

## Newsletter No.1 2013

Dear Colleagues,

Welcome to the first of the four WHTA Newsletters for 2013. I apologise that the start of the newsletter series has begun this late in the year but do hope you find both this and the coming newsletters helpful as they arrive in coming months.

### 1 The Growth of WHTA – *Reflections and a Thank YOU!!*

May I simply begin by thanking you all for joining WHTA for 2013. Obviously a big thank you to those who were previous members and have re-joined, but I would also like to welcome the new members linking with WHTA for the first time.

As many of you already know, the establishment of WHTA a couple of years ago was actually a venture I undertook simply as a result of a number of physiotherapists working in women's health asking me to do so. The expressed need was for there to be more professional development training events in the area of women's health and more easy access to new research in the field.

I must admit that it was actually with immense nervousness (*and self-doubt!!*) that I eventually took the plunge to set up the WHTA service. The journey since then has been an extremely humbling and challenging one. There is no doubt that the journey has taken more hours than I ever expected (I think my husband was doubting for a little while if I was actually still going to be alive when 2013 came around - LOL), but I must say it has been one of the most rewarding journeys I have ever undertaken in terms of my professional life. Thank you for all your words of encouragement – there were times where I don't think I would have continued without it, but I am so glad that I did. You are all amazingly inspirational and I really feel honoured to have had the chance to get to know you all.

### 2 Across Geographical Areas – an opportunity for the future

Just to let you know.... WHTA does now have members in every state and territory of Australia, as well as quite a number of members in New Zealand. Having taught across so many locations I have had first-hand experience that different locations definitely have different areas of expertise. Every geographical area seems to have certain skills that they have refined to an extremely high level that other geographical areas would probably benefit from learning from. I am really hoping that over the next 1-2 years that the broad membership base of WHTA across the states of Australia as well as New Zealand will actually allow me to facilitate some events where we all join together and share that immense degree of knowledge that is out there.

(INTRODUCTORY LETTER CUT for Online.....)

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## 2013 Newsletter No.1 Clinical Information

### Clinical Tip

**A new way to assess for risk  
of levator avulsion**

### Clinical Focus Topic

**Caffeine and Urinary  
Symptoms**

### Medications Update

**Mirabegron – a new  
treatment for OAB?**

### In the News

**A Look at Recent Research**

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**“Incontinence” 2013  
POP-Q App  
iUro App**

## CLINICAL TIP

### A new assessment for Risk of Avulsion

With the increasing evidence that levator avulsion is a major risk factor for anterior and central compartment prolapse there is mounting pressure for physiotherapists to be able to identify this specific form of pelvic floor trauma. Unfortunately, research on previous palpation methods has shown poor predictive ability to accurately make this diagnosis.

Recently, Kruger, Dietz and Dumoulin (2013 *Neurourology and Urodynamics*) have published research indicating that the measurement of the "Width Between Insertion Sites" has the highest sensitivity and specificity of the various digital methods in predicting levator avulsion.

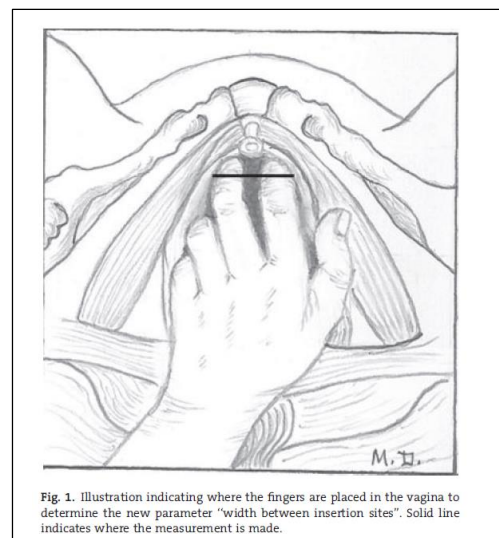
#### What is "Width Between Insertion Sites":

##### Protocol:

- Patient is asked to first perform a series of PFMC to facilitate muscle bulk and make palpation easier
- Distance between insertion sites of muscle is then estimated by parting the finger up behind the pubis until the muscle bulk can be palpated on either side of the examining fingers.

