milk – Low Fat and Whole
Fruits	Grapefruit, Lemon, Orange, Pineapple, Cranberry, Grapefruit	Bananas, Blueberries, Honeydew Melon, Pears, Raisins, Watermelon
Vegetables	Tomato and Tomato Products, Hot Peppers, Spicy Foods, Chilli, Horseradish, Vinegar, Monosodium Glutamate	Broccoli, Brussels Sprouts, Cabbage, Carrots, Cauliflower, Celery, Cucumbers, Mushrooms, Peas, Radishes, Squash, Zucchini, White Potatoes, Sweet Potatoes and Yams
Other	Artificial Sweeteners, Nutrasweet, Sweet N Low, Equal (Sweetener), Saccharin, Ethnic Spicy foods	Chicken, Eggs, Turkey Beef, Pork, Lamb Shrimp, Tuna Fish, Salmon Oat, Rice Popcorn

The best way to make a diet plan is to start with an elimination diet. Start with only boiled semi solids for a few days and then start adding new elements one at a time. Keep noting what suits and what flares your IC/BPS as usually the diet causing flares may vary from individual to individual.

### Behavioural and Lifestyle Changes:

Some important changes that can help reduce flares and alleviate symptoms include regular and active exercise schedule, improving work life balance and reducing stress and regulating fluid intake and timed voiding. The patient should be educated about each of these aspects in detail.

### Pelvic Floor relaxation therapy:

It is of utmost important to understand that Kegels exercises are contraindicated in patients with IC/BPS. These patients need pelvic floor relaxation, for which we recommend lying down on a flat surface for 10 - 15 minutes and imagining a light over the pelvic area relaxing the muscles of the pelvic floor with each deep breath. This can be done twice in a day.

### Oral Medications:

A large variety of medications are helpful in IC/BPS patients. These include non steroidal anti-inflammatory agents, opiates, anti-anxiety medications, antidepressants, nerve relaxants and medicines that help to restructure and repair the leaky urothelium. Here are some common medicines along with their daily doses:

Amitriptyline is a very useful nerve relaxant that is very helpful in patients with IC/BPS. Its good to start with 10 mg once a day and increase it to upto 75mg per day while balancing and slowly allowing the body to get used to side effects such as drowsiness, constipations, palpitations and dry mouth.

Hydroxyzine is very helpful if an allergic cause of IC/BPS is suspected and the dosage varies from 25 to 75 mg per day. It needs to be used with caution in elderly because of side effects like confusion and sedation.

Pentosan Polysulphate helps in regeneration of the urothelial barrier and can be initiated in a dose of 300mg/day. It is given in 3 divided doses of 100mg each.

Addition of tramadol or tapentadol is very useful to reduce pain due to central action of opioids. Tramadol in a dose of 50mg thrice a day and Tapentadol in a dose of 50mg twice a day titratable upto 150 mg twice a day can be initiated.

To reduce strain on pelvic floor muscles, relaxants such as cyclobenzaprine can be added in a daily dose of 15mg/day.

Assessment of response to medication and lifestyle and diet changes must be done on a regular basis so that maximum effectiveness of treatment can be ensured. If there is poor relief with above oral medications and lifestyle changes, intravesical therapy consisting of weekly instillations can be done.

Other forms of therapy include cystoscopy and installation of Botulinum toxin A, TENS, Sacral Neuromodulation and sometimes there may be a need for urinary diversion and cystectomy. Many patients who have developed a mental habit of this sensation or pain may still not be cured despite removing the bladder.

### References

1. Cole EE, Scarpero HM, Dmochowski RR. Are patient symptoms predictive of the diagnostic and/or therapeutic value of hydrodistention? *Neuro-urology Urodyn.* 2005; 24(7):638-42.
2. Wein AJ, Hanno PM, Gillenwater JY. Interstitial cystitis: an introduction to the problem. In: Hanno PM, Staskin DR, Krane RJ, et al, editors. *Interstitial cystitis.* London: Springer-Verlag, 1990:3-15.
3. Nordling J, Anjum FH, Bade JJ, Bouchelouche K, Bouchelouche P, Cervigni M, Elnell S, Fall M, Hald T, Hanus T, Hedlund H, Hohlbrugger G, Horn T, Larsen S, Leppilahti M, Mortensen S, Nagendra M, Oliveira PD, Osborne J, Riedl C, Sairanen J, Tinzl M, Wyndaele JJ. Primary evaluation of patients suspected of having interstitial cystitis (IC). *Eur Urol.* 2004 May; 45(5):662-9.
4. Killinger KA, Boura JA, Peters KM. Pain in interstitial cystitis/bladder pain syndrome: do characteristics differ in ulcerative and non-ulcerative subtypes? *Int Urogynecol J.* 2013 Aug; 24(8):1295-301.
5. Kim SJ, Kim J, Yoon H. Sexual pain and IC/BPS in women. *BMC Urol.* 2019 Jun 6; 19(1):47. doi: 10.1186/s12894-019-0478-0.

## Drugs in Urogynaecology

Dr. Jagdish Gandhi

### Introduction

Urogynaecology encompasses mainly the management of lower urinary tract disorders and genital prolapse. Some of these disorders may be managed with drugs especially bladder dysfunctions whilst surgical management may be inevitable in other disorders. This article reviews the drug management of Overactive bladder (OAB), Urinary Stress incontinence (USI), Bladder pain syndrome (BPS) / Interstitial cystitis, Nocturnal enuresis and Urogenital atrophy.

### Drugs for Overactive bladder (OAB)

Overactive bladder is defined by the International Continence Society as a syndrome of urinary urgency, often with urinary frequency and nocturia, in the absence of local pathological factors<sup>1</sup>. Overactive bladder is a common syndrome, and prevalence increases with age. In women, prevalence ranges from 9–43%<sup>2</sup>.

Drugs used in the management of overactive bladder works through one of the following mechanism.

1. Inhibition of the detrusor muscles contractions – Anticholinergics/ Antimuscarinics such as Solifenacin
2. Relaxation of the detrusor muscles – Beta 3 adrenoceptor agonist such as Mirabegron
3. Increasing bladder outlet resistance – Alpha adrenergic agonist
4. Decreasing urine production – Antidiuretics such as Desmopressin

**Anticholinergic drugs** – These drugs remain the mainstay of pharmacotherapy<sup>3</sup>.

Mechanism of action - Detrusor muscle contractility is primarily controlled by the parasympathetic nervous system via acetylcholine acting on muscarinic receptors<sup>4</sup>. Antimuscarinic drugs block acetylcholine from binding to muscarinic receptors. M2 is the most common receptor within the bladder but M3 is more active in detrusor function<sup>5</sup>. Drugs including Oxybutynin, Tolterodine, Fesoterodine and Trospium are antagonists of muscarinic receptors M2 & M3. Drugs including Solifenacin and Darifenacin are selective M3 receptor antagonists.

Side effects – (Figure 1) Antimuscarinic drugs are associated with systematic anticholinergic adverse effects, including dry mouth, constipation, blurring vision, urinary retention, confusion and tachycardia. These and other adverse effects contribute to low medication persistence<sup>5</sup>. Caution is needed for women with autonomic neuropathy, hiatus hernia and hepatic and renal impairment. Anticholinergics can worsen hyperthyroidism, coronary artery disease, congestive heart failure and arrhythmias. Anticholinergics are contraindicated in women with myasthenia gravis, closed angle glaucoma, significant bladder outflow obstruction or urinary retention, severe ulcerative colitis and gastrointestinal obstruction.

Studies by Akino et al.<sup>6</sup> showed that more patients withdrew because of adverse events than lack of efficacy. Hence, when selecting drug treatment for OAB, consideration of adverse events is as important, if not more important, than efficacy.

## Systemic impact of anticholinergics

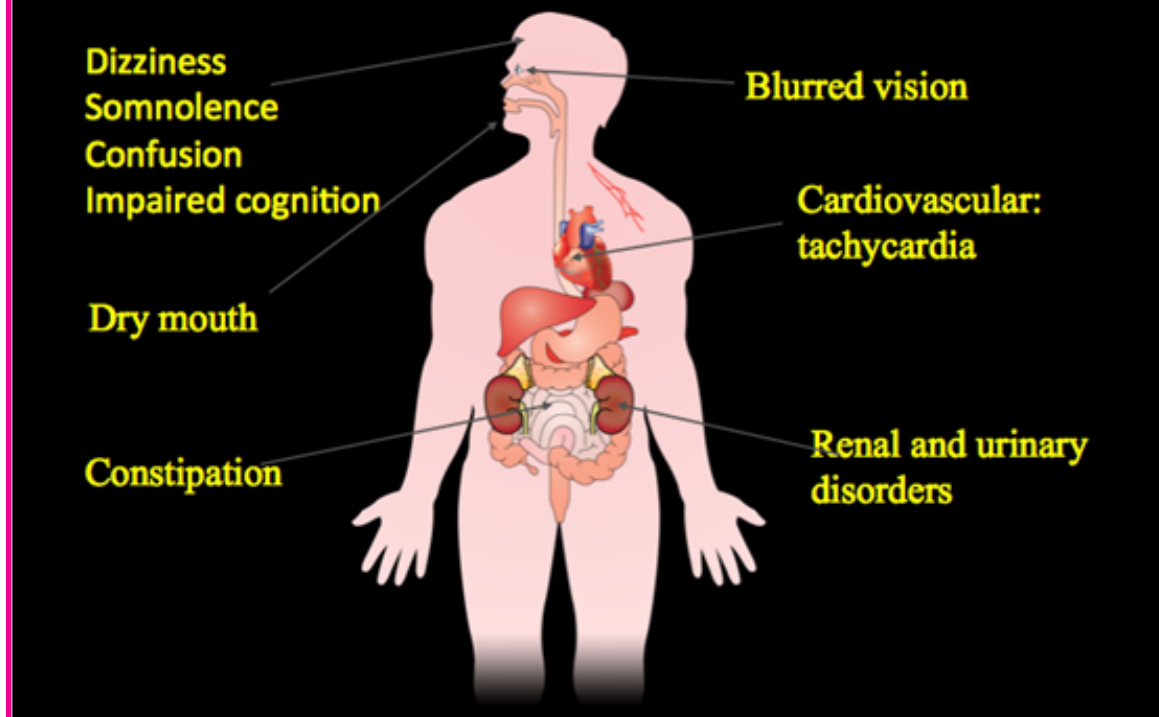


Figure 1

### Choosing medicine

Hsu et al.<sup>7</sup> reported that Fesoterodine 8 mg shows greater improvement in incontinence, urgency episodes, and micturition frequency than Tolterodine 4 mg. However, Fesoterodine appears to have a worse safety profile due to adverse events such as constipation, and dry mouth than Tolterodine.

NICE<sup>8</sup> recommends not offering women flavoxate, propantheline or imipramine to treat urinary incontinence or overactive bladder. Also not to offer oxybutynin (immediate release) to older women who may be at higher risk of a sudden deterioration in their physical or mental health. Offer a transdermal overactive bladder treatment to women unable to tolerate oral medicines.

Frail older women

Antimuscarinic drugs may work differently in frail older women and women with multiple co-morbidities of any age. These drugs have

differing affinities for antimuscarinic receptors within the brain and a variable ability to cross the blood brain barrier. This has the potential for adverse effects on cognitive function. Hence anticholinergics should be given only after a full medication review<sup>8</sup>.

Oxybutynin, is the one most likely to cross the blood-brain barrier. Newer agents such as tolterodine and darifenacin have low lipophilicity and are thought to be more suitable for older patients. Trospium is the least likely to impair CNS function based on neuropsychological and coordination tests<sup>9</sup>.

