Nottingham University Hospitals NHS
NHS Trust

How do I manage a patient with intractable daytime wetting:

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Nottingham Children's Hospital

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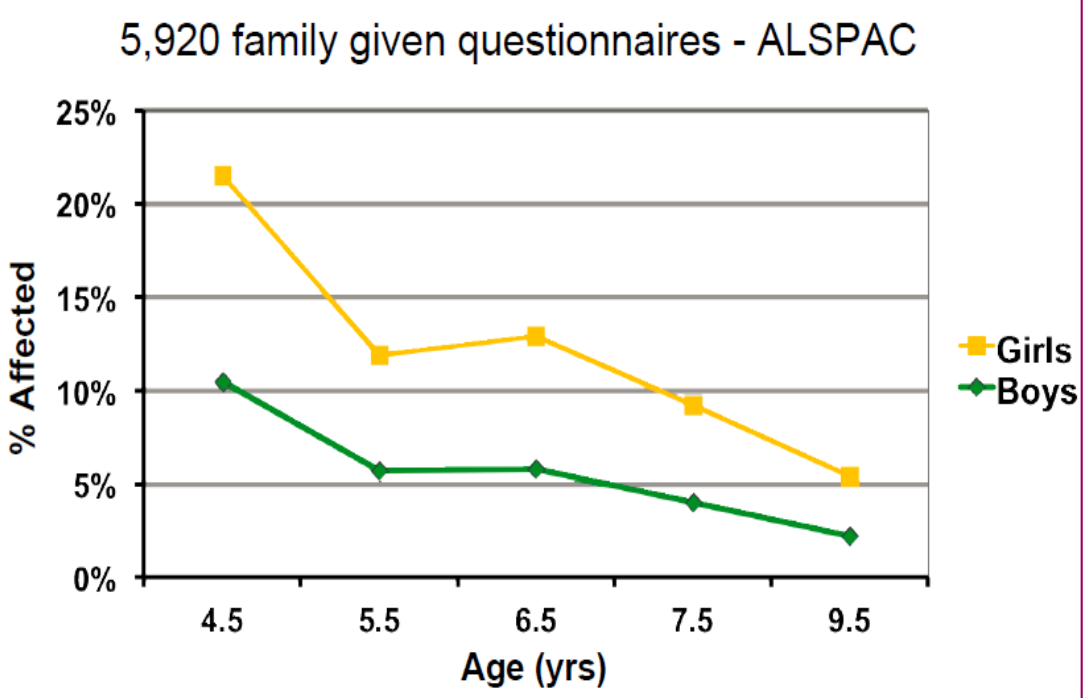
Natural History of Daytime Incontinence in Avon, UK



Heron J, et al: J Urol 179: 1970, 2008

Of 107 children aged 11-12 with day-wetting

91 (85%) were dry at 15-16 yr

Swithinbank et al BJU 1998

In 3 long-term outcome studies of treatment 60-75% were dry 3-5yr later, many still on treatment….

What I intend to discuss…

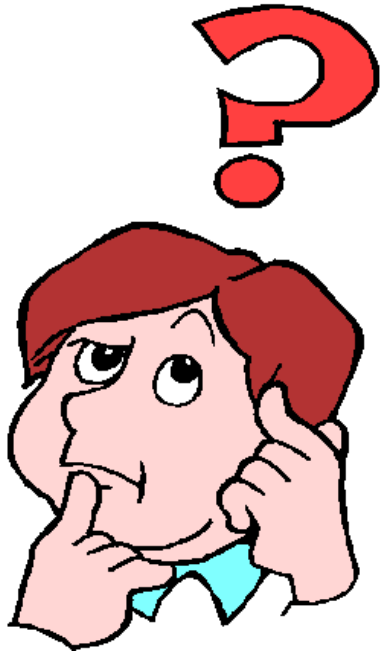
- Why is wetting intractable
- Diagnoses
- My Strategy
  - Assessment
  - Management
- Medications for Overactive Bladder (OAB)
- Medication for Incomplete Bladder emptying

I'm not discussing

- Bedwetting
- Antibiotics
- Laxatives
- Neurogenic Bladder
- Plumbing Problems
- Non pharmacological treatments

Why is the wetting intractable?

- Plumbing problem
- Neurogenic Bladder
- Psycho-Social, Behavioural, Neurodevelopmental, ADHD & ASD
- Non adherence & therapeutic relationship!
- Child abuse
- Wrong diagnosis / treatment
- ***Selection…***



Diagnosis & patterns of daytime incontinence

Symptom	Functional Disturbance	Pathology
Urge incontinence	Overactive bladder	Detrusor overactivity – functional or urological /neurogenic
Giggle wetting	Normal OAB Giggle micturition Dysfunctional voiding Underactive bladder	Depends on associated symptoms
Post micturation dribble	Normal or Vaginal reflux of urine	Normal, Vaginal reflux of urine
Stress (e.g with cough, sneeze, exertion)	Dysfunctional voiding, Underactive bladder, OAB	Dysfunctional voiding, Underactive bladder, OAB +/- Neurogenic, Urological
Continuous dribble	Ectopic ureter	Ectopic ureter
Unaware	Anything but Normal or OAB commonest!	Anything including Urological / neurogenic

Assessment

History

Voiding, Storage, Bowels, Co-morbidities, Psycho-social, Developmental, Attitudes, Values & Behaviours. *Variability of symptoms*

Examination

General + Abdomen, Bladder, Spine, Reflexes, BP, Ext Genitalia?

