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A multidisciplinary pelvic floor journal

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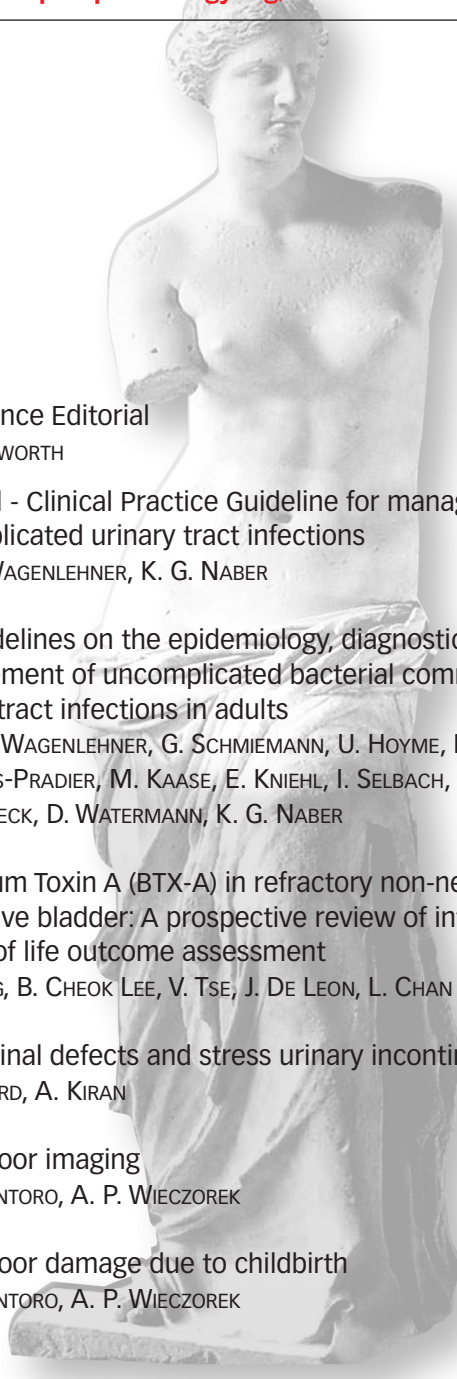

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PELVIPERINEOLOGY

Emphasising the multi-disciplinary approach to the assessment and treatment of pelvic pathology

Following the Annual General Meeting of AAVIS in Vienna last September AAVIS has become the International Society for Pelviperineology. The change of name reflects the fact that AAVIS has evolved into an international and multidisciplinary pelvic floor society. Once again we will be holding our Annual Scientific Meeting and International Pelviperineology Congress. The venue for the meeting is Dockside Convention Centre at Darling Harbour in Sydney with special Cadaver Workshops at Macquarie University. Plenary sessions will be held at Dockside on October 7th and 8th 2011 with workshops at Macquarie on October 9th. Social activities will include a welcome cocktail party on Thursday 6th October and a conference dinner on Friday 7th October.

Conference editorial

The upcoming ISPP International Pelviperineology Congress is a special event in the history of our society. AAVIS was founded in 1996 and has organised an Annual Scientific meeting every year since 1999. In recent years our meetings have developed a multidisciplinary and international focus until last year in Vienna it was decided to change the name of our society. In 2011 we return to Australia where our society was born and in particular to Sydney, the location of very successful meetings in 2005 and 2007.

This year The Plenary sessions will be held at the Dockside Convention centre which is a large modern venue in the heart of the Sydney Central Business District within walking distance of many hotels and apartments. Hands on cadaver workshops will be held at the impressive new facilities of the Australian School of Advanced medicine at Macquarie University. An interesting and varied program has been arranged and we look forward to welcoming you to Sydney in October. You can monitor the conference website at www.pelviperineology.com and make sure you book in early to secure your place at this landmark event.

BRUCE FARNSWORTH

Editorial

Clinical Practice Guideline for management of uncomplicated urinary tract infections

Urinary tract infections (UTI) are among the most common types of bacterial infection in outpatient medicine. Rising rates of antibiotic resistance and a better understanding of the ecological adverse effects (collateral damage) of antibiotics warrant a reevaluation of the treatment recommendations for uncomplicated UTI. The new German guideline contains updated recommendations.

The new German guideline is based on a review of publications on uncomplicated UTI retrieved by a systematic search of the Medline and Cochrane Library databases. Other guidelines were also considered in the review.

Uncomplicated UTI is classified as either uncomplicated cystitis (UC) or uncomplicated pyelonephritis (UP). The choice of a suitable antibiotic is determined by the following main criteria: the patient's individual risk profile and prior antibiotic treatment, if any; the spectrum of pathogens and antibiotic susceptibility; the proven efficacy of the antibiotic; the ecological adverse effects of antimicrobial therapy; the side effects for the patient under treatment. On the basis of these criteria, cotrimoxazole/trimethoprim and fluoroquinolones can no longer be recommended as first-line empirical treatment for UC. Fosfomycin-trometamol, nitrofurantoin, or pivmecillinam are now recommended as first choice drugs. High-dose fluoroquinolones are still recommended, however, as first-line oral treatment for UP. Asymptomatic bacteriuria should only be treated in exceptional situations such as pregnancy or before urological procedures that will probably injure the mucosa of the urinary tract.

The new German guideline on management of uncomplicated UTI incorporates a forward-looking approach to the use of antibiotics in treating this common type of infection. It is intended to bring up a sustained improvement in the quality of care.

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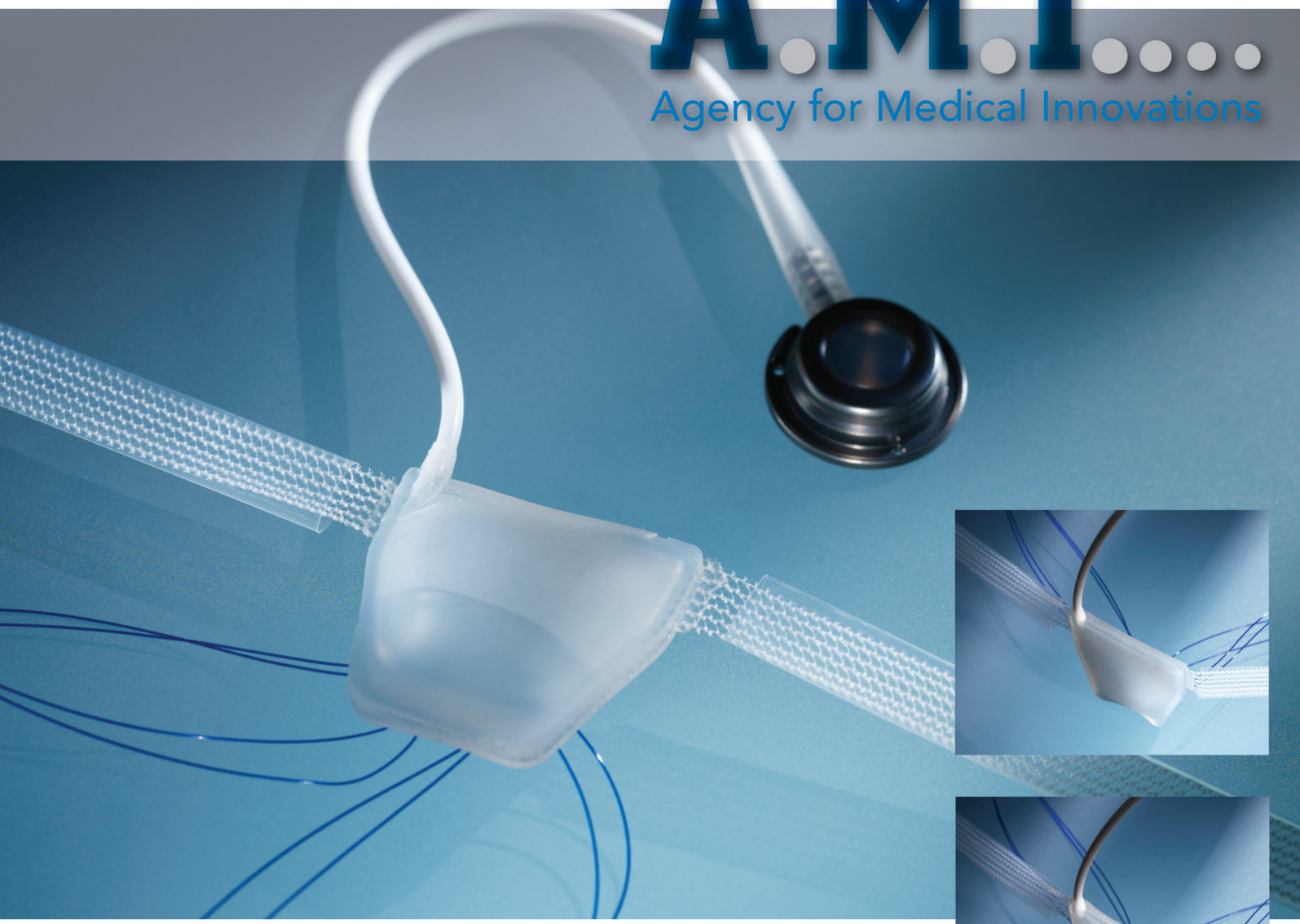

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Guidelines

S-3 Guideline uncomplicated urinary tract infections.

Guidelines on the epidemiology, diagnostics, therapy and management of uncomplicated bacterial community acquired urinary tract infections in adults

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Abstract: *Background:* Urinary tract infections (UTI) belong to the most frequent bacterial infections in outpatients. Increasing antibiotic resistance rates and a new appreciation of the epidemiological side effects of antibiotics ("collateral damage") have warranted an update of the guidelines of uncomplicated UTI as an S3 clinical guideline. *Methods:* The guideline was developed by the Deutsche Gesellschaft für Urologie (DGU), in collaboration with the Deutsche Gesellschaft für Allgemein- und Familienmedizin (DEGAM), Deutsche Gesellschaft für Gynäkologie und Geburtshilfe (DGGG), Deutsche Gesellschaft für Hygiene und Mikrobiologie (DGHM), Deutsche Gesellschaft für Infektiologie (DGI), Deutsche Gesellschaft für Nephrologie (DGfN), Paul-Ehrlich-Gesellschaft für Chemotherapie (PEG) and a patient representative. The systematic review of the literature on the topics of the guideline was performed for the time period 01.01.1998 to 30.04.2008 in the data-bases Cochrane Library and Medline. International guidelines of the years 1999 to 2007 were included. *Results*: Uncomplicated UTI comprise uncomplicated cystitis and uncomplicated pyelonephritis. The leading uropathogen is *Escherichia coli*. The choice of the antbiotic substance follwos the five primary aspects: 1. individual patient risk and antibiotic pretreatment; 2. bacterial spectrum and antibiotic susceptibility; 3. effectivity of the antimicrobial substance demonstrated in clinical studies; 4. epidemiological effects ("collateral damage") and 5. adverse effects. If antibiotics such as trimethoprim/ sulfamethoxazole or fluoroquinolones have been given prior, the risk for pathogens to become resistant against these substances is increased. Because of in-creasing resistance rates of *E. coli* against trimethoprim/ sulfamethoxazole also in uncomplicated UTI, trimethoprim alone or in combination with sulfamethoxazole is not regarded any more as first line agent in the empiric treatment of uncomplicated cystitis, unless the regional resistance rate is below 20%. The antibiotic resistance rates of fluoroquinolones in uncomplicated UTI are in Germany still below 10%. But there is a significant emergence of resistance compared to earlier years. Moreover fluoroquinolones and group 3 cephalosporines exhibit negative epi-demiological effects resulting in selection of multiresistant pathogens. Because these antibiotic classes are needed in therapy of life-threatening infections, such effects should be taken seri-ously. For substances like fosfomycin, nitrofurantoin or mecillinam "collateral damage" has not been documented or only to a lesser degree. Therefore for empiric therapy of frequent uncompli-cated cystitis fosfomycin-trometamol, nitrofurantoin or pivmecillinam (not listed in Germany) are recommended as first-line antibiotics. For oral first-line treatment of uncomplicated pyelo-nephritis fluoroquinolones are still recommended in sufficiently high dosage, due to the resist-ance rates of *E. coli* still beeing below 10% and the superior effectivity compared to other anti-biotics. Asymptomatic bacteriuria (ASB) should only be treated in exceptional cases such as pregnant women or prior to expected mucocutaneous traumatising interventions of the urinary tract. *Conclusion:* The S3 guideline „uncomplicated urinary tract infections" is a comprehensive set of evidence-and consensus-based recommendations dealing with epidemiology, diagnosis, therapy and management of uncomplicated bacterial UTI of adult outpatients. A broad implementation in all disciplines taking care of patients with UTI is necessary, in order to ensure a prudent anti-biotic policy in these frequent infections and thus improve patient care.

1. BACKGROUND

The clinical S3-guideline **uncomplicated urinary tract infections (UTI)** aims to implement evidence based guidelines on the diagnosis and therapy of uncomplicated bacterial community acquired UTI in adults, in order to prevent unbalanced use of certain antibiotic classes and thus prevent emergence of antibiotic resistance.

Guidelines in Germany are classified according to the "Arbeitsgemeinschaft Wissenschaftlich Medizinischer Fachgesellschaften (AWMF)" into three classes (S1, S2, S3), depending on the methodology of development[1]. A S3-guideline is the highest scientific level and encompasses a guideline with all elements of systematic development (logic-, decision- and outcome analysis)[1].

This S3-guideline was inititated by Prof. Dr. K.G. Naber and Prof. Dr. F.M.E. Wagenlehner and was endorsed by the Deutsche Gesellschaft für Urologie (DGU). The scientific societies, work-ing groups, organisations and authors with voting power are shown in figure 1.

The guideline was supported by the "Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF)" (Prof. Dr. I. Kopp). International reviewers have reviewed and evaluated this version of the guideline.

The full german long-version of the consented S3-guideline can be downloaded from the web-sites of the AWMF[2], the DGU[3] and other participating societies. This publication corres-ponds to the short-version, which is available in the German[4] and English version[5].

Figure 1.

Scientific Societies / Working Groups / Organisations	Authors with voting power
German Society for Urology (DGU) in charge	Prof. Dr. Dr. K.G. Naber Priv.-Doz. Dr. W. Vahlensieck Prof. Dr. F.M.E. Wagenlehner
German Society for General and Family Medicine (DEGAM)	Prof. Dr. E. Hummers-Pradier Dr. G. Schmiemann
German Society for Gynaecology and Obstretics (DGGG)	Prof. Dr. U. Hoyme Prof. Dr. D. Watermann
German Society for Hygiene and Microbiology (DGHM)	Dr. M. Kaase Dr. E. Kniehl
German Society for Infectiology (DGI)	Prof. Dr. Dr. K.G. Naber
German Society for Nephrology (DGfN)	Prof. Dr. R. Fünfstück Priv.-Doz. Dr. U. Sester
Paul-Ehrlich-Society for Chemotherapy (PEG)	Prof. Dr. R. Fünfstück Dr. M. Kaase Dr. E. Kniehl Prof. Dr. Dr. K.G. Naber Prof. Dr. F.M.E.Wagenlehner
Patient representative	I. Selbach

2. METHODS

The consensus-group of this S3-guideline consisted of 11 representatives of 7 societies and one patient representative (Figure 1). Defined topics were distributed in working groups. The rec-ommendations are based on the systematic literature research performed through the databases Cochrane Library and Medline, searching the period from 1st January 1998 through 30th April 2008. 13 international guidelines were included in the evidence process[6-18]. The evaluation of the scientific evidence was performed in five evidence grades (I-V) according to the Oxford Centre of Evidence Based Medicine[19] (Table 1). Four recommendations were given: A - strong recommendation; B - recommendation; C - recommendation uncertain; D - no recommendation possible.[11] consensus conferences were held, the consensus process was achieved by a nominal group process (NGP) lead by an external moderator of the AWMF with the represen-tatives of the involved societies.

TABLE 1. – Evidence level (I-V) according to the Oxford Centre of Evidence Based Medicine (1999).[19]

Studies on therapy, prevention and etiology	
Evidence level	**Description**
Ia	Systematic review of randomized controlled trials (RCT).
Ib	A well performed RCT (with small confidence interval).
Ic	All or none principle.
IIa	Systematic review of well performed cohort studies.
IIb	A well performed cohort study or a RCT of lower quality.
IIc	Effect and success studies, pharmacoeconomic and ecologic studies.
IIIa	Systematic review of well planned case-control studies.
IIIb	A case–control study.
IV	Case series or cohort studies and case-control studies of lower quality.
V	Expert opinion without explicit critical evaluation of evidence or based upon physiologic models / laboratory work.