Counseling - Women should be told explicitly about the likelihood of success and failure, known side-effects of each drug, such as dry mouth and constipation, and that side-effects may indicate that the treatment is working. It may take about 4 weeks before drug start showing benefit and hence women should be encouraged to persevere for at least this period of time if possible. If a woman shows limited improvement, no improvement or report-

ed intolerable adverse effects, then treatment should be revised. This amendment could be either a change in dosage, a change in drug or switching to another type of treatment<sup>8</sup>.

Reviewing drugs

A review at 4 weeks after starting a new medicine for overactive bladder and making necessary changes of dose or alternative medicine is advisable.

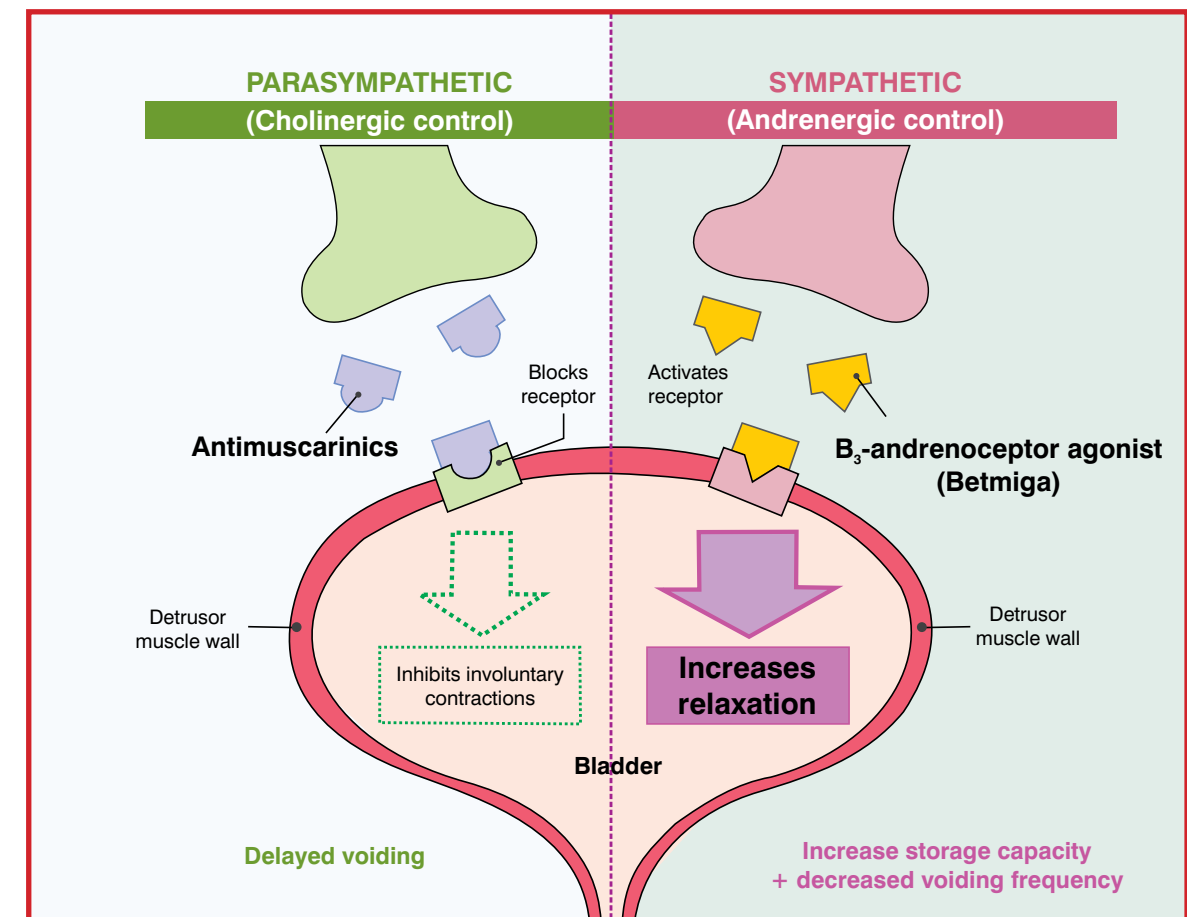
**Mirabegron** is recommended as an option for treating the symptoms of overactive bladder only for people in whom antimuscarinic drugs are not effective or suitable. Three recent systematic reviews found mirabegron had similar efficacy to most antimuscarinics<sup>10-12</sup>.

Mechanism of action - Mirabegron mimics sympathetic activity by stimulating the  $\beta_3$ -adrenoceptors on the detrusor muscle, promoting bladder relaxation during the filling stage<sup>13</sup>.

Side effects - Increased blood pressure, nasopharyngitis, urinary tract infection, and headache are common adverse effects with mirabegron, and dizziness and urinary retention have also been reported.

Drake et al.<sup>14</sup> noted that adding mirabegron 50mg to solifenacin 5mg improved OAB symptoms when compared with solifenacin 5 or 10mg, and it was well tolerated in OAB patients. However, combination therapy also showed higher incidences of adverse events vs. monotherapy. The small potential benefit in key OAB outcomes with combination therapy should be weighed against increased risk of adverse events<sup>7</sup>.

Mode of action of OAB treatments (Figure 2)

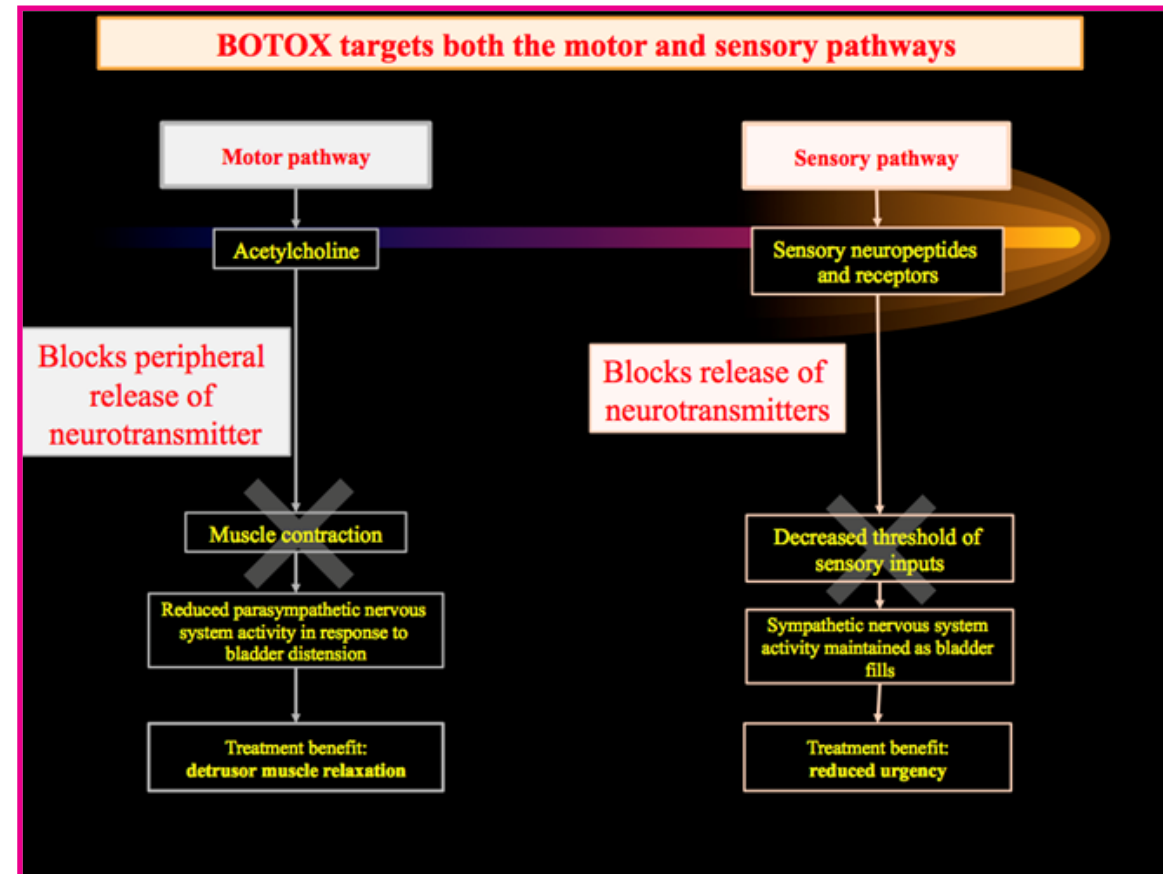


## Invasive procedures for overactive bladder

### Botulinum toxin type A injection (BOTOX)

NICE recommends offering bladder wall injection with botulinum toxin type A to women with overactive bladder caused by detrusor overactivity that has not responded to non-surgical management.

Mechanism of action - Botox blocks the pre-synaptic release of acetylcholine and causes full or partial paralysis and weakening of overactive muscle. (Figure. 3)



Current evidence - suggests that Botox may be effective for the symptomatic treatment of OAB. Its use should however be reserved for patients who fail to improve with conservative treatment and medical management with two different anticholinergic drugs<sup>15</sup>.

Drake et al.<sup>16</sup> concluded that after 12 weeks, Onabotulinumtoxin A 100 U provides greater relief of OAB symptoms compared with most other licensed medicines. Similarly multiple randomized, placebo-controlled trials demonstrated that botulinum toxin A to be an effective

treatment for patients with refractory idiopathic or neurogenic detrusor overactivity. The urinary incontinence episodes, maximum cystometric capacity, and maximum detrusor pressure were improved greater by botulinum toxin A compared to placebo. The adverse effects of botulinum toxin A, such as urinary retention and urinary tract infection, were primarily localised to the lower urinary tract<sup>17</sup>. Nitti et al.<sup>18</sup> noted that long-term Onabotulinumtoxin A treatment consistently decreased overactive bladder symptoms and improved quality of life with no new safety signals.

### Precautions & Counselling

The women need to be informed the likelihood of complete or partial symptom relief, possible voiding disorder and need for clean intermittent catheterisation, and increased risk of urinary tract infection. She should also be informed that there is not much evidence about how long the injections work for, how well they work in the long term and their long-term risks<sup>8</sup>.

The procedure is performed under local or general anaesthesia using a flexible or rigid cystoscope. BOTOX 100-200 units are dissolved in 10-20 mls of saline and 1 ml solution is injected at 10-20 sites into the bladder wall, avoiding trigone and ureteric orifices. A post operative review is required at 3 months and if treatment has been beneficial then a repeat procedure may be offered with adjusted dose when OAB symptoms recur.

### Drugs for Stress Urinary Incontinence

Duloxetine is licensed for use in moderate to severe stress UI. It is a serotonin and noradrenaline reuptake inhibitor that acts chiefly in the sacral spinal cord. It is thought that the resultant increase in pudendal nerve activity increases urethral sphincter contraction and closure pressure. A Cochrane systematic review concluded the effectiveness of serotonin and noradrenaline reuptake inhibitors (duloxetine) for the treatment of stress UI<sup>19</sup>.

Nausea was significantly more common with all daily dosages of duloxetine compared with placebo<sup>20</sup>. Other adverse effects were dry mouth, constipation, fatigue, insomnia, dizziness, increased sweating, vomiting and somnolence. NICE suggests not to use duloxetine as a first-line treatment for women with predominant stress UI<sup>8</sup>.

