Azienda
Unità Sanitaria Locale
Latina

REGIONE
LAZIO

L'INCONTINENZA URINARIA NELL'ANZIANO

UOC UROLOGIA
LATINA 29/09/2012

INCONTINENZA URINARIA

INVOLONTARIA O ANORMALE

PERDITA URINARIA

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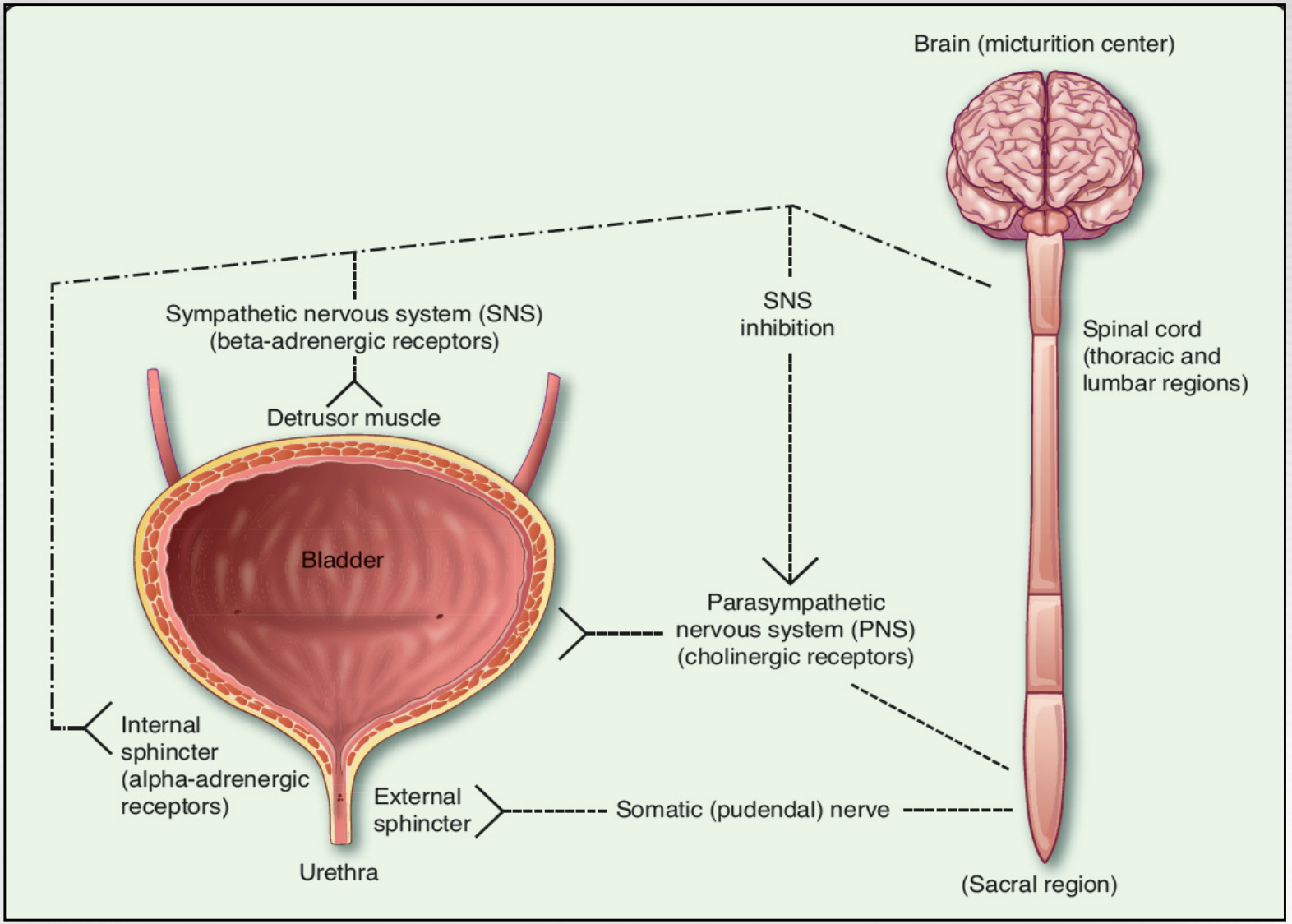