Basic Investigations

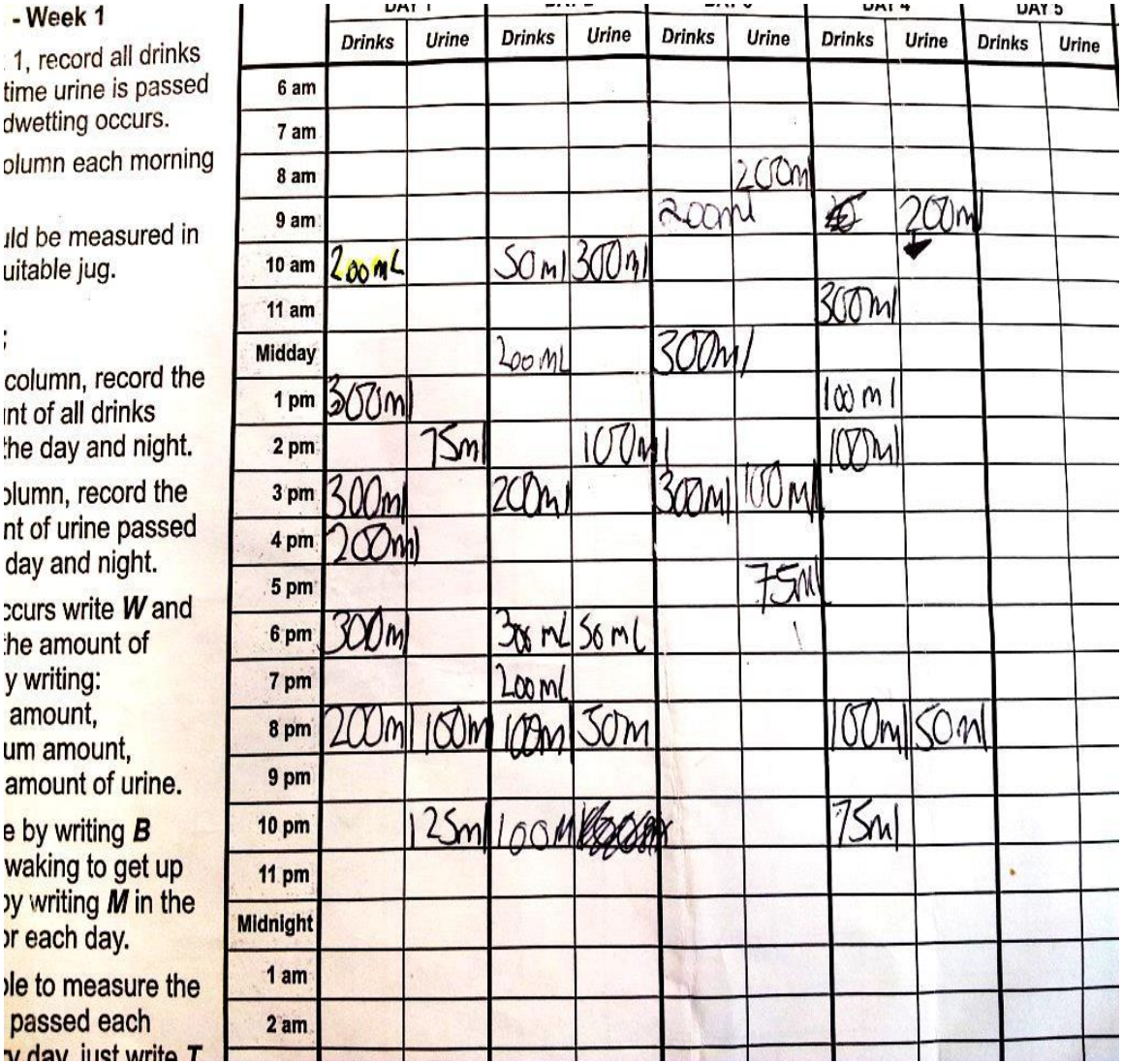
Urinalysis, Freq/Vol chart, Stool Chart,

Intermediate Investigations

Bladder Scan, Uroflow, Renal tract USS

Invasive Investigations

MCUG, Urodynamics, MRI Spine..



- Week 1

1, record all drinks
time urine is passed
dwetting occurs.

olumn each morning

uld be measured in
uitable jug.

column, record the
nt of all drinks
he day and night.

olumn, record the
nt of urine passed
day and night.

ccurs write ***W*** and
he amount of
y writing:
amount,
um amount,
amount of urine.