### Drugs for Nocturnal enuresis/ Nocturia

Desmopressin (DDAVP)

The use of desmopressin may be considered specifically to reduce nocturia in women with UI or OAB who find it a troublesome symptom. It increases the reabsorption of water, concen-

trates urine and reduces urine production. It needs to be taken at bedtime and advise the women to limit fluid intake from 1 hour before to 8 hours after administration. Use particular caution in women with cystic fibrosis and avoid in those over 65 years with cardiovascular disease or hypertension. It can cause fluid overload and hyponatraemia<sup>21</sup>.

### Drugs for Bladder pain syndrome (BPS) / Interstitial Cystitis

Bladder pain syndrome (BPS) is a chronic pain syndrome and the principles of management of chronic pain should be used for the initial assessment of this condition. BPS is a diagnosis of exclusion and other conditions should be excluded.

The initial treatment with analgesic drugs is recommended along with conservative management including dietary and fluid modification and exercise. If these fail then oral Amitriptyline or Cimetidine may be considered. A systematic review<sup>22</sup> that included a total of 281 patients who were treated with increasing titrated doses of amitriptyline between 10 mg and 100 mg over a 4-month period showed trends in improvement in urinary urgency, frequency and pain scores in both trials compared with non treated patients.

One RCT<sup>23</sup> compared 36 patients treated with a 3-month course of 400 mg cimetidine orally versus placebo twice daily. All patients had symptomatic improvements, but these were more pronounced in the treatment group, especially for pain and nocturia. Cimetidine is currently not licensed for the treatment of BPS.

Oral hydroxyzine or pentosan polysulfate does not appear to be an effective treatment for BPS<sup>24</sup>.

### Intravesical treatments

If initial treatments fail next approach is the intravesical instillations of Lidocaine, Hyaluronic acid, Dimethyl Sulfoxide (DMSO), Heparin or Chondroitin sulphate or indeed Intravesical injection of botulinum toxin A (Botox).

Lidocaine is a local anaesthetic that acts by

blocking sensory nerve fibres in the bladder. Matsuoka<sup>25</sup> reported on 102 patients treated with a 5-day course of 200 mg intravesically administered Lidocaine with alkalinised instillation of 8.4% sodium bicarbonate to a final volume of 10 ml versus placebo. Over a 29-day follow-up period, 30% of treated patients compared with 9.6% of the control group reported symptomatic improvement.

A systematic review of controlled and observational studies evaluated hyaluronic acid given in a weekly regimen for up to 4–10 weeks. It appears to be an effective intravesical treatment<sup>26</sup>.

A systematic review<sup>27</sup> evaluated 33 patients given placebo (saline) or 50% DMSO for two sessions each week for 2 weeks. Of the treatment group, 53% had marked symptomatic improvement compared with 18% of the placebo group. Adverse effects include a garlic-like taste and odour on the breath and skin, and bladder spasm. Full eye examination is needed prior to starting treatment and 6-monthly blood tests for renal, liver and full blood counts are advised.

One observational study<sup>28</sup> evaluated 48 patients treated with 10,000 units of heparin in 10 ml sterile water instilled three times a week for 3 months. The study reported that 56% of patients achieved clinical remission over 3 months and 50% of patients had symptomatic control after 1 year.

An individual participant meta-analysis of 213 patients<sup>29</sup> showed some benefit in the global response assessment using 2% intravesical chondroitin sulfate.

A systematic review<sup>30</sup> with a total of 260 patients evaluating intravesical injection of Botox in BPS patients found symptomatic improvement although, 7% of patients needed post-treatment self-catheterisation.

## Drugs for Urogenital atrophy

Vaginal lubricants and moisturisers are used to reduce vaginal dryness and pain during intercourse in women with mild to moderate Vulvo Vaginal Atrophy (VVA). Lubricants and moisturisers work in different ways and are particularly helpful for women who are not medically

suitable to take estrogen<sup>31</sup>. A variety of vaginal lubricants are commercially available and can be water-based, plant oil-based, mineral oil-based or silicone-based products. It is generally perceived that oil-based and silicone-based lubricants are thicker in composition and longer lasting compared with water-based lubricants. The effect of moisturisers is longer lasting compared with lubricants, if used regularly. Therefore, moisturisers are not only used by women with VVA who have painful intercourse, but also by symptomatic women who are not sexually active<sup>32</sup>.

### Topical vaginal estrogen

Atrophic vaginitis is treatable with topical estrogen, which improves lubrication and sexual function. Systemic absorption is insignificant with low-dose topical estrogen<sup>33</sup>.

Vaginal estrogen may reduce symptoms of urgency of micturition and recurrent urinary tract infections. Vaginal symptoms can persist even when on adequate systemic HRT; in such cases both topical and systemic estrogen are required.

Several vaginal estrogen preparations are available, including estradiol and estriol creams, tablets and rings. The lowest possible dose that provides effective relief of symptoms should be used as maintenance therapy.

A recent Cochrane review of 30 randomised controlled trials, representing 6235 postmenopausal women, compared intravaginal estrogenic preparations to one another or with placebo. The review concluded that there was no difference in efficacy between the various intravaginal estrogenic preparations when compared to each other<sup>34</sup>.

### Topical oestrogen – Prolapse

NICE guideline on menopause [2019] advises to consider vaginal oestrogen for women with pelvic organ prolapse and signs of vaginal atrophy. Also consider an oestrogen-releasing ring for women with pelvic organ prolapse and signs of vaginal atrophy who have cognitive or physical impairments that might make vaginal oestrogen pessaries or creams difficult to use.

Local Estrogen for genital/ breast cancer patients

A case–control study of 271 women with breast cancer on Tamoxifen or aromatase inhibitors concluded that there is no increased risk of recurrence in women on vaginal estrogen therapy, with a mean follow-up of 3.5 years<sup>35</sup>.

In 2014, a meta-analysis concluded that there is no increased risk of recurrence in women who are taking HRT following treatment of endometrial cancer<sup>36</sup>. Following ovarian cancer, although some concerns have been expressed about systemic treatment, there are no data to suggest an increased risk of recurrence with either systemic or local estrogen therapy<sup>37</sup>.

The benefits of topical vaginal estrogen to the genitourinary tract may outweigh the risk.

### Androgens and dehydroepiandrosterone

Androgens play an essential role in female sexual function. Multiple studies have compared the use of vaginal testosterone to other treatments and found it to be safe and effective<sup>38</sup>.

A recent study compared the effect of intravaginal DHEA (prasterone), conjugated equine estrogens and estradiol on moderate to severe dyspareunia and/or vaginal dryness. The authors concluded that 6.5 mg prasterone used daily appears to be as efficacious as 0.3 mg conjugated equine estrogens or 10 µg estradiol for the treatment of VVA<sup>39</sup>.

## Conclusion

Anticholinergic drugs remain the mainstay in the management of the overactive bladder, though side effects are the main reason for discontinuation by the patients. Mirabegron is a suitable for OAB treatment and has become a well-established alternative to the anticholinergics. Efficacy of BOTOX in treating OAB is excellent with low side effect profile. BOTOX has been used successfully for patient with Bladder pain syndrome / Interstitial cystitis. There is no suitable drug for stress urinary incontinence and use of Duloxetine has been short lived. Desmopressin is a well recognized and well proven for the management of Nocturnal enuresis but patient needs close monitoring. Use of Estrogen for urogenital atrophy meets with excellent results and is relatively a safe drug.

## References

- Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, Van Kerrebroeck P, Victor A, Wein A. The standardisation of terminology of lower urinary tract function: report from the standardization sub-committee of the International Continence Society. *Neurourol Urodyn*. 2002;21:167–178. doi:10.1002/nau.10052.
- Gormley EA, Lightner DJ, Faraday M, Vasavada SP. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline amendment. *J Urol*. 2015;193(5):1572–1580. doi:10.1016/j.juro.2015.01.087.
- Munjuluri N, Wong W, Yoong W. Anticholinergic drugs for overactive bladder: a review of the literature and practical guide. *The Obstetrician and Gynaecologist*. 2007; 9:9–1
- Abrams P, Andersson KE, Buccafusco JJ, Chapple C, de Groat WC, Fryer AD, Kay G, Laties A, Nathanson NM, Pasricha PJ, Wein AJ. Muscarinic receptors: their distribution and function in body systems, and the implications for treating overactive bladder. *Br J Pharmacol*. 2006;148(5):565–578. doi:10.1038/sj.bjp.0706780
- Kumar V, Templeman L, Chapple CR, Chess-Williams R. Recent developments in the management of detrusor overactivity. *Curr Opin Urol*. 2003;13(4):285–291. doi: 10.1097/00042307-200307000-00004.
- Akino H, Namiki M, Suzuki K, Fuse H, Kitagawa Y, Miyazawa K, Fujiuchi Y, Yokoyama O. Factors influencing patient satisfaction with antimuscarinic treatment of overactive bladder syndrome: results of a real-life clinical study. *Int J Urol*. 2014;21(4):389–394. doi: 10.1111/iju.12298.
- Hsu, FC, Weeks, CE, Selph, SS, et al. (2019) Updating the evidence on drugs to treat overactive bladder: A systematic review. *International Urogynecology Journal* 30: 1603-1617
- National Institute for Health and Care Excellence. Urinary incontinence: the management of urinary incontinence in women. NICE clinical guideline No. 171. Manchester: NICE; 2013.
- Kay GG, Granville LJ. Antimuscarinic agents: implications and concerns in the management of overactive bladder in the elderly *Clin Ther* 2005 27 127–38.
- National Institute for Health and Care Excellence. Mirabegron for Treating Symptoms of Overactive Bladder [NICE Technology Appraisal Guidance 290]. London: NICE; 2013. Available at: <http://www.nice.org.uk/guidance/ta290>. Accessed July 2017.
- Maman K, Aballea S, Nazir J et al. Comparative efficacy and safety of medical treatments for the management of overactive bladder: a systematic literature review and mixed treatment comparison. *EurUrol* 2014; 65: 755–65
- Selph S, Carson S, McDonagh M. Summary Review: Overactive Bladder Drugs. Portland, OR: Health & Science University, Pacific Northwest Evidence-based Practice Center, 2013
- Andersson KE. On the site and mechanism of action of beta3-adrenoceptor agonists in the bladder. *International neurourology journal*. 2017;21(1):6–11. doi: 10.5213/inj.1734850.425.
- Drake MJ, Chapple C, Esen AA, Athanasiou S, Cambroner J, Mitcheson D, Herschorn S, Saleem T, Huang M, Siddiqui E, Stolzel M, Herholdt C, MacDiarmid S, investigators Bs (2016) Efficacy and safety of mirabegron add-on therapy to solifenacin in incontinent overactive bladder patients with an inadequate response to initial 4-week solifenacin monotherapy: a randomised double-blind multicentre phase 3B study (BESIDE). *Eur Urol* 70 (1):136–145.
- Tincello D, Fowler CJ, Slack M. Botulinum Toxin for an Overactive Bladder. Royal College of Obstetricians and Gynaecologists. Scientific Impact Paper No. 42. February 2014. [https://www.rcog.org.uk/globalassets/documents/guidelines/sip\\_42\\_13022014.pdf](https://www.rcog.org.uk/globalassets/documents/guidelines/sip_42_13022014.pdf).
- Drake MJ, Nitti VW, Ginsberg DA, Brucker BM, Hepp Z, McCool R, Glanville JM, Fleetwood K, James D, Chapple CR. Comparative assessment of the efficacy of onabotulinumtoxinA and oral therapies (anticholinergics and mirabegron) for overactive bladder: a systematic review and network meta-analysis. *BJU Int*. 2017;120(5):611–622. doi: 10.1111/bju.13945.