The authors suggest a cut-off of >3.5cm as a high chance of avulsion.

(Distance is estimated with 3 finger width = ~4cm)



#### How accurate is using a cut-off of 3.5cm for diagnosis of avulsion?

	In women in whom Avulsion was present on ultrasound	In women whom Avulsion was not present on ultrasound
<b>Distance between Insertion Sites Method</b>	78% identified as having a distance >3.5cm and therefore avulsion	90% identified as having a distance <3.5cm and therefore no avulsion
<b>Palpation of Absence of Muscle - % Identified correctly</b>	60% identified as having an absence of muscle bulk and therefore avulsion.	92% Identified as having muscle bulk present and therefore no avulsion

**NOTE!** The authors do acknowledge however that width between insertion sites is unable to discriminate unilateral from bilateral avulsion.

**Reference:** Kruger J, Dietz H, Budgett S and Dumoulin C (2013), Comparison between transperineal ultrasound and digital detection of levator ani trauma. Can we improve the odds? *Neurourology and Urodynamics*.

## Clinical Focus Topic      *Caffeine & Urinary Sx*

### BACKGROUND INFORMATION

For everyone who knows me personally (which is most of you!!), you are probably thinking that there is a conflict of interest I need to disclose here..... So let's start with that. YES, I have an extreme caffeine addiction. I am probably the only physiotherapist in Australia who works in women's health who virtually never drinks a glass of water. I have about 6-7 cups of tea and 1 coffee each day and that is my total fluid intake. If I go to bed without having a cup of tea I wake up with a headache, and if I don't have a cup of tea in the morning I have a headache by 10am.

#### **What does this mean in terms of my opinion on advice we should give to women regarding caffeine?**

I think it is true to say that my own caffeine addiction probably does influence what I say about caffeine, but I don't think it is in a bad way (but maybe I am biased in that opinion). The fact is that I know what it is like to have a caffeine addiction. A lot of people say they have a caffeine addiction but often it is just their way of saying they love having a coffee in the morning, when in reality they can go without it if they have to. My addiction however is real.

#### **Why am I saying this?**

I suppose I would like to give a very personal first-hand explanation to all of you who don't tend to drink caffeinated substances about how very "REAL" caffeine addiction can be. My caffeine addiction is as real as a smoking addiction, or an alcohol addiction. When we ask people to try to stop smoking we give nicotine patches, we understand that people withdrawing from alcohol can have numerous very dangerous physiological side effects during the process. In contrast, I think health professionals often take very lightly advice about cutting out caffeine. If I was to come to you as a patient and you gave advice for me to cut out caffeine completely you would make me extremely sick for at least a few days and I would be in an enormous amount of pain. My head would feel like it is going to explode. My whole neck would ache and I would struggle to get out of bed. I am being honest when I say that if I ever went into hospital for an operation I would realistically need to declare my caffeine addiction as I would have a physiological withdrawal.

Now, I am not necessarily saying this is good.... But I am saying it is real. Whilst obviously reducing caffeine is no big deal for some people, for others it is. If we are going to tell people to reduce caffeine who are likely to go through a physical withdrawal, we had better be sure that the research actually backs us up on this.

### BACKGROUND INFORMATION ON CAFFEINE LEVELS

Gleason et al 2012 estimate that average caffeine levels in beverages are

➤ Coffee	95 - 206mg per 250ml	(average - 150mg)
➤ Tea	14 – 120mg per 250mls	(average - 65mg)
➤ Carbonated drinks	20 - 90mg per 375ml can	(average - 55mg)
➤ High Energy drinks	50 – 505mg/serve	(average - 275mg)

## RESEARCH REVIEW

### RESEARCH PAPER 1 *Is caffeine intake associated with urinary incontinence in Japanese Adults*

Authors            Hirayama and Lee  
Journal            J Prev Med Public Health, 2012 May, vol 45 (3), pp. 204-208