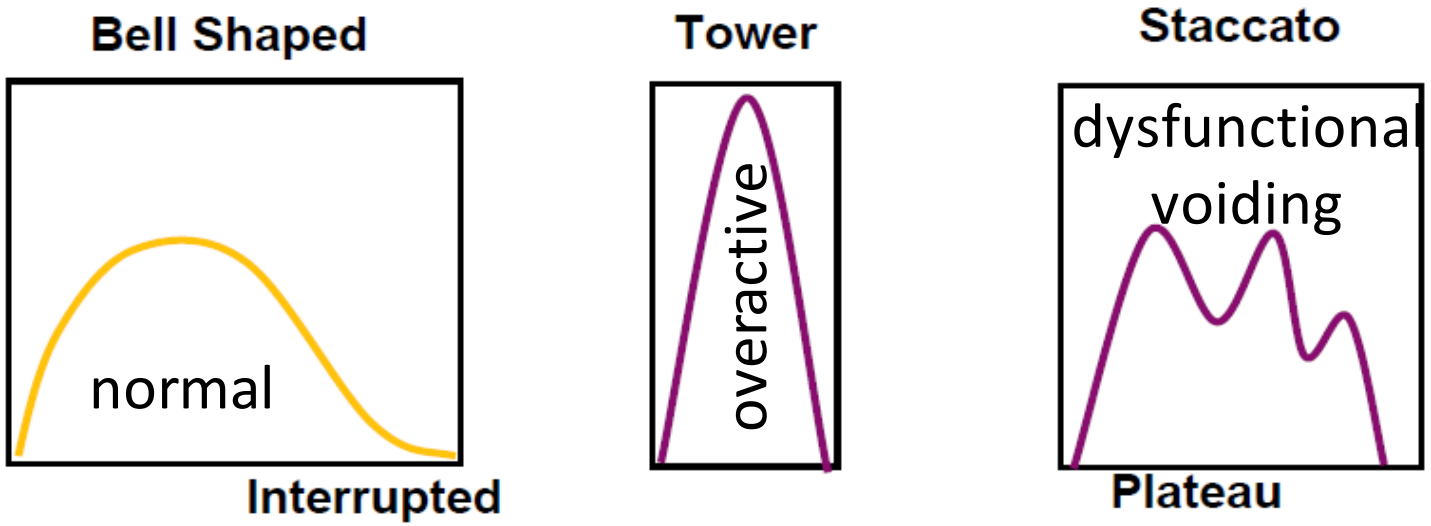
e by writing ***B***
waking to get up
y writing ***M*** in the
r each day.

le to measure the
passed each
y day, just write ***T***

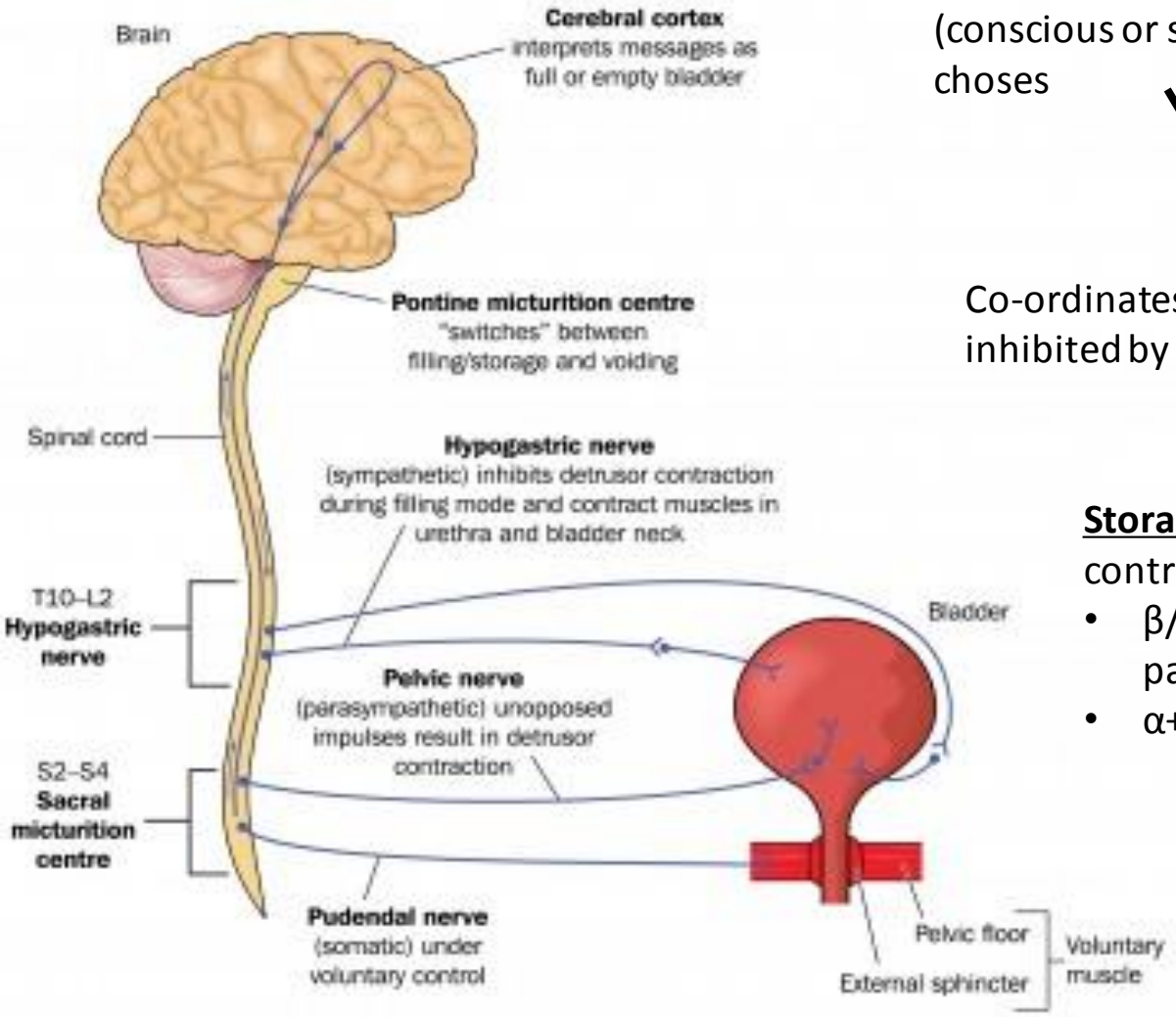
	DAY 1		DAY 2		DAY 3		DAY 4		DAY 5	
	Drinks	Urine	Drinks	Urine	Drinks	Urine	Drinks	Urine	Drinks	Urine
6 am										
7 am										
8 am						200ml				
9 am					200ml			200ml		
10 am	200mL		50ml	300ml						
11 am							300ml			
Midday			200mL		300ml					
1 pm	300ml						100ml			
2 pm		75ml		100ml			100ml			
3 pm	300ml		200ml		300ml	100ml				
4 pm	200ml									
5 pm						75ml				
6 pm	300ml		300mL	50mL						
7 pm			200mL							
8 pm	200ml	100ml	100ml	50ml			100ml	50ml		
9 pm										
10 pm		125ml	100ml				75ml			
11 pm										
Midnight										
1 am										
2 am										