17. Hsieh, P. F., Chiu, H. C., Chen, K. C., Chang, C. H. & Chou, E. C. Botulinum toxin A for the Treatment of Overactive Bladder. *Toxins* 8, (2016).
18. Nitti VW, Ginsberg D, Sievert KD, Sussman D, Radomski S, Sand P, De Ridder D, Jenkins B, Magyar A, Chapple C. Durable efficacy and safety of long-term On a botulinum toxin A treatment in patients with overactive bladder syndrome: final results of a 3.5-year study. *J Urol* 2016; 196:791-800.
19. Mariappan P, Ballantyne Z, N'Dow JMO, Alhasso AA. Cochrane Database of Systematic Reviews.1. Oxford: Update Software; 2006. Serotonin and noradrenaline reuptake inhibitors (SNRI) for stress urinary incontinence in adults. (Cochrane Review)
20. Dmochowski RR, Miklos JR, Norton PA, et al. Duloxetine versus placebo for the treatment of North American women with stress urinary incontinence. *Journal of Urology*. 2003;170(4 Part 1):1259-63.
21. Lose G, Galos O, Freeman RM, van Kerrebroeck P Efficacy of desmopressin (Minirin) in the treatment of nocturia: a double-blind placebo-controlled study in women *Am J Obstet Gynecol* 2003 189 1106-13 doi:10.1067/S0002-9378(03)00593-3.
22. Giannantoni A, Bini V, Dmochowski R, Hanno P, Nickel JC, Proietti S, et al. Contemporary management of the painful bladder: a systematic review. *Eur Urol* 2012;61:29-53.
23. Thilagarajah R, Witherow RO, Walker MM. Oral cimetidine gives effective symptom relief in painful bladder disease: a prospective, randomized, double-blind placebo-controlled trial. *BJU Int* 2001;87:207-12.
24. Tirilapur SABJ, Carberry CL, Khan KS et al. Management of bladder pain syndrome: Green-top guideline No. 70. *BJOG* 2016; 124: e46-72.
25. Matsuoka PK, Haddad JM, Pacetta AM, Baracat EC. Intravesical treatment of painful bladder syndrome: a systematic review and meta-analysis. *Int Urogynecol J* 2012;23:1147-53.
26. Barua JM, Arance I, Angulo JC, Riedl CR. A systematic review and meta-analysis on the efficacy of intravesical therapy for bladder pain syndrome/interstitial cystitis. *Int Urogynecol J* 2016;27:1137-47.
27. Dimitrakov J, Kroenke K, Steers WD, Berde C, Zurakowski D, Freeman MR, et al. Pharmacologic management of painful bladder syndrome/interstitial cystitis: a systematic review. *Arch Intern Med* 2007;167:1922-9.
28. Parsons CL, Housley T, Schmidt JD, Lebow D. Treatment of interstitial cystitis with intravesical heparin. *Br J Urol*1994;73:504-7
29. Thakkinian A, Nickel JC. Efficacy of intravesical chondroitin sulphate in treatment of interstitial cystitis/bladder pain syndrome (IC/BPS): Individual patient data (IPD) meta-analytical approach. *Can Urol Assoc J* 2013;7:195-200
30. Tirumuru S, Al-Kurdi D, Latthe P. Intravesical botulinum toxin A injections in the treatment of painful bladder syndrome/interstitial cystitis: a systematic review. *Int Urogynecol J* 2010;21:1285-300
31. Sinha A, Ewies AA. Nonhormonal topical treatment of vulvovaginal atrophy: an up-to-date overview. *Climacteric* 2013; 16: 305-12.
32. Khanjani S, Panay N. Vaginal estrogen deficiency. *TOG* 2019; 1: 37-42
33. S H Bakour, J Williamson. Latest evidence on using hormone replacement therapy in the menopause. *The Obstetrician & Gynaecologist*2014; <http://onlinelibrary.wiley.com/doi/10.1111/tog.12155/>.
34. Lethaby A, Ayeleke RO, Roberts H. Local oestrogen for vaginal atrophy in postmenopausal women. *Cochrane Database Syst Rev* 2016;( 8): CD001500.
35. Le Ray I, Dell'Aniello S, Bonnetain F, Azoulay L, Suissa S. Local estrogen therapy and risk of breast cancer recurrence among hormone-treated patients: a nested case-control study. *Breast Cancer Res Treat* 2012; 135: 603-9
36. Shim SH, Lee SJ, Kim SN. Effects of hormone replacement therapy on the rate of recurrence in endometrial cancer survivors: a meta-analysis. *Eur J Cancer* 2014; 50: 1628-37.
37. Guidozzi F. Estrogen therapy in gynecological cancer survivors. *Climacteric* 2013; 16: 611-7.
38. Lemke EA, Madsen LT, Dains JE. Vaginal testosterone for management of aromatase inhibitor-related sexual dysfunction: an integrative review. *Oncol Nurs Forum* 2017; 44: 296-301.
39. Archer DF, Labrie F, Montesino M, Martel C. Comparison of intravaginal 6.5mg (0.50%) prasterone, 0.3mg conjugated estrogens and 10µg estradiol on symptoms of vulvovaginal atrophy. *J Steroid Biochem Mol Biol* 2017; 174: 1-8

# Complete Perineal Tear

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## Introduction

Old complete perineal tear (also known as chronic perineal laceration) is defined as third degree obstetric perineal tear involving perineal body (perineal skin and perineal muscles) and anal sphincter with or without including anal mucosa which has not healed. It is a result of non-healed or non-sutured third and fourth degree of obstetric perineal tears and remains beyond three months after delivery or injury.<sup>1</sup>

It may occur due to: 1-4

### • Obstetric causes

It is the most common cause and occurs due to following risk factors:

1. Over stretched perineum
  - a. Large fetal weight
  - b. Midline episiotomy
  - c. Prolonged labour
  - d. Difficult labour
  - e. Instrumental delivery
  - f. Shoulder Dystocia
  - g. Occipito-posterior position
2. Rapid stretching of the perineum.
  - a. Precipitate labour
  - b. Breech delivery
3. Rigid perineum
  - a. Elderly primigravida
  - b. Vulvar edema

c. Scarred perineum as a result of previous surgeries

d. Previous perineal tear

### • Traumatic causes

1. Road traffic accidents with fracture pelvis and perineal tear.
2. Coital injuries mainly due to rape especially in young girls or elderly woman with inelastic perineum.
3. Surgical trauma

Past history of surgery on anal canal or perineum if not healed well. Past history of attempt to perform immediate suturing after complete perineal tear (third and fourth degree) during delivery which failed.

4. Fall from height with some sharp or blunt object directly hitting the perineum may result in complete perineal tear

## Clinical Features

It is generally seen in a primiparous woman with past history of difficult or obstructed labor or instrumental delivery with increased bleeding along with symptoms of anal incontinence following childbirth.<sup>1,4</sup>

### Symptoms

1. Fecal incontinence: It is varying based on the degree of damage to external anal sphincter. The fecal incontinence is only for loose stools (during diarrhea) if mild injury but may be for solid stools also in the event of complete damage to the sphincter.
2. Flatus incontinence is commonly present.

3. As a result of irritation by fecal matter, pain and redness in perineum may be seen.<sup>1,4</sup>

### Signs

1. The perineal body is frequently absent on inspection. The red shining mucus membrane of anal canal and rectum and pinkish vaginal wall are seen lying together with barely any perineum in between as shown in Figure 1.
2. On either side of anus (at around 3 and 9 o'clock positions), two dimples (depressions) are seen relative to the severed ends of external sphincter muscles.
3. Radial folds of skin which normally occur all around the anal verge are now seen only in posterior half (where external sphincter is present) whereas they are absent in anterior half (where external sphincter is torn).<sup>1,4</sup>



4. On speculum examination, upper vagina and cervix are mostly normal (old cervical tear may be seen in difficult labor). Any associated genital prolapse is looked for.<sup>1,4</sup>
5. On vaginal examination, cervix and uterus are normal. Bilateral adnexa are normal. Though, lower part of vagina may be torn.<sup>1,4</sup>
6. On rectal examination, there is no sphincteric grip on the examining rectal finger due to torn sphincter. Any associated rectal prolapse or hemorrhoids are looked for.<sup>1,4</sup>
7. On combined recto-vaginal examination, anal canal and vagina lie close to each other with only a small septum between the

two, which is felt when one finger inserted in vagina and one finger in rectum. Levator ani tone is examined which is normally good. Complete perineal tear is mostly not associated with genital prolapse because of better tone of levator ani muscles (forced daily contraction of levator ani muscles acts like routine pelvic floor exercises) preventing prolapse.<sup>1,4</sup>

### Investigations

Diagnosis is generally made clinically (from typical symptoms and clinical examination).

1. A defect in the anal sphincter can be detected by transperineal ultrasound or anal ultrasound especially three-dimensional ultrasound.
2. A defect in the external anal sphincter may be detected by magnetic resonance imaging.
3. Microscopic stool examination for any cysts or ova as helminthiasis (worm infestations) and amoebiasis are common. They should be treated before surgery.<sup>1,4</sup>

### Differential diagnosis

Rectovaginal fistula is a vital differential diagnosis since it also leads to fecal and flatus incontinence. Diagnosis can be confirmed by vaginal, rectal and recto-vaginal examination. Proctography can be done for high fistula.<sup>1</sup>

### Management

#### Prevention

Most perineal tears can be avoided by proper conduction of delivery, avoiding obstructed labor and difficult instrumental deliveries.<sup>1,4</sup> The various preventive steps to prevent perineal tear are:

1. Delivery of fetal head should be carried in a controlled way by ensuring flexion of the head with left hand and perineal support with right hand.
2. Episiotomy: Liberal use of episiotomy does not reduce the incidence of third degree

tears. It should only be given aptly for indications like instrumental delivery and large baby and must be performed timely.

3. Perineal massage help in relaxing the perineal muscles and may be starting a week before delivery.
4. Mode of delivery: Elective cesarean delivery prevents damage to perineum from labor-related events. Ventouse delivery is associated with reduced perineal injury than forceps delivery. If both instruments are used together then perineal damage is higher than when a single instrument is used.<sup>1,4</sup>

### Treatment

Surgery is the treatment of choice for complete perineal tear. It can either be done within 24 hours after delivery or within 3 months but before 6 months. The reason for delay is that by 3 months, infection and inflammation decreases, her general condition and nutritional status is restored. Delaying for more than 6 months causes dense scar tissue formation making surgery more challenging. However, in India it is frequent to see these patients present many years after its causation. In such cases, surgery must be done promptly to avoid discomfort to the patient.<sup>1,4</sup>

### Pre-operative management

1. Patient is admitted two days before surgery.
2. Soft or non residual diet (milk and fluids) is given. Full diet should not be given.
3. Local vaginal douching is done with Beta-dine or acriflavin.
4. Bowel emptying done by peglac (polyethylene glycol) and enema.
5. Bacterial intestinal flora is controlled by tablet neomycin 250 mg thrice daily or metronidazole 400 mg thrice daily.<sup>1,4</sup>

### Surgical repair

1. Layered method of CPT repair<sup>1,4-5</sup>
  - I. Under spinal anaesthesia (preferred) or general anaesthesia and after bowel

preparation, the patient is put in lithotomy position.