Brain (micturition center)
Sympathetic nervous system (SNS)
(beta-adrenergic receptors)
SNS
inhibition
Spinal cord
(thoracic and
lumbar regions)
Detrusor muscle
Bladder
Parasympathetic
nervous system (PNS)
(cholinergic receptors)
Internal
sphincter
(alpha-adrenergic
receptors)
External
sphincter
Somatic (pudendal) nerve
Urethra
(Sacral region)

Alterazione anatomo-funzionale di uno o più componenti che concorrono alla continenza urinaria

Risultato: la continenza

- Il risultato di questa attività riflessa è l'incremento del tono sfinterico a garanzia della continenza urinaria.
- Ciò accade sino a quando l'input afferente è modesto (vescica non distesa)

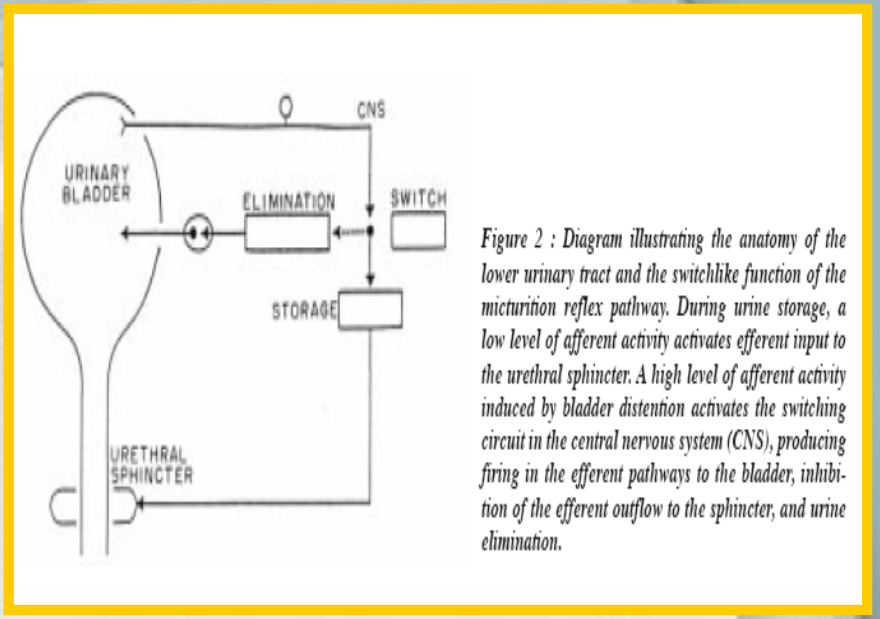
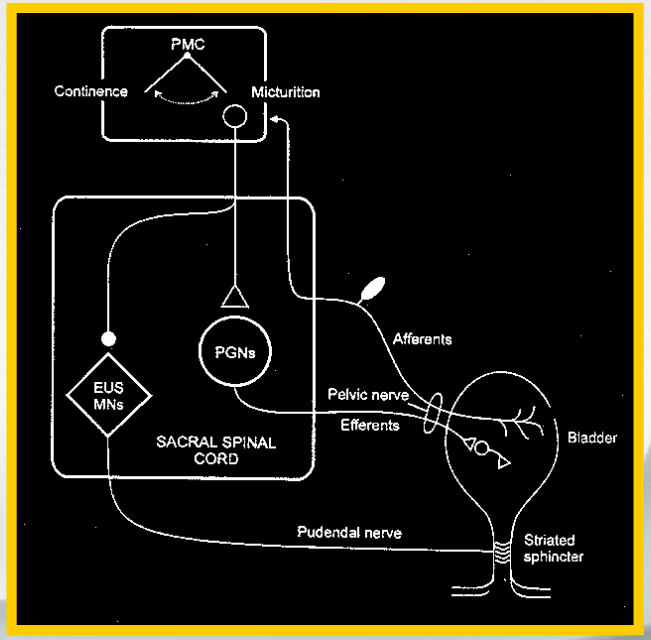


Figure 2 : Diagram illustrating the anatomy of the lower urinary tract and the switchlike function of the micturition reflex pathway. During urine storage, a low level of afferent activity activates efferent input to the urethral sphincter. A high level of afferent activity induced by bladder distention activates the switching circuit in the central nervous system (CNS), producing firing in the efferent pathways to the bladder, inhibition of the efferent outflow to the sphincter, and urine elimination.