- Avoid over interpretation!
- Need 2-3 days to be representative
- Freq = 4-7/d
- EBC= 30 x (Age+1)
- MVV = 75% EBC
- Ignore first morning wee
- If you don't drink you wont pee much!

Flow Rate Examples



Neveus T, et al: J Urol 176: 314-24, 2006
Kamenatsu A, et al: J Urol 184: 1674, 2010



The Master control – inhibits voiding (conscious or subconscious) until it choses

Co-ordinates micturition - inhibited by cortex

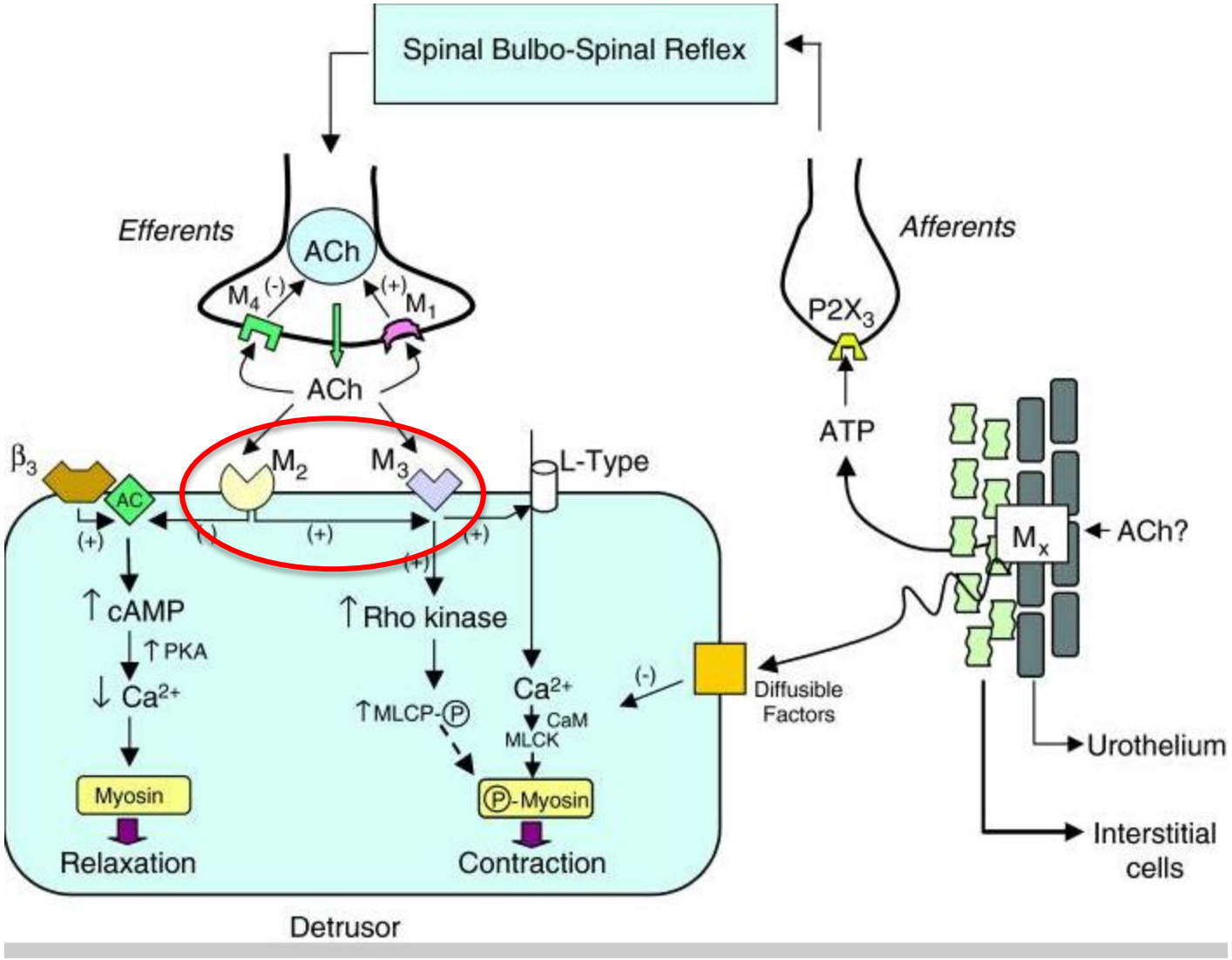
Storage/Filling – under SYMPATHETIC control:

