

CONGRESSO NAZIONALE
78
FIMMG-METIS 2021

MEDICINA GENERALE CONVENZIONATA, DIRITTO DELL'INDIVIDUO.

**RESIDENZIALE
E VIDEOCONFERENZA**
4 OTTOBRE 2021
9 OTTOBRE 2021

FAD ASINCRONE
12 OTTOBRE 2021
15 NOVEMBRE 2021



SCELTA FIDUCIARIA
PROSSIMITÀ
DOMICILIARITÀ

FIMMG[®]
Federazione Italiana Medici di Famiglia

Metis[®]
SOCIETÀ SCIENTIFICA DEI MEDICI
DI MEDICINA GENERALE



Cosa fare quando la terapia farmacologica
fallisce?

La tossina botulinica
intra-detrusoriale

Il PAC per l'incontinenza urinaria

Angelo Di Santo

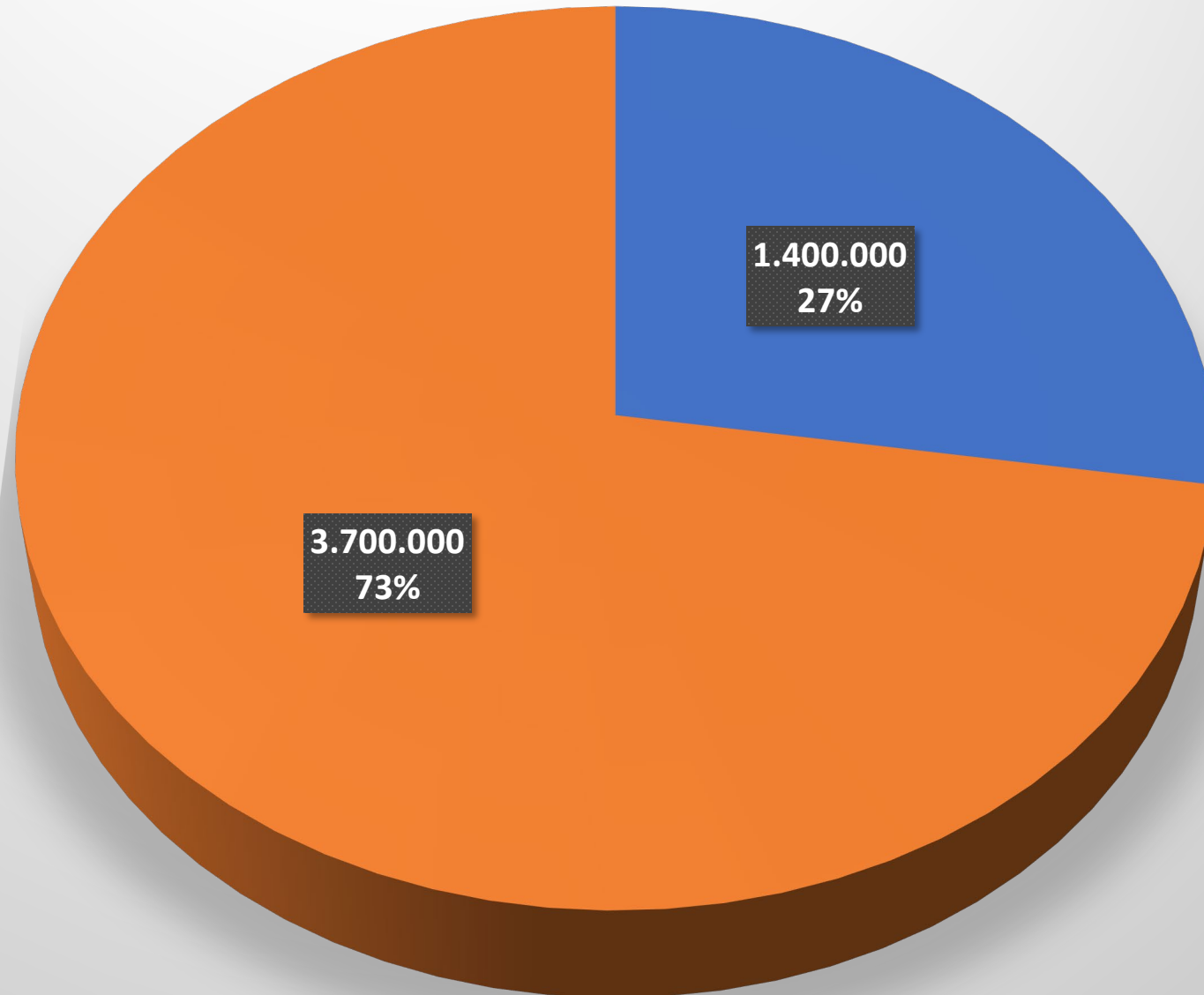


M.G. VANNINI
OSPEDALE RELIGIOSO
CLASSIFICATO ACCREDITATO
ISTITUTO FIGLIE DI SAN CAMILLO

INCONTINENZA

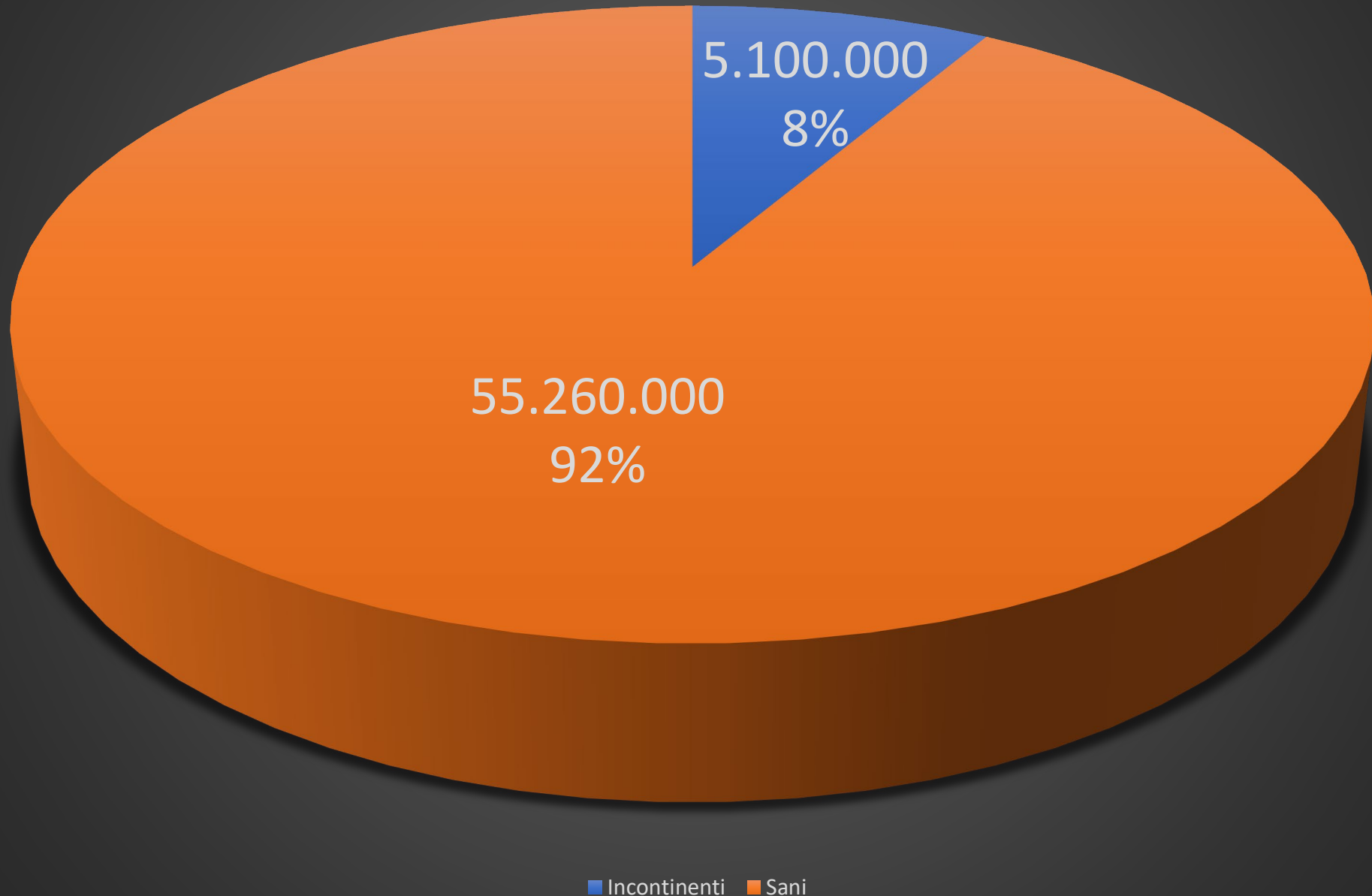
5.100.000 in Italia

**Nella Regione Lazio
quasi mezzo milione
di cittadini soffre di
incontinenza urinaria
e/o fecale in forme ed
intensità diverse**



Maschi
Femmine

60.360.000 popolazione italiana



Solo incontinenza urinaria maschile?





Solo
incontinenza
urinaria
femminile?





Inevitable...?

Incontinenza fecale





STOMIZZATI





Pz. MIELOLESI

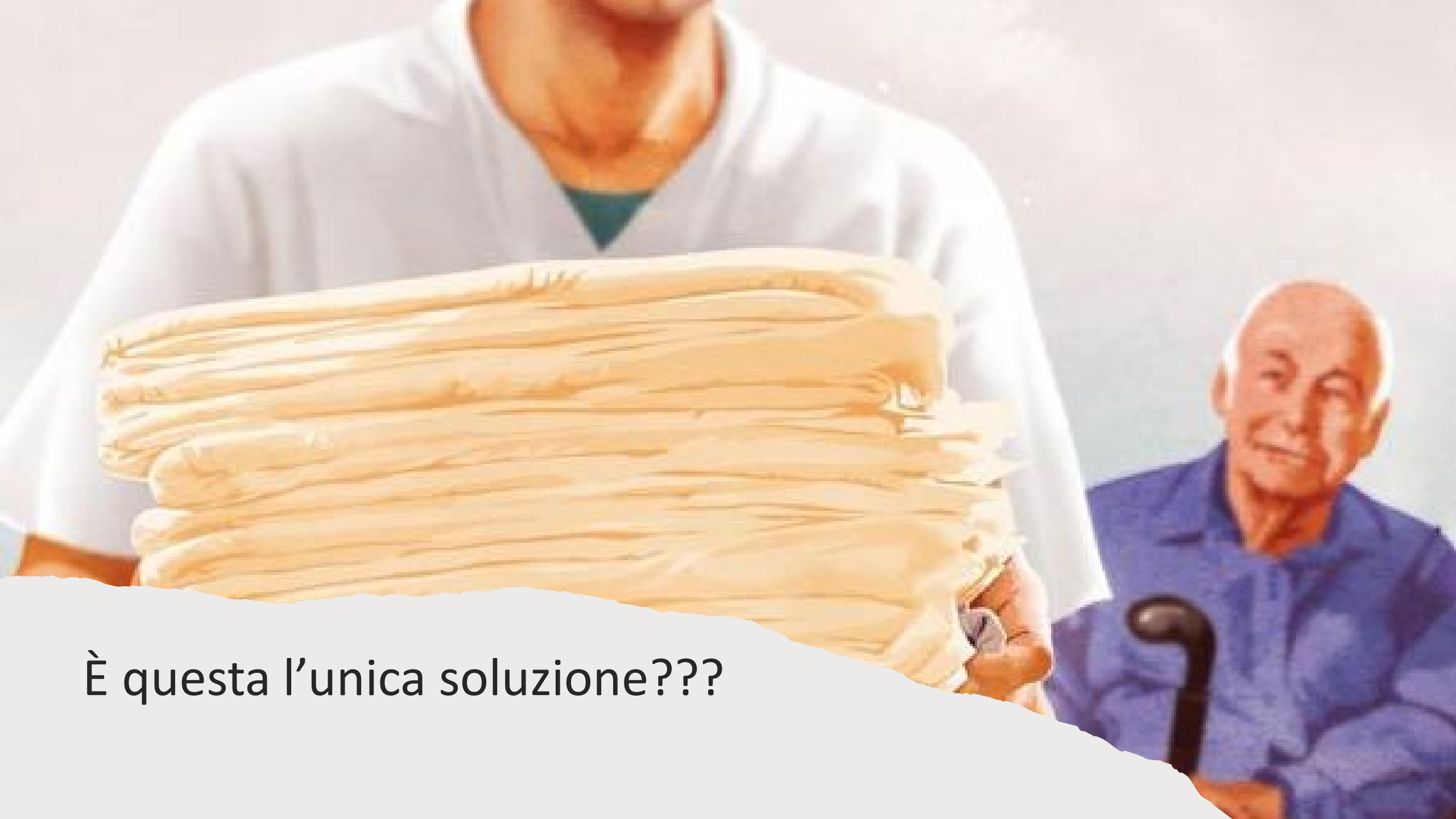
VESCICA ED
INTESTINO
NEUROGENI



M. DI PARKINSON

SCLEROSI MULTIPLA





È questa l'unica soluzione???