- II. Transverse incision is made at junction of rectal and vaginal mucosa. The incision is extended in the midline of the posterior vaginal wall.
- III. Rectal wall is separated from the posterior vaginal wall with sharp dissection. The ends of external anal sphincter are held with Allis forceps. Internal anal sphincter is identified as a white fibrous tissue between anorectal mucosa and external anal sphincter.
- IV. Anal mucosa is closed with continuous 2-0 or 3-0 vicryl (delayed absorbable polyglactin) sutures. The internal anal sphincter is then closed over anal mucosal sutures with 2-0 or 3-0 vicryl sutures.
- V. The ends of external anal sphincter are mobilized and are brought together over sutured internal anal sphincter. They are sutured together with two rows of delayed absorbable (vicryl 1-0) sutures. They can be stitched as end to end or by overlapping (one sphincter partly covering the other sphincter) technique. The results of both procedures are similar.
- VI. Levator ani (puborectalis) muscles are then brought together with interrupted delayed absorbable vicryl no.1 sutures.
- VII. The bulbocavernosus and superficial transverse perineal muscles are closed (like perineorrhaphy) with 1-0 vicryl sutures.
- VIII. The vaginal mucosa is closed with 1-0 or 2-0 vicryl sutures.
- IX. The perineal skin is closed with 1-0 or 2-0 vicryl sutures as interrupted sutures or subcuticular sutures.

### 2. Warren flap method of CPT repair<sup>1,4-5</sup>

- I. The preliminary work up, anaesthesia and position are similar.
- II. Inverted V shaped incision is given over posterior vaginal mucosa.
- III. The flap of vaginal mucosa is dissected free from above downwards and is turned back downwards.

- IV. The dissected vaginal flap is retracted downwards till the external anal sphincter ends are visible on both sides.
- V. The ends of external anal sphincter are caught with Allis forceps on both sides and are sutured end to end or with an overlapping technique with 1-0 or 2-0 delayed absorbable (vicryl or PDS) sutures.
- VI. Levator ani (puborectalis) muscles are then sutured over external anal sphincter sutures with vicryl no. 1 sutures.
- VII. The vaginal mucosa is closed with continuous 1-0 delayed absorbable (vicryl) sutures. The redundant vaginal mucosa may be trimmed.
- VIII. Perineorrhaphy is done by suturing bulbocavernosus, superficial transverse perineal muscles and perineal skin.

### Post-Operative Care <sup>1,4</sup>

It is similar in both the methods

1. Foley's catheter is kept for 24 hours.
2. Patient is kept nil orally for 24 hours.
3. Intravenous fluids only are given for first 24 hours. Oral fluids (coconut water, tea, soup, etc) are started on day 2.
4. Syrup lactulose (duphalac) 15ml twice daily is started from second day onwards to soften the stools. Usually she passes stools by third day.
5. If she does not pass motion by fourth day, then gentle olive oil enema may be given.
6. Antibiotics are given for about 5 to 7 days. 3rd generation cephalosporin along with metronidazole given intravenously initially for 1 to 2 days then orally for 5 to 7 days. Neomycin may also be continued for 7 days to kill intestinal flora.
7. Betadine (povidone iodine) wash at the repair site should be done daily.
8. Anti-inflammatory agents (ibuprofen with paracetamol) may be given for 5 to 7 days.

### Discharge and Follow-up

Woman is discharged on 6th or 7th day.

1. She should continue laxative (lactulose 15 to 20 ml daily) for about six weeks.
2. Contraceptive advice is given.
3. She should be reassessed after 6 weeks for any complication and the repair site along with anal sphincter tone is examined.
4. If any residual symptoms present, anal ultrasound or MRI may be done to identify any residual disease.
5. Though vaginal delivery with liberal medial episiotomy can be performed, generally elective cesarean delivery is preferred to avoid perineal tear again. <sup>1,4</sup>

### Complications <sup>1,4</sup>

1. Wound dehiscence
2. Infection
3. Residual effects with ongoing fecal and flatus incontinence.
4. Rectovaginal fistula
5. Constipation if repair is too tight.
6. Dyspareunia

#### REFERENCES

1. Sharma JB. Textbook of Gynecology. 1st ed. New Delhi: Avichal Publishing Company; 2018. 19 (iii) : Old Complete Perineal Tear or Chronic Perineal Laceration:431-436.
2. Pergialiotis V, Vlachos D, Protopapas A, Pappa K, Vlachos G. Risk factors for severe perineal lacerations during childbirth. *Int J Gynaecol Obstet.* 2014 Apr;125(1):6-14.
3. Wilson AN, Homer CSE. Third- and fourth-degree tears: A review of the current evidence for prevention and management. *Aust N Z J Obstet Gynaecol.* 2020 Apr;60(2):175-182.
4. Goh R, Goh D, Ellepola H. Perineal tears - A review. *Aust J Gen Pract.* 2018 Jan-Feb;47(1-2):35-38.
5. Aydin Besen M, Rathfisch G. The effect of suture techniques used in repair of episiotomy and perineal tear on perineal pain and dyspareunia. *Health Care Women Int.* 2020 Jan;41(1):22-37.

## Vesicovaginal Fistula

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### Introduction

A fistula is defined as an abnormal communication between more than one epithelial surfaces. In the context of gynaecology, genitor-urinary tract fistulae connect the genital tract (vagina, uterus or perineum) and the urinary tract (bladder, ureter or urethra). This chapter will discuss about vesicovaginal fistulae, that is, an abnormal communication between the urinary bladder and the vagina.

### Etiology

Vesicovaginal fistulae are mainly acquired. Acquired vesicovaginal fistulae can be divided, according to etiology, into obstetric, surgical, radiation, malignant and miscellaneous groups. In most developing countries, over

90% of fistulae are of obstetric etiology, whereas in the developed countries, over 70% follow pelvic surgery<sup>1</sup>.

The most common cause of obstetric fistulae is obstructed labour. Other rare obstetric causes are those following accidental injury at caesarean section, forceps delivery, fetal craniotomy or symphysiotomy and lastly criminal abortion, which sadly is still prevalent in most underdeveloped areas of the country.

Vesicovaginal fistulae following pelvic surgery can result from direct injury at the time of surgery or, more commonly, as a delayed event. The most common gynaecologic pelvic surgery is hysterectomy (laparoscopic, abdominal or vaginal). If the fistula is a delayed event, it is presumed that the fistula occurs as a result of compromised blood supply to part of the urinary tract leading to tissue necrosis and formation of fistula. Infection followed by discharge of a small pelvic hematoma at the vault might be the other explanation.

Other rare causes besides invasive carcinoma of the cervix and vagina include prolonged specific infection, penetrating trauma, neglected pessaries, catheter-related injuries and coital injury.

The true prevalence of vesicovaginal fistulae in the developing world is unknown because of the difficulties of obtaining accurate data, but the estimated prevalence is 1-2 per 1000 deliveries, with perhaps 50000 - 100000 new cases each year<sup>2</sup>.

VVFs can be classified in various ways. Simple fistulas are usually small in size ( $\leq 2.5$ cm) and are present as single non-radiated fistulas. Complex fistulas include previously failed fistula repairs or large-sized ( $\geq 2.5$  cm) fistulas, more often a result of chronic diseases or radiotherapy or fistulae involving urethra, bony margins and ureteric openings.

### Clinical Features

The most characteristic presentation of Vesicovaginal fistulae is continuous urinary incontinence. The clinical findings are often obvious when there is a large defect. However, post-surgical fistulae often present with an atypical history; the fistulae may be small and sometimes invisible. In these cases, a diagnosis may be difficult and might only become apparent after extensive investigation.

Symptoms usually develop between 5 and 14 days after the causative injury, but the time of presentation often varies which again depends on the severity of symptoms. Many patients with vesicovaginal fistulae are amenorrhoeic at the time of presentation which might be due to hypothalamic influence resulting from the physical and emotional effects of a traumatic labour, stillbirth and fistula development<sup>3</sup>.

## Investigations

In order to diagnose a vesicovaginal fistula, the leaking fluid must be confirmed as urine, the leakage must be

extra-urethral and the site of the leakage must be identified.

Careful examination, usually necessitating examination under anaesthesia (EUA), is required to identify the fistulae in the first place<sup>4-6</sup>. A malleable metallic probe (traditionally silver) is invaluable for exploration of the vaginal walls, and tissue forceps are helpful in creating tension to identify the smallest fistulae. Vaginal access can be assessed at the same time to enable a choice to be made between vaginal and abdominal approaches for the repair surgery.

For fistulae which cannot be seen clearly with naked eye, a carefully conducted dye study remains the investigation of first choice. Identification of the site of a fistula is best carried out by the instillation of a coloured dye, most commonly methylene blue, into the bladder, with the patient in the lithotomy position, so that any leakage can be directly visualised.

The traditional 'three-swab test' not only gives a less clear distinction between urethral and extra-urethral (ureteral) leakage, but also precludes the identification of multiple fistulae and hence is not recommended.

If leakage of clear fluid continues after instillation of the dye, a ureteric fistula is likely; this is most easily confirmed by a 'two-dye test' using phenazopyridine which is an oral formulation of an orange dye which is excreted by kidneys, to stain the renal urine and methylene blue to stain the bladder contents<sup>7</sup>. Indigo carmine may be used intravenously as an alternative to oral phenazopyridine.

Intravenous urography is an insensitive investigation in the diagnosis of vesicovaginal fistula; however knowledge of upper urinary tract status may have a significant influence on the treatment measures used and should therefore be looked upon as an essential investigation for any suspected or confirmed vesicovaginal fistula.

Cystourethroscopy should be performed in all cases which allow determination of the exact size & of site the fistula with relation to the ureteric orifices and bladder neck. This is important in determining the appropriate surgical technique and the likelihood of subsequent urethral incompetence. The condition of the tissues can also be carefully assessed, as the persistence of slough should defer definitive repair surgery. Malignant change has been reported in long-standing benign fistulae; thus, if there is any doubt about the nature of the tissue, biopsy should be undertaken<sup>8</sup>.

## Treatment

The fistula represents a distressing and unforeseen complication, causing symptoms much worse than those arising from the initial complaint. Counselling thus plays a crucial role in the management of these patients and a confident yet realistic attitude from the treating doctor is needed along with the support from the nursing staff.

Spontaneous closure of a small vesicovaginal fistula can occur if the outflow from the bladder is unobstructed<sup>9, 10</sup>. Consequently, catheterisation can result in spontaneous resolution and worth a prolonged trial of at least six to eight weeks prior to embarking on surgical repair.

Incontinence pads should be provided in generous quantities for the interval between diagnosis and repair. The vulval skin may be at considerable risk from ammoniacal dermatitis and liberal use of silicone barrier cream should be encouraged.

In the rare situation of a surgical fistula where leakage is evident within the first 24 hours after surgery, immediate reoperation and repair might be appropriate. However, in the majority of the cases of vesicovaginal fistulae, delay of about 3 months is warranted which allows slough to separate and inflammatory changes to resolve. Surgical success must not be compromised by operating too early, despite the fact that the waiting period is distressing for the patient. The timing of the fistula repair operation is one of the contentious aspects of vesicovaginal fistula management. Understandably, surgery for vesicovaginal fistulae should only be undertaken by surgeons with appropriate training and experience.

There is a debate between the two schools of thoughts pertaining to the route of repair, namely abdominal (laparoscopic or open) versus vaginal. Surgeons involved in fistula management must be capable of different approaches and should be prepared to modify their technique to select the most appropriate for the individual case. Where access is good and the vaginal tissues are sufficiently mobile, the vaginal route is usually most appropriate. If access is poor and the fistula cannot be brought down, the abdominal approach should be used. Occasionally, it may be appropriate with a vaginal approach to have the patient prone with head-up tilt (reverse lithotomy). Robotic approach is as good as endoscopic technique.