#### **Methods**

N = 683 ♂ and 298 ♀ aged 40-75years

#### **Results:**

1. There was no statistically significant difference in the caffeine intakes of those who reported urinary incontinence to those who did not

	Men	Women
<b>Caffeine Intake - Incontinent</b>	120mg	94mg
<b>Caffeine Intake - Not incontinent</b>	106	103mg
	P = 0.33	P = 0.44

2. Those with the highest level of caffeine intake were found to have a slightly increased risk of incontinence compared to the lowest intake (36% increased risk for men and 12% increased risk for women), however this became not statistically significant after allowing for confounding factors.

#### **Conclusion:**

No association was evident between caffeine intake and UI in middle-aged older Japanese adults.

#### **TARYN'S COMMENT**

Notes:

The study above did not distinguish out stress incontinence from urgency or urge incontinence. In addition, the above study had fairly small numbers which makes it hard to reach statistical significance. Looking at the raw numbers it could be argued that there was more of an effect in men than women.

The next studies separate gender. This could be relevant as urgency and urge incontinence in men does have a much higher association with Detrusor Overactivity than urgency in women. Therefore, if caffeine is related to DO it would be expected to be more of an associated for male urgency incontinence than female urgency incontinence.

We will start by looking at caffeine intakes association with urinary incontinence in women simply because more research has been conducted in women.

## Is caffeine intake a risk factor for women?

### RESEARCH 2

#### *Are smoking and other lifestyle factors associated with female urinary incontinence? The Norwegian EPINCOT\* Study*

Authors Hannestad YS, Rortveit G, Daltveit AK and Hunskaar S.  
Journal British Journal of Obstetrics and Gynaecology

#### **Background**

The Norwegian EPINCOT Study (\*EPINCOT = Norwegian Epidemiology of Incontinence in the County of Nord-Trøndelag) surveyed 27,936 women  $\geq 20$  years between 1995-1997. Questions covered smoking, BMI, physical activity, caffeine intake etc and their relationship with LUT disorders

#### **2 Main Findings Related to Caffeine**

- Tea Drinkers were at slightly higher risk for all types of incontinence
- No effect was found for consumption of alcohol or coffee

### RESEARCH 3

#### *Caffeine and Urinary Incontinence in US Women*

Authors Gleason JL, Richter HE, Redden DT, Goode PS, Burgio KL and Markland AD  
Journal International Urogynaecology Journal, February 2013

#### **Background**

The focus of this study was to characterise the association between caffeine consumption and severity of urinary incontinence in US women. Data was collected from the 2005-2006 and 2007-2008 National Health and Nutrition Survey and included 4,309 non-pregnant women aged  $>20$  with complete data.

Caffeine Intake was categorised into quartiles (0-27mg/day; 28-95mg/day; 96-204mg/day;  $>204$ mg/day)

Urinary Incontinence was categorised as either

1. Any urinary incontinence (including mild / drops / occasional) OR
2. Moderate / severe UI (defined as weekly incontinence or monthly incontinence of more than just drops)

#### **Main Results**

- Urinary Incontinence
  - 41.0% of women stated they experienced some degree of urinary incontinence
  - 16.5% of women stated they experienced moderate/severe urinary incontinence
- Caffeine Consumption
  - Average caffeine intake per day in women was 126.7mg
  - Caffeine intake in the highest quartile ( $>204$ mg/day) was associated with
    - 1.4x the risk of "Any" urinary incontinence, but
    - No increased risk of moderate to severe urinary incontinence
  - Type of UI (Stress, urgency, mixed) was not associated with caffeine intake

#### **Conclusion**

Caffeine intake  $>204$ mg/day was associated with any UI, but not with moderate to severe urinary incontinence in women.