3. INTRODUCTION

Uncomplicated UTI are amongst the most frequent infections in the outpatient setting and are together with respiratory infections responsible for the highest amount of antibiotic prescriptions. The first evidence based recommendations on uncomplicated UTI were published by the Infectious Dieseases Society of America in 1999.[20] Since then the resistance level of the uropatho-gens causing uncomplicated UTI has considerably increased and different therapeutical strat-egies have been evaluated. The knowledge and awareness for collateral effects of systemic anti-biotic substances has increased considerably. These aspects have internationally lead to a reconsideration of recommendations and guidelines in uncomplicated UTI.[21-23]. This short version contains the most important fundamentals and all consented recommendations. The exact description of the methods and the detailed explanations with corresponding references are to be found only in the long version.

4. DEFINITIONS OF UNCOMPLICATED URINARY TRACT INFECTIONS (UTIs)

A UTI is classified to be uncomplicated, if there are no relevant functional, anatomical or sig-nificant renal dysfunctions and no relevant comorbidities in the urinary tract favoring UTI or serious complications (A-V).

A lower UTI (cystitis) is assumed if the symptoms are limited to the lower urinary tract, e.g., dysuria, urgency, frequency, suprapubic pain (A-V).

An upper UTI (pyelonephritis) is assumed, if the symptoms comprise for instance flank pain, costovertebral angle tenderness and/or fever (> 38°C) (A-V).

A clinically symptomatic UTI is differentiated from an asymptomatic bacteriuria (A). The term "asymptomatic urinary tract infection" should not be used (B-V).

Recurrent UTI is assumed if a recurrence rate of > 2 symptomatic episodes per six months or > 3 symptomatic episodes per year exist (B-V).

5. GROUPS OF PATIENTS

Patients with uncomplicated UTI should be discerned into different groups with regard to diag-nostic procedure and therapy (B-V).

- otherwise healthy, non-pregnant premenopausal women (standard group)
- otherwise healthy pregnant women
- otherwise healthy postmenopausal women
- otherwise healthy young men
- otherwise healthy patients with diabetes mellitus and stable glycaemic metabolism

5.1. Otherwise healthy, non-pregnant premenopausal women

In otherwise healthy, non-pregnant women the following factors increase the risk for UTI (A).
- recent intercourse (IIb)
- use of diaphragm and spermicides (IIb)
- previous asymptomatic bacteriuria (IIb)
- UTI in the medical history (IIb)
- young age at first UTI (IIb)
- UTI in family medical history (IIb)

The incidence of cystitis and pyelonephritis is greater in women than in men in this age group (IIb).

Asymptomatic bacteriuria is often found during routine examinations in otherwise healthy non pregnant women. Asymptomatic bacteriuria does not require treatment in this group of patients apart from some exceptions (Ia).

5.2. Otherwise healthy pregnant women without risk factors

UTI and asymptomatic bacteriuria are more frequent in pregnancy (IIa).

The spectrum of pathogens and the bacterial resistance patterns are similar to non-pregnant premenopausal women (IIa).

The rate of pyelonephritis, compared to non pregnant women is increased (IIa).

There seem to be correlations between UTI and asymptomatic bacteriuria in pregnancy and pre-term delivery, reduced birth weight, increased neonatal mortality and preeclampsia (IIb).

5.3. Otherwise healthy postmenopausal women

Postmenopause is characterized by a significantly decreased estrogen production, which is often associated with atrophy of the vaginal mucous membranes. A change in pH and a reduced colo-nization by lactobacilli leads to an increased vaginal colonization with enterobacteriaceae and anaerobes. Their increasing concentration predisposes to UTI, with a correlation to increasing age (IIb).

According to an American epidemiological study 6.7 episodes of UTI are expected per 100 per-son years in postmenopausal diabetic women (IIb).

There are epidemiological studies on the incidence of cystitis and pyelonephritis in postmeno-pausal women (IIb).

For female nursing home residents, the prevalence of asymptomatic bacteriuria is about 25-50% (Ia).

Asymptomatic bacteriuria does not require treatment in postmenopausal women apart from some exceptions (A-Ia).

5.4. Otherwise healthy young men

Generally UTIs in men are complicated, but occasionally there are acute episodes of uncompli-cated UTI (IIb).

UTIs in men always need a differentiated diagnostic evaluation (A-GCP).

Asymptomatic bacteriuria in otherwise healthy young men usually does not require treatment (B-V).

5.5. Otherwise healthy patients with diabetes mellitus and stable glycaemic metabolism

In otherwise healthy patients with diabetes mellitus and stable glycaemic metabolism, UTIs can be assumed to be uncomplicated (B-IIa).

UTI in otherwise healthy patients with diabetes mellitus and unstable glycaemic metabolism can be problematic because of aggravated insulin resistance and an increasingly unstable glycaemic metabolism (III).

With unstable glycaemic metabolism and with manifest diabetic complications UTIs are consid-ered to be complicated (A-V).

6. DIAGNOSTICS OF UTIs

6.1. Introduction

A diagnosis based on clinical criteria alone is associated with an error rate up to one third (Ia).

Even the use of low-threshold test instruments such as urine dipsticks, can improve the diagnos-tic accuracy only to a limited extent (Ia).

6.2. Medical History

All patients, in which a UTI is to be confirmed or ruled out, have to undergo a thorough medical history of symptoms, diagnostic findings and risk factors, e.g. dysuria, frequency, urgency, in-creased or reoccurring incontinence, gross haematuria, suprapubic pain, flank pain, fever, urine smell and/or cloudy urine, previous UTI, conspicious vaginalis discharge or vaginal irritation, as well as risk factors for a complicated progress (A-Ia).

Type and frequency of complications may differ in individual groups of patients. Therefore group-specific diagnostic strategies should be used (B-IIb).

6.3. Diagnostics in different groups of patients

6.3.1. Diagnostics in otherwise healthy, non-pregnant premenopausal women

6.3.1.1. Acute uncomplicated cystitis in otherwise healthy, non-pregnant premenopausal women

An uncomplicated acute cystis can be assumed in otherwise healthy non-pregnant premeno-pausal women with typical acute complaints, such as dysuria, frequency, urgency and absence of vaginalis discharge, if pyelonephritis and complicated UTI are unlikely on the basis of medical history. Urinalysis and further diagnostics are unnecessary (C-Ia).

At the first manifestation of an acute UTI, or if the patient is unknown to the physician, symptom related investigations with medical history, physical examination and urinalysis (including mi-croscopy, if applicable) should always be performed (B-V).

6.3.1.2. Acute uncomplicated pyelonephritis in otherwise healthy, non-pregnant premeno-pausal women

In diagnostics of acute uncomplicated pyelonephritis in otherwise-healthy non-pregnant women, the medical history follows the general principles (see 3.2). In addition, a physical examination and urinalysis including culture should be performed (A-V).

In order to rule out complicating factors further examinations (e.g., ultrasound) are necessary (A-V).

6.3.1.3. Asymptomatic bacteriuria in otherwise healthy, non-pregnant, premenopausal women

Screening for asymptomatic bacteriuria in otherwise healthy, non-pregnant women is not neces-sary because usually it has no therapeutic consequences (A-Ia).

6.3.2. Diagnostics in otherwise healthy pregnant women without risk factors

6.3.2.1. Acute uncomplicated cystitis in otherwise healthy pregnant women without risk factors

Diagnostics of acute uncomplicated cystitis in otherwise healthy pregnant women are performed the same way as in non-pregnant patients regarding medical history. However, physical exami-nation and urinalysis including urine culture are always necessary (A-V).

During pregnancy bacteriological eradication should be verified by urine culture after antibiotic therapy (A-V).

6.3.2.2. Acute uncomplicated pyelonephritis in otherwise healthy pregnant women without risk factors

Diagnostics of acute pyelonephritis in otherwise healthy pregnant women are similar to diagnos-tics of non-pregnant patients (A-V).

Physical examination and urinalysis including a urine culture should be performed in each case (A-V).

Even in case of suspected pyelonephritis an ultrasound of the kidneys and urinary tract should be made in addition (A-V).

During pregnancy bacteriological eradication should be verified by urine culture after antibiotic therapy (A-V).

6.3.2.3 Asymptomatic bacteriuria in otherwise healthy pregnant women without risk factors

As the therapy of asymptomatic bacteriuria in pregnancy is recommended (A-Ib), a screening via urinalysis including urine culture should be performed, preferably at the end of the first trimester (A-V).

The use of dipsticks only is insufficient to diagnose asymptomatic bacteriuria (A-IV).

Bacterial eradication should be verified by additional urine culture after therapy (A-V).

6.3.3. Diagnostics in otherwise healthy postmenopausal women

6.3.3.1. Acute uncomplicated cystitis in otherwise healthy postmenopausal women

Diagnostics of acute uncomplicated cystitis in otherwise healthy postmenopausal women is made also by medical history as in otherwise healthy premenopausal woman (A-V).

At the first manifestation of an acute UTI, or if the patient is unknown to the physician, symptom related investigations with medical history, physical examination and urinalysis (including mi-croscopy, if applicable) should always be performed (B-V).

To what extent additional diagnostic procedures e.g. physical investigation, urinalysis including urine culture are required in this group, has not yet been proven by convincing studies (D-V).

6.3.3.2. Acute uncomplicated pyelonephritis in otherwise healthy postmenopausal women

Diagnostics of acute uncomplicated pyelonephritis in otherwise healthy postmenopausal women follows general principles concerning medical history (see 3.2). In addition, a physical examina-tion and urinalysis including urine culture is indicated (A-V).

In case of suspected urine transport disorders (e.g. increased residual urine) the exclusion of complicating factors by advanced examinations (e.g. ultrasound) is necessary (A-V).

6.3.3.3. Asymptomatic bacteriuria in otherwise healthy postmenopausal women

Screening for asymptomatic bacteriuria in otherwise healthy postmenopausal women is not nec-essary because usually no therapeutic consequences result (A-Ia).

6.3.4. Diagnostics in otherwise healthy young men

6.3.4.1./ 2. Acute uncomplicated cystitis and pyelonephritis in otherwise healthy young men

Complicating factors must be ruled out if the diagnosis of uncomplicated UTI (cystitis or pye-lonephritis) is made in men (A-IIb).

In cases of suspected urethritis the diagnostics of urethritis are indicated (A-V).

Besides medical history a physical (including a rectal) examination is indicated in otherwise healthy young men (A-V).

Diagnostics of UTI in otherwise healthy young men should be confirmed by urinalysis including urine culture (A-V).

Diagnostics by dipsticks only are not recommended because of insufficient sensitivity and speci-ficity (B-IIb).

6.3.4.3. Asymptomatic bacteriuria in otherwise healthy young men

Screening for asymptomatic bacteriuria in otherwise healthy men is not necessary, because de-tection of pathogens usually remains without therapeutic consequences (A-V).

6.3.5. Diagnostics in otherwise healthy patients with diabetes mellitus and stable glycaemic metabolism

6.3.5.1. Acute uncomplicated cystitis in otherwise healthy patients with diabetes mellitus and stable glycaemic metabolism

If there are typical and acute complaints such as dysuria, frequency, urgency, and if pyelonephri-tis and complicated UTI are unlikely based on the patients medical history, an uncomplicated acute cystitis should be assumed in otherwise healthy diabetic women with stable glycaemic me-tabolism (HbA1c <7.5%, no predisposition to hypo- or hyperglycaemia, no diabetic nephropa-thy). (B-V).

At the first manifestation of an acute UTI, or if the patient is unknown to the physician, symptom related investigations with medical history, physical examination and urinalysis (including mi-croscopy, if applicable) should always be performed (B-V).

To what extent additional diagnostic procedures (e.g. physical investigation, urinalysis including urine culture) are required in this group, has not yet been proved by convincing studies (D-V).

In otherwise healthy diabetic men diagnostics should be performed as described under 6.3.4.1/ 2. (A-V)

6.3.5.2. Acute uncomplicated pyelonephritis in otherwise healthy patients with diabetes mellitus and stable glycaemic metabolism

Diagnostics of acute uncomplicated pyelonephritis in otherwise healthy diabetic women with stable glycaemic metabolism follows general principles concerning medical history (see 3.2). In addition, a physical examination and urinalysis including urine culture is indicated (A-V).

Advanced examinations (e.g. ultrasound) are necessary to rule out complicating factors (A-V).

In otherwise healthy diabetic men diagnostics should be performed as described under 6.3.4.1/ 2. (A-V).

6.3.5.3. Asymptomatic bacteriuria in otherwise healthy patients with diabetes mellitus and stable glycaemic metabolism

Screening for asymptomatic bacteriuria in otherwise healthy diabetic patients with stable gly-caemic metabolism is not necessary because usually therapeutic consequences do not result (A-Ia).

6.4. Urinalysis

The gold standard for diagnosis of UTI is in case of a positive medical history and typical symp-toms, the urinalysis in-

cluding a quantitative urine culture and its assessment (A-Ia).

The so far usual typical criteria for microbiological diagnosis of UTI includes the detection of bacterial counts of > 105 colony forming units (CFU) / ml of typical uropathogens (A-Ia).

However, sensitivity and specificity respectivly positive / negative predictive values for an UTI are already relatively high with bacterial counts from 103 to 104 CFU / ml in case of monoinfec-tions (i.e. one species of bacteria only) of typical uropathogens (A-Ia).

In urine cultures from suprapubic bladder puncture specimens, any count of uropathogens has a clinical relevance. Therefore urine cultures from suprapubic bladder punctures should be pre-pared in such a way, that already bacterial counts of 102 CFU/ml can be detected reliably (at least 10 identical colonies) (B-Ia).

6.4.1. Urine sampling

Common recommendations with the goal to reduce contaminations are:

- spreading of the labia (B-IV)
- thorough cleansing of the urethral meatus of the women or the glans penis of the men with water (B-IV)
- collection of midstream urine (B-IV).

If only an exploratory urinalysis (e.g. dipsticks) is required, collection of midstream urine instead of spontaneous urine and cleansing of the vaginal introitus or the glans penis are unnecessary (C-IV). Nevertheless, advanced laboratory-chemical and / or microbiological examinations require an exact collection and processing of the urine, usually from midstream urine. Contaminations by urethral and/or surrounding flora are to be kept low (A-IV).

6.4.2. Urinary diagnostic procedures

Urine samples for microbiological diagnostics with culture should be processed without delay. In case of sampling in the afternoon or during the night urine should be kept refrigerated at 2 – 8oC in case the sample cannot be transported or processed immediately. This urine sample must be processed the following day. Reports of such urine samples should be labelled that storage of urine can change the number of pathogens (A-GCP).

6.4.2.1. Urine dipsticks

Also a combination of clinical symptoms and negative results of dipsticks does not completely exclude a diagnosis of UTI (A-IIb).

In a typical case of medical history (dysuria, frequency, urgency, exclusion of pathological vagi-nal discharge) the probability of a UTI is so high that the additional use of dipsticks can only marginally improve the diagnostic accuracy (A-Ia).

At the first manifestation of an acute UTI, or if the patient is unknown to the physician, symptom related investigations with medical history, physical examination and urinalysis (including mi-croscopy, if applicable) should always be performed (B-V).

6.4.2.2. Urine microscopy

With appropriate experience in urine microscopy UTI can be excluded to a large extent (B-Ia).

Centrifugation of urine for the microscopic detection of bacteria does not improve the accuracy of diagnosis (A-Ib).

The lack of microscopic evidence of leukocytes excludes a UTI (B-IIIb).

6.4.2.3. Dip slide culture

Bacteriuria with higher numbers of pathogens (> 104/ml) can be excluded by a dip slide culture (A-Ia).

The exclusion of bacteriuria with lower numbers of pathogens (<104/ml) is not possible because of method related reasons (A-Ia).

6.4.2.4. Urine culture

Urine samples for microbiological diagnostics with culture should be processed without delay. In case of sampling in the afternoon or during the night urine should be kept refrigerated at 2-8°C in case the sample cannot be transported or processed immediately. This urine sample must be processed the following day. Reports of such urine samples should be labelled that storage of urine can change the number of pathogens (A-GCP).

The quantitative urine culture with identification of pathogens and susceptibility testing is essen-tial for targeted and successful therapy especially in cases of complicated and recurrent UTI (A-V).

TABLE 2. – Indication for urine culture.

A. Asymptomatic patient
- leucocyturia, hematuria or a positive nitrit test in patients with specific risk factors (state after renal transplantation, vesicoureteral reflux) - after completing the antibiotic therapy in pregnant women, men, of pyelonephritis or complicated urinary infections
B. Symptomatic patient
- all patients with clinical suspicion of UTI, except in women with uncomplicated cystitis - signs of recurrent UTI in outpatients - signs of UTI with predisposing factors, e.g. complicated UTI in outpatients - all signs of nosocomial UTI - persisting symptoms under or after antibiotic therapy - fever or sepsis of unknown origin
C. Targeted indications in special clinical cases
- before and after urological interventions - pregnancy - immunosuppression - neurogenic bladder voiding disorders, e.g. meningomyelocele - unclear abdominal complaints or flank pain

6.4.2.5. Imaging diagnostics and endoscopy

For clarification of complicating factors ultrasound of the kidneys and urinary tract is the pri-mary diagnostic imaging procedure (A-GCP).