COSCIENTIZZAZIONE DELLO STIMOLO MINZIONALE

- Incremento dell'attività afferente conseguente all'aumentare dello stiramento dei tensocettori vescicali
- L'informazione raggiunge i centri sovraspinali pontini e corticali del lobo frontale
- La coscientizzazione si verifica a livello della sostanza grigia periacqueduttale (inizia il desiderio di mingere)

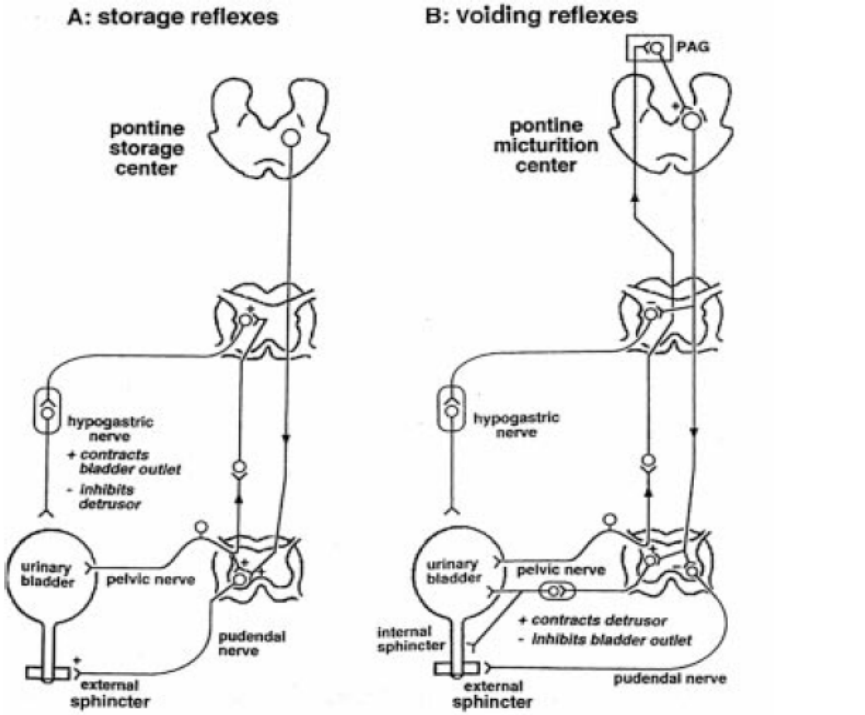


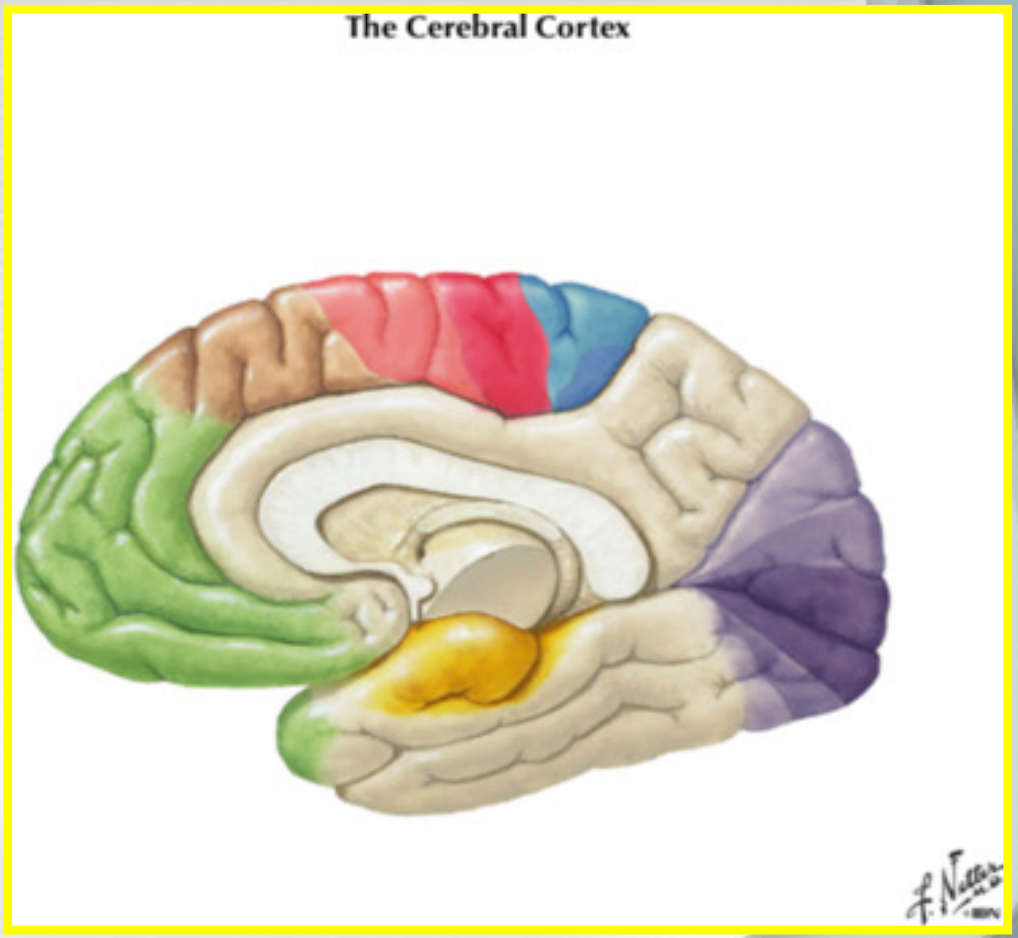
Figure 3 : Diagram showing neural circuits controlling continence and micturition. (A) Urine storage reflexes. During the storage of urine, distention of the bladder produces low level vesical afferent firing, which in turn stimulates (1) the sympathetic outflow to the bladder outlet (base and urethra) and (2) pudendal outflow to the external urethral sphincter. These responses occur by spinal reflex pathways and represent «guarding reflexes», which promote continence. Sympathetic firing also inhibits detrusor muscle and modulates transmission in bladder ganglia. A region in the rostral pons (the pontine storage center or «L» region) increases external urethral sphincter activity. (B) Voinding reflexes. During elimination of urine, intense bladder afferent firing activates spinobulbospinal reflex pathways passing through the pontine micturition center, which stimulate the parasympathetic outflow to the bladder and internal sphincter smooth muscle and inhibit the sympathetic and pudendal outflow to the urethral outlet. Ascending afferent input from the spinal cord may pass through relay neurons in the periaqueductal gray (PAG) before reaching the pontine micturition center.