## But what if we look at urgency incontinence and stress incontinence in women separately?

### RESEARCH 4

### *Caffeine intake, and the risk of stress, urgency and mixed urinary incontinence*

Authors

Jura YH, Townsend MK, Curhan GS, Resnick NM, Grodstein F

Journal

Journal of Urology

#### **Background**

A prospective cohort study of 65,176 women aged 37-39 years.

#### **Main Findings**

- Overall caffeine consumption was not associated with urinary incontinence of monthly or more
- High Caffeine consumption greater than 450mg showed a modest increased risk of weekly urinary incontinence compared to the lowest caffeine consumption (less than 150mg) Relative Risk = 1.19
- The increased risk was predominantly focused on increased urgency incontinence at caffeine levels >450mg compared to <150mg Relative Risk 1.34,
- There was no increased risk for high caffeine consumption >450mg for stress or mixed urinary incontinence.

#### **Conclusion**

Only high caffeine intake >450mg (not low or moderate) is associated with increased incidence of urinary incontinence, and this association only applies to urgency urinary incontinence (moderate intake does not increase the risk). There is also no association with any level of caffeine intake and stress or mixed urinary incontinence.

## Does Caffeine make urinary incontinence get worse over time??

### RESEARCH 5

### *Caffeine intake and risk of urinary incontinence progression among women*

Authors

Townsend MK, Resnick NM, Grodstein F

Journal

Obstetric Gynecology, 2012 vol 119, no. 5, pp. 950-957

#### **Background**

A prospective cohort study of 21,564 women with moderate UI.

Measures: Baseline Caffeine intake in the previous year  
Change in caffeine intake over the previous four years  
2 Years follow up of incidence of urinary incontinence

#### **Main Findings**

- The change in urinary incontinence progression was similar across categories of baseline caffeine intake and change in caffeine intake before baseline.
  - 21% of women with caffeine intake of 450mg or more had an increase in urinary incontinence
  - 22% of women with caffeine intake less than 150mg had an increase in urinary incontinence

#### **Conclusion**

Long term high level caffeine intake is not associated with an increased risk of progression of urinary incontinence.

## WHAT ABOUT IN MEN??

### RESEARCH 6

Authors

Journal

### Caffeine and Urinary Incontinence in US Men

Davis NJ, Vaughan CP, Johnson TM, Goode PS, Burgio KL, Redden DT and Markland AD

Journal of Urology 2013, Jun, vol 189, pp. 2170

#### **Background**

Whilst research has previously looked at the association between urinary incontinence and caffeine in women, little has been done on the association between UI and caffeine in men. The focus of this study was to characterise the association between caffeine consumption and severity of urinary incontinence in US men. Data was collected from the 2005-2006 and 2007-2008 National Health and Nutrition Survey and included 3,960 men aged 20yrs or older

Urinary Incontinence was categorised as

3. Any urinary incontinence OR
4. Moderate / severe UI defined as scoring >3 on a standardized Incontinence Severity Index.

#### **Main Results**

- Urinary Incontinence
  - 12.9% of men stated they experienced some degree of urinary incontinence
  - 4.4% of men stated they experienced moderate/severe urinary incontinence
- Caffeine Consumption
  - Average caffeine intake per day was 169mg/day
  - Caffeine intake in the
    - >234mg/day was associated with 1.72x the risk of mod-severe urinary incontinence
    - >392mg/day was associated with 2.08x the risk of mod-severe urinary incontinence

#### **Conclusion:**

In men, caffeine consumption equal to or greater than 2 cups of coffee per day was significantly associated with moderate to severe urinary incontinence

*High caffeine consumption appears to have a stronger relationship to moderate to severe urinary incontinence in men than women.... This could be due to the fact that urge urinary incontinence has a fairly low association with detrusor overactivity in women in the first place.*



## So is it related to detrusor overactivity??

### RESEARCH 7

#### *Dietary Caffeine and the risk for detrusor instability: a case control study*

Authors

Arya LA, Myers DL and Jackson ND

Journal

Obstetrics and Gynaecology, 2000 July, vol 96, no. 1, pp 85-89

#### **Background**

The focus of this study was to determine whether there is an association between caffeine intake and detrusor overactivity. All women in the study had urinary incontinence, however half also had urodynamically proven detrusor overactivity and half did not. Comparison was made between the caffeine intake of the 131 women with 'UI + DO' vs the caffeine intake of the 128 women with urinary incontinence but no detrusor overactivity. All women had a maximum urethral closure pressure on urodynamics >20cmH<sub>2</sub>O to rule out UI from intrinsic sphincter deficiency.