Additional imaging diagnostic procedures should be performed in case of specific clinical prob-lems (B-V).

Routine cystoscopy is not indicated in otherwise healthy women with recurrent UTI (A-IIb).

6.4.2.6. Differential diagnosis

In cases with unclear clinical symptoms, atypical complaints, non-conclusive urine analysis in-cluding negative urine culture, differential diagnosis should be considered at an early stage. (A-GCP).

UTI: Urinary tract infection

* at the first manifestation of an acute UTI, or if the patient is unknown to the physician, symp-tom related investigations with medical history, physical examination and urinalysis (including microscopy, if applicable) should always be performed

7. SPECTRUM OF PATHOGENS

Escherichia coli is the most causative pathogen of uncomplicated UTIs, followed by Staphylo-coccus saprophyticus, Klebsiella pneumoniae, and Proteus mirabilis. Other pathogens are rare (Ia). Enterococci are mostly found in mixed infections (Ic). Therefore, their pathogenicity in un-

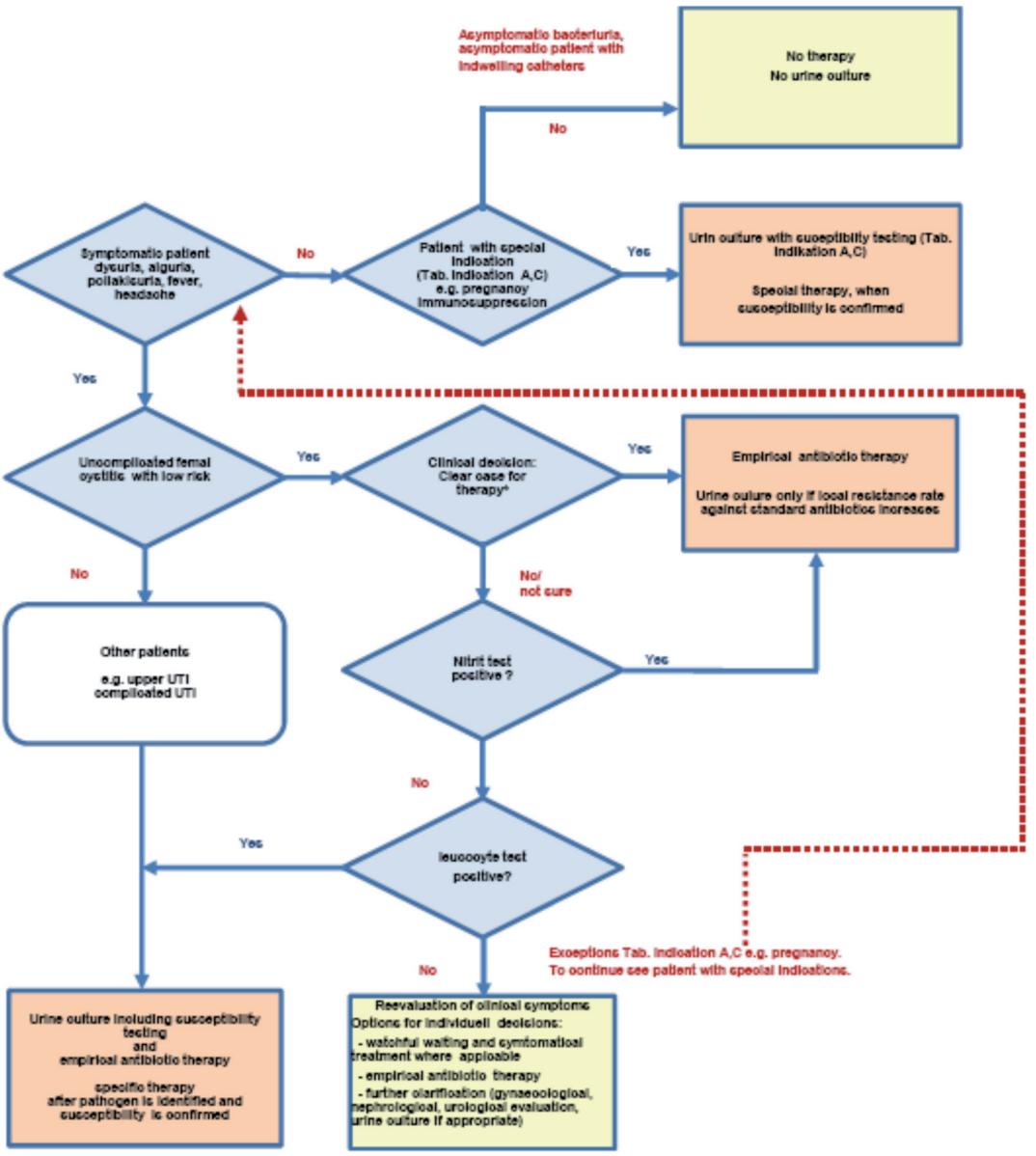

Figure 2. – Decision tree - diagnostics and therapy of symptomatic patients (clinical-microbio-logical path of diagnostics).

TABLE 3. – Spectrum of pathogens in women with uncomplicated cystitis in Germany compared with nine other European countries and Brazil (ARESC study).[24]

	Germany		Total	
Escherichia coli	243	76.7	2,315	76.7
Proteus mirabilis	15	4.7	104	3.4
Klebsiella pneumoniae	8	2.5	107	3.5
Enterobacter spp.	4	1.3	34	1.1
Citrobacter spp.	2	0.6	29	1.0
Other Enterobacteriaceae	5	1.6	36	1.2
Non Enterobacteriaceae	0	0	6	0.2
Staphylococcus saprophyticus	9	2.8	108	3.5
Staphylococcus aureus	7	2.2	32	1.1
Other coagulase-negative staphylococci	14	4.4	68	2.3
Enterococcus spp.	8	2.5	123	4.1
Streptococcus spp.	2	0.6	56	1.9
Total	317	100	3,018	100

complicated UTIs is uncertain.

TABLE 4. – Number and percentage of sensitive and resistant strains of Escherichia coli and of the entire spectrum of pathogens from female patients with uncomplicated cystitis in Germany for 9 antibiotics (CLSI criteria) (ARESC study) (Ia).[24]

	Escherichia coli				Total bacterial spectrum			
	susceptible		resistant		susceptible		resistant	
	n	%	n	%	n	%	n	%
Ampicillin	144	59.2%	85	34.9%	157	56.6%	105	37.9%
Amoxicillin/ Clavulan acid	215	88.8%	3	1.2%	241	87.0%	9	3.2%
Cefuroxime	222	91.3%	1	0.4%	274	89.2%	7	2.2%
Ciprofloxacin	232	95.4%	11	4.5%	291	92.3%	21	6.6%
Cotrimoxazole	180	74.0%	63	25.9%	227	73.9%	80	26.0%
Fosfomycin	238	97.9%	2	0.8%	274	96.1%	4	1.4%
Mecillinam	235	97.5%	3	1.2%	235	97.5%	3	1.2%
Nalidixic acid	220	90.5%	23	9.4%	251	90.6%	26	9.3%
Nitrofurantoin	232	95.4%	11	4.5%	272	86.3%	15	4.7%

8. SUSCEPTIBILITY OF PATHOGENS

Susceptibility strongly depends on the substance. In the ARESC study the susceptibility of Es-cherichia coli (total spectrum) was highest for fosfomycin trometamol with 97.9% (96.1%) fol-lowed by mecillinam with 97.5% (97.5%), ciprofloxacin with 95.4% (92.3%), nitrofurantoin with 95.4% (86.3%), cefuroxime, with 91.3% (89.2%), nalidixic acid with 90.5% (90.6%), amoxicillin/clavulanic acid with 88.8% (87.0%), cotrimoxazole 74.0% (73.9%) and ampicillin with 59.2% (56.6%).

In another German investigation[25] of urine cultures from uncomplicated and complicated UTIs in female patients from general practices the resistance rate of Escherichia coli against amoxicillin, amoxicillin/clavulan acid, oral cephalosporins (group 1 by PEG) and cotrimoxazole was between 25 and 40%. 9% of the isolates were resistant to fluoroquinolones. The resistance rate of Escherichia coli against nitrofurantoin (2%) and oral cephalosporins (group 1 by PEG) 3 (3%) was low. In elder patients with complicated UTIs the resistance rate of Escherichia coli against most antibiotics was significantly higher (2-5 fold).

9. ANTIBIOTIC THERAPY

9.1. Indication for an antibiotic therapy

If an uncomplicated UTI is limited to the bladder, even in recurrent episodes no serious compli-cations are to be expected (IIc).

The basic intention of antibiotic therapy is to rapidly relieve clinical symptoms (B-V).

In acute uncomplicated cystitis an antibiotic therapy should be recommended (B-Ib) (1).

In acute uncomplicated pyelonephritis an effective antibiotic therapy should be applied as soon as possible. (A-Ic).

Asymptomatic bacteriuria increases the risk of infection in pregnant women and in patients with expected mucocutaneous traumatising interventions of the urinary tract. In these cases the patient should be screened for asymptomatic bacteriuria and treated if necessary (A-Ib).

9.2. Preferred form of therapy

An oral antibiotic therapy should be the preferred method of treatment (B-GCP).

For therapy of acute uncomplicated cystitis a short course therapy with an appropriate antibiotic should be possibly preferred (B-Ia).

9.3. Choice of antibiotics

Selecting an antibiotic the following criteria have to be considered:

- individual risk of the patient (A-GCP)
- spectrum of pathogens and susceptibility against antibiotics (A-IIa)
- effectiveness of antimicrobials (A-Ia)
- adverse effects from the drug (A-GCP)
- effects on the individual patients (collateral damage) and/or general public (epidemiol-ogical effects) bacterial resistance situation (A-IIc).

From the group of oral antibiotics or antibiotic classes basically appropriate for the therapy of UTI - aminopenicillins in combination with a betalactamase inhibitor, cephalosporins group 2 and 3 (by PEG), fluoroquinolones, fosfomycin trometamol, nitrofurantoin, pivmecillinam, trimethoprim or cotrimoxazole – the risk of microbiological "collateral damages" by selection of multiresistant pathogens or the risk of clostridium difficile-related colitis is highest with fluoro-quinolones and cephalosporins (IIIb).

Regarding inevitable use of fluoroquinolones and/or cephalosporins for other indications, the clinical consequence of an increased resistance towards these substances should be assessed as more significant than that of previously mentioned antibiotics (B-V).

As long as there are therapeutic alternatives with comparable efficacy and acceptable adverse effects, fluoroquinolones and cephalosporins should not be used as antibiotics of the first choice in uncomplicated cystitis (B-V).

Physicians dealing with the therapy of UTI should get informed about the spectrum of pathogens and local changes in resistance patterns. Sources for these analyses are national studies, analyses of the physicians' associated microbiological laboratories and the physicians' own evaluations (B-IIa).

9.4. Antibiotic therapy

9.4.1. Aminopenicillins ± Beta-lactamase inhibitors

Ampicillin, the better absorbable ampicillinesters and amoxicillin can no longer be recom-mended for empiric therapy because of the low / high susceptibility / resistance patterns (A-IIa).

Aminopenicillins + betalactamase inhibitors are not the first choice for the empiric short course therapy of uncomplicated cystitis (A-Ib).

There are, however, no sufficient studies for the therapy of pyelonephritis (D).

9.4.2. Cephalosporins

There are only a few convincing studies for oral cephalosporins. But oral cephalosporins should not be used as antibiotics of first choice for empiric therapy of uncomplicated UTI (B-V).

In uncomplicated cystitis a 3-day course with cefpodoxime proxetil (100 mg bid) is equivalent to a 3-day course with cotrimoxazole. Therefore cefpodoxime proxetil is an alternative in the treatment of uncomplicated cystitis when other antibiotics are unsuitable (B-Ib).

A 10-day therapy with cefpodoxime proxetil (200 mg bid) was clinically (not microbiologically) equivalent to a 10-day therapy with ciprofloxacin in uncomplicated pyelonephritis Therefore cefpodoxime proxetil can be considered an alternative in the treatment of uncomplicated pye-lonephritis, when other antibiotics are unsuitable (C-Ib).

9.4.3. Fluoroquinolones

Fluoroquinolones (ciprofloxacin, levofloxacin, ofloxacin) are well effective in a 3-day treatment of uncomplicated cystitis (Ib). However, they are no longer recommended as antibiotic of the first choice for treatment of uncomplicated cystitis, since they are used (have to be used) in other indications and given that other antibiotics are available, which are exclusively used for the ther-apy of uncomplicated cystitis (B-V).

Fluoroquinolones at a sufficiently high dose - Ciprofloxacin 500-750 mg daily bid (Ib) or Levofloxacin 500-750mg qd (Ib) – are considered oral antibiotics of the first choice for empiric treatment of mild and moderate uncomplicated pyelonephritis, if the local resistance rate of Es-cherichia coli is <10% (A-V).

9.4.4. Fosfomycin

In clinical trials a single dose of fosfomycin trometamol was not inferior to cotrimoxazole, trimethoprim or nitrofurantoin in the empiric treatment of uncomplicated cystitis

(1) *Minority vote of the German Society for General and Family Medicine:* In acute uncomplicated cystitis symptomatic treatment by itself is a justifiable alternative to im-mediate antibiotic therapy (C-Ia).

in otherwise healthy women (Ia).

Due to low resistance rates and due to low collateral damage fosfomycin trometamol is deemed to be a drug of the first choice in the empiric treatment of uncomplicated cystitis in otherwise healthy women (A-Ib).

Oral treatment with a single dose of fosfomycin trometamol is not indicated for the therapy of pyelonephritis or the treatment of men (A-V).

9.4.5. Nitrofurantoin

In clinical trials macrocrystalline nitrofurantoin (extended release form 100mg bid for 5 days) was as effective as a 3-day course with cotrimoxazole in the empiric treatment of uncomplicated cystitis (Ib).

Due to low resistance patterns and low collateral damage nitrofurantoin is a drug of choice in empiric treatment of uncomplicated cystitis in otherwise healthy women (A-Ib).

Nitrofurantoin was investigated in a short-term course of 3 days only against placebo. Prolonged treatment (5-7 days) showed better results (A-IIb).

9.4.6. Pivmecillinam (available in Austria and Scandinavia, not in Germany)

In clinical trials pivmecillinam (400 mg bid for 3 days) was clinically (not microbiologically) as effective as a 3-day course with norfloxacin in the empiric treatment of uncomplicated cystitis in women (Ib).

In clinical trials women with uncomplicated cystitis were empirically more effectively treated with pivmecillinam at a dosage of 200 mg bid for 7 days than with pivmecillinam at a dosage of 400 mg bid for 3 days (Ib).

Due to low resistance rates and due to low collateral damage pivmecillinam is an antibiotic of the first choice for empiric treatment of uncomplicated cystitis in otherwise healthy women. The recommended duration of therapy (3-7 days) depends on the dosage (see Table 5) (A-Ib).

9.4.7. Trimethoprim mono or in combination with a sulfonamide

In the past cotrimoxazole (trimethoprim/sulfamethoxazole) and trimethoprim were the standard in empiric treatment of cystitis (Ia).

Due to existing resistance rates, which according to the ARESC study in Germany are > 20% for Escherichia coli and also for the total spectrum of pathogens, a higher failure rate is now to be expected (IIb). Therefore, cotrimoxazole and trimethoprim are recommended only as antibiotics of first choice for empiric treatment, if rates of resistance below 20% can be verified (B)[2].

10. ANTIBIOTIC THERAPY OF ACUTE UNCOMPLICATED UTI IN SPECIAL PATIENT GROUPS

10.1. Antibiotic therapy of acute uncomplicated UTI in otherwise healthy premenopausal women

10.1.1. Acute uncomplicated cystitis in otherwise healthy premenopausal women

In otherwise healthy premenopausal women with typical medical history and complaints of un-complicated cystitis, a routine urine culture is unnecessary before therapy, as clinical cure is ex-pected within a few days and as no more consequences are drawn from the results of the urine culture (A-V).

At the first manifestation of an acute UTI, or if the patient is unknown to the physician symptom related investigations with medical history, physical examination and urinalysis (including mi-croscopy, if applicable) should always be performed (B-V).

To optimize this treatment strategy regular contemporary and local epidemiological studies of pathogen susceptibility are recommended, since pathogen susceptibility varies regionally and also changes with time (B-IIa).

Antibiotics of the first choice are fosfomycin trometamol, nitrofurantoin and pivmecillinam, be-cause the susceptibility of Escherichia coli pathogens to these antibiotics is high and because they cause little collateral damage. These antibiotics are primarily used for the therapy of uncomplicated cystitis (A-Ib). Consensus 10/12 (2 abstentions – see minority vote of DEGAM).