Absorbable sutures should be used throughout all urinary fistula repair procedures. Polyglactin (Vicryl<sup>TM</sup>) 2/0 suture on a 25-mm heavy taper-cut needle is preferred for bladder and vagina. Fistula repairs may require additional tissue with intact vascular pedicle to provide support and create an extra layer to the repair. This tissue can be provided by way of an interposed graft of muscle, peritoneum or omentum, which can help to fill dead space and bring new blood supply into the area. The Martius graft, consisting of labial fat and bulbocavernosus muscle, is most commonly used to cover vaginal repair of urethral and bladder neck fistulae<sup>11</sup>.

Postoperative period is probably more important than the surgery itself. Continuous bladder drainage in the postoperative period is crucial to success; nursing staff should check catheters hourly throughout the postoperative period to confirm free drainage and to check output. Where failure occurs after a straightforward repair, it is almost always possible to identify a period during which free drainage was interrupted. The catheter must be of sufficient diameter to prevent blockage but whether the suprapubic or urethral route is used is contentious. Both can be used as a 'belt and braces' approach. This also allows the suprapubic catheter to be used once the patient is voiding to assess residual volumes<sup>12</sup>. The duration of free drainage depends on the type of fistula repaired but a period of 12 to 14 days is usually adequate.

Restricting patient mobility in the postoperative period helps preventing kinking of the urinary

catheters, which can obstruct free drainage and endanger the repair. Consequently, continuous bed rest during this period is necessary. Graduated compression stockings and Low Molecular Weight Heparin should be considered for this period.

## Conclusion

In developing countries, over 90% of the vesicovaginal fistulae are obstetric in origin, resulting from pressure necrosis during obstructed labour. Prevention of the obstetric factors is the key to avoid these dreadful complications. The successful management of fistulae in the setting of developing nations involves improving access to proper health care services, patient education and tackling the cases by trained personnel appropriately.

## References

1. Hilton P, Ward A. Epidemiological and surgical aspects of Urogenital fistulae: a review of 25 years experience in south-east Nigeria. *Int J Urogynecol* 1998;9:189-94
2. Waaldijk K, Armiya'u Y. The obstetric fistula: a major public health problem still unsolved. *Int J Gynecol* 1993;4:12G8
3. Evoh NJ, Akinla O. Reproductive performance after the repair of obstetric vesico-vaginal fistulae. *Ann Clin Res* 1978;10:30M
4. Jonas U, Petri E. Genitourinary fistulae. In: Stanton S, editor. *Clinical Gynecologic Pathology*. St Louis: Mosby; 1984. p. 238-55
5. Lawson J. The management of genito-urinary fistulae. *Clin Obstet Gp* 1978;6:2W36
6. Chdssar Moir J. *The Vagino-ginul Fistula* 2nd ed. London: Bailliere Tindall; 1967
7. Raghavaiah N. Iuhedye test to diagnose various types of vaginal fistulas. *J Urol* 1974;112:811-12
8. Hudson C. Malignant change in an obstetric vesico-vaginal fistula. *Proc R Soc Med* 1968;61:121-4
9. Waaldijk K. The immediate surgical management of fresh obstetric fistulas with catheter and/or early closure. *Znt J Gynaecol Obsrct* 194;45:1 1-6
10. Davits R, Miranda S. Conservative treatment of vesico-vaginal fistulas by bladder drainage alone. *RrJ [Jrol]* 191;68:155-6
11. Martius H. Die operative Wiederherstellung der vollkomnen fehlenden Harnrohre und des Schiessmuskels Derselben. *Zentralbl Gynabl* 1928;52:43&6
12. Hilton P. Bladder drainage. In: Stanton S, Monga A, editor. *Clinical Gynaecological Urology* Edinburgh: Churchill Livingstone; 2000. p. 541-50

Rectovaginal fistulas are abnormal epithelial-lined connections between the rectum and vagina. The incidence is low in the developed countries due to better obstetric care and access to Health.

Fistulas can be the result of congenital malformations or acquired etiologies. In this article, we will address acquired rectovaginal fistulas.

### Etiology of RVF

CHILDBIRTH	<p>Prolonged labor with necrosis of the rectovaginal septum or obstetric injury with a third- or fourth-degree perineal tear or episiotomy can lead to rectovaginal fistula .</p> <p>Infection and breakdown of the repair also leads to fistula</p>
INFECTIONS	<p>Cryptoglandular anorectal abscesses and Bartholin gland infections may spontaneously drain causing a low rectovaginal fistula. Diverticular disease in the setting of previous hysterectomy is the most common infectious cause of a <b>high</b> fistula. Lympho granuloma venereum and TB can also cause TB</p>
MALIGNANCY	<p>These are usually seen in the setting of rectal, uterine, cervical, or vaginal malignancies that have significant local extension or have been treated with radiation therapy. The Radiation and hysterectomy are associated with higher rates of Fistula. A biopsy is always indicated to r/o an active malignancy. Post radiation Rectal ulcers can progress to fistula formation around 6 months to 2 years post therapy.</p>
OPERATIVE TRAUMA	<p>Low fistulas may be the result of anorectal and vaginal operations. Pelvic procedures can result in High RVF. Hysterectomy following radiation treatment or with unrecognized intraoperative rectal injury may result in fistula development.</p>

INFLAMMATORY BOWEL DISORDER	<p>Inflammatory bowel disease is another possible culprit. Both ulcerative colitis and Crohn disease can be associated with rectovaginal fistula. Crohn disease is more frequently associated with rectovaginal fistula because it causes transmural inflammation of the rectal wall. The incidence may increase with the severity of a Crohn's flare-up.</p>
Rare causes	<p>Cryptoglandular anorectal abscesses and Bartholin gland infections may spontaneously drain causing a low rectovaginal fistula. Diverticular disease in the setting of previous hysterectomy is the most common infectious cause of a <b>high</b> fistula. Lympho granuloma venereum and TB can also cause TB</p>
MALIGNANCY	<p>Fecal impaction, vaginal dilatation after radiation to the vaginal cuff, viral and bacterial infections in patients with human immunodeficiency virus (HIV), and sexual assault could also result in RVF<sup>6,7,8,9</sup></p>

### Classification

Size, location, and etiology are used as the criteria to classify rectovaginal fistulas as simple or complex. Classification of the fistula helps determine appropriate therapy.

#### Size –

In using size as a criterion, fistulas less than 2.5 cm in diameter are

considered small; those greater than 2.5 cm are described as large.

#### Location-

The location of a rectovaginal fistula can be described in relation to the rectum, vagina, and rectovaginal septum.

In low fistulas, the rectal defect is at the dentate line with the vaginal opening inside the vaginal fourchette.

In high fistulas, the vaginal opening is at the level of the cervix.

Middle fistulas are found between the two.

Preoperative localization helps determine the appropriate surgical approach. High fistulas are more easily approached through a laparotomy, whereas a perineal approach is usually suitable for the majority of low and middle fistulas.

#### Etiology

Post radiation and malignant fistulae are hard to treat

A Simple RVF consist of small, low fistulas secondary to infection or trauma. These fistulas generally have healthy, well-vascularized surrounding tissue, which can be repaired with local techniques.

#### COMPLEX RVF

Large (>2.5 cm), high, or caused by inflammatory bowel disease. Recurrent fistulas are also considered complex due to their association with tissue scarring and decreased blood supply. In all, complex fistulas require more complicated surgical procedures for repair.

## EVALUATION-

History:

Patient symptoms usually depend on the size and location of a rectovaginal fistula.  
Passage of flatus or liquid stool per vagina.  
A malodorous vaginal discharge  
Recurrent vaginitis.  
A detailed bowel history is important to rule out inflammatory bowel disease as a cause.  
A history of pelvic malignancy should be elicited.

## EXAMINATION

The physical examination is important to locate the fistula and to assess the integrity of surrounding tissue.

There may be a palpable depression in the an-

terior midline of the rectum, or a pit like defect if the fistula is small. These changes may be visible on anoscopy.

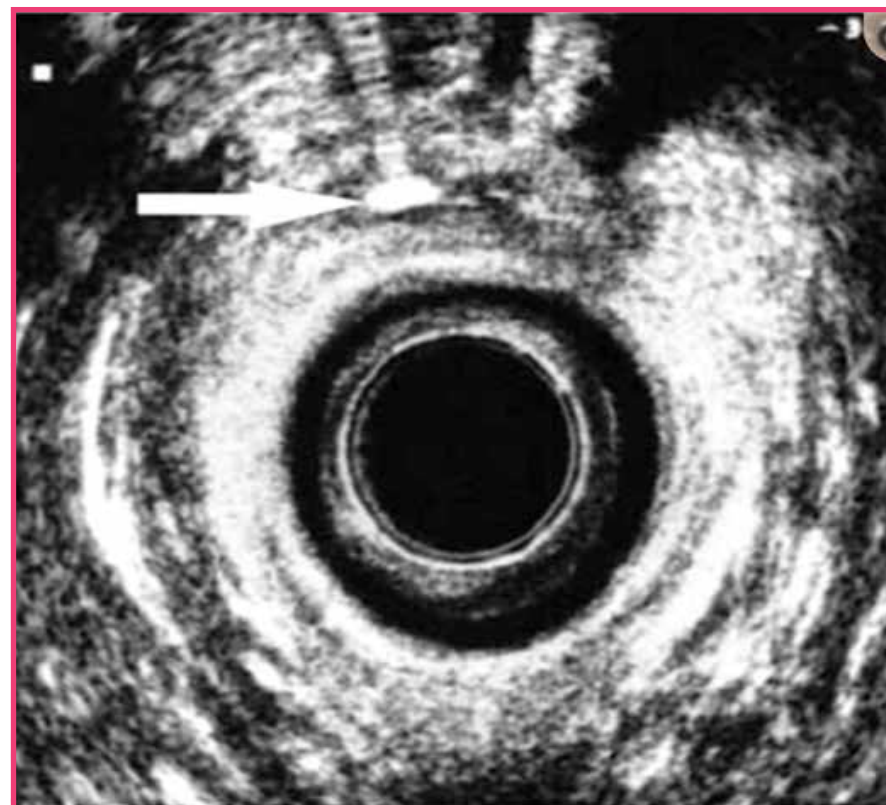
On vaginal examination, the darker mucosa in the fistula track may be apparent, contrasting with the light vaginal mucosa. There may be visible stool or signs of vaginitis.

Probing the tract may be very painful and is therefore not recommended.

An assessment of anal sphincter integrity in the same sitting will assist in surgical planning.

## SUPPLEMENTAL TESTS

1. Endorectal and transvaginal ultrasounds may be used to identify a low fistula tract



Hydrogen peroxide highlighting a fistula in an anal scan

A vaginal tampon can be inserted followed by instillation of a methylene blue Enema. The tampon is removed after retaining the enema for 15 to 20 minutes. If there is no staining, the diagnosis of rectovaginal fistula is highly unlikely.

More proximal fistulas are best diagnosed with vaginography or computed tomography with rectal contrast (Fig. 2).



Lateral view of contrast rectal study demonstrating contrast in vagina (rectovaginal fistula)

## Endoscopy

If inflammatory bowel disease is suspected. Examination under anesthesia with biopsies may be necessary in patients with prior irradiation for malignancy.

All patients require assessment of fecal continence and its cause. They may need MRI or u/s to study the sphincter

## Treatment

Conservative management works in very few cases. The major mode of treatment is Surgery

## Simple Rectovaginal Fistulas

Advancement flaps are the most popular transanal procedure among colorectal surgeons.

Excision and closure of the rectal portion of the fistula

Coverage with a vascularized mucosal flap on the high pressure side of the fistula.