- β/ β3+ suppresses detrusor & parasymp/muscarinic/cholinergic
- α+ stimulates internal sphincter

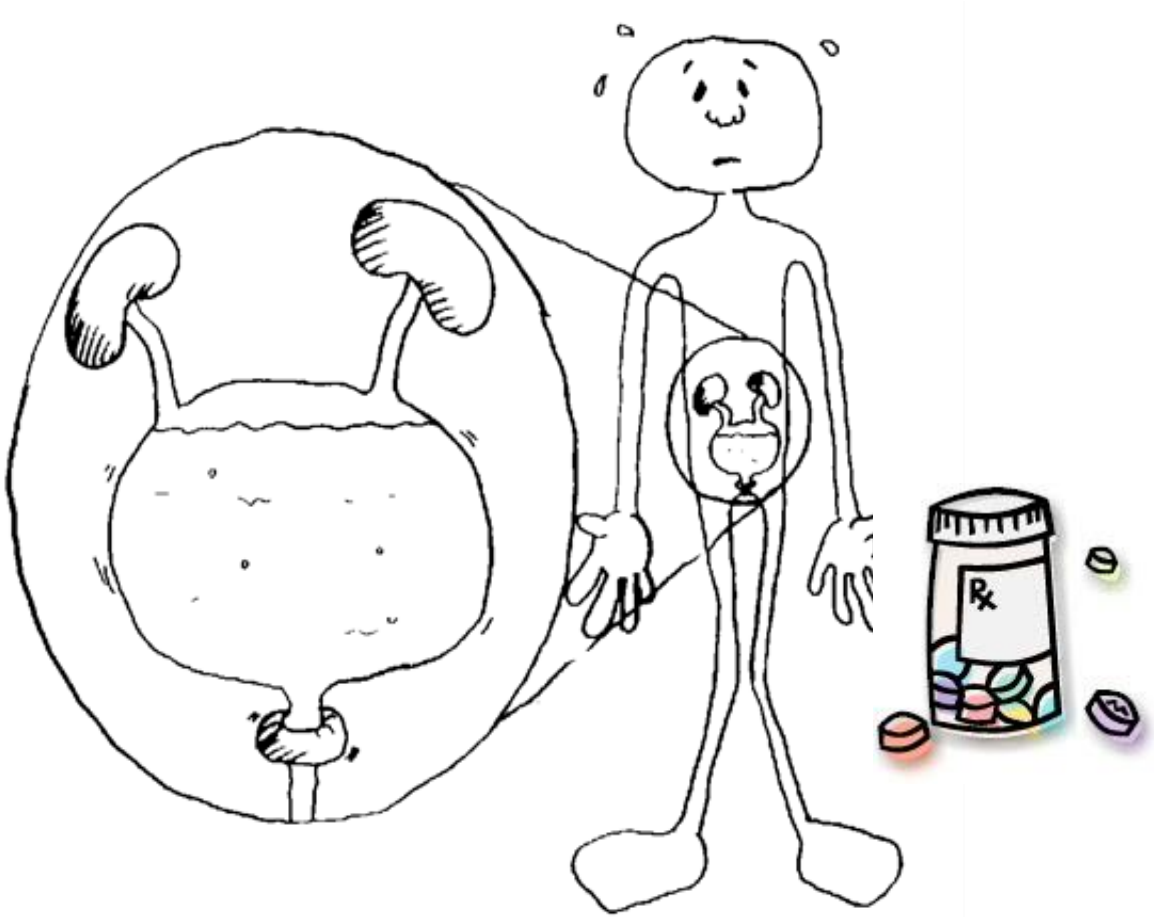
Voiding/Micturition – by SYMPATHETIC inhibition –

- α- relaxes internal sphincter
- release of parasymp/muscarinic/cholinergic stimulation ➡ detrusor contraction

Muscarinic receptor subtypes in the bladder



Drugs for Bladder Disorders



Drugs that might be used for incontinence

Category	Drug	Mechanism	Condition
Anticholinergics	Oxybutinin + Numerous others	Inhibit detrusor contraction	OAB
α agonist	Pseudoephedrine Midodrine	Increase bladder outlet resistance	OAB Stress Inc
α blocker	Doxazocin + others	Decrease bladder outlet resistance	Prostate Dysf Void?
B3 agonist	**Mirabegron** Solabegron	Suppresses detrusor both directly & by inhibiting muscarinic stimulation	OAB
CNS stimulant	Methylphenidate	CNS stimulation suppresses micturition reflex?	Giggle micturition
SSRI/SNRI	Duloxetine	inhibits serotonin and norepinephrine reuptake at spinal level increases striated muscle tone in sphincter	Stress incontinence
Tricyclics	Imipramine	? CNS sympathetic agonist plus weak anticholinergic inhibit detrusor	OAB (NE)
Others	Antibiotics Desmopressin	UTI Reduce bladder filling!	