Cotrimoxazole, trimethoprim, fluoroquinolones, cephalosporins and aminopenicillins in combi-nation with a beta-lactamase-inhibitor should only be used alternatively in empiric treatment, if local resistance patterns (<20%) permit and first choice drugs cannot be used (B-V) .

Monitoring the efficacy of treatment of uncomplicated cystitis in otherwise healthy premeno-pausal women is unnecessary if they had become asymptomatic (B-V).

If therapy fails (within 2 weeks), non-compliance of patients, resistant pathogens or so far unrec-ognized risk factors should be considered. In these cases, differentiated instructions and a physi-cal examination of the patient; a urinalysis including urine culture; and possibly a switch of the antibiotic regimen are indicated before starting the next attempt of antibiotic treatment (B-V).

A clinical recurrence may be caused by the same or a different pathogen. As frequently a chnge of resitance patterns is observed, urinalysis including urine culture is recommended (B-IIa).

TABLE 5. – Recommended short-term course for uncomplicated cystitis in otherwise healthy premenopausal women (without risk factors).

Drug	Daily dosage	Duration
Antibiotic of first choice (A)		
Fosfomycin trometamol	3000mg qd	1 d
Nitrofurantoin	50mg q6h	7 d
Nitrofurantoin RT	100mg bid	5 d
Pivmecillinam*	200mg bid	7 d
Pivmecillinam*	400mg bid	3 d
Antibiotic of second choice (B)		
Ciprofloxacin	250mg bid	3 d
Ciprofloxacin RT	500mg qd	3 d
Levofloxacin	250mg qd	3 d
Norfloxacin	400mg bid	3 d
Ofloxacin	200mg bid	3 d
Cefpodoxime proxetil	100mg bid	3 d
If local resistance patterns are known (Escherichia coli resistence rate < 20%) (B)3		
Cotrimoxazole	160/800mg bid	3 d
Trimethoprim	200mg bid	5 d
RT= slow releasing form (= macrocrystalline form) *available in Austria and Scandinavia, not in Germany		

10.1.2. Acute uncomplicated pyelonephritis in otherwise healthy premenopausal women

Pyelonephritis with mild and moderate symptoms in

(2) *Minority vote of the German Society of General and Family Medicine:* Despite higher resistance rates, the vast majority of patients are successfully treated with trimethoprim (A-Ib).

(3) *Minority vote of the German Society of General and Family Medicine:* Despite higher resistance rates, the vast majority of patients are successfully treated with trimethoprim (A-Ib).

otherwise healthy premenopausal women should be treated with oral antibiotics (B-Ib). In severe infections with systemic side effects, like nausea, vomiting, and/or cardiovascular instability, therapy should be started with high dose parenteral antibiotics (B-Ib)(Figure 3).

In mild or moderate pyelonephritis with clinically uneventful course 2 weeks of treatment are generally sufficient in otherwise healthy premenopausal women. With fluoroquinolones, the therapy can be shortened to 7-10 days. If used at higher doses, e.g. Levofloxacin 750 mg qd, the treatment duration can even be reduced to 5 days (B-Ib).

Fluoroquinolones should be considered as first choice antibiotics if the local Escherichia coli resistance rate is <10% (B-Ib).

Cefpodoxime proxetil should be considered in situations where other antibiotics e.g. fluoroqui-nolones cannot be applied (B-Ib).

Cotrimoxazole should not be used anymore for empiric therapy of pyelonephritis (A-Ib). But Cotrimoxazole can be given as an oral sequence therapy after initial parenteral therapy, if patho-gens are tested susceptible for cotrimoxazole (C-Ib). Trimethoprim has not been studied in this context.

TABLE 6. – Recommended empiric antibiotic therapy of uncomplicated pyelonephritis in otherwise healthy premenopausal women (without risk factors).

Oral therapy of mild to moderat cases		
Antibiotic of first choice (A)[4]	Daily dosage	Duration
Ciprofloxacin1	500-750mg bid	7-10 d
Ciprofloxacin RT	1000mg qd	7-10 d
Levofloxacin1	(250-) 500mg qd	7-10 d
Levofloxacin	750mg qd	5 d
Antibiotic of second choice (B) (similar clinical efficacy, microbiologically not equivalent with fluoroquinolones)		
Cefpodoxime proxetil	200mg bid	10 d
Ceftibuten	400mg qd	10 d
If susceptibility of pathogens is confirmed (B) (not for empiric therapy)		
Cotrimoxazole	160/800mg bid	14 d
Amoxicillin/Clavulanic acid[2,3]	0,875/0,125g bid	14 d
Amoxicillin/Clavulanic acid[2,3]	0,5/0,125g tid	14 d
[1] Low doses studied, high dosage recommended by experts [2] Not investigated in convincing clinical studies. [3] Primarily for Gram-positive pathogens [4] If Escherichia coli resistance is <10%		
Initial parenteral therapy of severe pyelonephritis		
After clinical improvement therapy can be switched to one of the above-mentioned oral therapy regimens if susceptibility of pathogens is confirmed. The total duration of therapy is 1-2 weeks, therefore duration of parenteral antibiotic therapy is not noted.		
Antibiotic of first choice (A)[7]	Daily dosage	
Ciprofloxacin	400mg bid	
Levofloxacin[1]	(250-) 500mg qd	
Levofloxacin	750mg qd	
Antibiotic of second choice (B)		
Cefepim[1,4]	1-2g bid	
Ceftazidim[2]	1-2g tid	
Ceftriaxon[1,4]	1-2g qd	
Cefotaxim[2]	2g tid	
Amoxicillin/Clavulanic acid[2,3]	1,0/0,2g tid	
Amoxicillin/Sulbactam[2,3]	1,0/0,5g tid	
Piperacillin/Tazobactam[1,4]	2,5-4,5g tid	
Amikacin[2]	15mg/kg qd	
Gentamicin[2]	5mg/kg qd	
Doripenem[4,5]	0,5g tid	
Ertapenem[4,5]	1g qd	
Imipenem/Cilastatin[4,5]	0,5/0,5g tid	
Meropenem[4,5,6]	1g tid	

[1]Low doses studied, high dosage recommended by experts
[2]Not investigated in convincing clinical studies.
[3]Primarily for Gram-positive pathogens
[4]Same protocol for acute uncomplicated pyelonephritis and complicated UTI (stratification not always possible)
[5]Only if ESBL resistance >10% (ESBL-extended spectrum beta-lactamases)
[6]Only high dosage studied
[7]*If Escherichia coli* resistence <10%

10.1.3. Asymptomatic bacteriuria in otherwise healthy premenopausal women

Asymptomatic bacteriuria in otherwise healthy premenopausal women is not associated with adverse outcomes. Therefore neither screening nor therapy are generally necessary (A-Ia).

10.2. Antibiotic therapy of acute uncomplicated UTI in otherwise healthy pregnant women without risk factors

When selecting drugs possible adverse reactions on the embryo/fetus have to be taken into ac-count. Mainly penicillins, cephalosporins or fosfomycin trometamol should be considered (A-GCP).

Asymptomatic bacteriuria and symptomatic UTI in pregnancy have to be treated with antibiotics to avoid serious consequences for mother and child (A-Ia).

10.2.1. Acute uncomplicated cystitis in otherwise healthy pregnant women without risk factors

Short-term therapy of acute cystitis in pregnant women is not as well investigated as in non-pregnant women. For treatment fosfomycin trometamol (single dose), pivmecillinam, oral cepha-losporins of group 2 or 3 are primarily recommended (B-IIa).

10.2.2. Acute uncomplicated pyelonephritis in otherwise healthy pregnant women without risk factors

During pregnancy inpatient treatment of pyelonephritis has to be considered (A-V).

For empiric treatment cephalosporins of group 2 and 3 are mainly recommended (B-V).

After therapy of pyelonephritis a follow-up urine culture is necessary to demonstrate success, because asymptomatic bacteriuria has to be treated as well (A-Ia).

10.2.3. Asymptomatic bacteriuria in otherwise healthy pregnant women without risk fac-tors

Treatment of asymptomatic bacteriuria during pregnancy should be initiated according to resis-tance patterns, when pathogens are identified and their susceptibility is known. (B-V).

10.3. Antibiotic therapy of acute uncomplicated UTI in otherwise healthy postmenopausal women

10.3.1. Acute uncomplicated cystitis in otherwise healthy postmenopausal women

The short-term therapy of acute cystitis in postmenopausal women is not as well established as in premenopausal woman. Recent studies, however, demonstrate the possibility of short-term ther-apy (C-Ib).

Selection and dosage of antibiotics comply with treatment regimens of premenopausal women (B-V).

10.3.2. Acute uncomplicated pyelonephritis in otherwise healthy postmenopausal women

For the antibiotic treatment of acute uncomplicated pyelonephritis in postmenopausal women an approach similar to the treatment of premenopausal women is recommended

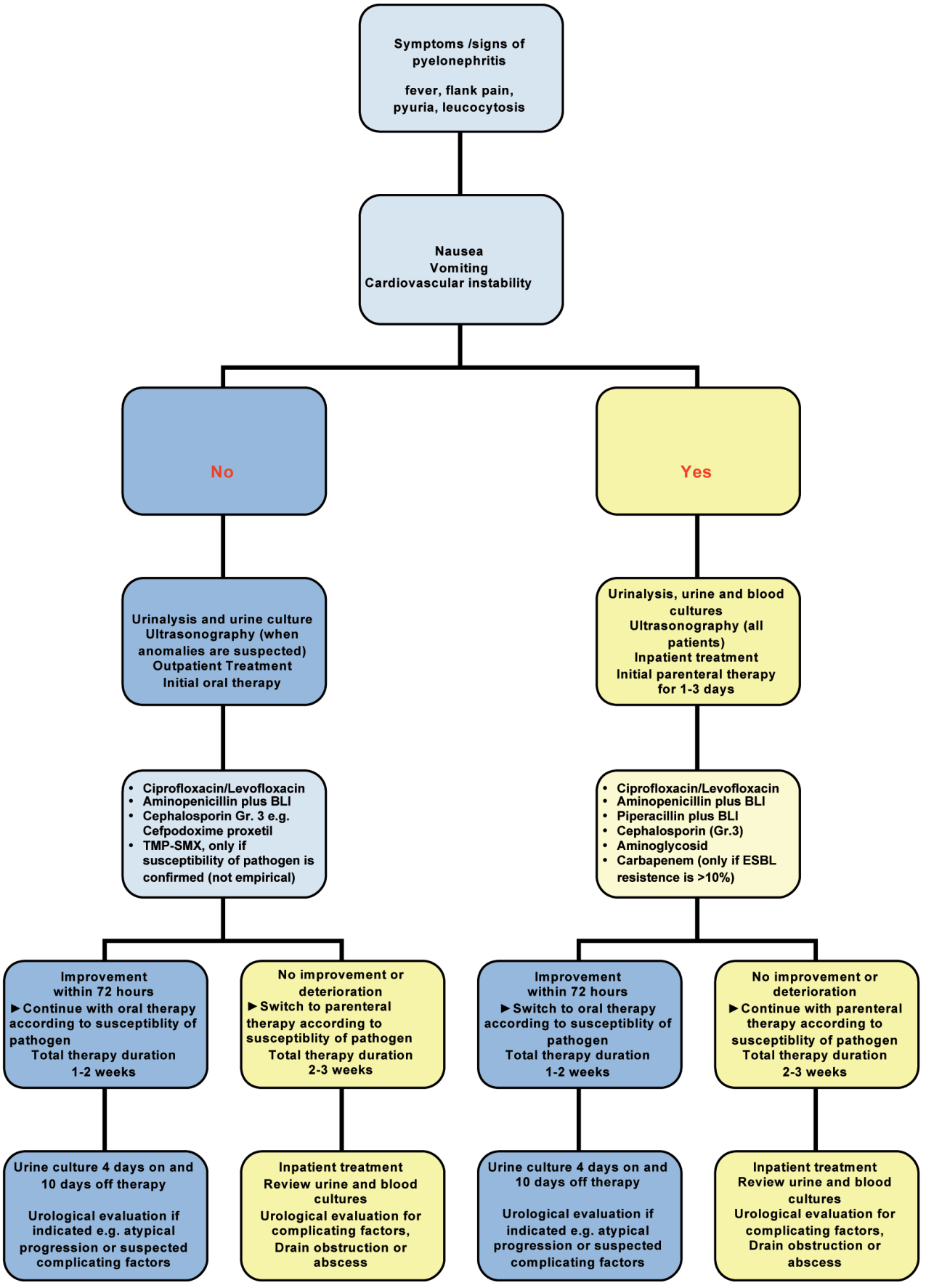

Figure 3. – Clinical management of acute pyelonephritis in female adult patients
BLI = betalactamase inhibitor; TMP = Trimethoprim; SMX = Sulfamethoxazole.

(B-V).

10.3.3. Asymptomatic bacteriuria in otherwise healthy postmenopausal women

Asymptomatic bacteriuria in otherwise healthy postmenopausal women is apparently not associ-ated with adverse outcomes. Therefore neither screening nor therapy are generally necessary (A-IIb).

10.4. Antibiotic therapy of acute UTI in otherwise healthy young men

10.4.1. Acute uncomplicated cystitis in otherwise healthy young men

For the empiric oral therapy of acute uncomplicated cystitis in young men, the same antibiotics are recommended as in women (Table 4), with the exceptions of fosfomycin trometamol (single dose), pivmecillinam and nitrofurantoin (B-V).

10.4.2. Acute uncomplicated pyelonephritis in otherwise healthy young men

For the empiric oral therapy of mild and moderate acute uncomplicated pyelonephritis in young men fluoroquinolones are recommended as fist choice, if the local resistance rate of Escherichia coli is < 10% (A-Ib).

Duration of therapy is usually 7-10 days (B-IIa).

10.4.3. Asymptomatic bacteriuria in otherwise healthy young men

Also in men asymptomatic bacteriuria is probably not associated with adverse outcomes. There-fore therapy is generally unnecessary if complicating factors are excluded (B-V).

10.5. Antibiotic therapy of acute UTI in otherwise healthy patients with diabetes mellitus and stable glycaemic metabolism

10.5.1. Acute uncomplicated cystitis in otherwise healthy patients with diabetes mellitus and stable glycaemic metabolism

In patients with uncomplicated UTI and diabetes mellitus, the spectrum of pathogens does not differ significantly from UTI in patients without diabetes mellitus. The predominant species is Escherichia coli (A-Ia).

Acute uncomplicated cystitis in patients with diabetes mellitus and stable glycaemic metabolism (HbA1c <7.5%, no predisposition to hypo- or hyperglycaemia, no diabetic nephropathy) should be treated in the same way as corresponding UTIs in patients without diabetes mellitus (B-V).

In acute uncomplicated cystitis in patients with diabetes mellitus and stable glycaemic metabo-lism a short-term antimicrobial therapy is justified (C-V).

In severe insulin resistance, threatening organ complications and a tendency to metabolic de-compensation inpatient treatment should be considered (A-V).

10.5.2. Acute uncomplicated pyelonephritis in otherwise healthy patients with diabetes mel-litus and stable glycaemic metabolism

Antimicrobial treatment of otherwise healthy patients with diabetes mellitus and stable glycae-mic metabolism (HbA1c <7.5%, no predisposition to hypo- or hyperglycaemia, diabetic neph-ropathy) is the same as treatment in patients without diabetes mellitus. Controls of metabolic parameters, however, are necessary. The duration of antimicrobial therapy should depend on the clinical course of infection (B-V).

10.5.3. Asymptomatic bacteriuria in otherwise healthy patients with diabetes mellitus and stable glycaemic metabolism

In otherwise healthy patients with diabetes mellitus with stable glycaemic metabolism (HbA1c <7.5%, no predisposition to hypo- or hyperglycaemia, diabetic nephropathy) and without ob-structive anatomical changes no antibiotic therapy is necessary (A-Ib).

11. ASYMPTOMATIC BACTERIURIA

Asymptomatic bacteriuria increases the risk of infection in pregnant women and in patients with expected mucocutaneous traumatising interventions of the urinary tract. In these cases patients should be screened for asymptomatic bacteriuria and treated if necessary. Supporting studies are available for pregnancy and transurethral resection (A-Ib).

Asymptomatic bacteriuria obviously has no adverse effects in the following groups of patients. Therefore neither screening nor treatment are recommended.

- premenopausal, non pregnant women (A-Ib)
- . diabetic women* (A-Ib).
- . older persons living in the community (A-llb)
- . elderly institutionalized subjects (A-lb)
- patients with spinal cord injury (A-IIb)
- . catheterized patients while the catheter remains in situ (A-la).

*this applies to diabetics with stable glycaemic metabolism.