Caffeine Intake was classified as either

- |            |                 |   |
|------------|-----------------|---|
| - Minimal  | < 100mg / day   | (~1-2 caffeinated drinks per day – depending on caffeine level) |
| - Moderate | 100-400mg / day | (~1-6 caffeinated drinks per day –depending on caffeine level)  |
| - High     | >400mg / day    | ( >5 caffeinated drinks per day – depending on caffeine level)  |

#### **Main Findings**

- There was a statistically significant association between high caffeine intake and detrusor overactivity
  - OR = 2.4                      p =0.018 (ie women with high caffeine were 2.4x more likely to have DO)
- Average caffeine intake of women with UI + DO (484mg) was significantly higher than the average caffeine intake of those with urinary incontinence without DO (194mg) p = 0.002
- Women with minimal caffeine intake had slightly lower risk of DO than those with moderate caffeine intake, but this did not reach statistical significance (p=0.093)

*Women can have a range of aetiologies underpinning their urgency incontinence. It may be that when the urgency is known to be associated with DO that caffeine may be a factor, but when the urgency is related to other factors caffeine intake becomes irrelevant?*

## SO DOES REDUCING CAFFEINE ACTUALLY MAKE A DIFFERENCE?

## INTERVENTION STUDIES

### RESEARCH 8

#### *Caffeine Reduction Education to improve urinary symptoms (Australian Study)*

Authors

Bryant CM, Dowell CJ and Fairbrother G

Journal

British Journal of Nursing, 2002, vol 11, no. 8, 560-565

#### **Background**

This was a randomised controlled trial of 95 consecutive adult patients (male and female) presenting to two nurse continence advisers. Treatment group underwent 1month trial of bladder training plus reduction of caffeine to less than 100mg, compared to control group who received bladder training only.

Frequency, urgency and leakage outcomes were tested 1month post-enrolment.

#### **Main Findings**

- Caffeine reduction resulted in a statistically significant reduction in symptoms of urgency ( $p=0.002$ ) and frequency ( $p = 0.037$ ) when compared to the control group.
- Caffeine reduction resulted in no difference for incontinence episodes

#### **QUESTION/ THINKPOINT**

**BUT WAS IT THE REDUCTION IN CAFFEINE OR JUST A REDUCTION IN FLUID**

### RESEARCH 9

#### *The impact of fluid intake on urinary symptoms in women*

Authors

Switnbank, Hashim and Abrams

Journal

Journal of Urology, 2005, vol 174, no. 1, 187-9

#### **Background**

This was a 4 week randomised, prospective crossover study that followed 69 women with either urodynamic stress incontinence ( $n = 39$ ) or urodynamically proven detrusor overactivity ( $n = 30$ ) whilst implementing caffeine restriction and fluid manipulation.

#### **Main Findings**

- **Detrusor Overactivity Group**
  - Reduction in fluid intake resulted in significantly decreased urgency, frequency and incontinence episodes, and a statistically significant increase in quality of life.
  - Change from caffeinated to decaffeinated resulted in no change in symptoms
- **Stress Incontinence Group**
  - Reduction in fluid intake resulted in a significant decrease in incontinence episodes
  - Change from caffeine to decaffeinated produced no change in symptoms

Final Study....

## RESEARCH 10

### *Dietary caffeine, fluid intake and urinary incontinence in older rural women*

Authors

Tomlinson BU, Dougherty MC, Pendergast JG, Boyington AR, Coffman MA, Pickens SM

Journal

International Urogynaecology Journal of Pelvic Floor Dysfunction

## Background

41 women with urinary incontinence had nurse home visits with the most common recommendation being to decrease caffeine intake and increased fluid intake.