Oppure questa...???

A large orange circle is positioned on the left side of the slide, partially cut off by the edge.

2015 Decreto del Ministro della Salute

- costituito il “**Gruppo di lavoro sui problemi legati all’incontinenza urinaria e fecale**”

- Il Gruppo di lavoro ha prodotto un

**“Documento tecnico di indirizzo sui
problemi legati all’incontinenza
urinaria e fecale”**



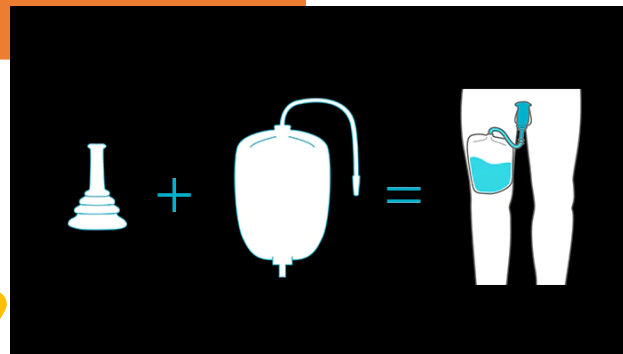
Documento
tecnico di
indirizzo sui
problemi legati
all'incontinenza
urinaria e fecale

- Prevede:
 - la predisposizione di linee di indirizzo per un razionale utilizzo dei dispositivi medici previsti nella attività chirurgica complessa ed avanzata



Documento tecnico di indirizzo sui problemi legati all'incontinenza urinaria e fecale

- Prevede:
 - l'ottimizzazione e razionalizzazione del percorso di fornitura di dispositivi medici monouso (ausili monouso) per incontinenza già a partire dalla prescrizione anche alla luce delle ricerche e delle sperimentazioni internazionali



Documento tecnico di indirizzo sui problemi legati all'incontinenza urinaria e fecale

- Prevede:
 - l'attuazione di campagne di educazione e sensibilizzazione sui temi dell'incontinenza, a livello regionale, che affianchino la “Giornata nazionale per la prevenzione e cura dell'incontinenza” del 28 giugno istituita dal Ministero della Salute.

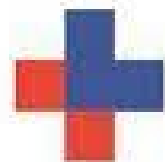


28 GIUGNO 2021

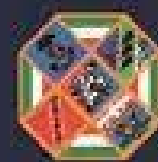
XVI GIORNATA NAZIONALE PER
LA PREVENZIONE E LA CURA
DELL'INCONTINENZA

Documento
tecnico di
indirizzo sui
problemi legati
all'incontinenza
urinaria e fecale

- Prevede:
 - l'attivazione e l'implementazione di percorsi diagnostico-terapeutici assistenziali (PDTA) in grado di garantire la presa in carico della persona incontinente erogando i necessari interventi multiprofessionali e multidisciplinari



SALUTE LAZIO
SISTEMA SANITARIO REGIONALE



REGIONE
LAZIO

Direzione: SALUTE E INTEGRAZIONE SOCIOSANITARIA

Area: RETE OSPEDALIERA E SPECIALISTICA

DETERMINAZIONE (con firma digitale)

N. G05042 del 04/05/2021

Proposta n. 13792 del 28/04/2021

Oggetto:

Approvazione del documento regionale "Rete regionale dei Centri per la prevenzione, diagnosi e cura dell'incontinenza urinaria e fecale"

Proponente:

Estensore	URSO ANTONELLA	_____ firma elettronica _____
Responsabile del procedimento	URSO ANTONELLA	_____ firma elettronica _____
Responsabile dell'Area	G. SPIGA	_____ firma digitale _____
Direttore Regionale	M. ANNICCHIARICO	_____ firma digitale _____

Firma di Concerto

DETERMINA

per le motivazioni espresse in premessa, che si intendono integralmente richiamate:

- di approvare il documento regionale denominato "Rete regionale dei Centri per la prevenzione, diagnosi e cura dell'incontinenza urinaria e fecale"

MODELLO DI
RETE
REGIONALE CHE
GARANTISCE...

- **tempestiva presa in carico** del paziente in tutto il **territorio regionale**;
 - **adeguati livelli di cura**;
 - **equità** a livello territoriale nelle condizioni **di accesso e di fruizione dei servizi**;
 - un percorso di cura **multidisciplinare e multiprofessionale** in tutto il territorio regionale.
- 



Criteri per la classificazione dei Centri dell'incontinenza urinaria e fecale

expertise dei Professionisti;

equipe multidisciplinari;

posizione geografica rispetto alle caratteristiche
e alle esigenze del territorio al fine di fornire
adeguata risposta al bisogno di salute.



MODELLO DELLA RETE (circolare)

Livello di Assistenza Primaria
(MMG/PLS)

Centri di Livello I

Centri di Livello II

Centri di Livello III

Sono pertanto previsti "link" tra i vari Centri, di pari e diverso livello, a partire dal territorio, affinché si possano complementare, utilizzando ciascuno le professionalità e le risorse previste per lo specifico livello; sia tra Centri dello stesso livello, per condividere gli stessi protocolli ed uniformare gli standard, e, auspicabilmente, per raccogliere i risultati. In questo modello di rete la presa in carico del cittadino con problemi di continenza, permette accesso all'expertise appropriato e standard Regionale pur rispettando il criterio della prossimità dell'accesso alle cure.

È previsto, oltre all'interscambio per motivazioni cliniche, una collaborazione diffusa dei centri della rete per esigenze di formazione ed aggiornamento del personale, che vede direttamente impegnati come referenti, delle suddette attività, i Centri di livello III (e le loro strutture accademiche di riferimento), oltre alla Regione, qualora vi fosse necessità.

Il documento definisce un modello di rete di servizi per la prevenzione, la diagnosi e la cura dell'incontinenza, che a partire dal territorio prevede, per le Strutture Sanitarie, al fine di garantire la presa in carico, l'inquadramento diagnostico e la continuità delle cure.

3.1 MODELLO DELLA RETE

Viene descritto un modello di rete di servizi per la prevenzione, la diagnosi e la cura dell'incontinenza, strutturata in tre livelli ben definiti.

Qualsiasi sia il livello a cui accede il paziente deve essere assicurata un'adeguata presa in carico indirizzando il paziente al percorso assistenziale più idoneo al suo bisogno clinico.

Livello di Assistenza Primaria

Il medico di medicina generale (MMG) e il pediatra di libera scelta (PLS), nell'ambito delle loro attività di assistenza primaria, hanno un ruolo primario nella rilevazione e diagnosi dell'incontinenza, in virtù del rapporto fiduciario (e quindi confidenziale) con il paziente, dell'abitudine della frequentazione e della conoscenza che il MMG/PLS ha degli eventi che colpiscono l'assistito.

Centri di Livello I – Diagnostico - Riabilitativo

I Centri di I livello svolgono una funzione di diagnosi e trattamento *iniziale* dell'incontinenza urinaria e/o fecale per il paziente uomo, donna, bambino e anziano. Assicurano, quindi, la presa in carico dell'assistito da parte di una figura medica specialistica (urologici, ginecologici, proctologici e riabilitativi) integrata in un team multidisciplinare e interprofessionale e l'inserimento del paziente nel percorso assistenziale, secondo il suo bisogno clinico.

Questi Centri provvedono all'esecuzione degli accertamenti di inquadramento, forniscono le informazioni utili relative alla situazione generale del paziente e avviano il percorso riabilitativo efficace ed efficiente, nell'ambito dell'appropriatezza clinico-organizzativa.

Sono in stretto contatto con l'Assistenza Primaria e i Centri di livello superiore per supportare l'assistito per eventuali passaggi di setting e la prosecuzione dei percorsi di cura.

Centri di Livello II – Specialistico (Urologico, Ginecologico, Coloproctologico)

Il Centro di secondo livello è identificato all'interno dell'azienda ASL e deve garantire l'assistenza specialistica, sia ambulatoriale che ospedaliera. Per ogni azienda ASL si prevede un unico Centro di secondo livello e l'individuazione di un coordinatore delle attività sia ambulatoriali che ospedaliere e del monitoraggio delle liste di attesa. L'assistenza ambulatoriale è garantita da un *ambulatorio*

Qualsiasi sia il livello a cui accede il paziente deve essere assicurata un'adeguata presa in carico indirizzando il paziente al percorso assistenziale più idoneo al suo bisogno clinico.

Livello di Assistenza Primaria

Il medico di medicina generale (MMG) e il pediatra di libera scelta (PLS), nell'ambito delle loro attività di assistenza primaria, hanno un ruolo primario nella rilevazione e diagnosi dell'incontinenza, in virtù del rapporto fiduciario (e quindi confidenziale) con il paziente, dell'abitudine della frequentazione e della conoscenza che il MMG/PLS ha degli eventi che colpiscono l'assistito.

Neuromodulazione sacrale	Tecnica di elettrostimolazione dei nervi sacrali volta a correggere una disfunzione del basso apparato urinario
Basso apparato urinario	Unione funzionale di vescica, uretra e sfintere striato uretrale
PDTA	Percorsi diagnostici-terapeutici-assistenziali
DRG	Diagnosis-Related Group
Diagnosi	giudizio clinico, effettuato da medico autorizzato, che consiste nel riconoscere una condizione morbosa in base all'esame clinico del malato e alle ricerche di laboratorio e strumentali
MMG	Medici di Medicina Generale
PLS	Pediatrati di Libera Scelta

5.0 MODALITA' ESECUTIVE

In questo capitolo vengono identificati i requisiti minimi, compiti e funzioni dei diversi setting assistenziali per la prevenzione, diagnosi e cura dell'incontinenza urinaria e fecale nella Regione Lazio.

Il MMG/PLS risulta centrale nell'intercettazione del problema, sia che il/la paziente si rivolga per il problema specifico, che in corso di accessi per altre problematiche. Potranno essere altresì attuati appositi protocolli che prevedono diversi gradi di intensità di cura secondo il bisogno assistenziale, per l'orientamento del paziente al centro per lui più idoneo perché inizi quanto prima una terapia riabilitativa o un percorso di cura.

Il Centro di I livello assistenziale esegue le seguenti attività:

- attività di diagnosi e trattamento iniziale dell'incontinenza urinaria e/o fecale per il paziente uomo, donna, bambino e anziano secondo i rispettivi Percorsi Diagnostici Terapeutici Assistenziali (PDTA);
- identificare i soggetti con "incontinenza urinaria e/o fecale complicata" (i.e. incontinenza urinaria associata a dolore, ematuria, infezioni urinarie complicate, prolasso, e incontinenza fecale associata a sospetta patologia infiammatoria cronica, fistola, prolasso), o associata a patologia neurologica, per indirizzarli ad una gestione specialistica a seconda delle necessità; i pazienti con lesione midollare (di origine traumatica e non) seguono un percorso assistenziale in strutture dedicate (i.e. Unità Spinali) che non rientrano nella rete dell'incontinenza.