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Botulinum Toxin A (BTX-A) in refractory non-neurogenic overactive bladder: A prospective review of intermediate-term quality of life outcome assessment

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Abstract: *Objective:* To evaluate the efficacy of BTX-A in non-neurogenic (idiopathic) overactive bladder (OAB) patients. *Materials and methods*: All drug refractory non-neurogenic OAB patients that received intravesical BTX-A between January 2004 and January 2009 were recruited prospectively. Patient demographics, voiding diary and urodynamics studies were recorded. King's Health Questionnaires (KHQ) was completed pre and post therapy at 3, 6 and 9 months. The primary end point assessments were number of urgency and urge incontinence as well as quality of life outcomes. All adverse events were also documented. *Results:* A total of 60 patients (28 men, 32 women) with the mean age of 64.2 (28 to 84) years old and a mean follow up was 26.2 (12 to 58) months, were recruited during the 5 years period. No significant adverse side effects or mortality were documented. Three patients (6%) developed a temporary increase in post void residuals requiring short-term catheterisation (< 5 days). Fifty patients (83%) demonstrated significant improvement with regards to their KHQ scores pre and post BTX administration ($p < 0.001$), with the symptomatic benefits diminishing at subsequent 6 and 9 months follow up ($p>0.05$). 48 patients (80%) reported recurrence of OAB symptoms at the 6 months follow up visit, necessitating reintroduction of anticholinergic therapy for symptomatic control. When looking at specific KHQ domains, significant reduction was noted in storage symptoms specifically of frequency, nocturia, urge and urge incontinence ($p < 0.001$). The improvement in stress incontinence and bladder pain were not significant ($p>0.05$). The functional bladder capacity increased from 192.7 (60 to 300) mls to 341 (140 to 550) mls while the number of pad use decreased from 3.7 (3 to 7) pads to 0.75 (0 to 1) pad ($p < 0.001$). *Conclusion:* Our results indicate that BTX-A treatment for non-neurogenic OAB appears to be safe and well-tolerated with most patients electing for repeated treatments.

Key words: Overactive bladder; Intravescical BTX-A; Urge incontinence; Stress incontinence.

INTRODUCTION

Overactive bladder (OAB) affects more than 12% of adult population[1] and is characterised by symptoms of urinary urgency, with or without urge incontinence, usually with frequency and nocturia.[2] OAB is most commonly caused by detrusor overactivity (DO), which is defined as the presence of involuntary detrusor contractions during the filling phase of cystometry, which may be spontaneous or provoked.[2] In the absence of local or neurological causes, this DO is termed idiopathic or non-neurogenic detrusor overactivity (NNDO).

Management approaches to this debilitating condition usually comprises of bladder retraining and antimuscarinic agents. However a proportion of patients remained affected[3] either because they are refractory to antimuscarinics, have discontinued treatment due to significant side effects or have contraindication to these agents. Other treatment options for these drug-refractory patients consist conventionally of more invasive procedures including sacral neuromodulation, augmentation cystoplasty or urinary diversion.[4] However the advent of intravesical use of botulinum toxin (BTX) has offered another minimally invasive option in the armamentarium of agents which can be used to treat DO.[5-9]

Although data is abundant on the use of BTX in neurogenic DO,[5,7,8,10] few studies have evaluated the efficacy of BTX in managing idiopathic DO.[11-14] To our knowledge, this is the first Australasian series that reports on the clinical effects of BTX on the treatment of non-neurogenic DO and its impact on the patient quality of life.

MATERIALS AND METHODS

From January 2004 to January 2009, patients from the Concord hospital urodynamic clinic with non-neurogenic OAB who were refractory to at least 2 anticholinergic agents and/or have ceased anticholinergic therapy due to unwanted side effects were enrolled prospectively into the study. All patient demographics, voiding diary and outcome of multi-channel urodynamics studies were recorded. Patients were required to fill a validated King's Health Questionnaires (KHQ) pre and post therapy at 3, 6 and 9 months. Exclusion criteria included neurogenic bladder, bladder outlet obstruction, active urinary tract infection and muscular weakness such as myasthenia gravis.

Doses of 200 IU of BTX-A (Botox®, Allergan Inc, CA, USA) were constituted with 10 mls of sterile normal saline for intra-detrusor injection. The injection was administered with a 23G Williams needle (Cook, Queensland, AUSTRALIA) via a 22 French rigid cystoscope transurethrally, as a day procedure under general anaesthesia. The needle tip was placed into detrusor muscle and 1 ml aliquots each containing 20 units were injected without raising any submucosal blebs. 200 IU of BTX-A was injected in 2 rows of fives injections to the base of the bladder sparing the dome and trigone. Ureteric orifices were used as markers of the lateral extent of the injection sites. Each patient received a prophylactic dose of cephalothin 1g intravenously and the bladder was emptied at the end of procedure. No urethral catheter was used. Patients were then kept in the day surgery unit for 6 hours to ensure satisfactory voiding.

Patients were followed up prospectively every 3 monthly with further history and examination, voiding diary and KHQ. The primary end point assessments were number of urgency and urge incontinence as well as quality of life outcomes. Adverse events such as acute urinary retention, clot retention, transient weakness and bladder or urethral pain were documented. The results were analysed using a 2-sample student *t test* with equal variance to compare the results pre and post BTX-A treatment.

RESULTS

A total of 60 patients (28 men, 32 women) with the mean age of 64.2 (28 to 84) years old and a mean follow up was 26.2 (12 to 58) months, were recruited during the 5 years period. The causes of bladder dysfunction requiring Botox-A treatment include 42 patients with idiopathic DO, 6 patients with non-neurogenic poor detrusor compliance and 12 patients with OAB symptoms but no demonstrable DO on urodynamics.

No significant adverse side effects or mortality were documented. Three patients (6%) developed a temporary increase in post void residuals requiring short-term catheterisation (< 5 days). Two patients who were previously on clean intermittent self catheterisation (CISC) due to under-

lying poor bladder compliance continued with CISC practice post BTX-A administration. No patient was admitted with gross hematuria or clot retention.

Of the patient cohort, 50 patients (83%) demonstrated significant improvement with regards to their KHQ scores pre and post BTX administration ($p < 0.001$). The most significant improvement was reported at 3 months ($p < 0.001$) with the symptomatic benefits diminishing at subsequent 6 and 9 months follow-up ($p > 0.05$) (Table 1). The domains with the greatest improvement were incontinence impact (domain 2), physical limitation (domain 4) and emotion (domain 7) (Figure 1). Most patients (80%) reported recurrence of OAB symptoms at the 6 months follow up visit, necessitating reintroduction of anticholinergic therapy for symptomatic control. A total of 37 (62%) patients have repeated BTX-A injection with a mean interval of 11 (7 to 14) months. For those patients who received further intravesical administration of BTX-A, all patients reported similar efficacy and improvement of their urinary symptoms. Out of the 60 patients, 4 were lost to follow-up while the remaining 11 patients did not request for further BTX-A treatment.

Significant reduction was noted in storage symptoms specifically of frequency, nocturia, urge and urge incontinence ($p < 0.001$). The improvement in stress incontinence and bladder pain were not significant ($p > 0.05$). The functional bladder capacity increased from 192.7 (60 to 300) mls to 341 (140 to 550) mls while the number of pad use decreased from 3.7 (3 to 7) pads to 0.75 (0 to 1) pad ($p < 0.001$). For the 6 patients who had poor detrusor compliance as sole finding on the preoperative urodynamics, there was significant improvement noted ($p < 0.001$) with the detrusor compliance normalised on urodynamics at 6 months post injection.

DISCUSSIONS

Botulinum toxin (BTX) is a complex and potent neurotoxin protein produced by anaerobic bacterium *Clostridium botulinum*. It was first isolated by Ermengem in 1897 and later introduced into the field of urology by Schurch and Stohrer for the treatment of detrusor sphincter dyssynergia in patients with spinal cord injuries[6,7] prior to use in non-neurogenic DO.[15]

The role of BTX at the neuromuscular junction has been well described and consisted of inhibition of acetylcholine neurotransmitter release resulting in temporary chemo-denervation and striated muscle relaxation.[8] However there is also increasing evidence suggesting a much greater extent of neurologic effects of BTX. BTX has been found to inhibit the release of a number of neurotransmitters (including acetylcholine, adenosine triphosphate, and the neuropeptides such as substance P) and down-regulate the expression of purinergic and vanilloid receptors on afferent neurons within the bladder suburothelium;[8-11] hence potentially treating DO and OAB by both sensory and motor pathways. Of the seven serotypes of BTX, type A and B have been used

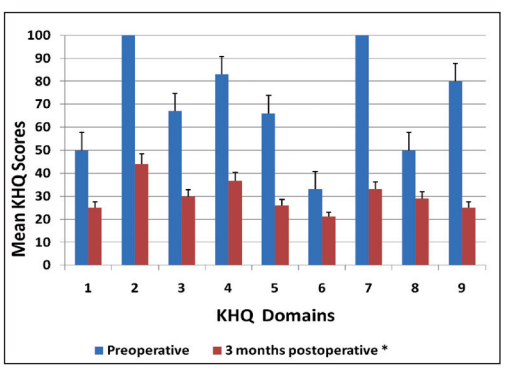

Figure 1. – Mean KHQ scores pre and post BTX-A (at 3 months) ($p < 0.01$).

Table 1. – Mean KHQ scores pre and post BTX-A.

KHQ Domains	Preoperative	3 months postoperative*	6 months postoperative**	9 months postoperative**
1. General Perception	50	25	40	50
2. Incontinence Impact	100	44	63	100
3. Role Limitations	67	29.9	33	63
4. Physical Limitations	83	36.7	41	81
5. Social Limitations	66	25.9	41.2	63.3
6. Personal Relationships	33	21	26.1	31.4
7. Emotions	100	33	56	88.7
8. Sleep/Energy	50	29	40	46.7
9. Severity Measures	80	25	41	76.5

* denotes $p < 0.001$ between preoperative and 3 months postoperative;
** denotes $p > 0.05$ (NS) between 3 months and subsequent 6 and 9 months postoperative.

with clinically beneficial outcomes in various neurologic disorders.[3] Recently BTX-A has been shown to inhibit the release of norepinephrine, suggesting a potential role in inhibiting afferent/sensory innervations of lower urinary tract and central desensitisation through a decrease in central uptake of substance P[9] contributing to overall decrease in frequency and urgency.[10] Although there have been numerous published literature on the efficacy of BTX-A in the treatment of DO and OAB, this drug is not yet approved by many government regulatory bodies.[3,15]

At present there is no consensus on the dose, percentage of dilution, injection site (intradetrusor or suburothelium), the number of injections and rate of BTX use in neurogenic or non-neurogenic OAB. Recent studies have shown that doses of 100 or 200IU of BTX-A is effective in treating idiopathic DO[16] while doses over 200IU are commonly used in patients with neurogenic DO.[10,17] In a double-blind, placebo-controlled randomized dose ranging trial, Dmochowski[18] have shown either 100 or 150 units of BTX to have the best efficacy and safety profile in the treatment of idiopathic OAB. There have been published literature revealing similar efficacy of BTX-A in both suburothelial or detrusor injections.[9,19] This may be attributed to the diffusion of BTX-A between detrusor and suburothelial space as evident in magnetic resonance study.[20] Kuo[19] reported superior clinical efficacy of BTX-A when administered in suburothelial and into detrusor compared to bladder base injections, with no documented incidence of vesico-ureteric reflux when injecting BTX-A into the trigone.

Several large volume studies published on BTX-A in idiopathic OAB refractory to anticholinergics such as by Schmid[21] has shown significant improvement in bladder function with regards to subjective symptoms, quality of life and urodynamics parameters. Rajkumar[22] published the use of 300 IU BTX-A in his group of idiopathic non-anticholinergic responders showing significant improvement in the bladder symptoms after the initial 6 weeks follow up; with therapeutic effects of BTX-A lasting over 20-24 months. Although all the patients were able to void following the administration of 300 units of BTX-A, 4 patients demonstrated post void residuals of more than 200 mls. Jeffrey[23] also reported similar efficacy with Dysport 500IU with significant subjective and objective improvements in patients with refractory IDO. Our series has shown significant improvement in patients' quality of life events as well as symptoms of frequency, urgency and urge incontinence. The effects of BTX lasted for an average of 6 months in our experience and majority of patients were happy to undergo the treatment again. As with most published literature, the beneficial effects of BTX were maintained throughout the 24 weeks period with most patients electing for repeat treatment when the clinical effects wear off. Therefore the safety of repeated BTX injection on the structural changes in the bladder caused by either the toxin or repeated micro-scarring of

bladder is a potential source of concern. Apostolidis[24] concluded that repetitive injection of BTX did not appear to produce any significant inflammatory changes, fibrosis, or dysplastic changes apart from presence of eosinophils which might be treatment-related effect. Nonetheless the patient numbers are too small from which to draw definitive conclusion. Grosse[25] found no evidence of increased drug tolerance after multiple treatments. BTX produced from 1997 onwards has much lower antigenic potential and the development of resistance to BTX treatment is uncommon.

Several factors have been shown to limit the therapeutic efficacy of BTX. Patients with pre-existing bladder wall fibrosis and low bladder compliance or OAB symptoms with painful bladder or interstitial cystitis appeared to respond less favourably.[26] In our experience, the administration of intravesical BTX does not appeared to improve symptoms of painful bladder; perhaps there were other sensory pathways not accounted by BTX. However we have demonstrated improvement in bladder symptoms in patients with poor bladder compliance as well as significant increase in the mean functional bladder capacity following administration of BTX; validating the effects of BTX in temporary chemodenervation and smooth muscle relaxation. In contrast to the reported literature[14] that up to 45% of patients who received high doses of BTX would require clean intermittent self catheterisation (CISC), we did not identify any new patient with prolonged voiding dysfunction apart from those who previously perform CISC for poorly compliant and hypocontractile bladder. While we acknowledge the modest numbers of patients, our series has excellent intermediate term follow up and a consistent protocol was instituted for each patient. Unfortunately the literature pertaining to longer-term use and outcome of BTX is sparse. To our knowledge this is the first published study on BTX-A in non-neurogenic OAB in an adult Australasian patient cohort. Despite the numerous longitudinal studies on BTX in refractory non-neurogenic OAB, only a well-designed randomised double blinded control trial can address the issues surrounding BTX and its cost-effectiveness over other therapeutic options.

CONCLUSIONS

BTX-A significantly reduce the symptoms and improve quality of life in patients with drug refractory non-neurogenic OAB. Our results indicate that BTX-A treatment appears to be safe and well tolerated with most patients electing for repeated treatments. However the lack of general consensus with regards to BTX would require more well-designed, randomised controlled trials before BTX could be accepted and approved by various government bodies for use in treating this debilitating condition.

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Review

Paravaginal defects and stress urinary incontinence

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Abstract: *Objective:* To analyze the literature on the role of paravaginal defects in pathophysiology and management of stress urinary incontinence and to formulate an idea on the management according to the underlying pathophysiology in each individual patient with stress urinary incontinence. *Materials and Methods:* This is a clinical review of literature on paravaginal defects. A medline search was performed using the Medical Subject Headings (MeSH) terms "Paravaginal defect", "stress urinary incontinence", and "Colposuspension". Literature from the year 1990 to 2010 is reviewed. Anatomical, clinical, imaging and surgical evidences for the existence and role of paravaginal defects is summarized and analyzed. Role of colposuspension in correcting paravaginal defects and stress urinary incontinence is discussed. *Results:* Paravaginal defects are real entities and play an important role in the patho-physiology of stress urinary incontinence. Current clinical practice ignores the anatomical causes underlying the causation of stress urinary incontinence and instead the use of a single procedure (in most cases mid-urethral slings) for all women with stress incontinence is becoming a trend. *Conclusion:* Evaluation of a woman with stress urinary incontinence should include searching for possible underlying causes (anatomical and functional) and management should be based accordingly. In the presence of paravaginal defect, a colposuspension will be a better management option. Urethral hypermobility (or a hypotonic urethra) in the absence of a paravaginal defect may be treated with mid-urethral slings.

Key words: Paravaginal defect; Stress urinary incontinence; Colposuspension; Mid-urethral slings.