## Main Findings

- **Decreased Caffeine** resulted in a non-significant reduction in incontinence episodes  $p = 0.074$
- **Increased fluid intake** only resulted in an increase in average volume voided  $p = 0.0479$

Taryn's Note – the non-significance ( $p > 0.05$ ) could simply be because of the small numbers in the trial though.

## TARYN'S SUMMARY

There appears to be fairly consistent research showing an association between caffeine and detrusor overactivity. Whilst there is no evidence that caffeine causes detrusor overactivity it may worsen detrusor overactivity in those already affected.

Whilst caffeine may be related to detrusor overactivity, the inconsistent research on whether DO is actually related to LUT symptoms makes this finding less clinically relevant. The more important association is whether caffeine relates to symptoms.

There does not appear to be any link between caffeine intake and stress incontinence.

There is only one trial on caffeine intake specifically in men – which seems to show a fairly strong association with symptoms. As male urge incontinence has a much stronger relationship to detrusor overactivity this is a logical result.

There seems to be little evidence that there is an association between general urinary incontinence and caffeine intake in women. However, these generalised results are probably diluted due to the high number of women whose urinary incontinence is actually SUI. In addition, women have a much more multivariate nature to their urge urinary incontinence (not being always related to DO). It is therefore not surprising that the research seems to come out less strong in women than it does in men.

If there is an association between urge incontinence and caffeine in women it only appears to be at very high levels of caffeine consumption. There appears to be no increased risk at moderate intake vs low intake. A woman presenting with a caffeine intake of 1-2 cups per day really has no increased risk compared to no caffeine intake.

There is only one small trial that indicates a reduction in caffeine may help symptoms – and even then the reduction in symptoms is with reference to urgency but not urge incontinence. In addition, it could be argued that the reduction in symptoms in women is more related to a reduction in fluid intake than necessarily a reduction in caffeine.

Finally, there appears to be no evidence that people who consume caffeine will have a worsening of their condition at a faster rate than people who do not consume caffeine.

**WHAT'S THE UPSHOT OF ALL THIS.....** In some people there is a link between caffeine and symptoms. It is definitely worthwhile to trial a reduction in caffeine and see if there is an improvement in symptoms. But we may not need to be as militant on caffeine as we sometimes think.

## MEDICATIONS UPDATE

### Mirabegron - a new option for OAB?

#### What is Mirabegron?

Mirabegron (trademark "Myrbetriq" to the public) is the first in an entirely new class of drug now being marketed for the management of OAB. It is already approved in some parts of Europe and the USA, and is likely to hit the Australian market in the next 6-12 months.



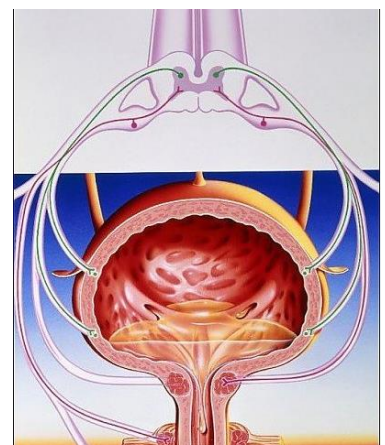
#### How is Mirabegron different to previous OAB Drugs?

Unlike all previous drugs for OAB, Mirabegron is **NOT** an **antimuscarinic**. Mirabegron is a **β3 Adreno-Receptor Agonist (β3-AR)**. To fully understand this difference we need to first review the normal neurological control of the LUT.

#### LUT PHYSIOLOGY REVIEW

The lower urinary tract (LUT) obviously consists of the **Bladder** (designed to store urine) and the **Urethra** (designed to release urine at a convenient time).