Il Centro di primo livello oltre alla presenza dello specialista urologo e/o ginecologo e/o coloproctologo deve preferibilmente prevedere la presenza del fisiatra. Deve, inoltre, essere prevista la presenza di un/dei fisioterapisti/i e di un/degli infermieri/i, possibilmente con competenze specifiche, rispettivamente nella riabilitazione pelvi-perineale e negli aspetti assistenziali di uro-riabilitazione. Si sottolinea inoltre l'importanza della presenza, ove possibile, dell'ostetrica per le attività di prevenzione e cura della incontinenza urinaria e fecale in gravidanza e nel puerperio.

Il Centro di primo livello è tenuto ad alimentare regolarmente, secondo le modalità previste, che verranno trasmesse a tutti i Centri interessati, dalla Struttura detentrica, con apposita procedura operativa, il Registro Regionale dell'Incontinenza affidato al Policlinico di Tor Vergata. La mancata ottemperanza alla tempestiva e puntuale condivisione dei dati nel Registro costituisce un elemento negativo di valutazione dell'operato del Centro.

Il MMG/PLS risulta centrale nell'intercettazione del problema, sia che il/la paziente si rivolga per il problema specifico, che in corso di accessi per altre problematiche. Potranno essere altresì attuati appositi protocolli che prevedono diversi gradi di intensità di cura secondo il bisogno assistenziale, per l'orientamento del paziente al centro per lui più idoneo perché inizi quanto prima una terapia riabilitativa o un percorso di cura.





U.O.S.D. UROLOGIA VANNINI

Ambulatorio Urologia Femminile

Ambulatorio Incontinenza Urinaria

Ambulatorio Neuro-Urologico

(L'ambulatorio del Centro di II livello deve essere in grado di: eseguire l'anamnesi generale e del sintomo, la somministrazione di un diario minzionale e/o dell'incontinenza fecale, di questionari generali e specifici (QoL, etc), la valutazione del desiderio e delle aspettative di trattamento – o se già precedentemente eseguiti, effettuare la valutazione approfondita degli stessi; eseguire un opportuno esame fisico obiettivo generale e del pavimento pelvico (testing perineale, esame neurologico di minima dell'area sacrale, stress test, etc...)



U.O.S.D. UROLOGIA VANNINI

- Rete con altri centri (Es. PTV, Fondazione Santa Lucia, Fondazione don Carlo Gnocchi, Ospedale Pediatrico Bambino Gesù)

(Inviare il paziente con incontinenza complicata o con nota o sospetta incontinenza neurologica alle UO afferenti al centro specialistico più idoneo a seconda del problema)





U.O.S.D. UROLOGIA VANNINI

Ecografia dedicata

(eseguire gli accertamenti diagnostici di prima linea (ad es. ecografia pelvica, valutazione del residuo vescicale post-minzionale)



BLADDER TRAINING PREVENTS INCONTINENCE

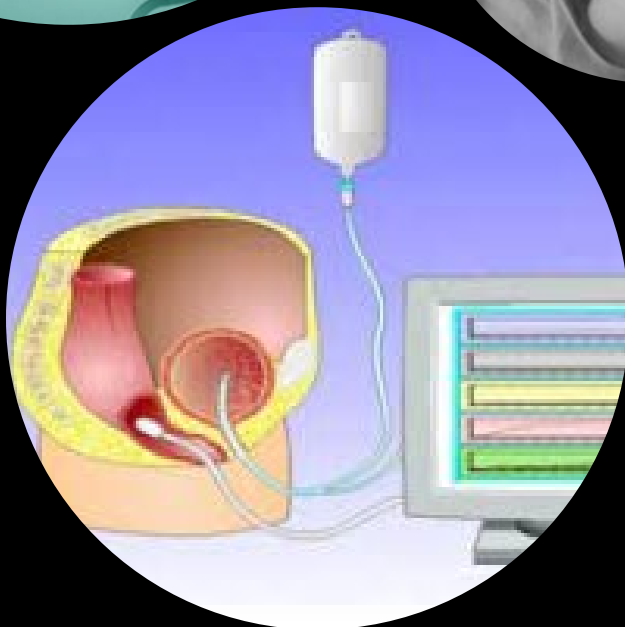
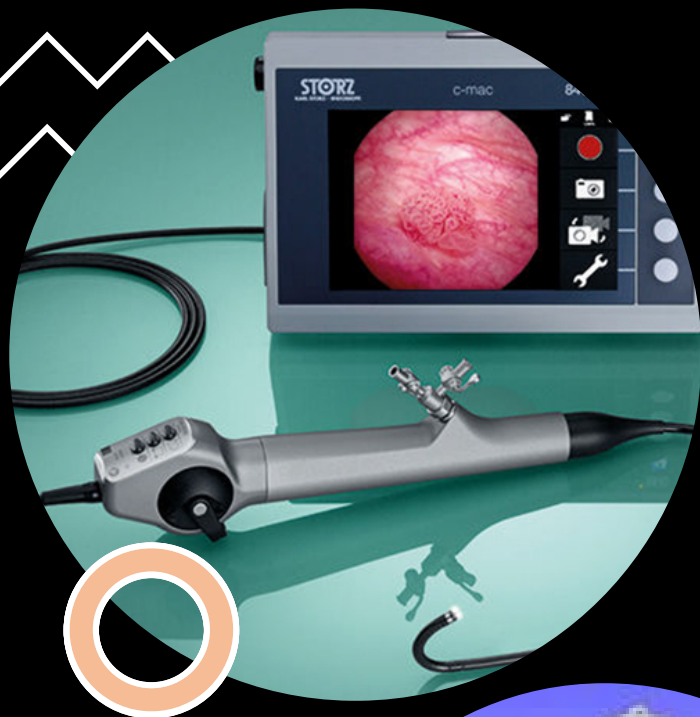
U.O.S.D. UROLOGIA VANNINI

- Bladder Training e Timed-voiding vescicale + farmacoterapia

(Nel caso di incontinenza non-complicata, definire una diagnosi e iniziare un trattamento di tipo comportamentale-rieducativo (interventi/consigli sullo stile di vita, rieducazione vescicale e intestinale), riabilitativo (ad es. rieducazione del pavimento pelvico), farmacologico, se non già eseguito dal Centro di I livello.



U.O.S.D. UROLOGIA VANNINI



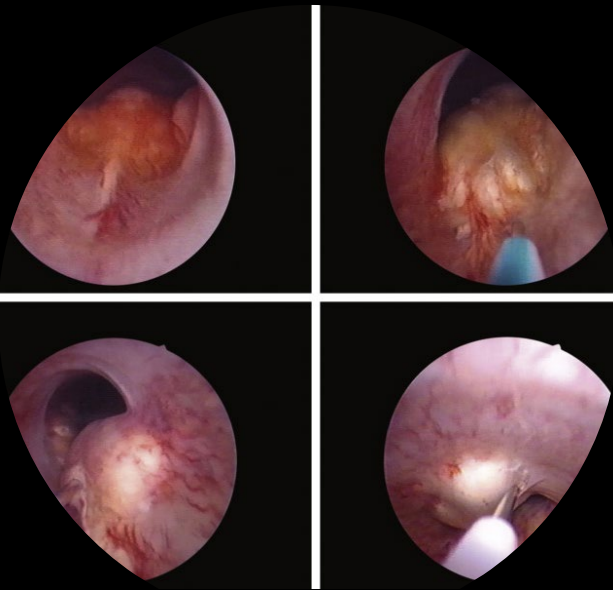
- Esame Urodinamico invasivo (Cistomanometria e Studio Pressione/Flusso)
- RX-Cistografia
- Cine-Uretro RM
- Cistoscopia diagnostica ed operativa.

(A seconda della categoria di paziente, ovvero a seconda che si tratti di paziente uomo, donna, bambino o anziano, potrebbero essere necessari ulteriori esami diagnostici o trattamenti e/o strategie di trattamento diverse tra loro, che verranno dettagliati in specifici PDTA, definiti in maniera condivisa tra i diversi profili di professionisti coinvolti nella presa in carico. L'assistenza ospedaliera è garantita dalle UU.OO di Urologia e/o Ginecologia e/o Chirurgia generale e/o Medicina Fisica (a seconda dell'origine patologica dell'incontinenza o della tipologia di paziente). Le suddette UU.OO, afferenti al Centro di secondo livello per l'assistenza ospedaliera, devono essere in grado di: ☐ svolgere un'attività di livello I in assenza di Centri riabilitativi Territoriali ☐ assicurare la valutazione multidisciplinare del paziente ad opera degli specialisti urologo, ginecologo, chirurgo generale con esperienza in chirurgia coloretale a seconda dell'origine patologica dell'incontinenza, integrata con altre figure professionali in ragione delle caratteristiche del paziente (ad es. pediatra e geriatra o neurologo per la valutazione – rispettivamente – del paziente pediatrico, anziano o con patologia neurologica); ☐ eseguire una diagnosi specialistica attraverso una strumentazione di diagnostica morfofunzionale urologica e uro-ginecologica e coloretale endoscopici; ☐ eseguire indagini di uro-radiologia e di urodinamica e di diagnostica anorettale; ☐

U.O.S.D. UROLOGIA VANNINI

- Chirurgia dell'Incontinenza Urinaria:
 - Bulking-agents
 - Sling tension-free (maschili e femminili)
 - Sfintere artificiale
 - Colposacropessi
- Videolaparoscopica

(assicurare il trattamento terapeutico con soluzioni chirurgiche specialistiche (in particolare trattamenti chirurgici mini invasivi quali iniezioni di sostanze volumizzanti, di tossina botulinica, inserzione di sling - tension free, trattamento chirurgico fasciale vaginale del prolasso quando associato all'incontinenza, riparazione sfinteriale anale da lesioni ostetriche), secondo PDTA definiti e condivisi; ☐ garantire il collegamento diretto ai Centri di terzo livello per i casi più complessi e nello stesso tempo mantenere un collegamento con i Centri di pari livello, di livello I e con il MIMG/PLS; ☐ effettuare in maniera continuativa e non occasionale gli interventi diagnostico-terapeutici previsti dai PDTA; Il Centro di secondo livello è tenuto ad alimentare regolarmente, secondo le modalità previste, che verranno trasmesse a tutti i Centri interessati, dalla Struttura detentrica, con apposita procedura operativa, il Registro Regionale dell'Incontinenza affidato al Policlinico di Tor Vergata. La mancata ottemperanza alla tempestiva e puntuale condivisione dei dati nel Registro costituisce un elemento negativo di valutazione dell'operato del Centro.)



U.O.S.D. UROLOGIA VANNINI

- PAC INCONTINENZA (Pacchetti Ambulatoriali Complessi (PAC)
 - PAC per la gestione dell'incontinenza urinari a da urgenza di origine idiopatica o neurologica refrattaria a gli antimuscarinici (P788.31)

(assicurare il trattamento terapeutico con soluzioni chirurgiche specialistiche (in particolare trattamenti chirurgici mini invasivi quali iniezioni di sostanze volumizzanti, di tossina botulinica, ...)



The Standardisation of Terminology of Lower Urinary Tract Function: Report from the Standardisation Sub-committee of the International Continence Society

Paul Abrams, Linda Cardozo, Magnus Fall, Derek Griffiths, Peter Rosier, Ulf Ulmsten, Philip van Kerrebroeck, Arne Victor, and Alan Wein

This report presents definitions of the symptoms, signs, urodynamic observations and conditions associated with lower urinary tract dysfunction (LUTD) and urodynamic studies (UDS), for use in all patient groups from children to the elderly.