INTRODUCTION

The diversity of the pathologies of the pelvic floor, their origin, their degree, and their clinical relevance makes comparison of studies on diagnosis and treatment of pelvic floor disorders difficult. The focus of research in recent years was the search of a numeric classification. The description of single compartments and stages of their descent disregards quality of tissue and complex pathologies of the pelvic tissues. Even though, the entity "Paravaginal defects" is known for decades, its clinical importance is under discussion. In the last decade, a rapidly growing number of novel surgical techniques are being introduced into daily clinical practice to cure female stress urinary incontinence (SUI). Looking at abstracts of major meetings and publications, it seems that alloplastic slings are the solution for everything and these have replaced other well established procedures. The widespread acceptance of tension-free slings worldwide apparently forced colposuspension onto sidelines, even though it is accepted as an effective procedure in the long term cure of SUI by Cochrane collaboration and other groups. The aim of this paper is to analyze the literature on the role of paravaginal defects (at the level of urethra) in the pathophysiology and management of stress urinary incontinence and to formulate an idea on the management according to the underlying pathophysiology in each individual patient with stress urinary incontinence. Paravaginal defect (PVD) is defined as the medial displacement of the vaginal wall and pubocervical fascia (PCF) from its normal line of attachment to the pelvic sidewall at the Arcus tendinus fascia pelvis (ATFP).[1] As early as 1909, George White described attachments and supports of vagina and their role in the development of cystocele. White describes "……the real support of the vagina comes from its attachment to the white line of the pelvic fascia, and especially a thick bundle of fibers attached to the spine of the ischium and radiating out on both the anterior and posterior surfaces of the vagina. … a cystocele is caused by the breaking loose of the vagina from the white line, which can readily occur during labor and especially in an instrumental delivery".[2] The existence of pubocervical fascia as a separate structure (or sheath) is disputed. However, most authors agree that the structural layer that supports the bladder is composed of the anterior vaginal wall and its attachment through the endopelvic fascia to the pelvic wall.[3] Whether it is the detachment of pubocervical fascia or the detachment of anterior vaginal wall (through its attachment to the endopelvic fascia) from the ATFP, it is purely a matter of nomenclature. The process of detachment of the supporting structure from ATFP (or broadly lateral pelvic wall), called paravaginal defect, is undisputed. Paravaginal defects may occur at the level of urethra (when it can cause urethral hypermobility) (Figure 1) or bladder (causing lateral cystocele) or at both levels.

MATERIALS AND METHODS

This is a clinical review of literature on paravaginal defects in stress urinary incontinence. A medline search was performed using the MeSH terms "Paravaginal defect", "stress urinary incontinence", and "Colposuspension". Literature from the year 1990 to 2010 is reviewed. Anatomical, clinical, imaging and surgical evidences for the existence and role of paravaginal defects is summarized and analyzed. Role of colposuspension in correcting paravaginal defects and stress urinary incontinence is discussed.

RESULTS AND DISCUSSION

Anatomical studies on paravaginal defects

The arcus tendineus fasciae pelvis (ATFP), or white line, attaches to the pubic bone 1 cm lateral to midline and 1 cm superior to its inferior margin. The arcus tendinus levator ani (ATLA - tendinous origin of levator ani muscle from the lateral pelvic wall) originates from the pubic bones several centimeters above the origin of the ATFP. As the ATFP fans out from its origin, it lies on the inner surface of the levator ani fascia. According to Haderer et al. the most common 'paravaginal' defect occurs when the ATFP peels away from the levator ani fascia. This may also occur after the ATLA detaches from the pubic bone or, more rarely, from the ischial spine.[4] Because the endopelvic fascia provides support to the anterior vaginal wall and urethra, detachment of its lateral attachments can have a deleterious effect on the support of the urethrovesical junction. It is to be emphasized that the lateral portions of the pubourethral ligaments fuse strongly with the fascia of levator ani at ATLA.[5] Considering this fact, any detachment of ATLA also causes loss of support to the pubourethral ligaments and hence a failure of urethral suspensory mechanism. Contraction of

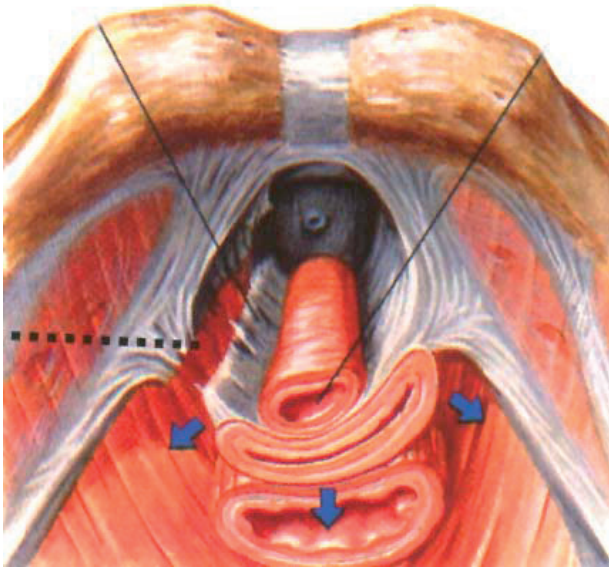

Figure1. – Illustration of paravaginal defect from abdominal route.

the levator ani muscles is a requisite for the normal maintenance of urethral support. Levator ani muscles support the urethra through the endopelvic fascia.[6] If there is a break in the attachment of this endopelvic fascia to the levator ani muscle, then urethral support during increased intra-abdominal pressure is lost and may result in stress urinary incontinence.

Imaging studies on paravaginal defects

The first report on imaging of paravaginal defects, were described by Huddleston et al. in a magnetic resonance imaging (MRI) study of 12 women with cystourethrocele and stress urinary incontinence.[7] They performed MRI scans pre and post operatively on the 12 women. They describe "Mustache" sign formed by white fat in prevesical space against bilateral sag of detached vagina from arcus tendineus fascia pelvis, and "saddlebags" or "paddle" sign caused by displaced fluid-filled bladder wall into bilateral paravaginal defects. The authors were able to demonstrate a correlation between the preoperative MRI scans and the intraoperative findings. Furthermore, there was disappearance of the defects in the postoperative (all patients underwent abdominal paravaginal repair) MRI scans in all but two patients who had surgical failure. The persistence of the defects in the patients who were failures seems to be confirmation of the possible value of this technique to predict procedure failures. De Souza et al. compared paravaginal fascial volume in 11 continent women and 10 women with stress incontinence using MRI with endovaginal coil.[8] They documented the presence of high-signal-intensity tissue and its extent in relation to the urethra (enveloping or extending lateral to urethra). The paravaginal fascia (connective tissue containing venous plexus) was identified as a hyperintense structure surrounding the vaginal wall anteriorly, laterally, and posteriorly with variable thickness on both T2-weighted and short inversion time inversion-recovery MRI images. It was proposed that the high signal intensity of this tissue was a result of its vascularity. They reported that extension of paravaginal fascia either totally or laterally around the urethra was present in all reference subjects but in only 50% (five of 10) of SUI patients. Also the mean urethral paravaginal fascial volume was reduced in patients with SUI (3.5 cm3 ± 2.0) compared with that in reference subjects (5.3 cm3 ± 0.6, P = .017). Although this study does not provide a direct evidence for the presence of paravaginal defect, it gives an indirect clue to the role of paravaginal fascia in maintaining continence. Tunn et al. studied morphology of levator ani, endopelvic fascia and urethra in 54 women with SUI using MRI in supine position.[9] Lateral fascial defects were identified on both sides in 31% of the women (n = 17) and on one side in 15% (n = 8), as suggested by absence of a low-intensity tissue bridge indicating fusion of the lateral vaginal wall and levator ani muscle at the level of the middle urethra. They also reported central defects of the endopelvic fascia in 39% (n = 21), and levator abnormalities such as unilateral loss of substance in 30%, a higher signal intensity in 28%, and altered origin in 19% of the patients. An interesting finding in this study was a significant association between loss of the symphyseal concavity of the anterior vaginal wall and lateral fascial defects (p = 0.001) and levator ani changes (p = 0.016). It is to be noted that some of the morphological changes observed in this study, can also occur because of normal variations in individual anatomy. Even in healthy, nulliparous women, variations in morphology of levator ani and attachment of endopelvic fascia to the pelvic side wall are documented. Tunn et al. remark that it is difficult to ascertain whether the abnormal morphology in a particular patient is a result of pathological injury sustained during labor, or an incomplete development of major anatomical components of continence support system.[10] In a prospective study, El Sayed et al. used dynamic MRI to analyze association of SUI, pelvic organ prolapse (POP) and anal incontinence with specific pelvic floor structural abnormalities.[14] In this well designed study of 59 women, 15 nulliparous women were taken as controls and the remaining 44 women were assigned to four groups depending on their symptoms (POP without SUI, n = 10; SUI without POP, n = 10; SUI with bladder and/or genital prolapse n = 16; and anal incontinence associated with POP, n = 8). This study reported that POP was associated with levator muscle weakness in 16 (47%) of 34 patients, with level I and II fascial defects in seven (21%) of 34 patients, and with both defects in 11 (32%) of 34 patients. SUI was associated with defects of the urethral supporting structures in 25 (86%) of 29 patients but was not associated with bladder neck descent. Of the 26 women with SUI, 12 had isolated paravaginal defects, 2 had isolated central defects and 10 had combined central and paravaginal defects. Ultrasound imaging has also been used for studying pelvic floor structures. Ostrzensky and Osborne were the first to report imaging of paravaginal defects using ultrasound.[11] Early studies used abdominal ultrasound to image PVD, but this method was not found to be reliable because of the confounding effect of bladder filling, uterine position and size. Imaging of paravaginal support structures requires axial or transverse view of pelvis which can be obtained by 3D ultrasound. Tenting of the vagina (presence of ventrolateral vaginal groove) is considered to represent normal paravaginal support and any loss

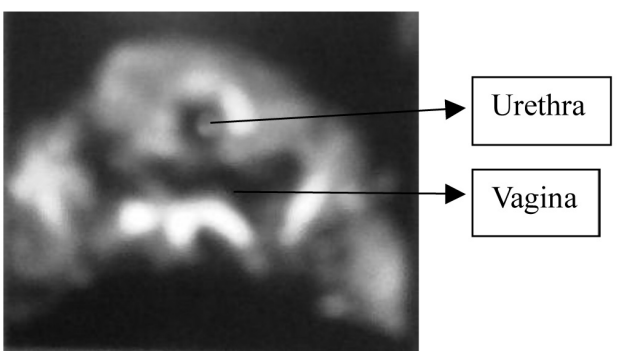

Figure 2. – 3D Perineal ultrasound showing loss of antero-lateral vaginal sulci-indicating bilateral paravaginal defect.

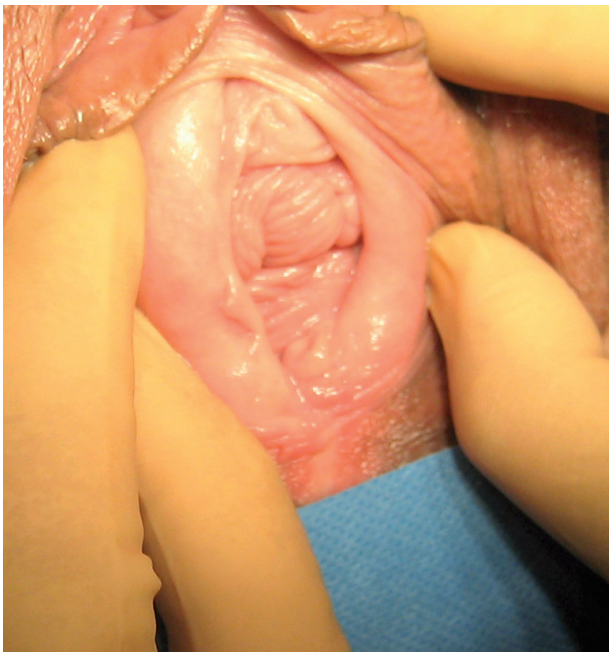

Figure 3. – Clinical demonstration of paravaginal defect.

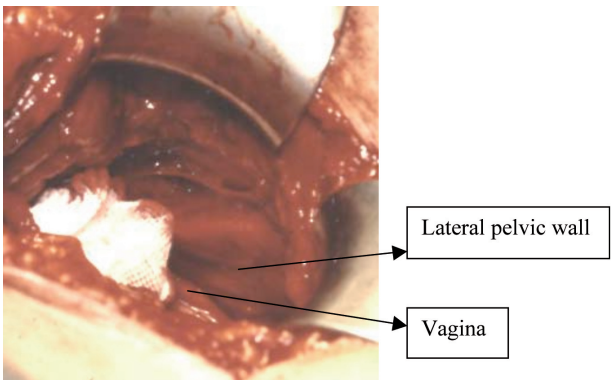

Figure 4. – Intra-operative view showing the gap between vagina and lateral pelvic wall.

of tenting is an indication of PVD (Figure 2). Dietz et al. compared paravaginal supports in 26 nulliparous women before and after 2-5 months of delivery.[12] Tenting was visible in all women antenatally, and in five of 21 women studied postnatally. Interestingly, there was no significant correlation between absence of tenting and bladder neck descent and the authors concluded that in some women delivery-related changes may be due to attenuation rather than disruption of structures. This study was limited by insufficient power to detect differences and lack of standardization and quantification of paravaginal support and defects. Further, the predictive value of bladder neck mobility in stress urinary incontinence is poor as demonstrated by Ultrasound and MRI studies.[13,14] Dietz et al. analyzed correlation between clinical detection and 3D ultrasound detection of paravaginal defects in women with anterior vaginal wall descent and reported that pelvic floor ultrasound in midsagittal, axial or coronal planes does not correlate well with clinical assessment for PVD. This result is not surprising considering the fact that clinical detection (during vaginal examination) of PVD has poor sensitivity[15] when compared with intra-operative detection. Further studies are required to correlate identification of PVD in imaging studies to intra-operative detection (which is the gold standard to detect

Figure 5. – Colposuspension – attachment of lateral vagina to the Cooper's ligament.

PVD) which may help in formulating guidelines for the management of SUI based on underlying morpho-pathological changes.

Clinical and surgical studies

A woman with paravaginal defect may present with complaints of SUI, protrusion of vaginal walls, involuntary leak of urine during intercourse, or colpophony. Colpophony was first described by Kohorn in the year 2000.[16] Colpophony or vaginal wind or vaginal noise is defined as a noise, typically related to the back passage, occurring during physical activity such as vaginal examination or intercourse. Clinically presence of PVD is indicated by the following signs: descent of anterior vaginal wall with intact rugae, absence of anterior vaginal groove on straining and restoration of normal position of a descended anterior vaginal wall upon supporting the anterolateral groove (Figure 3). Further confirmation of the role of a paravaginal defect in cystocele can be confirmed by supporting the lateral vaginal groove which causes restores position of the anterior vaginal wall to its normal position.

There is wide inter-observer and intra-observer variability in clinically detecting the presence of PVD.[17] Also clinical examination is a poor predictor for the actual presence of PVD noted intra-operatively.[18,19] Intra-operative identification of PVDs has been the gold standard for detecting PVDs. From the abdominal route, PVD can be seen as detachment of lateral edge of pubocervical fascia (PCF) (white structure with linear vessels running along the edge) from the ATFP, when bladder is pushed slightly away from the pelvic side wall (Figure 4). Surgical approximation of the detached edge of the PCF to ATFP is termed as Paravaginal repair (PVR). ATFP may not always be visible or accessible and in such cases, PCF can be attached to the obturator fascia. This method can be used to treat anterior vaginal wall prolapse and SUI. PVR for the treatment of SUI has lower success rates compared to Burch colposuspension, where the paraurethral fascia is attached to the iliopectineal (Cooper's) ligament on either side (Figure 5).[20] In a randomized controlled trial of Burch colposuspension versus PVR with follow-up of 1-3 years, Colombo et al. reported that the

subjective and objective cure rates favored the Burch colposuspension over the paravaginal repair: 100% versus 72% (p = 0.02) and 100% versus 61% (p = 0.004), respectively.[21] The higher success rate of Burch colposuspension compared to PVR in treating SUI could be because of provision of stronger point of attachment of the iliopectineal ligament as compared to ATFP.[22] Also, in some women ATFP may not be well formed, or ATFP itself might be detached from lateral pelvic wall.[23,1] It is nevertheless, a fact that Burch colposuspension corrects an existing paravaginal defect at the level of urethra. Presently there is level 1A evidence that Burch colposuspension is an effective procedure for the surgical management of SUI providing long term durability.[24,25] Midline fascial defects, attenuation of endopelvic fascia and intrinsic sphincter deficiency are the other proposed pathophysiologic mechanisms for the development of SUI. At present, all these defects can be visualized by MRI[14] and intrinsic sphincter deficiency can be documented by urodynamic studies.

We have observed an increasing incidence of obstructive voiding in patients having midurethral slings in presence of paravaginal defects (unpublished data). In our audit of 351 cases of complications of mid-urethral slings, 153 patients (44%) had underlying paravaginal defects. PCF is a broad trampoline like structure that, to some extent, supports pelvic floor against intra-abdominal pressure. It is easy to deduct that inserting a midurethral sling in presence of a PVD will lead to intra-abdominal pressure being transmitted entirely on the sling (and not uniformly across the PCF). This can lead to obstructive voiding symptoms. Given this scenario, it is our opinion that it will be illogical to place a midurethral tape in a woman with documented PVD. An important advance in the management of SUI would be to identify the underlying structural abnormality using ultrasound imaging, and functional disturbance using urodynamics, and tailor the treatment accordingly. For example, in a stress incontinent woman with midline fascial defect/attenuation of endopelvic fascia, a midurethral sling would be an ideal choice. On the other hand a stress incontinent woman with PVD would definitely benefit from retropubic colposuspension. Such an approach based on an understanding of pathophysiology would be logical and will definitely help to avoid many of the complications encountered with mid urethral slings.