Treatment of Overactive Bladder

Drink enough to avoid dehydration

Caffeine avoidance

Treat/prevent constipation

Treat/prevent symptomatic UTIs

Regular or timed voiding

- Reminder alarm

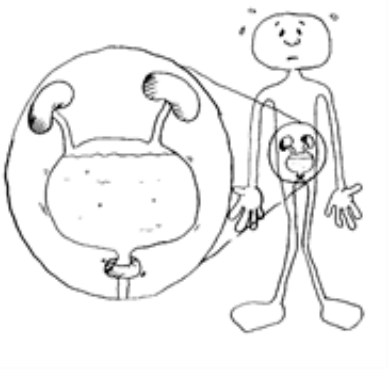
Anticholinergics

β3 agonist? (Mirabegron)

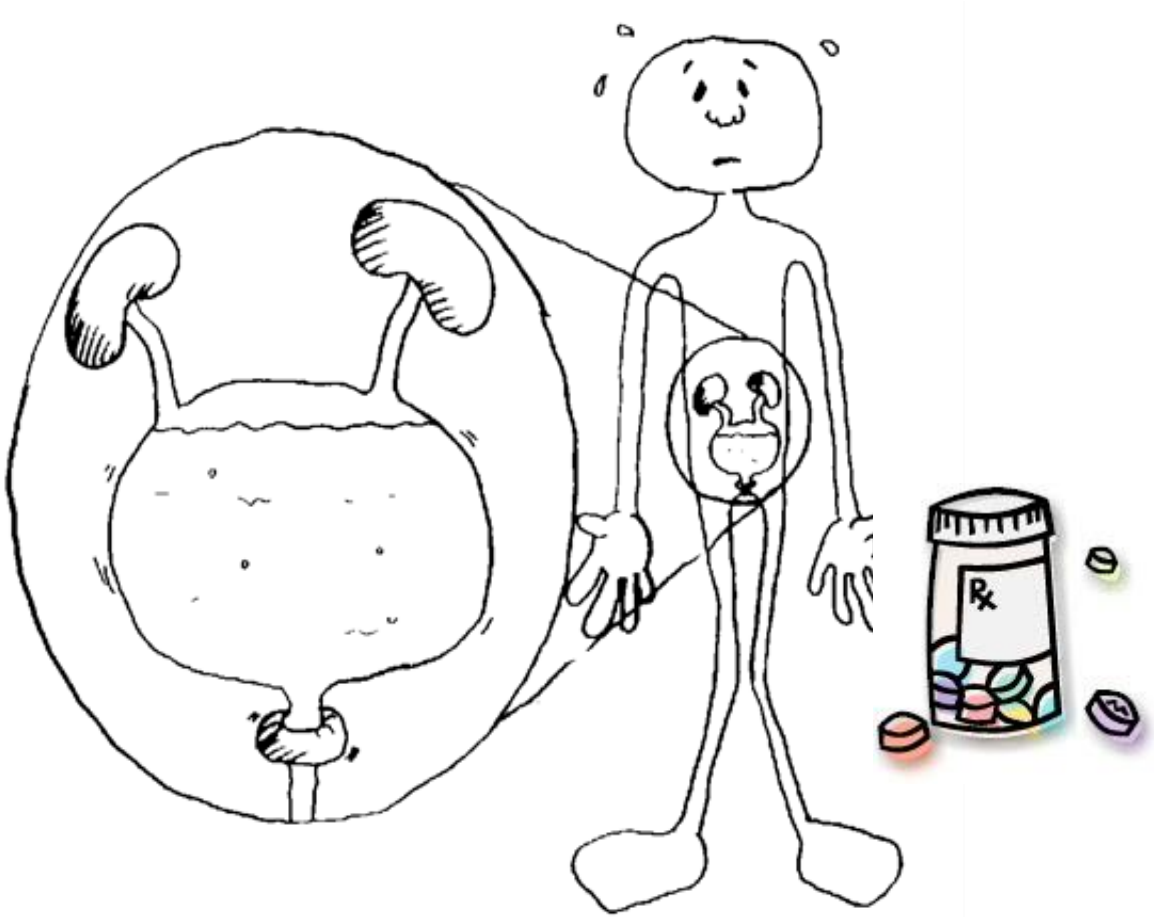
Neuromodulation (sacral/tibial nerve)?