Sistema limbico e corteccia parietale e frontale

Regolano la funzione vesicosfinteriale in rapporto all'emotività e alle contingenze comportamentali (suscitare o interrompere volontariamente la minzione)

LA CORTECCIA CEREBRALE: L'INIBIZIONE E L'INDUZIONE

- **Quando lo stato di riempimento ha determinato la coscientizzazione, la corteccia frontale ha il compito di INIBIRE lo svuotamento sino al luogo e momento opportuno (atto volontario/induzione)**



INCONTINENZA URINARIA

10 milioni hanno I.U.

25 milioni episodio di I.U.

A ≤ 80 anni prevalentemente le donne

Dopo 80 anni uomini e donne in egual misura

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INCONTINENZA URINARIA

Paziente anziano e' importante ricercare la causa perché c'è la concezione che la I.U. sia normale in età avanzata

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DA URGENZA

Associata ad urgenza minzionale

DA SFORZO

Associata a specifica attività

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MISTA

Include parte da urgenza e parte da sforzo

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DA RIGURGITO

- Vescica ipotonica
- Ostruzione vescicouretrale
- Altre forme di ritenzione urinaria

  LUTS + piccole perdite urinarie
  causa principale - BPH (IPB)

VESCICA IPERATTIVA

INCONTINENZA URINARIA

Serie di sintomi: Urgenza

Con o senza I.U.