Colposuspension – An effective way of correcting SUI due to paravaginal defect and urethral hyper mobility

The aim of colposuspension is restoration of urethral function and maintenance of continence by positioning and well supporting the proximal urethra with in the abdominal cavity, thereby raising the pressure transmission ration over 100% in the upper third of the urethra. Downward and backward movement of the bladder neck during stress (urethral hypermobility) is supposed to be an important cause of SUI. It is sufficient to elevate paravaginal tissue just to achieve some support for the bladder neck area; attempts to completely approximate vaginal wall to cooper's ligament area is likely to induce voiding difficulties, de novo urge symptoms and does not achieve long lasting results. In our practice indications for colposuspension include primary and secondary urethral incompetence in the presence of good vaginal mobility and capacity, mainly in presence of a paravaginal defect. In patients with MUCP<20 cm H_2O colposuspension is more likely to fail.

Evidences for efficacy of colposuspension: Since the early description of the Classical Burch,[26,27] many variations in the procedural aspects of colposuspension have been described in literature.[28,29,30] In our experience with more than 250 re-operations after "Burch" in other institutions, more than 90% have been anything but Burch colposuspensions. The many modifications and sub-modifications explain the wide variation in success and complication rates published, because very different procedures have been performed. A recent Cochrane evaluation of open retro-pubic colposuspension included 46 trials involving a total of 4738 women and reported an overall cure rates were 68.9% to 88.0% for open retropubic colposuspension with a few studies demonstrating lower failure rates than with conservative treatment, needle suspension, Marshall Marchetti Krantz procedure and anterior colporraphy. One important finding in this meta-analysis was that the benefit of colposuspension was maintained over time (RR of failure 0.51; 95% CI 0.34 to 0.76 before the first year, RR 0.43; 95% CI 0.32 to 0.57 at one to five years, RR 0.49; 95% CI 0.32 to 0.75 in periods beyond 5 years).[31] Even though Bombieri and Freeman stated that the position of the bladder neck and the amount of elevation do not influence the continence outcome, majority of authors using perineal or introital ultrasound found significant differences in bladder neck position, mobility at rest and during valsalva maneuver, funneling and urethral angles correlating with success or failure.[32,33,34] Using introital ultrasound it was demonstrated that over-elevation resulted in signs of over active bladder.[34]

Personal experience of the senior author: The senior author (EP) started with colposuspension after having seen the technique impressively demonstrated by Stuart Stanton, Sir Richard Turner-Warwick, Emil Tanagho and others in the late 70s and early 80s. He has performed more than 4600 colposuspensions in the last 30 years. Even though it was impossible to follow-up all these patients over such a long period of time, over the years, major unselected groups have been followed, looking for short term and long-term complications as well as subjective and objective success rates and satisfaction of the patients. In spite of the introduction of mid-urethral slings and injectables, the number of colposuspensions remains stable for many years in a specialized referral center in which 60% of colposuspensions are done for recurrent incontinence after mid-urethral slings. A randomized control trial of midurethral slings versus colposuspension in patients with SUI and paravaginal defects was planned. Within a short time it was observed that patients in the midurethral sling group had increasing incidence of lower urinary tract obstruction and other complications. Further continuation of this study was deemed to be unethical and the trial was terminated prematurely.

The available evidence indicates that open colposuspension is one of the most effective treatment modality for SUI especially in the long term. In competition with mid-urethral slings, colposuspension will remain the first choice for all laparotomies necessitated by other pathologies, especially in cases with paravaginal defects and in women with overactive bladders caused by anatomic defects.

CONCLUSION

Paravaginal defects are real entities and play an important role in the pathophysiology of stress urinary incontinence. Current clinical practice ignores the anatomical causes underlying the causation of stress urinary incontinence and instead, the use of a single procedure (in most cases mid-urethral slings) for all women with stress incontinence is becoming a trend. Studies are needed to standardize the ultrasound detection, establish its efficacy and cost-effectiveness before ultrasound can be routinely used for pre-op diagnosis. Evaluation of a woman with stress urinary incontinence should include searching for possible underlying causes (anatomical and functional) and management should be

based accordingly. In the presence of paravaginal defect, a colposuspension will be a better management option. Urethral hyper mobility in the absence of a paravaginal defect may be treated with mid-urethral slings.

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Book review

As announced (Pelviperineology 2011; 30:5) these are the second and third of a series of articles highlighting the different sections of the book "Pelvic Floor Disorders, Imaging and a Multidisciplinary Approach to Management" edited by G.A. Santoro, P. Wieczorek, C. Bartram, Springer Ed, 2010.

Pelvic floor imaging

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The *second section* of the book "Pelvic floor disorders - Imaging and Multidisciplinary Approach to Management" is entitled "Pelvic Floor Imaging" and consists of six chapters describing the different imaging techniques of normal female pelvic floor.

In the first chapter "*Endovaginal Ultrasonography: Methodology and Normal Pelvic Floor Anatomy*" Santoro et al. describe the role of high-resolution three-dimensional endovaginal ultrasonography (3D-EVUS) in the assessment of pelvic floor structures including muscles and the levator ani complex, the lower urinary tract, and the anorectal region. The methodology of this examination is reported in details including patient preparation, and position, technique of examination and manner of performing measurements. Many types of ultrasound transducers have been developed for pelvic floor assessment (mechanical radial probes with 360° field of view, electronic biplanar probes with linear and transverse curved arrays, and endfire probes).

Endovaginal US performed with 360° rotational transducer gives an overall view of pelvic structures, allows their precise assessment and to perform reliable measurements. In the axial plane four standard levels for the evaluation are defined (Figure 1): Level 1: corresponding to the bladder base and the inferior one-third of the rectum; Level 2: corresponding to the bladder neck, the intramural part of the urethra, and the anorectal junction. At this level the levator ani muscle subdivisions (puboperinealis, puboanalis, pubovaginalis, puborectalis, iliococcygeus) can be identified; Level 3: corresponding to the inferior pubic rami and symphysis pubis, the midurethra, and the upper one-third of the anal canal; Level 4: corresponding to the superficial perineal muscles, the perineal body, the distal urethra, and the middle and inferior one-third of the anal canal. In the axial plane can be measured levator hiatus dimensions; paravaginal spaces area; pubovisceral muscle thickness; urogenital hiatus diameters and superficial perineal muscles lengths.

Endovaginal US performed with an electronic biplane 180° rotational transducer provides an accurate evaluation of urethral morphology (rhabdosphincter and urethral smooth muscle) and vascularity and gives images of the posterior compartment (internal and external anal sphincters, anorectal junction, perineal body, rectovaginal septum) in the mid-sagittal plane. Using this transducer, it is also possible a dynamic assessment during contraction or Valsalva maneuvers.

The second chapter "*Translabial Ultrasonography: Methodology and Normal Pelvic Floor Anatomy*" by Peter Dietz describes technical requirements, equipment, and the methodology of transperineal ultrasound (2D/3D/4D TPUS) in the diagnostics of pelvic floor and lower urinary tract disorders. A convex transducer (frequency 3.5- 8 MHz) is placed on the perineum providing midsagittal view of the pelvic organs (symphysis pubis, bladder, urethra, vagina, anorectum). 3D data is obtained with the use of volumetric probe that combines an electronic curved array of 3-8 MHz with mechanical sector technology, allowing fast motorized sweeps through a field of vision. 4D-US implies the real-time acquisition of volume US data, which can be represented in multiplanar reconstructions or rendered volumes. 4D-TPUS performed during Valsalva maneuver allows to visualize downwards displacement of the pelvic organs, to reveal pelvic organ prolapse, and to demonstrate distensibility of the levator hiatus. Measurements of diameters and areas of the levator hiatus in this plane appear highly repeatable and correlate well with those obtained on MRI.

For the identification of levator trauma (detachment of the muscle from the inferior pubic rami) rendered volumes are used. However, the most reproducible method for identifying abnormalities of the puborectalis muscle at present seems to be tomographic or multislice imaging obtained during pelvic floor maximal contraction.

The third chapter entitled "*Endoanal and Endorectal Ultrasonography: Methodology and Normal Pelvic Floor Anatomy*" written by G.A. Santoro and G. Di Falco reports in details the technique of 3D-EAUS and 3D-ERUS performed with 360° rotational transducer. In the axial plane, the anal canal is divided in three levels: Level 1 (upper level): corresponding to the puborectalis sling, the deep part of the external anal sphincter (EAS) and the complete ring of the internal anal sphincter (IAS); Level 2 (middle level): at this level the superficial transverse perinei muscles and the two complete rings of the EAS and the IAS are identified; Level 3 (lower level): corresponding to the subcutaneous part of the EAS. The muscles of the lower and the upper part of the anal canal are different. The deep part of the EAS cannot be differentiated from puborectalis muscle posteriorly due to similar echogenicity. Moreover, the differences between genders exist in the anterior part of the EAS: it is symmetrical at all levels in males; while in females, it is shorter anteriorly, and there is no evidence of an anterior ring high in the anal canal. EAUS provides excellent measurements of sphincter dimensions, however its most relevant utility is the detection of localized sphincter defects.

Endorectal US is performed with a water-filled latex balloon covering the transducer in order to achieve good acoustic contact with the rectal wall and to have its adequate distension. Five layers are visualized: the first hyperechoic layer corresponds to the interface of the balloon with the rectal mucosal surface; the second hypoechoic layer corresponds to the mucosa and muscularis mucosae; the third hyperechoic layer corresponds to the submucosa; the fourth hypoechoic layer corresponds to the muscularis propria; the fifth hyperechoic layer corresponds to the serosa or to the

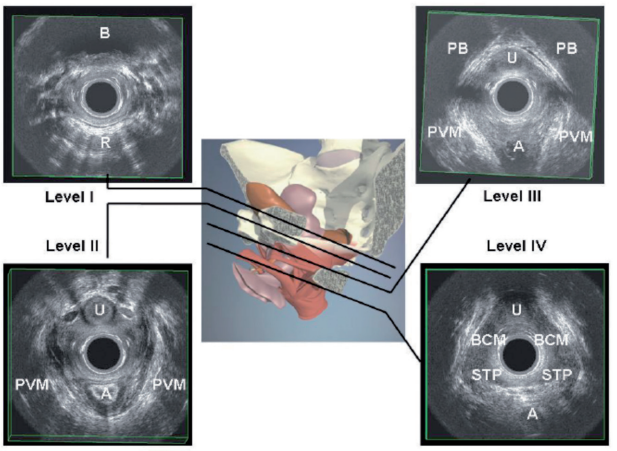

Figure 1. – Four standard levels of assessment of the female pelvic floor with 3D-EVUS. With the use of 360° rotational transducer. *A*-anal canal; *B*-bladder; *BCM*-bulbocavernosus muscle; *PB*-pubic bone; *PVM*-pubovisceral muscle; *R*-rectum; *STP*-superficial transverse perinei muscle; *U*-urethra.

interface with the mesorectum. 3D-ERUS is highly important in the staging of rectal cancer.

The fourth chapter "*Technical Innovations in Pelvic Floor Ultrasonography*" by Santoro et al. presents the most recent developments in the ultrasonographic imaging of the pelvic floor. Volume render mode (VRM) is a technique for analysis of the information inside a 3D volume by digitally enhancing individual voxels. Opacity, luminance, thickness and filter could be used as post-processing functions in order to provide better visualization of pelvic floor structures. Maximum Intensity Projection (MIP) improves the visualization of the spatial distribution and localization of urethral vessels, reducing the intensity of the gray scale voxels. Sculpting is a post-processing tool that allows to mark and to remove volume voxels, during off-line assessment. It can be performed in two ways: drawing an outline and removing everything within that outline or drawing an outline and removing everything outside this outline. It might facilitate the assessment of pelvic floor structures allowing comparison of the morphology in different disorders. Fusion imaging (simultaneous capturing of scans obtained by two different examinations - US/MRI) provides the information gathered by both modalities fused, compensating the deficiencies of one method and retaining the advantages of another one. PixelFlux is a dedicated software that allows an automated calculation of blood flow velocity, area of the vessels and perfusion intensity in arbitrary regions of interest (ROIs) of different organs. It can be used for the evaluation of vascular parameters in different part of the urethra in continent as well as incontinent patients. Motion tracking is a modality for the assessment of biomechanical properties of tissues and organs and it appears to be a feasible and valuable tool for the assessment of bladder neck mobility and the evaluation of the anorectal angle displacement during TPUS and Valsalva manoeuvre. Motion tracking provides quantitative assessment (displacement, velocity, acceleration, trajectory, motility, strain) of pelvic floor muscles, which allows to distinguish continent from incontinent females.

The fifth chapter entitled "*Magnetic Resonance Imaging: Methodology and Normal Pelvic Floor Anatomy*" by Jaap Stoker describes the MRI anatomy of the female pelvic floor obtained with either an endoluminal coil or an external phased array coil. On T2-weighted turbo spin-echo sequences, muscles are relative hypointense appearing grey on the images, ligaments and fascia are hypointense (black), and fat and smooth muscles are hyperintense (white). The anatomy of the urethra and its supportive structure including endopelvic fascia, periurethral ligaments and compressor urethrae is precisely visualized by MRI such as the complex anatomy of the perineal body with its muscular and fascial attaching structures (longitudinal muscle, EAS, perineal membrane, superficial transverse perinei muscle, and bulbospongiosus).

The IAS is easily recognized on MRI as a circular hyperintense structure. The intersphincteric space is the fat-containing space between the IAS and the outer striated muscle layer. The longitudinal muscle is the continuation of the smooth muscle longitudinal layer of the rectum and courses through the intersphincteric space. The puborectalis muscle forms the upper outer striated layer of the anal sphincter and appears as a sling that opens anteriorly. Anal and rectal support as well as perineal membrane, pelvic diaphragm and levator ani morphology are also precisely described by MRI.

In the last chapter of Section II "Technical Innovations in Magnetic Resonance Imaging of the Pelvic Floor" Dominik Weishaupt and Caecilia S. Reiner present the role of dynamic MRI in detection and characterization of functional pelvic floor abnormalities. The authors describe their own imaging protocol, which starts with the sequences allowing the assessment of anatomy and continues with fast sequences enabling good visualization at squeezing, straining, and during defecation.

Development of fast multislice sequences, has resulted in the possibility of performing dynamic MRI of the pelvic floor. Due to the fact that the posterior compartment is traditionally in the focus of interest, it is often called MR defecography. Dynamic pelvic MRI may be performed in an open configuration MR system in the sitting position, or in a closed-configuration MR system in the supine position. Although, the sitting position is the physiological position during defecation, it has been reported that MR defecography in the supine position and in the seated position are

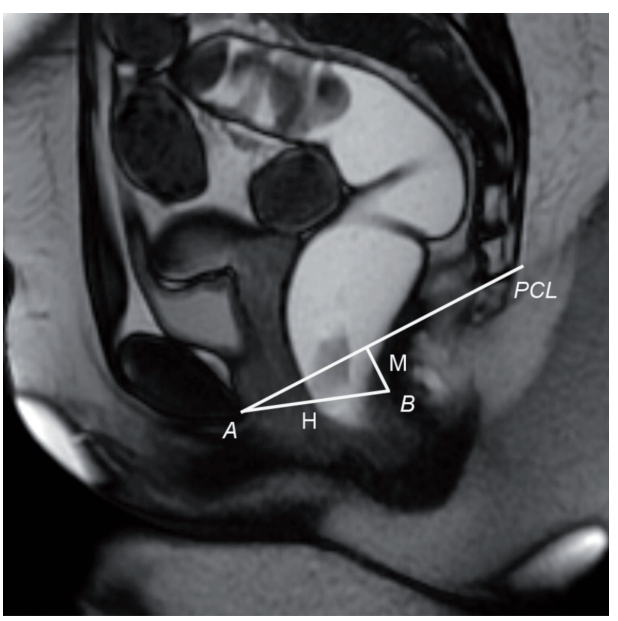

Figure 2. – Midsagittal balanced SSFP T2-weighted image, during straining with landmarks used in the HMO system. *A*-the inferior aspect of the symphysis pubis, *B*-the posterior wall of the rectum at the level of the ano-rectal junction. The H line (*H*) represents the anteroposterior hiatal width and extends from *A* to *B*. The M line (*M*) represents hiatal descent and extends perpendicularly from the pubococcygeal line (*PCL*) to the posterior end of the H line.

equally effective in identifying most of the clinically relevant abnormalities of the pelvic floor.

Image analysis is performed for three compartments by the assessment of morphological changes at different pelvic floor positions. The most commonly used reference line for image evaluation is the pubococcygeal line (PCL), defined on midsagittal images as the line extending from the inferior border of the symphysis pubis to the last or second-last coccygeal joint. The length of the bladder base, the cervix, or vaginal vault, and the ano-rectal junction is measured at a 90° angle to the PCL in the different pelvic floor positions. To determine pathologic pelvic floor descent, the measurements are made on the images showing maximal organ descent.