Botulinum Toxin

Bladder Augmentation



Drugs for Overactive Bladder



Comparison of Anticholinergics for OAB

	Pharmacology	Significant Features
Oxybutinin	Non selective antagonist. Direct smooth muscle action Available as immediate release (tds), slow release (od) & transdermal (od)	Dry mouth common Confusion (in elderly) with short acting Licensed for children over 5yr NICE 1st line (OAB Adult female)
Tolterodine	Non selective, short acting (bd), slow release (od)	Fewer A/E? BNFC listed but not licenced NICE 1st line (OAB Adult female)
Propiverine	Non selective, short acting (bd)	RCT shows effectiveness in children with OAB! Not licensed for children
Solifenacin	Some M2&3 selectivity, long acting (od)	May be more effective Much "Expert use" in UK Not licensed in children
Darifenacin	M3 selective ++, long acting (od)	May be more effective (adult) NICE 2nd line (OAB adult female) Not licensed
Trospium	Non selective, short acting (bd) Doesn't cross BBB	Fewer CNS effects Not licensed

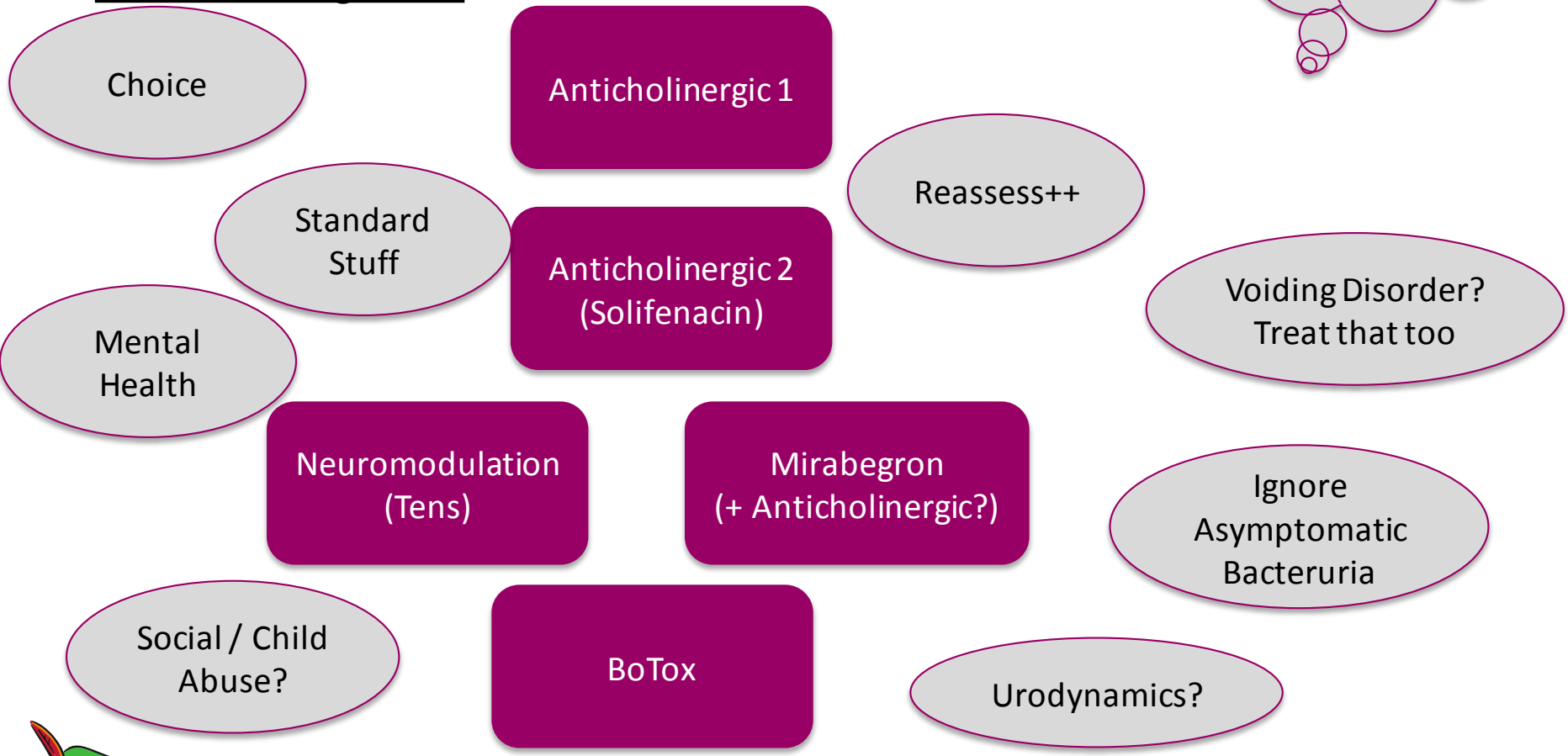
Mirabegron (Betmiga)

- A β3 agonist – suppresses detrusor and augments the sympathetic inhibition of cholinergic receptors
- Efficacy similar to anticholinergics
- NICE TA290 (2013) - an option for adults in whom antimuscarinic drugs are ineffective, or have unacceptable side effects
- MHRA alert 2015 – severe hypertension
- Anecdotal use in children…