Pollachiuria

Nicturia

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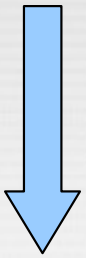
INCONTINENZA URINARIA

Comorbidità:



Ipertensione

Depressione

M. di Parkinson

Idrocefalo normoteso

Non pienamente conosciute

INCONTINENZA URINARIA

Idrocefalo normoteso

- Disturbi della deambulazione
- Deterioramento mentale
- Incontinenza urinaria
- Dilatazione ventricolare
- Normale pressione del fluido cerebrospinale

Eufunzione detrusoriale e sfinterica

-Sovrapontino inibitorio

-pontino- coordinazione

-Sacrale- facilitatorio

Cause iperattività detrusoriale

Iperreflessia detrusoriale

- lesioni neurologiche sovraspinali e spinali soprasacrali

Instabilità detrusoriale

- non neurologiche

INCONTINENZA URINARIA

URODINAMICA

- Flusso urinario
- Residuo minzionale
- Cistometria di riempimento
- Pressione vescicale
- Pressione uretrale

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INCONTINENZA URINARIA

FATTORI MULTIPLI

Cambiamenti

- tratto genitourinario

- tratto non genitourinario

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INCONTINENZA URINARIA

FATTORI MULTIPLI

Cambiamenti in funzione eta':

- iperattività detrusoriale
- contrattilità detrusoriale
- riduzione pressione chiusura uretrale
- atrofia area uretrale
- IPB

INCONTINENZA URINARIA

Disturbi funzione vescicale

- disordini degenerativi CNS
- demenza multiinfartuale
- idrocefalo

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INCONTINENZA URINARIA

CAUSE FISIOPATOLOGICHE

Lesioni centri minzionali piu' alti

- corda spinale sacrale
- aree neurologiche

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INCONTINENZA URINARIA

CNS

- controlla minzione(svuotamento) e riempimento

Controllo sopraspinale vescicale

Tre aree corteccia frontale

Ipotalamo

Tronco cerebrale

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INCONTINENZA URINARIA

- **POLLACHIURIA**
- **NICTURIA**

Perdita controllo volontario sovraspinale della minzione (non inibizione)

Iperattività e compromissione della minzione

INCONTINENZA URINARIA

Perdita controllo volontario della minzione

(non inibizione)

- iperattività detrusoriale
- insufficienza sensibilità vescicale

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IDROCEFALO NORMOTESO

- Incontinenza da lobo frontale (non ricordano quando e dove urinano)
- Valutazione urodinamica:
- iperattività vescicale (non inibizione)

IDROCEFALO NORMOTESO

Dopo CSF

- riduzione iperattività
- riduzione confusione mentale
- riduzione deterioramento mentale

INCONTINENZA URINARIA

I tre sintomi principali dell'idrocefalo normoteso, incluso l'incontinenza, potrebbero migliorare con lo shunt ventricolo-peritoneale

(Hakim and Adams)

Type of Incontinence	Common Causes	Common Symptoms	Treatment Options
Urge urinary incontinence (UUI)			

Idiopathic detrusor overactivity	Urinary tract infections	Urgency and frequency, day or night	• Anticholinergic drugs
			  • Oxybutynin
			  • Tolterodine
			• Surgery
			  • Intravesical Botox
			  • Sacral nerve stimulation

Neurogenic detrusor overactivity	• Neurological disorders
	  • Parkinson's disease
	  • Alzheimer's disease
	• Cerebrovascular accidents (e.g., stroke)
	  • Trauma
	  • Medications		

Stress urinary incontinence (SUI)			
Stress incontinence (outlet incompetence)	• Pelvic surgery • Parity (childbirth) • Constipation	Small volumes of urine loss with coughing or sneezing	• Weight loss • Kegel (pelvic floor) exercises with or without biofeedback • Sling procedures • Transurethral collagen denaturation (Renessa procedure) • Transurethral bulking agents
Mixed urinary incontinence (MUI)			
Mixed UUI and SUI	• Pelvic surgery • Parity (childbirth) • Constipation	Symptoms may include urge and stress features	Treatment depends on predominant symptoms