"Methods, definitions and units conform to the standards recommended by the International Continence Society, except where specifically noted".

The report covers the following areas:

The definitions restate or update those presented in previous International Continence Society Standard Terminology reports (see references) and those already published on Urinary Function [Lose et al., in Nocturia [van Kerrebroeck et al., 2002]. The present report on the technical aspects of urodynamic studies [Rowan et al., 1987] will be complemented by the report on urodynamic practice to be published [Schäfer et al., 2002]. In addition there are four ICS outcome reports [Fonda et al., 1998; Lose et al., 1998; Mattiasson et al., 1998; Nordling et al., 1998].

New or changed definitions are all indicated. Recommendations concerning technique are not in the main text of this report.

The definitions have been written to be compatible with WHO publication ICDH-2 [International Classification of Functioning, Disability and Health] published in 1989. In ICD10, the International Classification of Diseases, the definitions are descriptive of observations without implying underlying assumptions that may later be incorrect or incomplete. By following this principle, the International Continence Society (ICS) aims to facilitate comparison of results and enable effective communication between investigators who use urodynamic methods. It restates the ICS principle that symptoms, signs and urodynamic observations are separate categories, and adds a category of urodynamic observations. In addition, terminology related to urodynamic observations is included [Andersen et al., 1992].

When a reference is made to the whole anatomic structure, the correct term is the bladder, the smooth muscle structure known as the detrusor, being discussed, then the correct term is detrusor.

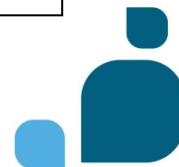
It is suggested that acknowledgement of these standards in written publications be indicated by a footnote to the section "Methods and Materials" or its equivalent, to read as follows:

Definizione incontinenza sec. I.C.S.

Neurourology and Urodynamics 21:167–178 (2002)
DOI 10.1002/nau.10052

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Urinary incontinence is the complaint of any involuntary leakage of urine. (NEW)²



Neurourology and Urodynamics 21:167–178 (2002)
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- *Stress urinary incontinence* is the complaint of involuntary leakage on effort or exertion, or on sneezing or coughing. (CHANGED)⁴



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- *Urge urinary incontinence* is the complaint of involuntary leakage accompanied by or immediately preceded by urgency. (CHANGED)⁵



Neurourology and Urodynamics 21:167–178 (2002)
DOI 10.1002/nau.10052

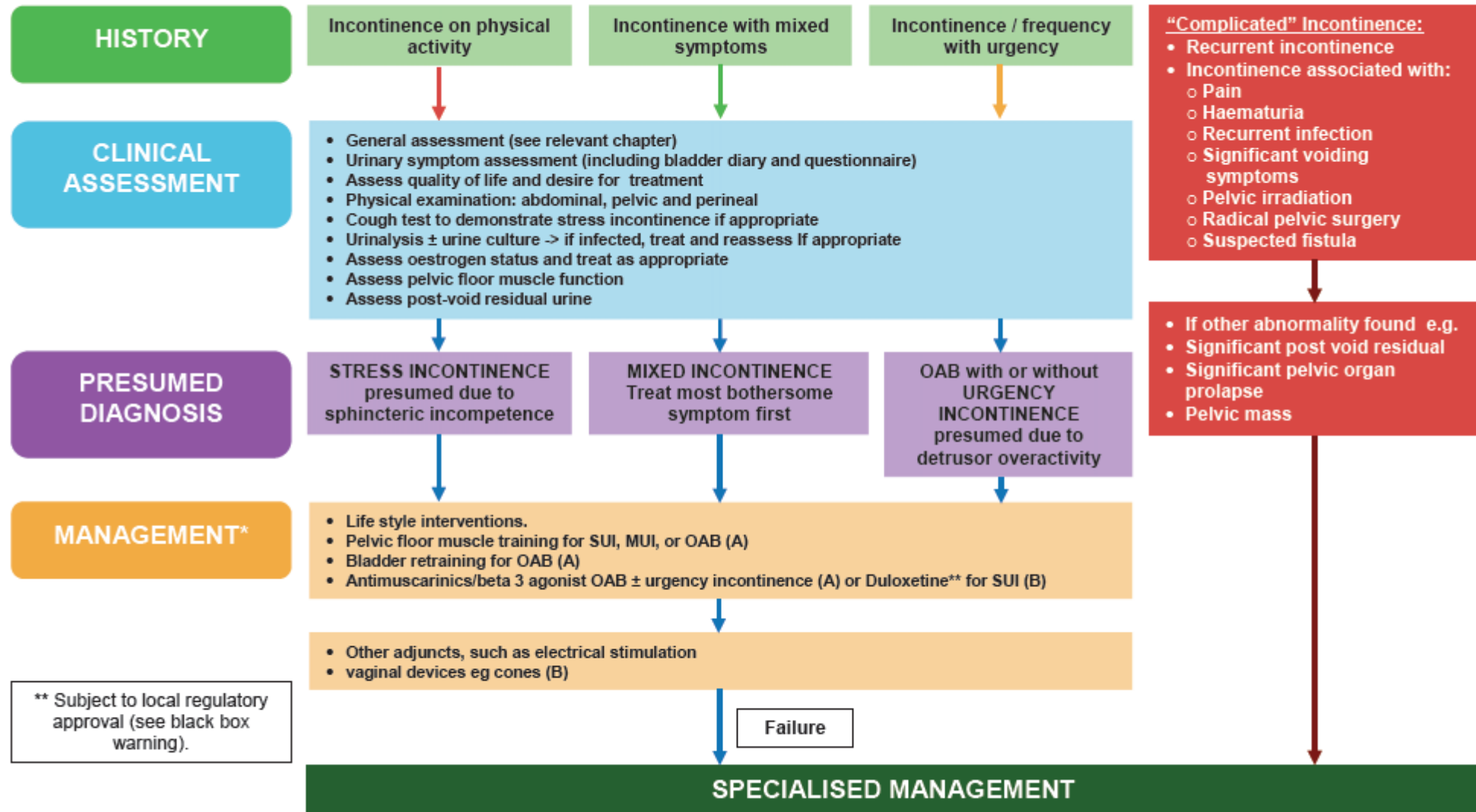
The Standardisation of Terminology of Lower Urinary Tract Function: Report from the Standardisation Sub-committee of the International Continence Society

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- *Mixed urinary incontinence* is the complaint of involuntary leakage associated with urgency and also with exertion, effort, sneezing or coughing. (NEW)