Personal Practice – Intractable OAB

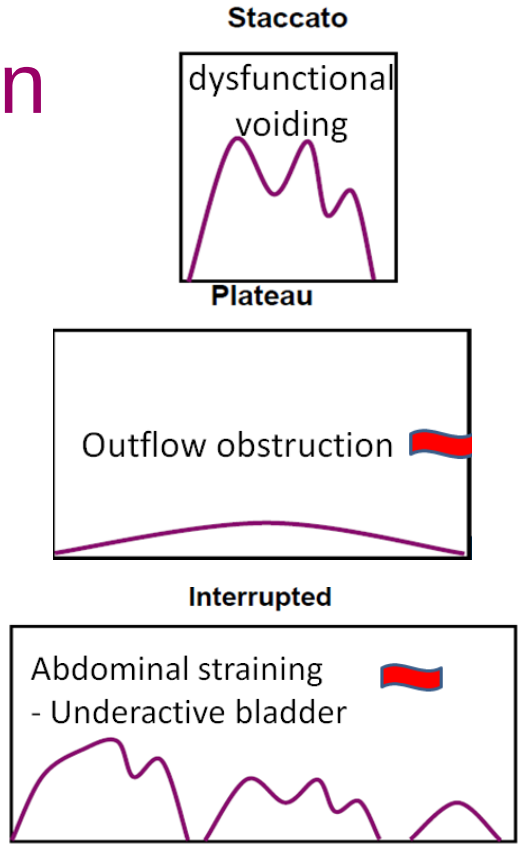
Usually had a lot of Rx already – don't repeat!

Clinical Diagnosis



α Blockers for voiding dysfunction

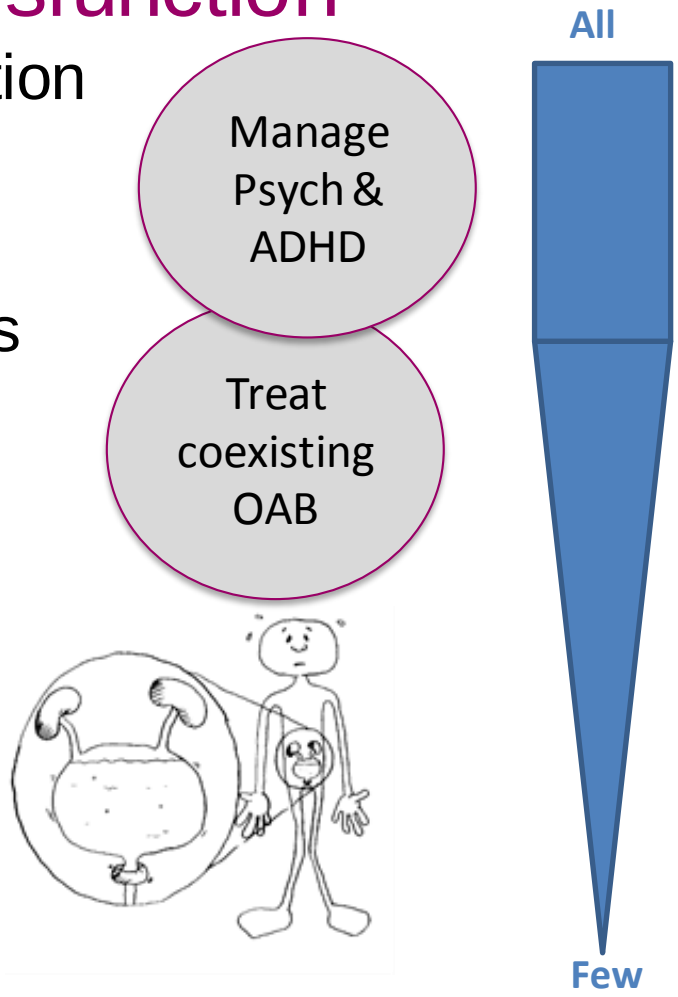
- Main use = antihypertensive
- Decrease bladder outlet resistance via relaxation of internal sphincter
- NICE approved for moderate to severe symptoms of benign prostatic hyperplasia
- NICE not approved for neurogenic bladder emptying problems
- Unlicensed in children - anecdotal and case series reports of successful use
- A double blind placebo RCT failed to show improvement (Kramer et al J Urol 2005)
- Largest children's cohort study (n=74) reports 72% improved, 43% dry using Doxazocin (Thom et al J Ped Urol 2012)



I have rarely used alfa blockers for voiding dysfunction Why?

Treatment of Voiding Dysfunction

- Drink enough to avoid dehydration
- Caffeine avoidance
- Treat/prevent constipation
- Treat/prevent symptomatic UTIs
- Regular or timed voiding
  - Double voiding
  - Reminder alarm
- Biofeedback
- **Anticholinergics?**
- **α blocker????**
- Self Catheterisation



How do I manage a patient with intractable daytime wetting: Drugs

- There are many drugs available but only Oxybutinin is licensed!
- Drugs are an add on not a substitute for the other measures

For OAB

- I Try more than one anticholinergic and increase to full dose.
- If it doesn't work I stop
- If it works continue for at least 6 months then try weaning
- I Re-evaluate regularly
- I sometimes use Mirabegron with variable success

For Voiding Dysfunction & Underactive Bladder

- I treat UTIs and coexisting OAB but rely on voiding training rather than medicines
- Despite using Alfa Blockers a lot for hypertension I rarely use them for voiding dysfunction. I *may* reconsider…