Another system for grading pelvic floor abnormalities is the "HMO system". This system distinguishes pelvic organ prolapse and pelvic floor relaxation. In pelvic floor relaxation, the pelvic floor becomes weakened, leading to hiatal descent and widening. The degree of pelvic floor relaxation is measured with two reference lines: the H line, representing hiatal widening and extends from the inferior aspect of the symphysis pubis to the posterior wall of the rectum at the level of the anorectal junction, and the M line, representing hiatal descent and extends perpendiculary from the PCL to the posterior end of the H line (Fig. 2). Abnormal pelvic floor relaxation is present, when the H line exceeds 6 cm, and when the M line exceeds 2 cm.

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Pelvic floor damage due to childbirth

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The *third section* of the book "Pelvic floor disorders - Imaging and Multidisciplinary Approach to Management" is entitled "Pelvic Floor Damage Due to Childbirth" and consists of three chapters describing mechanisms of pelvic floor trauma during vaginal delivery as well as ways of prevention.

In the first chapter "*Mechanisms of Pelvic Floor Trauma during Vaginal Delivery*" Minini et al. describe physical consequences of vaginal childbirth, which may vary from mild subclinical conditions to significant severe pathologies appearing immediately or in the long-term. Among various events during woman's lifetime affecting muscles of the pelvic floor and other supporting structures of the pelvic organs, pregnancy, childbirth, menopause and ageing have got the most pronounced influence on damage of pelvic organs. The long-term gynecological sequelae of pelvic floor weakness are pelvic organ prolapse, stress urinary incontinence, dyspareunia, fecal incontinence, and perineal pain.

Pelvic organ prolapse is a common condition affecting up to 15% of the female population and is responsible for about 20% of women on waiting lists for major gynecological surgery. The main risk factors associated with prolapse are parity and increasing age, while smoking and obesity are secondary factors. Parity shows the strongest correlation to prolapse as women who delivered four or more babies vaginally are found to have 11 times risk of significant pelvic organ prolapse compared to nulliparous women.

Rates of urinary incontinence range from 20% to 30% in the general population. Risk factors for the development of urinary incontinence are ageing and childbirth. Stress incontinence is more common in parous women compared with nulliparous women. Urinary symptoms are found antenatally in up to 60% of pregnant women. Postnatally, the reported prevalence of urinary incontinence varies from 6% up to 34%, and its increase is observed during pregnancy, immediately after birth, and with age 30 years or greater at the time of the second vaginal delivery.

Physiologically the uterus and vaginal apex are supported by a muscular component, requiring an intact nerve supply, and by a fascial component. Damage of any of these structures can lead to prolapse of the pelvic organs. Three factors are implicated in the etiology of prolapse and stress urinary incontinence: myogenic damage, neuromuscular injury, and damage to the endopelvic fascia. Damage of the nerve supply of the pelvic floor caused by childbirth may determine progressive denervation of the musculature. Subsequent reinnervation of the pelvic floor leads to an altered function. Trauma may affect the pudendal nerve and its branches, the anal sphincter, the levator ani complex, or the pelvic fascial structures.

Many women undergo significant trauma to pelvic floor structures as a consequence of attempts at vaginal delivery. Many risk factors for perineal damage at delivery have been identified, among which the most important are multiparity, forceps application during operative delivery, sacral rotation of the occiput, prolonged second stage of labor, epidural analgesia, third-degree tears, and fetal macrosomia. Some forms of trauma may also occur as a result of rapid labor. Regarding prolapse, pregnancy and childbirth are well documented as major risk factors.

The identification of women at high risk for delivery-related pelvic floor trauma should be a priority for everyday good clinical practice. Obstetric perineal damage cannot be avoided, but it certainly can be limited, by means of preventive strategies and therapeutic improvement: that is perineal risk factors, improving assistance, and timely rehabilitation.

The second chapter entitled "*Posterior compartment disorders and management of acute anal sphincter*" written by Abdul H. Sultan and Ranee Thakar focuses on obstetric trauma to posterior compartment. The posterior compartment consists of all the structures that include the posterior vaginal wall and structures posterior to it. During the process of vaginal delivery, fascia, muscles, and nerves may be stretched or disrupted. However, while these changes could

be attributed to the physiological process of childbirth, in some women they can lead to pathological events with long-term consequences. Obstetric trauma to the posterior compartment has been implicated in the development of rectoceles, perineoceles, and fecal incontinence. However, as many women develop these conditions many years after childbirth, either a direct link to its causation is not considered or it is attributed to the effects of ageing or the menopause.

A rectocele may be the result of overdistensibility of an intact rectovaginal septum, disruption of the perineal membrane and detachment from the perineal body. It remains to be established whether modification of obstetric practice, and in particular meticulous restoration of the perineal and vaginal anatomy when repairing episiotomies and genital lacerations, may minimize the development of rectoceles.

Obstetric anal sphincter injuries (OASIS) are reported to occur in 1.7% (2.9% in primiparae) of women in center where mediolateral episiotomies are practices, compared to 12% (19% in primiparae) in centers practicing midline episiotomy. In order to standardize the classification of perineal trauma, Sultan proposed the following classification that has been adopted by the Royal College of Obstetricians and Gynaecologists and also recommended by the International Consultation on Incontinence.

Obstetric trauma to the posterior compartment can result in pelvic floor denervation, disruption of the fascial supports, and injury to the anal sphincter. Injuries to the anal sphincter can give rise to anal incontinence, and therefore accurate detection and diagnosis of the full extent of the injury is mandatory at delivery. Repair of OASIS should only be conducted by a doctor who has been formally trained (or under supervision) in primary anal sphincter repair and the aim should be to restore the normal high-pressure zone of the anal canal represented by the anal length. Failure to identify and repair the internal sphincter at the time of the acute injury will increase the risk of fecal incontinence and jeopardize the ability to repair at a later date. Attention needs to be focused on training of doctors and midwives internationally in the identification and repair of OASIS.

In the third chapter "*Prevention of perineal trauma*" authors Abdul H. Sultan and Ranee Thakar describe how obstetrical perineal trauma might be minimized. Proven strategies include the practice of perineal massage in the antenatal period, delayed pushing in the second stage of labor with an epidural in situ, restrictive use of episiotomy, preference of a mediolateral over a midline episiotomy, and the use of a vacuum extractor instead of forceps for instrumental delivery.

Perineal trauma may occur spontaneously during vaginal birth or when surgical incision (episiotomy) is intentionally made to enlarge the diameter of the vaginal outlet. Approximately 85% of women sustain some form of perineal trauma during vaginal delivery. The prevalence of perineal trauma is dependent on variations in obstetric practice, including rates and types of episiotomy.

Perineal massage during the last month of pregnancy may increase the flexibility of the perineal muscles, leading

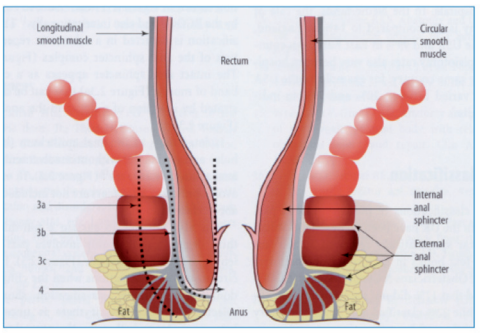

Fig. 13.2 Diagrammatic representation of the anal sphincters demonstrating the classification of major degrees of perineal tears (*3a–c* and *4*). Reproduced from [9], with permission

to a reduction in muscular resistance. This would allow the perineum to stretch at delivery without tearing, thereby avoiding the need for episiotomy. Water birth shows no significant difference in second-, third-, or fourth-degree tears, instrumental delivery, or sectarian section. Whether the upright or lying down position during labor and birth can be beneficial is still controversial. The method of pushing during second stage of labor plays an important role in prevention of perineal trauma - passive descent increases a woman's chance of having a spontaneous vaginal birth, decreases the risk of having instrumental delivery, and shortens the pushing time. Systematic vaginal application of obstetric gel shows significant reduction in second-stage duration and a significant increase in perineal integrity, without any adverse effects. Perineal warm packs potentially reduce risk of perineal trauma and increase comfort during late second stage of labor due to dilatation of blood vessels, increasing blood flow, and reducing the level of nociceptive stimulation, and collagen extensibility. Second-stage perineal massage does not decrease perineal trauma, postpartum pain, or urinary or anal incontinence.

Among proposed techniques reducing perineal trauma antenatal pelvic floor muscle training, epidural analgesia, head flexion, and active restrain of delivery of the head are described.

Obstetric perineal trauma can have a devastating effect on a woman's social life, with associated psychological sequelae. It is important to implement interventions that may be used to minimize perineal trauma. While cesarian section may eradicate perineal trauma, it is associated with an increased risk of mortality and morbidity and therefore should only be offered selectively.

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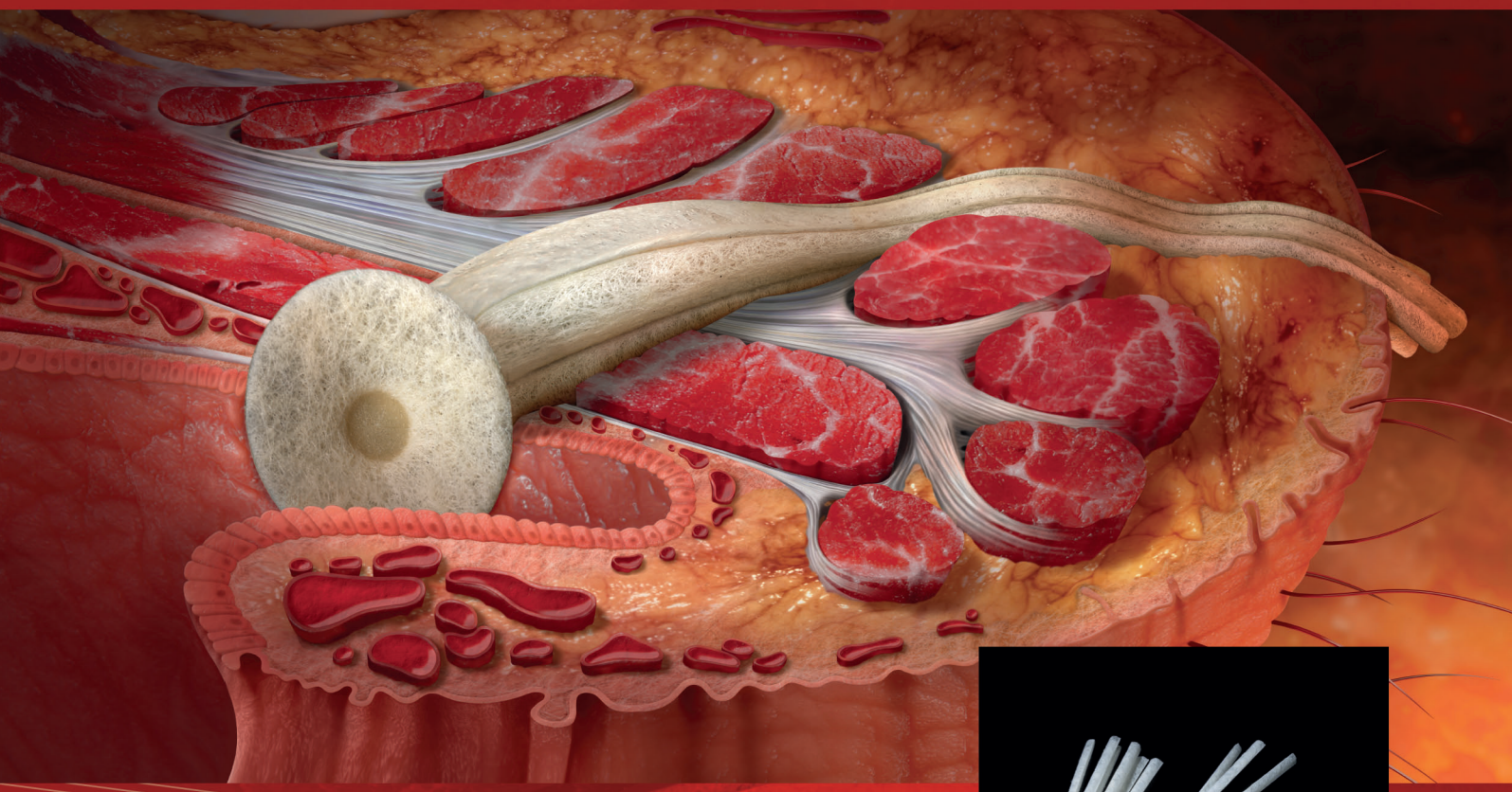

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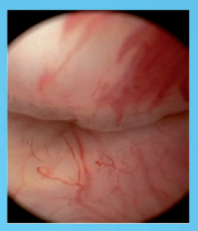

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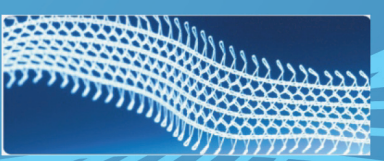

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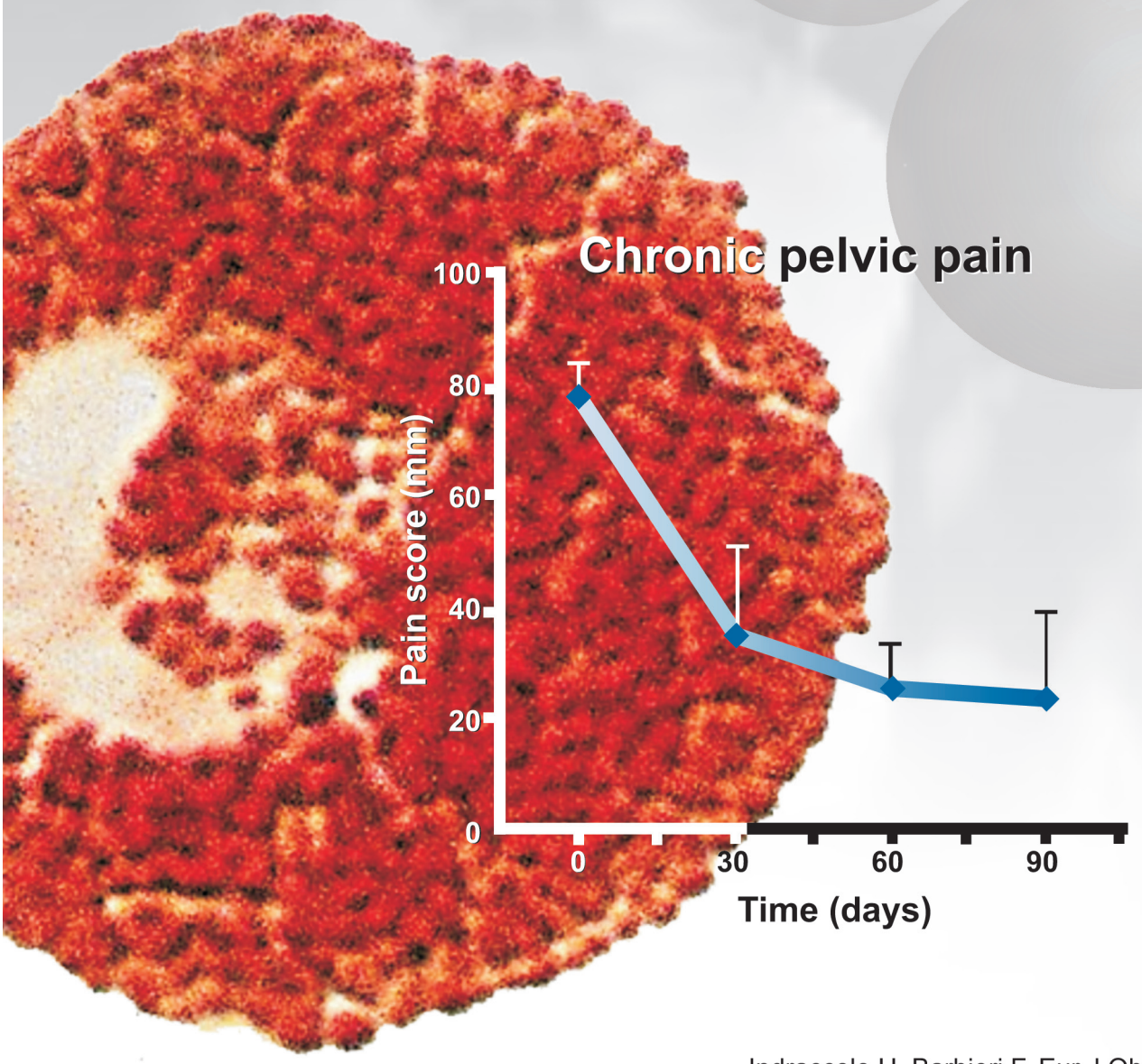

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