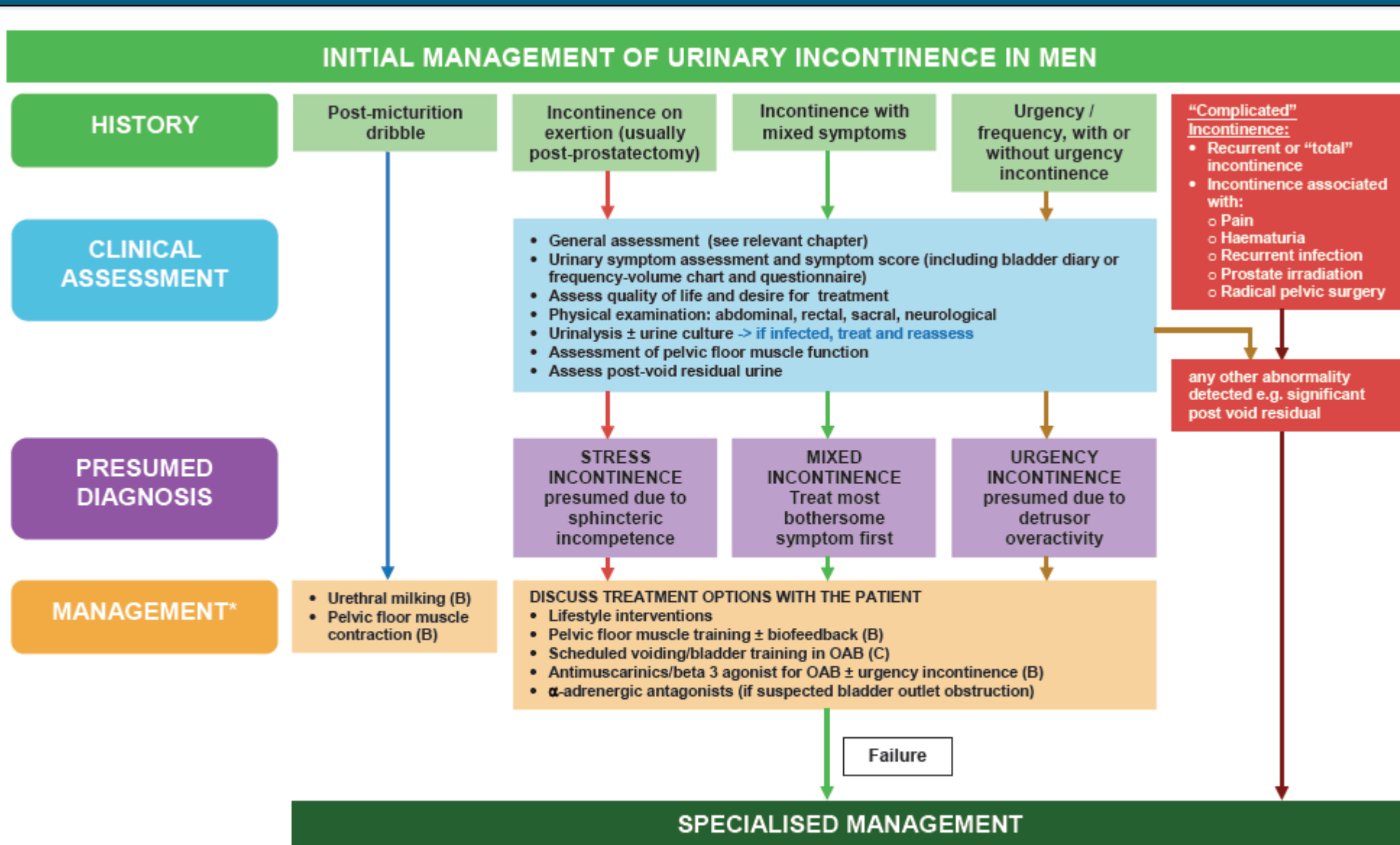


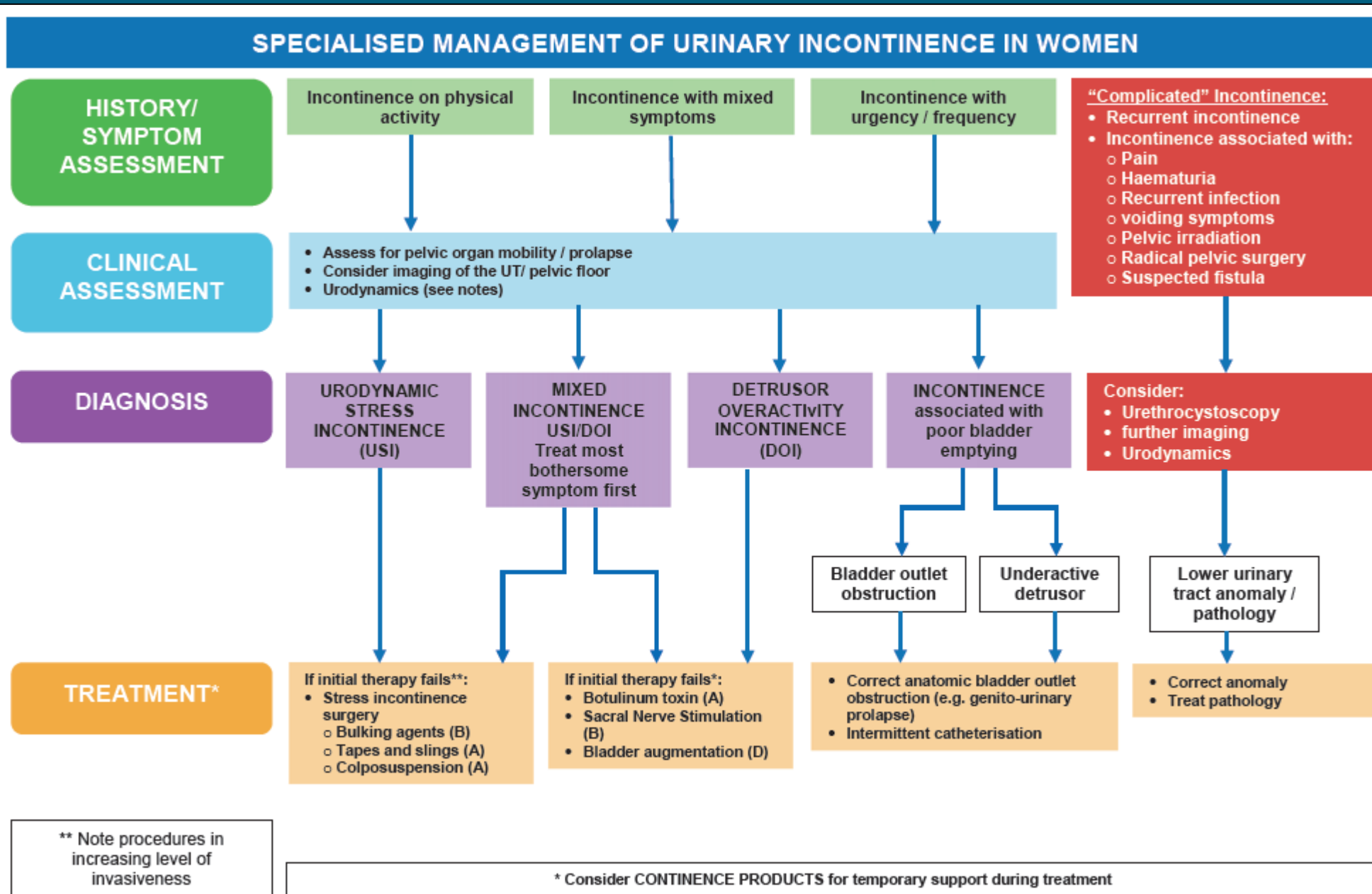
INITIAL MANAGEMENT OF URINARY INCONTINENCE IN WOMEN

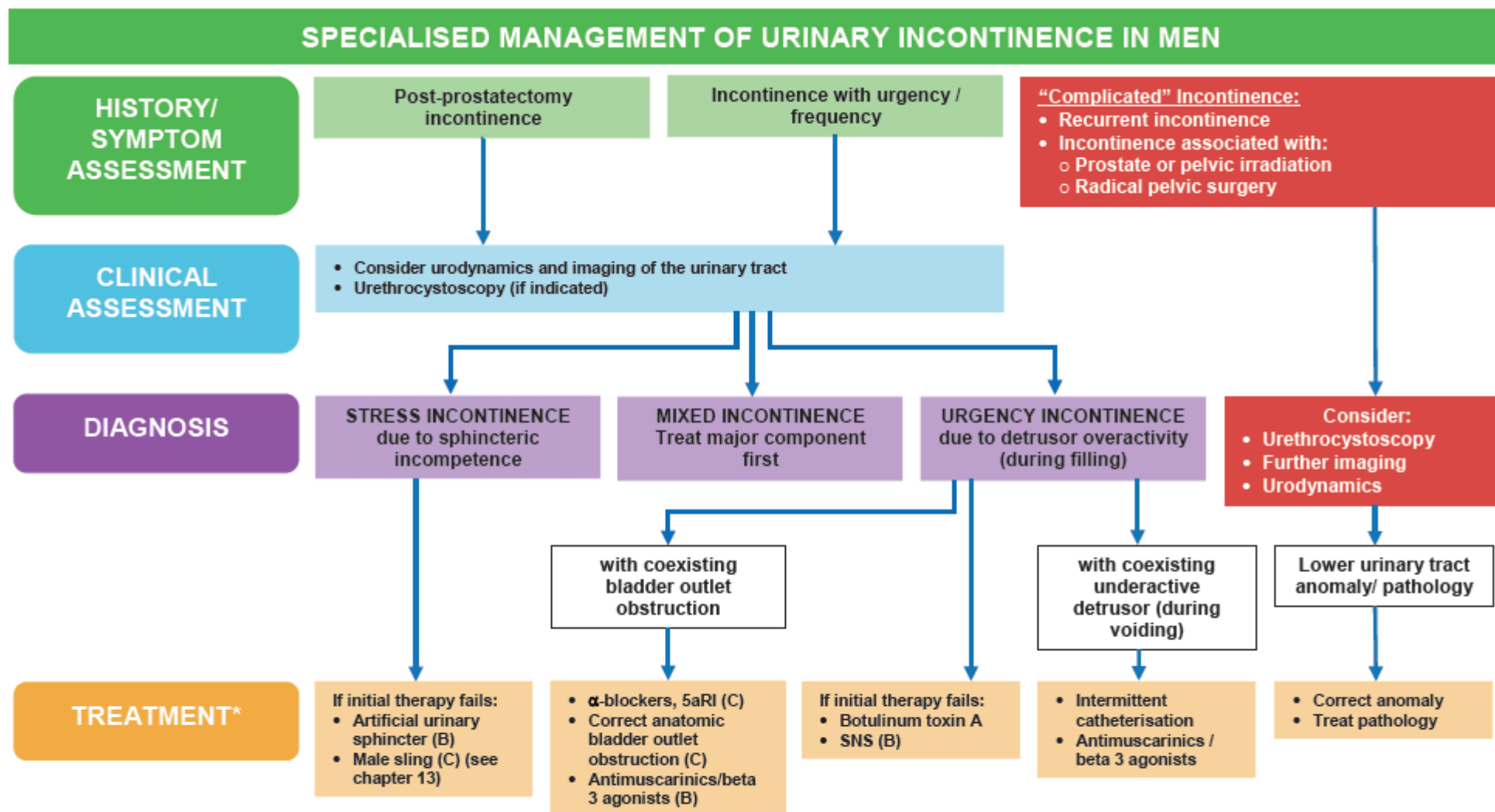


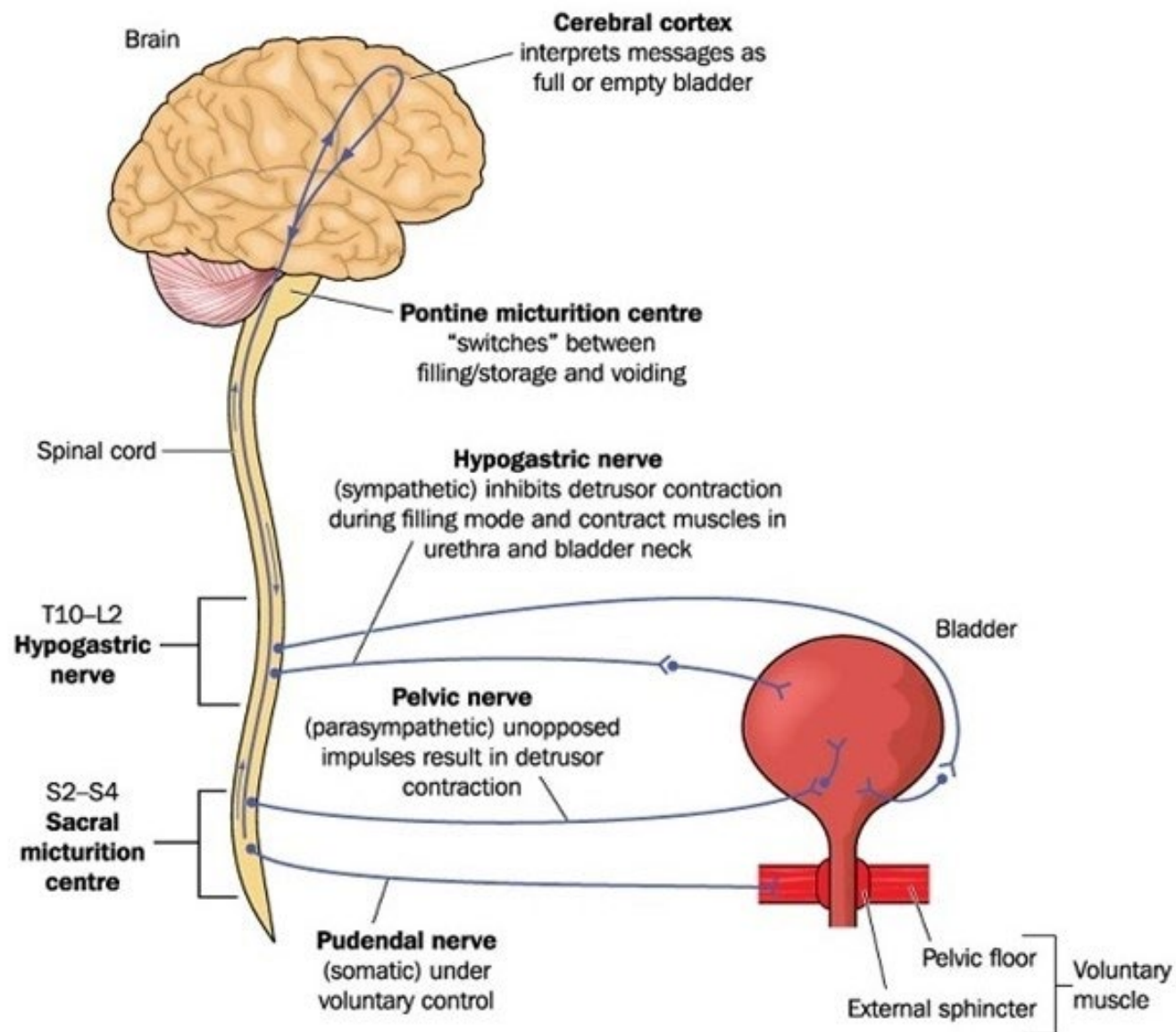
** Subject to local regulatory approval (see black box warning).

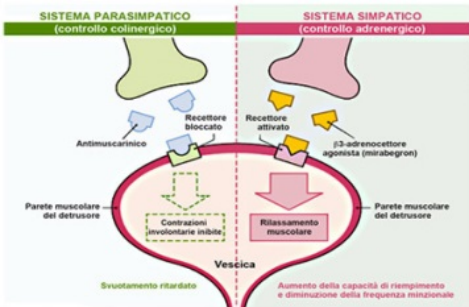
* Consider CONTINENCE PRODUCTS for temporary support during treatment











Meccanismo d'azione degli antimuscarinici e dei beta-3 agonisti

- Durante la **fase di riempimento vescicale** - in cui il muscolo detrusore dovrebbe rimanere rilassato - avviene una prevalente stimolazione del sistema nervoso simpatico (o **ortosimpatico**).
- Le terminazioni nervose ortosimpatiche rilasciano come neurotrasmettitore la **noradrenalina** che - legandosi ai recettori beta-adrenergici presenti a livello vescicale - determina un incremento delle concentrazioni cellulari di *adenosina monofosfato ciclico* (cAMP) che è direttamente responsabile del **rilassamento** del muscolo detrusore.





Meccanismo d'azione degli antimuscarinici e dei beta-3 agonisti

- Al contrario, durante la fase di svuotamento della vescica prevale la stimolazione del fibre nervose **parasimpatiche**
- L'**aceticolina** rilasciata dalla terminazioni nervose parasimpatiche si lega ai **recettori muscarinici M2 e M3 vescicali** ed è in grado di ridurre la quantità di cAMP cellulare, determinando la contrazione del muscolo detrusore.