Classification	Medication	Activity
Alpha-adrenergic agonists	Nasal decongestants	Urinary retention in men with overflow incontinence related to BPH
Alpha-adrenergic antagonists	Prazosin, terazosin, doxazosin, silodosin, alfuzosin	Urethral relaxation; may cause or exacerbate stress incontinence in women
Anticholinergic drugs	Antihistamines, tricyclic antidepressants, some antipsychotics	Anticholinergic actions; urinary retention in overflow incontinence or impaction
Antineoplastic drugs	Vincristine	Urinary retention
Calcium-channel blockers	Dihydropyridines (e.g., nifedipine)	Urinary retention; nocturnal diuresis resulting from fluid retention
Diuretics	Furosemide, bumetanide	Polyuria; frequency; urgency
Narcotic analgesics	Opiates	Urinary retention; sedation
Sedatives/hypnotics	Long-acting benzodiazepines (e.g., diazepam, flurazepam)	Sedation; delirium; immobility

Drug	Recommended Adult Dose	Pharmacokinetic Properties
Darifenacin (Enablex ER, Novartis)	7.5–15 mg q.d.; swallowed whole with liquid; should not be chewed, divided, or crushed	• Bioavailability, 17%; peak levels, 7 hours post-dose; protein binding, 98% (alpha$_1$-acid-glycoprotein) • Extensively metabolized by CYP2D6/3A4*; half-life, 13–19 hours; elimination: 60% in urine, 40% in feces • Dose adjustment for moderate hepatic impairment; poor CYP2D6 metabolizers may have higher drug levels
Fesoterodine (Toviaz ER, Pfizer)	4–8 mg q.d.; swallowed whole with liquid; should not be chewed, divided, or crushed	• Bioavailability, 52% peak levels, 5 hours post-dose; protein binding, 50%; metabolized by CYP2D6/3A4*; active metabolite, 5-hydroxymethyl-tolterodine (5-HMT) • Higher parent drug levels may occur in poor CYP2D6 metabolizers • Elimination: 70% renal as 5-HMT; half-life, 7 hours • Dose adjustments for moderate hepatic impairment and severe renal impairment (CrCl < 30 mL/minute); not recommended in severe hepatic impairment
Oxybutynin IR (Ditropan, Janssen)	2.5–5 mg b.i.d. or t.i.d.; maximum dosage, 5 mg q.i.d.	• Rapidly absorbed; peak levels, 1 hour post-dose; dose-dependent, linear pharmacokinetics; bioavailability, approximately 6%; extensively metabolized by CYP3A4*; active metabolite, desethyloxybutynin; half-life, 2–5 hours • May have direct smooth muscle-relaxant properties and local anesthetic effects • Caution recommended in renal impairment
Oxybutynin gel 10% (Gelnique, Watson) Oxybutynin gel 3% (Anturol, Antares)	1 g (sachet) applied daily to dry, intact skin; rotate application sites (abdomen, thigh, shoulder, upper arm) Three pumps (84 mg); applied as above; may rotate site if necessary	• Enters systemic circulation by passive diffusion across stratum corneum • Bypasses first-pass GI and hepatic metabolism, reducing formation of *N*-desethyl-oxybutynin metabolite • Steady state: achieved within 3–7 days of continuous dosing • Metabolized primarily by CYP3A4*; half-life: ~30 hours (3%); ~70 hours (10%) • Kinetic profiles similar to that of transdermal formulation (Oxytrol) • After application, wait 1 hour before showering; may apply sunscreen 30 minutes before or after application
Oxybutynin transdermal patch (Oxytrol, Watson)	36-mg patch applied twice weekly (every 3–4 days); delivers 3.9 mg daily; rotate administration sites (abdomen, hip, buttock)	• Enters systemic circulation by passive diffusion across stratum corneum • Bypasses first-pass GI and hepatic metabolism, reducing formation of *N*-desethyl-oxybutynin metabolite; half-life, approximately 7–8 hours • Kinetic profile similar to that of gel formulations