The tract is identified by palpation and probing. The fistula tract is debrided and excised. A flap is created that includes mucosa, submucosa, and muscle placed over reapproximated rectovaginal septum. The flap base should be

at least 2 to 3 times the width of the apex to ensure adequate vascular supply. Flap mobilization should continue 4 to 5 cm cephalad to the fistula defect.

These principles ensure a tensionless suture closure. The complications are minimal but the success rate is highly variable from 19% to 100%.

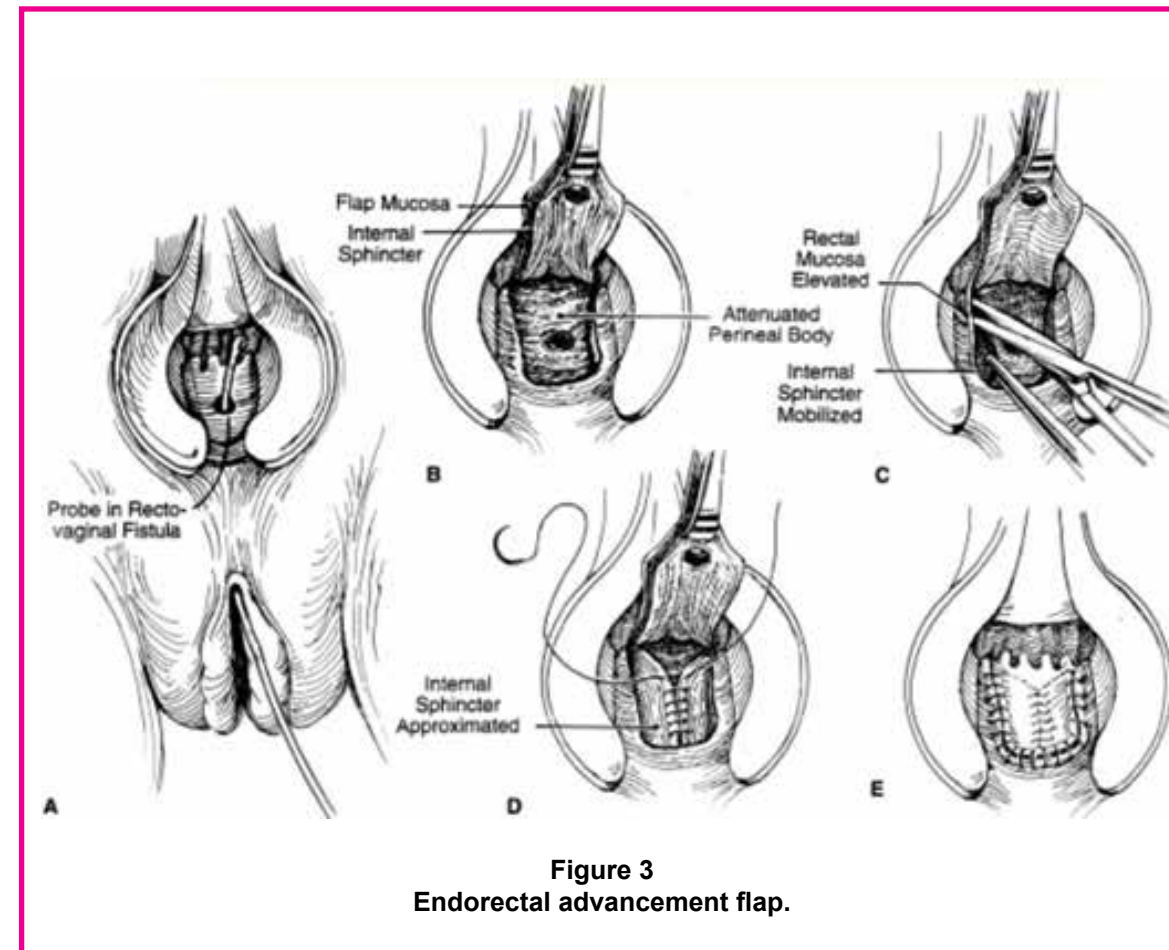


Figure 3  
Endorectal advancement flap.

Newer approaches have been developed for the treatment of intersphincteric anorectal fistulas and have been adopted for treatment of simple rectovaginal fistulas.

One approach involves the use of a **bioprosthetic fistula plug made from porcine intestinal submucosa (Anal Fistula Plug, Cook Surgical Inc., Bloomington, IN)**. After management of local sepsis with drainage procedures, a tapered plug is placed through the rectovaginal fistula tract. Excess plug length is excised at both the rectal and vaginal ends. The plug is then secured with 2–0 absorbable suture in a figure-of-eight fashion on the rectal side and the vaginal side left open to drain.

Trials that compare rectal mucosal flap advancement to bioprosthetic plug placement for the treatment of fistula in ano are ongoing. Smaller studies show that bioprosthetic plugs are more successful in the treatment of simple compared with complicated anorectal fistulas.<sup>22</sup> Recent modifications to the bioprostheses to accommodate anatomic features of a rectovaginal fistula may make this approach more successful<sup>23</sup>; however, additional experience is needed to determine the utility of bioprosthetics in the use of rectovaginal fistula treatment.

A second procedure for fistula in ano has been adopted to treat rectovaginal fistula. The procedure is called LIFT (ligation of intersphincteric

fistula tract), involves dissection in a bloodless plane between the internal and external anal sphincters beyond the fistula tract. The tract is then ligated and closed on both the rectal and perineal side. The intersphincteric dissection is then closed at the skin.

High success rates after LIFT treatment of fistula in ano are encouraging (60–94%).

But experience with LIFT treatment of rectovaginal fistula is limited. The bioprosthetic plug and LIFT repair for both rectovaginal fistula and fistula in ano are attractive because they allow the surgeon to avoid anal sphincter muscle division. Long-term impact on fecal continence in patients with other risk factors for incontinence remains a high priority for both patient and surgeon

The surgical treatment of complex fistulas is invasive and the procedures complex. They range from Low anterior resection, Abdominoperineal resection or pelvic exenteration. A good colorectal surgeon's help is needed.

#### References

1. Champagne BJ, McGee MF. Rectovaginal fistula. *Surg Clin North Am.* 2010;90(1):. doi:10.1016/j.suc.2009.09.003
2. Das B, Snyder M. Rectovaginal Fistulae. *Clin Colon Rectal Surg.* 2016 Mar;29(1):50-6.
3. Byrnes JN, Schmitt JJ, Faustich BM, Mara KC, Weaver AL, Chua HK, Occhino JA. Outcomes of Rectovaginal Fistula Repair. *Female Pelvic Med Reconstr Surg.* 2017 Mar/Apr;23(2):124-130.
4. Abu Gazala M, Wexner SD. Management of rectovaginal fistulas and patient outcome. *Expert Rev Gastroenterol Hepatol.* 2017 May;11(5):461-471.
5. Sharma JB. *Textbook of Gynecology.* 1st ed. New Delhi: Avichal Publishing Company; 2018. 18 (xiii): Rectovaginal Fistula:424-426

## Introduction

Sexual Health is utmost important for the women well-being and provides a sense of self and quality. Sexual function in women are associated with menopause, health, economic status, mental well-being. Sexual dysfunction is often unaddressed, undiagnosed and thus untreated. The incidence of women sexual dysfunction (WSD) is around 30% - 50%<sup>1</sup>. It is a highly underreported problem, as approximately 1/3rd of women never initiate any discussion about their sexual issues<sup>2</sup>, and it has been rarely reported spontaneously as a symptom<sup>3</sup>. Thus, a routine sexual assessment should be made in all women presenting with urinary symptoms<sup>4</sup>.

With the development of DSM-55 in 2013 Female sexual dysfunction (FSD) was recently redefined, and now includes Female Sexual Interest/ Arousal Disorder (FSIAD), Female Orgasmic Disorder and Genito pelvic Pain/ Penetration Disorder<sup>6,7</sup>.

To be considered dysfunctional, these symptoms must cause distress and must occur at least 75% of the time over a 6-month period<sup>8</sup>.

## Pathophysiology

The cause of FSD are multiple and variable and often difficult to understand the initial aetiology and is often a challenge for the clinician. Aetiology include organic elements such as hormonal, neurological, vascular issues, psychosocial factors such as relationship issues, social stressors, mood, history of physical or sexual abuse, and psychiatric history, neurotransmitters too play an important role.

For appropriate female sexual function, delicate balance of dopamine for desire, and epinephrine, norepinephrine, and serotonin for arousal and orgasm. Disorders and medications that disrupt these elements may lead to FSD. Hormonal deficits may be another factor

in pathophysiology. The decrease in estrogen associated with menopause may induce decreased sexual desire and atrophy of genital tissue that leads to painful intercourse<sup>6</sup>.

## Epidemiology

The incidence of FSD is around 30-50%<sup>1</sup>. Approximately 10% in women if distress is used as a criterion and 75% in menopausal women, if symptoms alone are used as the criterion. The peak age group for FSD is 51-59 year, around the time of menopause, however FSD can occur for women at all ages<sup>9,10</sup>.

## Clinical Presentation

**HISTORY:** A thorough sexual history is vital in making a diagnosis of sexual dysfunction and identifying contributing elements. Most of the women with sexual dysfunction are very reluctant in disclosing their sexual problems due to social stigma, fear and concern of embarrassment, and distrust in their clinicians ability to help.

Sexuality questionnaires and scales are thus integral in the diagnosis of FSD<sup>11</sup>, as they allow quantitative analysis of impact of FSD in sexual life of women requiring treatment. Using a routine screening question during history-taking is therefore essential to open a dialogue about sexual concerns. Examples of questionnaires include the 19 question Female Sexual Function Index, a 12 item Female Sexual Distress Scale<sup>5</sup>. Thus, standardized assessment of sexual dysfunction is important to actually understand what the patient experiences and without being able to measure it in a reproducible way, we cannot draw reliable conclusions<sup>12</sup>.

Questions should specifically address the nature of the concern, and whether the patient has difficulty with sexual desire, arousal, orgasm, sexual pain, or some combination thereof.

Duration, onset, its temporal relation to historical event such as childbirth, assault, any previous surgery, relationship with her partner, any other social problem, psychological history is important, eliciting elements such as depression symptoms, history of psychiatric disease, whether the patient has experienced past sexual or physical abuse, and any history of alcohol or substance abuse. The sexual history of a woman complaining of sexual pain should target the nature and severity of the pain, the location, and the time course. Questions about sexual practices or positions that bring on or improve the pain may be helpful as well. Patients with a primary complaint of orgasmic difficulty, questions should be directed to their experience of orgasm, patient with a complaint of "low libido" or "decreased sex drive," specific information about their libido is important<sup>13</sup>.

## Physical Examination

Physical examination may be focused with the following in mind. Thyroid disease may be contributory to FSIAD, and a thyroid exam must be included. In examining external female genitalia, look for any skin lesions or atrophy. Pelvic examination is most helpful in women who are complaining of sexual pain, and should specif-

ically look for findings of atrophy or areas of tenderness that may relate to their complaints. Some specific areas should be focussed in the pelvic exam are- the vulvar vestibule (provoked vulvodynia), levator and perineal body muscle soreness (vaginismus), rectovaginal nodularity (endometriosis), and anterior wall/ bladder (interstitial cystitis or painful bladder syndrome)<sup>6</sup>.

## Diagnosis

Most FSD diagnoses are made based on history alone, and laboratory evaluation is rarely helpful. A fraction of patients with desire complaints may have underlying thyroid dysfunction, so a TSH (Thyroid Stimulating Hormone) screen may be helpful. Serum testing for estrogen and androgens is rarely necessary. Occasionally testing of gonadotropins or estrogen may be helpful in women for whom the diagnosis of menopause is in doubt, for example following hysterectomy<sup>6</sup>.