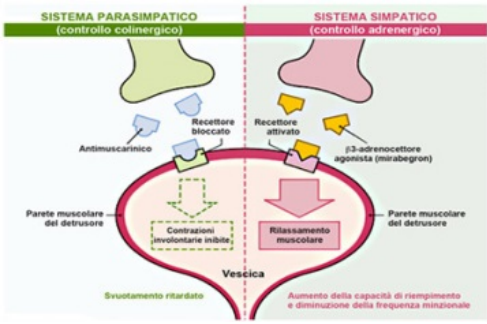




Meccanismo d'azione degli antimuscarinici e dei beta-3 agonisti

- Per favorire il rilassamento del detrusore possiamo quindi utilizzare farmaci
 - con azione beta-adrenergica
 - con azione anticolinergica

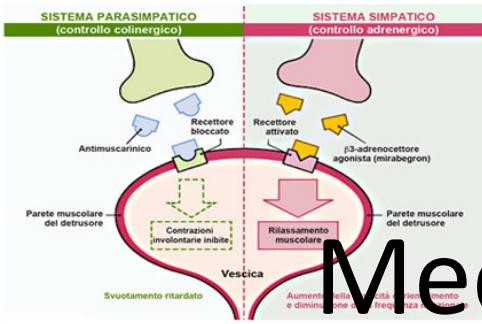




Meccanismo d'azione degli antimuscarinici

- I farmaci **antimuscarinici** agiscono **bloccando l'azione dell'acetilcolina sui recettori muscarinici** e riducono pertanto le contrazioni del detrusore vescicale.
- Effetti collaterali:
 - indebolimento della contrazione del detrusore durante lo svuotamento
 - costipazione, secchezza della bocca e disturbi della vista (glaucoma o sintomi urinari prevalentemente ostruttivi – controindicazioni)





Meccanismo d'azione dei beta-3 agonisti

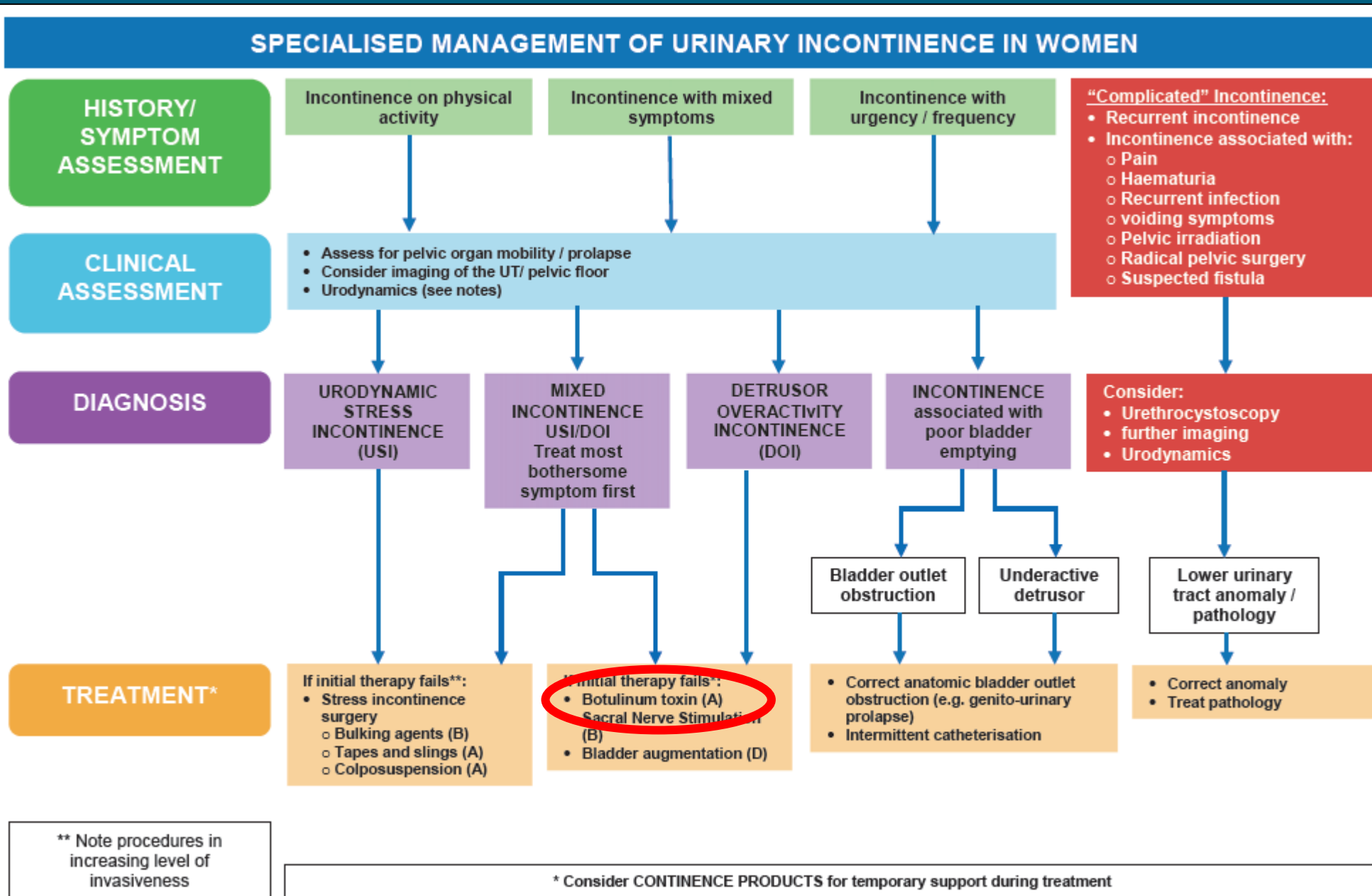
- Agonisti selettivi dei **recettori beta 3 adrenergici**: a livello vescicale sono presenti 3 tipi di recettori beta adrenergici: beta 1, 2 e 3. Tra questi i recettori Beta-3 costituiscono il 95% del totale e sono localizzati sulle cellule muscolari lisce del detrusore, sulle cellule uroteliali e su cellule interstiziali.
- Gli agonisti selettivi dei recettori Beta-3, legandosi selettivamente ai recettori beta 3, inducono il rilassamento del detrusore mediante l'aumento della concentrazione intracellulare del cAMP.
- Minimi effetti collaterali sistemici dovuti alla stimolazione dei recettori beta 1 e 2, maggiormente presenti a livello circolatorio, cardiaco e polmonare

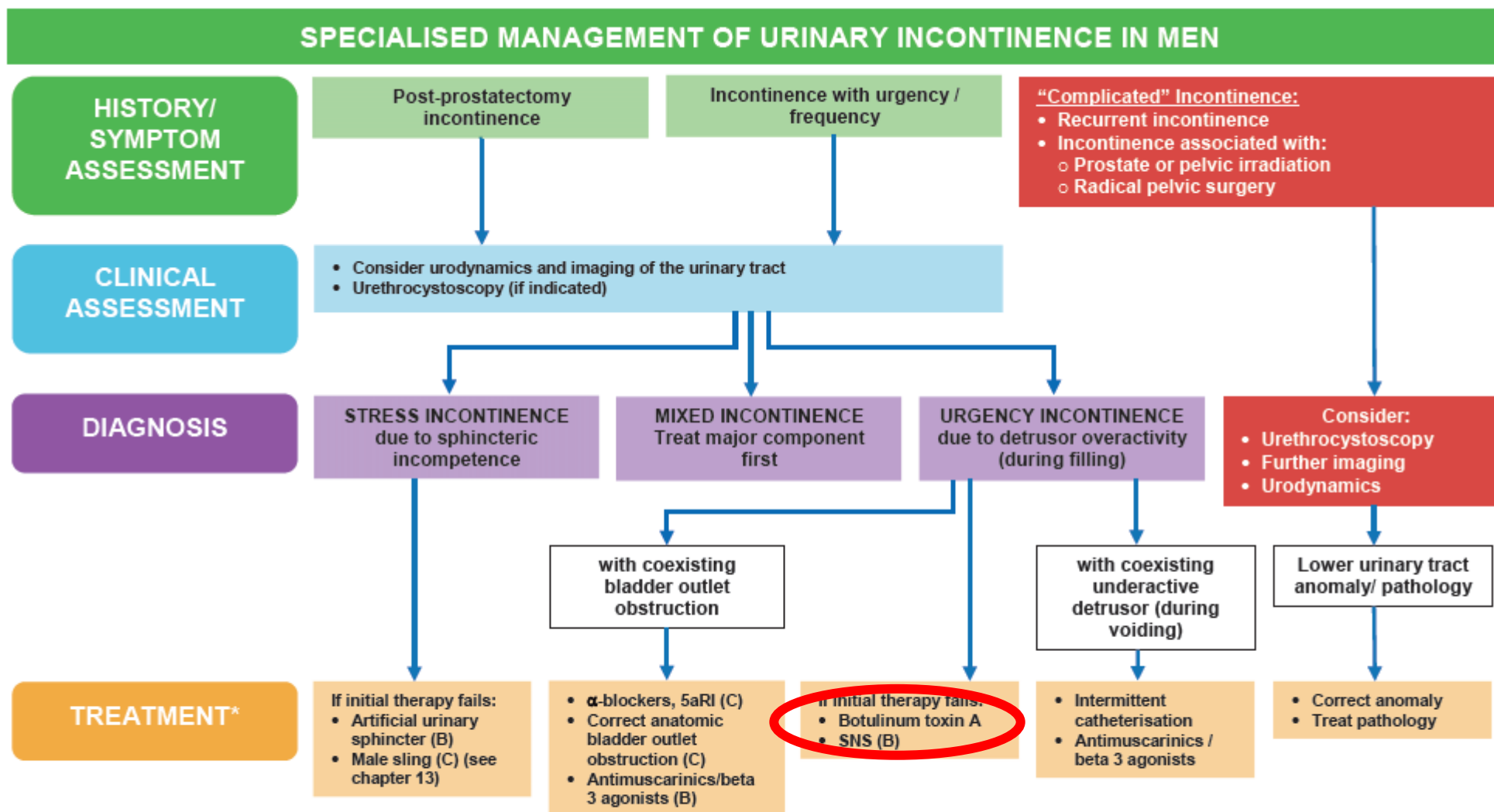




E quando non è sufficiente???









La tossina botulinica





- <https://m.infox.ru/news/281/209051-krasota-strasnaa-sila-ili-3-veskie-priciny-otkazatsa-ot-desevyh-ukolov-molodosti>





- <https://www.medicinaplasticaroma.it/medicina-estetica/corpo/trattamento-iperidrosi/>







Review

Botulinum toxin A for the Treatment of Overactive Bladder

Po-Fan Hsieh ¹, Hung-Chieh Chiu ¹, Kuan-Chieh Chen ², Chao-Hsiang Chang ^{1,3} and Eric Chieh-Lung Chou ^{1,3,*}

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Keywords: botulinum toxin A; overactive bladder; detrusor overactivity

1. Introduction

Overactive bladder (OAB) is a clinical diagnosis defined by the International Continence Society as “urgency, with or without urge incontinence, usually with frequency and nocturia” [1]. The overall prevalence of OAB was 12%–17% in the general population and it poses a great impact on daily activities and quality of life (QOL) [2–5]. In contrast to the clinical diagnosis of OAB, detrusor overactivity (DO) is a urodynamic observation characterized by involuntary detrusor contraction during the filling phase which may be spontaneous or provoked [1]. There is a substantial overlapping between OAB and DO, and DO is generally regarded as a major underlying physiology of OAB [6]. The standard treatment for OAB starts with patient education and behavior therapies. Among pharmacologic treatments, antimuscarinic agents are widely used but associated with adverse effects such as dry mouth, constipation, and blurred vision [7,8]. Due to the bothering side effects, the long-term adherence was consequently very low for antimuscarinic agents (12.0% to 39.4% at 12 months and 0% to 16% at 36 months) [9]. Beta3-adrenoceptor agonist is an alternative to antimuscarinic

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- In contrast to the clinical diagnosis of OAB, **detrusor overactivity (DO)** is a **urodynamic observation** characterized by involuntary detrusor contraction during the filling phase which may be spontaneous or provoked [1].