Oxybutynin XR (Ditropan XL, Janssen)	5–10 mg q.d.; may be increased to a maximum of 30 mg/day; swallowed whole; should not be chewed, divided, or crushed	• Peak levels, 4–6 hours post-dose; consistent plasma concentrations • Osmotically active bilayer; released over 24 hours • Metabolized by CYP3A4*; half-life, 12–13 hours
Solifenacin (VESIcare, Astellas Pharma US)	5–10 mg q.d.; swallowed whole with water	• Bioavailability, 90%; protein binding, 98%; metabolized by CYP3A4* • Elimination: 70% renal (<15% unchanged), 22% feces; half-life, 55 hours • Dose adjustments for moderate hepatic impairment and severe renal impairment (CrCl < 30 mL/minute); not recommended for use in severe hepatic impairment
Tolterodine IR (Detrol, Pfizer)	1–2 mg b.i.d.	• Rapidly absorbed; bioavailability, at least 77%; peak levels, 1–2 hours post-dose; protein binding, 96% (mainly to $alpha_1$-acid glycoprotein) • Extensively metabolized by CYP2D6 to active metabolite (5-HMT); metabolized by CYP3A4* in patients devoid of CYP2D6 • Half-life in extensive/poor metabolizers, 3 hours/9.6 hours • Elimination: approximately 77% of dose in urine, 17% in feces (metabolites) • Dose adjustments for substantially reduced hepatic or renal function
Tolterodine (Detrol LA, Pfizer)	2–4 mg q.d.; swallowed whole with liquid	• Rapidly absorbed; bioavailability, at least 77%; peak levels, 2–6 hours post-dose; protein binding, 96% (mainly to $alpha_1$-acid glycoprotein) • Extensively metabolized by CYP2D6 to active metabolite (5-HMT); 7% of Caucasians are poor metabolizers of CYP2D6 • Half life in extensive/poor metabolizers, 7 hours/18 hours • Elimination: approximately 77% of dose in urine, 17% in feces (metabolites) • Dose adjustments for substantially reduced hepatic or renal function

Trospium IR (Sanctura, Allergan)	20 mg b.i.d., at least 1 hour before meals or on empty stomach	• Bioavailability: <10%; peak levels, 5–6 hours post-dose • Metabolism: ester hydrolysis with subsequent conjugation (minimal CYP450 involvement) • Elimination: 85% in feces, 6% in urine (60% unchanged); half-life, approximately 20 hours • Dose adjustments or avoid in severe renal impairment; should be used with caution in moderate/severe hepatic impairment
Trospium (Sanctura XR, Allergan)	60 mg q.d. in morning, at least 1 hour before breakfast, with water or on empty stomach	• Peak levels, 5 hours post-dose; protein binding, 50%– 85% • Metabolism: ester hydrolysis with subsequent conjugation (minimal CYP450 involvement) • Elimination: 85% in feces, 6% in urine (60% unchanged); half-life, approximately 35 hours • Not recommended in severe renal impairment; no information on effect of severe hepatic impairment

Nonselective Alpha-Adrenergic Blockers	

General comments	• Used for both BPH and hypertension
	• Dosing based on patient response
	• Monitor for orthostatic hypotension (first dose)
	  • Educate patients to rise slowly from supine position
	  • Bedtime dosing for immediate-release formulations
	• Monitor efficacy, e.g., urine flow rates, symptoms
	• Potential for intraoperative floppy iris syndrome (cataract surgery)
	• Use with caution with antihypertensive drugs and other drugs that lower blood pressure (e.g., vardenafil)
	• Hepatic metabolism (primarily by CYP2D6/3A4*)
	• Highly protein-bound
	• Mechanism: nonselective alpha$_1$-receptor blockade in bladder neck and prostate

Doxazosin (Cardura and Cardura XL, Pfizer)	• Dosage (immediate release): 1–8 mg q.d. • Dosage (extended release): 4–8 mg q.d. with breakfast; titrate dose every 3–4 weeks (maximum, 8 mg/day) • Elimination: fecal 60%, renal 9% • Half-life: 15–20 hours
Prazosin (Minipress, Pfizer)	• FDA-approved for hypertension; not approved for BPH • Dosage: 0.5–1.0 mg b.i.d.; titrate dose every 2–7 days (maximum, 2 mg/day) • Half-life: 2.5 hours
Terazosin (Hytrin, Abbott)	• Dosage: 1–5 mg q.d; titrate dose every 2–7 days (maximum, 20 mg/day) • Elimination: fecal 60%, renal 40% (10% unchanged) • Half-life: 12–14 hours