## DIFFERENTIAL DIAGNOSIS

Orgasmic Dysfunction	Sexual Interest/arousal Dysfunction	Genitopelvic Pain/ Penetration Disorder
Lack of Education	Relationship issues	Vulvovaginal Atrophy
Lack of Sexual Desire and stimulation, Arousal Disorder	Vascular Disease	Vulvodynia Vaginismus Vestibulodynia Vulvitis/Vaginitis Endometriosis Adenomyosis Uterine Leiomyomas
Neuropathy	Prior Pelvic Surgery	Survivor of Physical, Sexual, Emotional, or Mental Abuse
Relationship issues	Depression and other Psychiatric Disorders	GI Etiologies (Irritable bowel syndrome, Irritable bowel disease, chronic constipation)
	Medications (Psychiatric, antihypertensive, opioid medications)	Genitourinary Causes (Painful bladder syndrome)
	Survivor of Physical, Sexual, Emotional, or Mental Abuse	Vulvar intraepithelial, neoplasia, vulvar atrophy, lichen sclerosis, condyloma
	Possible Sex Hormone Deficiency	Pelvic Inflammatory Disease

**History-taking is the most important aspect of the workup.** Establishing an honest and trusting relationship is important and assuring the patient that privacy and confidentiality are guaranteed. A focused physical examination may or may not be appropriate, which can be determined after the history is obtained<sup>14,15</sup>

**Laboratory testing for hormones is rarely helpful.** The diagnosis of estrogen deficiency is usually made clinically based on symptoms of menopause, **but estrogen or FSH levels may be helpful when the diagnosis is in doubt, as in women post-hysterectomy. A TSH screen** may be helpful for patients with Female Sexual Interest/ Arousal Disorder to rule out thyroid etiology, particularly when other symptoms such as irregular menses are present<sup>6</sup>.

**Transvaginal ultrasound may be helpful for sexual pain patients with cervical, bladder, uterine, or adnexal tenderness or masses on pelvic exam. In the absence of a palpable lesion, imaging is rarely useful<sup>6</sup>.**

### Treatment

Reassurance and education and allaying patient concerns are the most important part of management of sexual dysfunction. Setting reasonable goals and expectations is important, as sexual dysfunction of long duration is often unlikely to resolve quick<sup>16</sup>.

Treatment of sexual dysfunction depends on the underlying disorder. Treatment may include counseling, education, and reassurance. Once correctable causes have been ad-

ressed or ruled out, medical intervention may be considered.

### Female Sexual Interest/ Arousal Disorder (FSIAD)

Because FSIAD may be a side effect of medications, a frequent solution is adjustment of other prescriptions. Antihistamines, beta blockers, diuretics and hormonal contraceptives, the most common culprits are SSRI antidepressants. Dose adjustment is very important for improving sexual function<sup>17</sup>.

One medication that is **FDA-approved** to treat Female Sexual Interest/ Arousal Disorder is **flibanserin, a 5HT1A/2B agonist/antagonist**. It is indicated for premenopausal women with low sexual desire. It is taken nightly and requires daily use. Side effect include syncope and hypotension<sup>18</sup>.

The **FDA approved bremelanotide in June 2019** for acquired, generalized **hypoactive sexual desire disorder (HSDD)** in premenopausal women. It is administered as a subcutaneous injection about 45 minutes before an anticipated sexual activity. Approval was based on the **RECONNECT clinical trials** (N=1247). Results from these trials showed approximately 25% of patients treated with bremelanotide had an increase of 1.2 or more in their sexual desire score<sup>19,20</sup>.

Supplemental androgens have not been approved in the for sexual dysfunction<sup>21</sup>.

### Genitopelvic Pain/ Penetration Disorder

They are benefitted from **topical estrogen**, which improves vaginal epithelial integrity, reduces sensitivity and improves elasticity of the vaginal tissues. **Topical estrogen is available as a cream, tablet, or continuous-release ring. Topical prasterone (DHEA) has recently been FDA-approved** for the same indication, and can be applied nightly as a vaginal suppository. **Ospemifene, an oral selective estrogen receptor modulator, is also approved to treat dyspareunia by reversing genital atrophy<sup>22</sup>.**

Nonestrogen lubricants and moisturizers may also be helpful for patients with Genitopelvic Pain/ Penetration Disorder.

When sexual pain is associated with restrictive disease from vaginismus or narrowing of the introitus, additional therapy may be needed. Pelvic floor physical therapy may be necessary in conjunction with specific counseling to help with painful muscular contraction of the vaginal muscles.

For patients with restrictive disease due to atrophy or radiation injury, dilator therapy is another useful tool<sup>23</sup>.

### Female Orgasmic Disorder

Inhibition of orgasm is another common side effect of SSRIs. As with FSIAD, women with orgasmic dysfunction may benefit from an adjustment in antidepressant therapy. Again, **consideration must be given to the balance between the medication side effects and benefits of continuing effective antidepressants<sup>6</sup>.**

### Other Treatment Modality

- Patients with **relationship stagnation**, infidelity, other relationship problems, and/ or survivors of abuse may benefit from **psychological counseling referral**.
- **Referral to a gastroenterologist or urologist** is helpful for patients with gastrointestinal or urologic conditions that are suspected causes of their sexual pain.
- Patients for whom sexual pain is thought to arise from a musculoskeletal etiology often benefit from **pelvic floor physical therapy**.
- Patients with a neuropathy related to poorly controlled diabetes may benefit from **neurology referral**
- Patients may benefit from **routine exercise with moderate physical exertion** 150 minutes per week, or 75 minutes per week of high intensity exertion, as appropriate for the patient.

### Prevention

- There is evidence that **continued sexual activity is protective against later development of sexual dysfunction in menopausal women**. It is physiologically plausi-

ble that sexual stimulation leads to increased blood flow and preserved elasticity that may protect against vulvovaginal atrophy and its sexual sequelae.

## Follow Up

There are no formal guidelines to recommend an interval at which sexual dysfunction patients should be followed after successful treatment, patients may benefit from an appointment to evaluate treatment progress every 3-6 months while improving, and then yearly thereafter.

## Conclusion

It is a very debilitating condition and causes discomfort, social withdrawal and adversely affects physical and mental health and has a profound effect on the quality of life. It is a highly underreported problem, as approximately 1/3rd of women never initiate any discussion about their sexual issues, and it has been rarely reported spontaneously as a symptom. Thus, a routine sexual assessment and offering appropriate treatment may help women to combat such sensitive issue and help them to gain confidence and improve their quality of life.

## REFERENCES

- 1) Andrea Salonia, Griseeppe Zanni, Rossella E, Nappi, Alberto Bryant. Sexual Dysfunction is common in women with lower urinary tract symptoms and urinary incontinence: Results of a cross-sectional study. *European Urology*. 2004;45:642-48
- 2) Coyne KS, Margolis MK, Jumadilova Z, Bavendam T. Overactive bladder and women's sexual health: what is the impact? *J Sex Med*. 2007 Mar;6:656-66
- 3) Moutounaick M, Muget G, Teng M, Kerviniot, Chesnel C. Coital Incontinence. *Prog Urol*. 2018 Sep;28(11):515-22
- 4) Gray T, Li W, Campbell P, Jha S, Radley S. Evaluation of Coital Incontinence by electronic questionnaire: prevalence, associations and outcomes in women attending urogynecology clinic. *Int Urogynecol J*. 2018 Jul;29(7):969-78
- 5) American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. Fifth Edition. Washington, DC: American Psychiatric Publishing; 2013.
- 6) American College of Obstetricians and Gynecologists Committee on Practice Bulletins-Gynecology. ACOG Practice Bulletin No. 119: Female sexual dysfunction. *Obstet Gynecol*. 2011 Apr. 117 (4):996-1007.
- 7) Wright JJ, O'Connor KM. Female sexual dysfunction. *Med Clin North Am*. 2015 May. 99 (3):607-28.
- 8) World Health Organization. *Defining sexual health: report of a technical consultation on sexual health 28-31 January 2002*. Geneva. Geneva: WHO; 2006
- 9) Satcher D, Hook EW 3rd, Coleman E. Sexual Health in America: Improving Patient Care and Public Health. *JAMA*. 2015 Aug 25. 314 (8):765-6.
- 10) Shifren JL, Monz BU, Russo PA, Segreti A, Johannes CB. Sexual problems and distress in United States women: prevalence and correlates. *Obstet Gynecol*. 2008 Nov. 112 (5):970-8.
- 11) Gray T, Li W, Campbell P, Jha S, Radley S. Evaluation of Coital Incontinence by electronic questionnaire: prevalence, associations and outcomes in women attending urogynecology clinic. *Int Urogynecol J*. 2018 Jul;29(7):969-78
- 12) Claudine Domoney, Tara Symonds. Questionnaires to assess sexual function. In: Linda Cardozo, David Staskin (eds). *Textbook of female urology and urogynecology*. 4th edn. Florida, CRC Press; 2017. p.98
- 13) Kingsberg SA. Taking a sexual history. *Obstet Gynecol Clin North Am*. 2006 Dec. 33 (4):535-47.
- 14) Kingsberg SA. Taking a sexual history. *Obstet Gynecol Clin North Am*. 2006 Dec. 33 (4):535-47.
- 15) ACOG Committee Opinion No. 518: Intimate partner violence. *Obstet Gynecol*. 2012 Feb. 119 (2 Pt 1):412-7.
- 16) Buster JE. Managing female sexual dysfunction. *Fertil Steril*. 2013 Oct. 100 (4):905-15.
- 17) Montejo AL, Llorca G, Izquierdo JA, Rico-Villademoros F. Incidence of sexual dysfunction associated with antidepressant agents: a prospective multicenter study of 1022 outpatients. Spanish Working Group for the Study of Psychotropic-Related Sexual Dysfunction. *J Clin Psychiatry*. 2001. 62 Suppl 3:10-21.
- 18) Nappi RE, Cucinella L. Advances in pharmacotherapy for treating female sexual dysfunction. *Expert Opin Pharmacother*. 2015 Apr. 16 (6):875-87.
- 19) Clayton AH, Kingsberg SA, Jordan E. Efficacy of the investigational drug bremelanotide for hypoactive sexual desire disorder (HSDD): results from the RECONNECT study. Presented at: Annual Meeting of the American Society of Clinical Psychopharmacology; May 30, 2017. Miami, FL.
- 20) DeRogatis L, Althof S, Clayton A, et al. Changes in arousal and desire in bremelanotide RECONNECT study. Presented at: Annual Meeting of the International Society for the Study of Women's Sexual Health (ISSWSH); February 23-26, 2017; Atlanta, GA.
- 21) Taylor MJ, Rudkin L, Bullemor-Day P, Lubin J, Chukwujekwu C, Hawton K. Strategies for managing sexual dysfunction induced by antidepressant medication. *Cochrane Database Syst Rev*. 2013 May 31. CD003382.
- 22) Labrie F, Archer D, Bouchard C, Fortier M, Cusan L, Gomez JL, et al. High internal consistency and efficacy of intravaginal DHEA for vaginal atrophy. *Gynecol Endocrinol*. 2010 Jul. 26 (7):524-32.
- 23) Al-Abbadey M, Liossi C, Curran N, Schoth DE, Graham CA. Treatment of Female Sexual Pain Disorders: A Systematic Review. *J Sex Marital Ther*. 2016. 42 (2):99-142



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