Review

Botulinum toxin A for the Treatment of Overactive Bladder

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- Among **pharmacologic treatments**, **antimuscarinic agents** are widely used but associated with adverse effects such as **dry mouth, constipation, and blurred vision** [7,8].
- Due to the **bothering side effects**, the long-term **adherence** was consequently very low for antimuscarinic agents (**12.0% to 39.4%** at 12 months and **0% to 16%** at 36 months) [9].
- **Beta3-adrenoceptor agonist** is an **alternative** to antimuscarinic agents.
- The **efficacy** was **similar** among beta3-adrenoceptor agonists and antimuscarinic agents, but beta3-adrenoceptor agonists **produce less rates of dry mouth and constipation** [7].





Review

Botulinum toxin A for the Treatment of Overactive Bladder

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- Botulinum toxin was first isolated from Clostridium botulinum by van Ermengem [10].
- There were **seven serotypes** of botulinum toxin, and botulinum toxin A (BoNT/A) was used most frequently in the urologic field.
- The efficacy of BoNT/A in treating OAB has been supported by literatures [11–13].
- Currently both **AUA and EAU** guidelines suggested that intravesical injection of BoNT/A should be offered to patients with urgency urinary incontinence (UUI) refractory to antimuscarinic and beta3-adrenoceptor agonist therapy, and the FDA approved dose was **100 U of BoNT/A for idiopathic detrusor overactivity (IDO) and 200 U for neurogenic detrusor overactivity (NDO)** [7,14].





Review

Botulinum toxin A for the Treatment of Overactive Bladder

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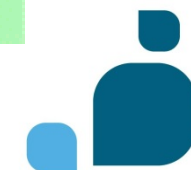
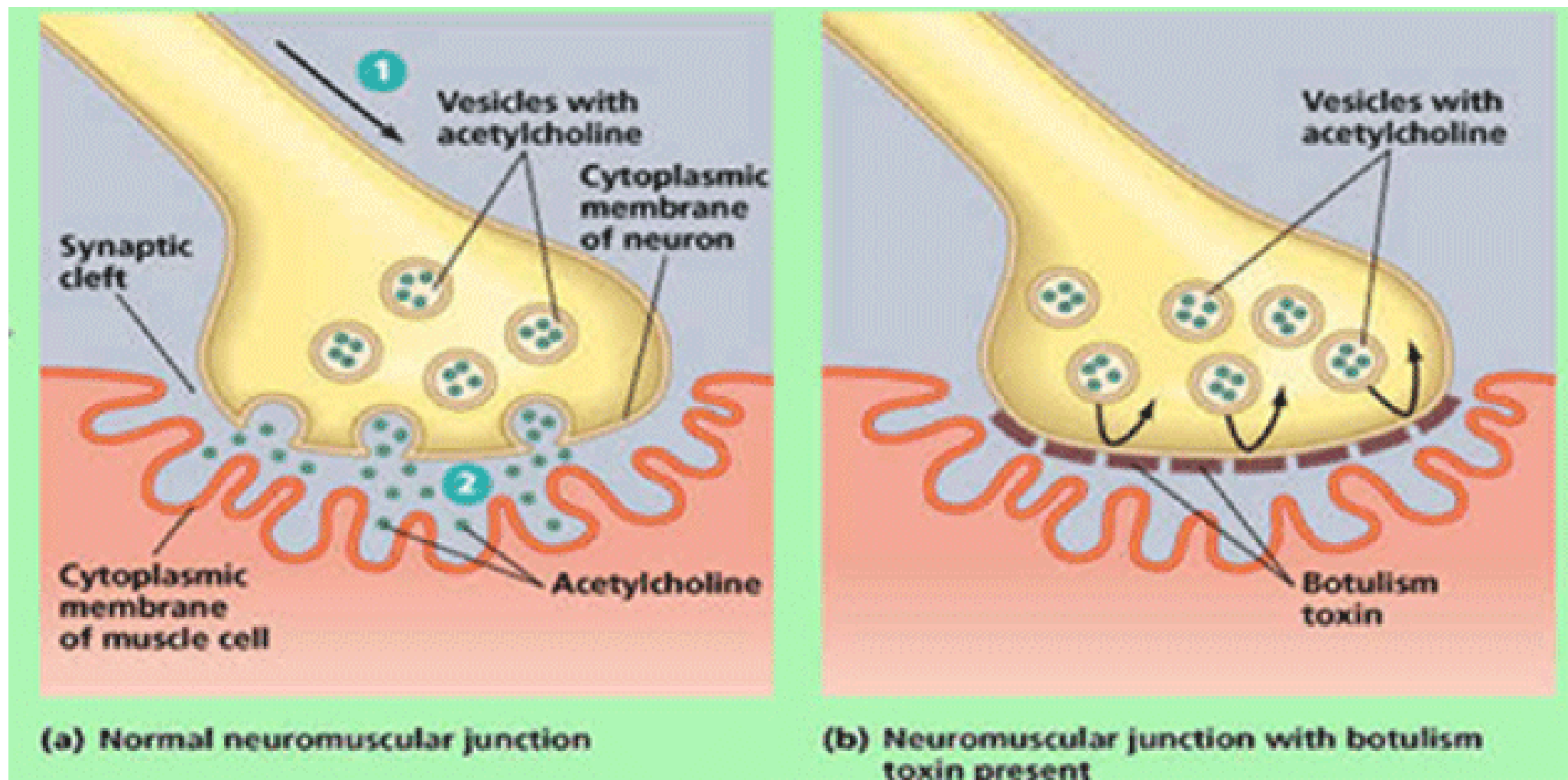
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- BoNT/A is composed of a 100 kDa heavy chain polypeptide and a 50 kDa light chain polypeptide, as is joined via a disulfide bond [15].
- The initially-proposed mechanism of BoNT/A was that by attachment of the heavy chain to the protein receptor SV2 on axon terminals, the toxin could enter the neuron by endocytosis [16]. Then the light chain cleaves synaptosomal-associated protein (25 kDa) (SNAP-25), a protein from the soluble N-ethylmaleimide-sensitive factor attachment receptor (SNARE) family.
- As a result, **the fusion of neurosecretory vesicles and release of acetylcholine(Ach) from presynaptic nerve terminals are blocked** [17]. With inhibition of Ach release, the effect on suburothelial afferent and detrusor parasympathetic nerve endings was abolished, which was similar to the action of anticholinergic agents [8,18].
- However, **emerging studies** indicated that BoNT/A also exerts complex inhibitory effects on other neurotransmitters, neuropeptides, and receptors mediating neurotransmission [19].







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• ...

• ... In other words, BoNT/A works through not only localized peripheral mechanism but also a CNS effect through retrograde axonal transport.

• In summary, it was proposed that the action of BoNT/A on human overactive bladders followed a sequential mechanism [19].

• First, the immediate effect of BoNT/A is inhibition of vesicular release of Ach, ATP, and SP and the axonal expression of TRPV1 and P2X3, leading to peripheral denervation [18,30,31].

• Second, after SNAP-25 was cleaved by BoNT/A, this exocytosis inhibitor could persist for a long time (up to 40 days in a mouse model) [17].

• Third, through retrograde transport into CNS BoNT/A would result in attenuation of central sensitization, leading to further peripheral desensitization.

Table 1. Randomized controlled trials of botulinum toxin A for idiopathic detrusor overactivity.

Authors/Year	No. Patients	Injection Method	UI Episode (%Change)	Frequency (%Change)	MCC (%Change)	Pdetmax (%Change)	Urinary Retention Requiring CIC (%)	Duration of Benefit
Sahai <i>et al.</i> /2006 [33]								
Placebo	18	Intravesical injection (trigone sparing)	−18	−7	−15	−4	None	NA
Botox 200 U	16		−70	−49	+72	−59	37.5%	>24 weeks
Brubaker <i>et al.</i> /2008 [34]								
Placebo	15	Intravesical injection (trigone sparing)	−5	NA	NA	NA	None	62 days
Botox 200 U	28		−75	NA	NA	NA	43%	373 days
Flynn <i>et al.</i> /2009 [36]								
Placebo	7	Intravesical injection (trigone sparing)	9.3	−6.8	NA	NA	None	NA
Botox 200 U or 300 U	15		−57.5	−12.2	NA	NA	7	>6 weeks
Dmochowski <i>et al.</i> /2010 [39]								
Placebo	44	Intravesical injection (trigone sparing)	−17.4	NA	NA	NA	0	NA
Botox 50 U	56		−20.7	NA	NA	NA	5.4	18 weeks
Botox 100 U	55		−18.4	NA	NA	NA	10.9	24 weeks
Botox 150 U	50		−23	NA	NA	NA	20	36 weeks
Botox 200 U	52		−19.6	NA	NA	NA	21.2	36 weeks
Botox 300 U	55		−19.4	NA	NA	NA	16.4	36 weeks
Dowson <i>et al.</i> /2010 [37]								
Placebo	13	Intravesical injection (trigone sparing)	45	0	0	NA	0	12 weeks
Botox 100 U	10		−8.3	−4.5	+40.9	NA	30	12 weeks
Rovner <i>et al.</i> /2011 [40]								
Placebo	44	Intravesical injection (trigone sparing)	−51.7	−15.6	+4.7	−10.7	0	NA
Botox 50 U	57		−69.9	−23.9	+8	0	3.6	12 weeks
Botox 100 U	54		−64.6	−26.4	+15.1	+24	9.1	12 weeks
Botox 150 U	49		−89.6	−14.4	+19.3	+3.4	12.7	36 weeks
Botox 200 U	53		−80	−24.8	+17.2	+5.5	18.2	36 weeks
Botox 300 U	56		−77.6	−27.1	+21.8	+23.1	16.4	36 weeks
Fowler <i>et al.</i> /2012 [41]								
Placebo	44	Intravesical injection (trigone sparing)	−53.5	NA	NA	NA	0	NA
Botox 50 U	57		−68.3	NA	NA	NA	14.6	12 weeks
Botox 100 U	54		−66.2	NA	NA	NA	-	24–36 weeks
Botox 150 U	49		−81.3	NA	NA	NA	-	24–36 weeks
Botox 200 U	53		−73	NA	NA	NA	-	24–36 weeks
Botox 300 U	56		−72.3	NA	NA	NA	-	24–36 weeks

Table 1. Cont.

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Denys <i>et al.</i> /2012 [42]								
Placebo	31	Intravesical injection (trigone sparing)	29% had UUI reduction > 50%		+10.5	−49.3	3.2	NA
Botox 50 U	23		37% had UUI reduction > 50%	NA	+8	−51.2	13	6 months
Botox 100 U	23		65% had UUI reduction > 50%	NA	+8	−36.5	4.3	6 months
Botox 150 U	30		56% had UUI reduction > 50%	NA	+9.5	−49.5	13.3	6 months
Tinello <i>et al.</i> /2012 [35]								
Placebo	118	Intravesical injection (trigone sparing)	−3.2	−9.6	NA	NA	4	NA
Botox 200 U	122		−73.1	−19.1	NA	NA	16	6 months
Chapple <i>et al.</i> /2013 [43]								
Placebo	271	Intravesical injection (trigone sparing)	−13.9	−6	NA	NA	0.7	NA
Botox 100 U	277		−53.2	−19.7	NA	NA	6.9	12 weeks
Nitti <i>et al.</i> /2013 [38]								
Placebo	277	Intravesical injection (trigone sparing)	−17.1	4.1	NA	NA	0.4	NA
Botox 100 U	280		−48.2	−16.9	NA	NA	5.4	12 weeks

Table 2. Randomized controlled trials of botulinum toxin A for neurogenic detrusor overactivity.