Uroselective Alpha-Adrenergic Blockers (Alpha$_{1A}$ Receptors)	
General comments	• Used only for BPH • Dosing based on patient response • Mechanism: selective alpha$_1$-receptor blockade in bladder neck and prostate; selectively reduce urinary tract alpha$_{1A}$-receptors
Alfuzosin (Uroxatral, Sanofi)	• Dosage: 1 extended-release tablet (10 mg) q.d. • Contraindication: moderate/severe liver disease • Elimination: fecal 70%, renal 25% (10% unchanged) • Half-life: 10 hours
Silodosin (Rapaflo, Watson)	• Dosage: 4–8 mg q.d. with food • Elimination: fecal 55%, renal 33% • Half-life: 14–24 hours; glucuronide conjugate • Contraindication: hepatic Child–Pugh score > 10
Tamsulosin (Flomax, Boehringer Ingelheim)	• Dosage: 0.4–0.8 mg q.d. • Elimination: renal 75% (<10% unchanged), fecal 20% • Half-life: 15 hours • Associated with intraoperative floppy iris syndrome (cataract surgery) • Avoid use in patients with sulfa allergy

5-Alpha-Reductase Inhibitors	
General comments	• Used only for BPH • Administered as monotherapy or with alpha-adrenergic blockers • Contraindications: pregnancy, including pregnant blood transfusion recipient if donor had dose within 6 months; pediatric patients; cutaneous absorption (avoid capsule handling by pregnant or potentially pregnant women) • Monitor PSA and side effects: abnormal ejaculation, reduced libido, signs and symptoms of BPH (urine flow)
Dutasteride (Avodart, GlaxoSmithKline)	• Dosage: 0.5 mg q.d. • Metabolized by CYP3A4*/3A5; active metabolites • Elimination: feces 45%, urine < 1% • Half-life: 5 weeks • Mechanism: inhibits type-1 and type-2 5-alpha-reductase • Possible risk of heart failure
Dutasteride/ tamsulosin (Jalyn, GlaxoSmithKline)	• Dosage: 1 capsule (dutasteride 0.5 mg/tamsulosin 0.4 mg) q.d., taken 30 minutes after same meal each day • See comments for dutasteride and tamsulosin on previous page
Finasteride (Proscar, Merck)	• Dosage: 5 mg q.d. • Metabolized by CYP3A4*; active metabolites • Elimination: feces 60%, urine 40% • Half-life: 6–8 hours • Mechanism: inhibits type-2 5-alpha-reductase • Minimal drug interactions reported; monitor when used with CYP3A4 inhibitors; caution in patients with hepatic impairment

Overflow incontinence (OFI)			
Overflow incontinence	• Benign prostatic hyperplasia (BPH) • Bladder outlet obstruction • Fecal impaction • Hypotonic/neurogenic bladder • Urethral stricture disease	Poor stream, incomplete emptying, and dribbling	• Alpha-adrenergic blockers • 5-alpha-reductase inhibitors • Intermittent catheterization • Surgical options
Other types of incontinence			
Post-prostatectomy incontinence	Disruption or denervation of pelvic floor muscle fibers	Stress incontinence and dribbling	• Kegel pelvic floor exercises • Male urethral sling • Artificial urinary sphincter
Fistula (e.g., colovesical or vesicovaginal)	• Postsurgical complications • Crohn's disease • Diverticulitis • Cancer	Continuous, steady incontinence	Surgical repair
Functional incontinence	• Limited mobility • Change in mental status	Symptoms vary	Eliminate causes

	Men	Women
Initial management options (treat most bothersome symptom first)	• Pelvic floor muscle training with/without biofeedback for post-prostatectomy SUI • Scheduled voiding (bladder training) • Incontinence products • Antimuscarinic drugs for OAB with/without UUI • Alpha-adrenergic antagonists for bladder outlet obstruction	• Pelvic floor muscle training for SUI or OAB • Bladder training for UUI or OAB • Vaginal cones • Electrical stimulation • Duloxetine for SUI • Antimuscarinic drugs for OAB with/without UUI
Specialized management options (if initial therapy fails)	• Artificial urinary sphincter • Male sling • Neuromodulation	• Bulking agents • Tapes and slings • Colposuspension (Burch) procedure • Artificial urinary sphincter • Botulinum toxin • Neuromodulation • Bladder augmentation

INCONTINENZA URINARIA

Paziente anziano e' importante ricercare la causa perché c'è la concezione che la I.U. sia normale in età avanzata

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