Authors/Year	No. of Patients	Patients Type	Injection Method	Continence (%) / UI Episode (%Change)	MCC (%Change)	Pdetmax (%Change)	Urinary Retention Requiring CIC (%)	Duration of Benefit
Schurch <i>et al.</i> /2005 [46]								
Placebo	21	53 SCI, 6 MS	Intravesical injection (trigone sparing)	24/−10	+18	−13	-	NA
Botox 200 U	19			71/−58	+85	−59	-	>24 weeks
Botox 300 U	19			53/−54	+63	−56	-	>24 weeks
Cruz <i>et al.</i> /2011 [47]								
Placebo	92	121 SCI, 154 MS	Intravesical injection (trigone sparing)	7.6/−36	+3	+15	12	13.1 week
Botox 200 U	92			38.0/−67	+64	−55	30	42.1 week
Botox 300 U	91			39.6/−62	+64	−64	42	42.1 week
Herschorn <i>et al.</i> /2011 [49]								
Placebo	29	38 SCI, 19 MS	Intravesical injection (trigone sparing)	NA/0	−21.9	+4	-	NA
Botox 300 U	29			NA/−25	+21.5	+49.1	-	9 months
Ginsberg <i>et al.</i> /2012 [48]								
Placebo	149	189 SCI, 227 MS	Intravesical injection (trigone sparing)	NA/−31.1	+6.3	−4.7	10	92 days
Botox 200 U	135			NA/−65	+59.9	−68.4	35	256 days
Botox 300 U	132			NA/−73	+65.6	−70.7	42	254 days



Review

Botulinum toxin A for the Treatment of Overactive Bladder

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Abstract: The standard treatment for overactive bladder starts with patient education and behavior therapies, followed by antimuscarinic agents. For patients with urgency urinary incontinence refractory to antimuscarinic therapy, currently both American Urological Association (AUA) and European Association of Urology (EAU) guidelines suggested that intravesical injection of botulinum toxin A should be offered. The mechanism of botulinum toxin A includes inhibition of vesicular release of neurotransmitters and the axonal expression of capsaicin and purinergic receptors in the suburothelium, as well as attenuation of central sensitization. Multiple randomized, placebo-controlled trials demonstrated that botulinum toxin A to be an effective treatment for patients with refractory idiopathic or neurogenic detrusor overactivity. The urinary incontinence episodes, maximum cystometric capacity, and maximum detrusor pressure were improved greater by botulinum toxin A compared to placebo. The adverse effects of botulinum toxin A, such as urinary retention and urinary tract infection, were primarily localized to the lower urinary tract. Therefore, botulinum toxin A offers an effective treatment option for patients with refractory overactive bladder.

Keywords: botulinum toxin A; overactive bladder; detrusor overactivity

1. Introduction

Overactive bladder (OAB) is a clinical diagnosis defined by the International Continence Society as “urgency, with or without urge incontinence, usually with frequency and nocturia” [1]. The overall prevalence of OAB was 12%–17% in the general population and it poses a great impact on daily activities and quality of life (QOL) [2–5]. In contrast to the clinical diagnosis of OAB, detrusor overactivity (DO) is a urodynamic observation characterized by involuntary detrusor contraction during the filling phase which may be spontaneous or provoked [1]. There is a substantial overlapping between OAB and DO, and DO is generally regarded as a major underlying physiology of OAB [6]. The standard treatment for OAB starts with patient education and behavior therapies. Among pharmacologic treatments, antimuscarinic agents are widely used but associated with adverse effects such as dry mouth, constipation, and blurred vision [7,8]. Due to the bothering side effects, the long-term adherence was consequently very low for antimuscarinic agents (12.0% to 39.4% at 12 months and 0% to 16% at 36 months) [9]. Beta3-adrenoceptor agonist is an alternative to antimuscarinic

• Adverse Events

- According the meta-analysis of BoNT/A in treating IDO patients, BoNT/A significantly increased
 - **PVR** (32.77 vs. 2.01, SMD = 31.73),
 - proportions of **urinary tract infection** (UTI) (19.69% and 5.94%, OR = 3.89), and proportions of **CIC** (8.41% and 0.46%, OR = 13.39) versus placebo [12].
- In treating NDO patients, BoNT/A also led to a higher risk of UTI (relative risk [RR] = 1.48), hematuria (RR = 1.81), and urinary retention (RR = 5.87) requiring catheterization [13].
- The effect of increased post-void residual volume (**PVR**) was **dose dependent**, and doses **>150U** was found to be more commonly associated with **PVR > 200 mL** [39,40].
- It was reported that age >61 years, low maximum flow rate, low voiding efficiency (a percentage of the voided volume compared to the prevoid bladder volume <90%), and large PVR at baseline were risk factors for these adverse events [51].
- The effect of increased PVR peaked by 2 weeks following BoNT/A injection, with a gradual decrease thereafter [39,49].
- For **urinary retention requiring catheterization**, the duration was **6 weeks** or less in more than half of the patients [12]. On the other hand, a meta-analysis showed there was no significant difference between trigonal and extratrighonal BoNT/A injection in terms of adverse events [52].



Review

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• Finally, these results indicated that:

- the adverse events of BoNT/A were **primarily localized to the urinary tract**, in contrast to the systemic effects of anticholinergic agents.
- Although **muscle weakness or hyposthenia** has been reported after BoNT/A injection, the incidence of systemic adverse events was **rare and the duration was transient** [54,55].





Come si somministra la tossina botulinica in vescica

Angelo Di Santo



M.G. VANNINI
OSPEDALE RELIGIOSO
CLASSIFICATO ACCREDITATO
ISTITUTO FIGLIE DI SAN CAMILLO

Preparazione

- **PROCEDURA AMBULATORIALE!!!**

- Urinocoltura negativa/in terapia
- Profilassia antibiotica



Preparazione

- Vescica vuota



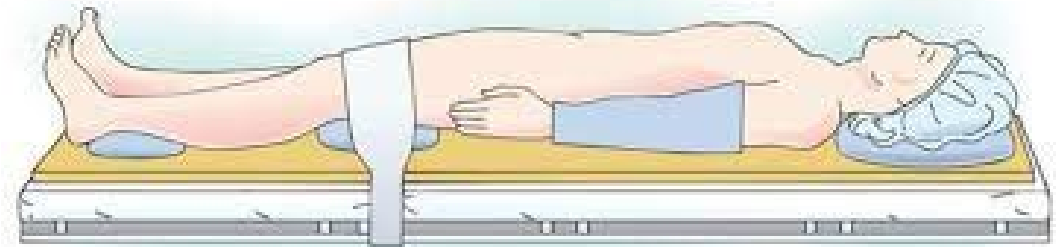
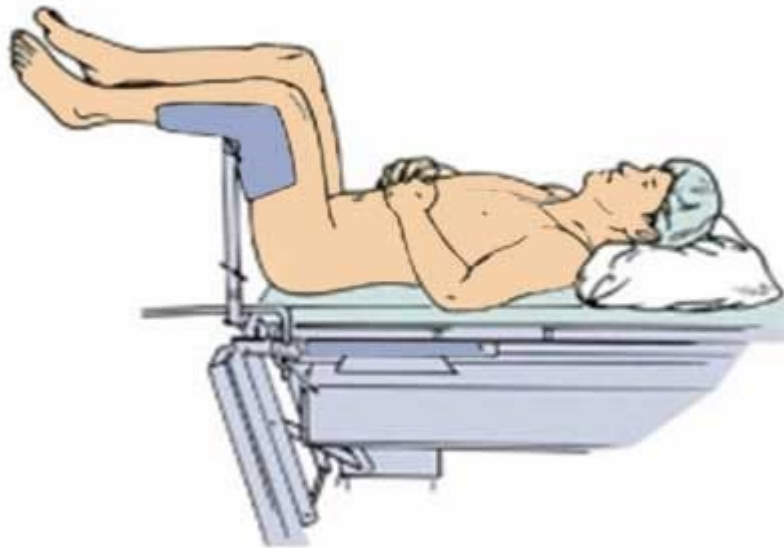
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- Auto-cateterismo intermittente



Preparazione

- Posizione litotomica/supina (cistoscopia rigida/flessibile), campo sterile



Preparazione

- Anestesia?



Procedura iniettiva con cistoscopio flessibile

IT/BTOX0309/14



INQUADRAMENTO SINTETICO DEL PROBLEMA

L'incontinenza urinaria e l'incontinenza fecale rappresentano condizioni cliniche che compromettono in misura rilevante la qualità della vita di chi ne è affetto, limitandone le attività individuali, portando ad una restrizione della partecipazione alla vita sociale ed influenzandone pesantemente l'immagine di sé. Nel caso di persone non autosufficienti l'incontinenza aumenta significativamente il carico di lavoro per i caregivers. La patologia inoltre comporta il rischio di insorgenza di complicanze quali infezioni urinarie e lesioni cutanee; nei casi più gravi, come nei soggetti affetti da patologie neurologiche, l'incontinenza urinaria rappresenta l'espressione clinica di una disfunzione neurogena a carico dell'apparato vescico-uretrale che può essere causa di morte o di gravi complicanze.

L'incontinenza presenta una prevalenza nel contesto della popolazione generale decisamente elevata e rappresenta inoltre una delle patologie con maggiori spese per il SSN e per il cittadino, per i costi diretti ed indiretti che comporta.

LE MAGGIORI CRITICITÀ

Si registrano una serie di problematiche, molte volte segnalate ma che per motivazioni diverse non hanno mai trovato una adeguata soluzione.

In sintesi si segnalano le seguenti maggiori criticità:

- Allo stato attuale non è possibile garantire pari opportunità di accesso alle cure ed uniformità degli interventi socio-sanitari, non essendo stata attivata in tutte le Regioni una Rete integrata di centri per la prevenzione, diagnosi e cura dell'incontinenza. Si segnala inoltre la carenza, anche nelle reti attivate ed in quelle in via di attivazione, dei Centri di Neuro-Urologia, delle Unità Pelviche e dei Centri Pediatrici. La creazione della Rete dei Centri consentirebbe anche di realizzare l'obiettivo di implementare percorsi di cura conseguenti a PDTA basati sulle evidenze e sulle Linee Guida internazionali, con l'effetto di indurre l'appropriatezza diagnostica, terapeutica e gestionale. Consentirebbe inoltre di affrontare un'altra criticità rappresentata da una non adeguata interazione tra il territorio (Cure Primarie) e l'ambito specialistico per una gestione integrata del problema

Altro elemento di disomogeneità sul territorio nazionale riguarda l'argomento della non razionale distribuzione dei dispositivi chirurgici complessi e l'argomento dei dispositivi medici monouso (pannoloni e cateteri), in particolare per quanto riguarda l'appropriatezza prescrittiva, l'acquisto e la distribuzione degli ausili

- Grave carenza dei Centri di Riabilitazione, a fronte di una presenza forte ed abbastanza omogeneamente distribuita sul territorio nazionale dei Centri di riferimento Urologico, Ginecologico e Coloproctologico

- Nonostante l'attivazione da parte della Presidenza del Consiglio dei Ministri e del Ministero della Salute della "Giornata nazionale per la prevenzione e la cura dell'incontinenza", che ogni anno si svolge il 28 giugno, non sono mai stati attivati adeguati piani di comunicazione per la sensibilizzazione dell'opinione pubblica e delle istituzioni sulle problematiche connesse alle difficoltà provocate dalla incontinenza ed alla rimozione di quegli stereotipi che rendono il disagio un problema della persona e non della collettività; e soprattutto non è sufficientemente reso noto il dato di una possibile risoluzione del problema con le terapie oggi a disposizione. Affrontare il problema rappresenterebbe tra l'altro anche il modo migliore per attuare una politica di razionalizzazione della spesa.



*Piccoli incontinenti
crescono...*

GRAZIE!





GRAZIE
PER L'ATTENZIONE