The bladder wall is largely made up of a **smooth muscle** layer known as the ***detrusor*** which is designed to remain relaxed during storage and contract during voiding. The urethra is also partially controlled by smooth muscle. The ***internal urethral sphincter*** consists of smooth muscle fibres that begin as extensions of the smooth muscle detrusor fibres at the bladder neck and extend down the length of the urethra.



## THE SMOOTH MUSCLE COMPONENTS OF THE LOWER URINARY TRACT –

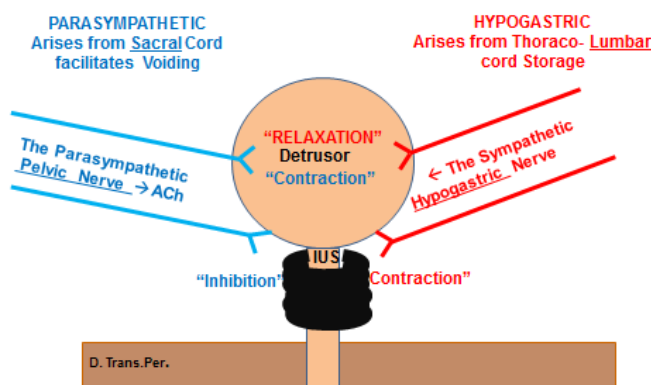
### Detrusor and Internal Urethral Sphincter

Being smooth muscles, both the detrusor and internal urethral sphincter are under the influence of the autonomic nerves. The two autonomic nerves that co-ordinate the actions of the detrusor and internal urethral sphincter are the:

1. **Pelvic Splanchnic Nerve** – a **parasympathetic nn**
  - I. Originates from the sacral spine
  - II. Sends motor efferents to facilitate **voiding**.
  - III. → Detrusor Contractoin and IUS relaxation
2. **Hypogastric Nerve** – a **sympathetic nn**
  - a. Originates from T10-L2
  - b. Sends motor efferents to facilitate storage.
  - c. → Detrusor Relaxation and IUS relaxation

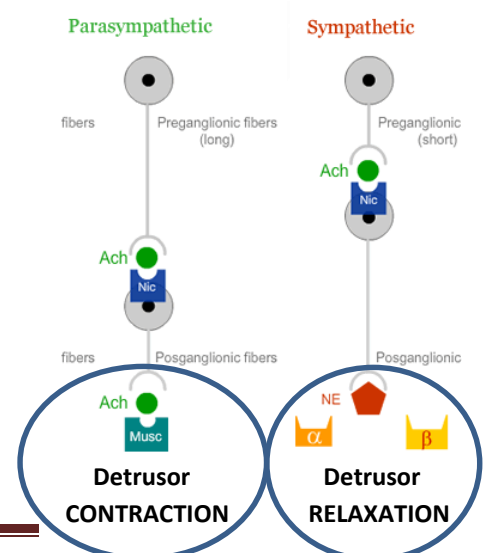
#### AUTONOMIC INNERVATION OF THE LUT

Dual Innervation of Detrusor and Internal Urethral Sphincter (smooth mm of LUT)



The two nerves work in different ways because they release different neurotransmitters into different receptors on the detrusor cells:

- Activation of the **Parasympathetic Pelvic** nerve facilitates voiding by releasing AcetylCholine into **muscarinic** receptors on the detrusor cells that facilitate **contraction**
- Activation of the **Sympathetic Hypogastric** Nerve facilitates storage by releasing Nor-Epinephrine (Nor-Adrenaline) into  $\alpha$  &  $\beta$  Receptors on the detrusor cells that induce **relaxation**.



## So how is Mirabegron different??

All previous drugs for overactive bladder could be grouped under the term “antimuscarinics” (historically also termed ‘anticholinergics’). They were all designed to block the muscarinic receptors in the bladder, thereby preventing the neurotransmitter Ach binding to smooth muscle cells. They worked by **stopping the detrusor contraction mechanisms**.

**Mirabegron** is a  $\beta_3$  adrenergic receptor ( $\beta_3$ -AR) agonist. It improves the symptoms of OAB by instead activating the  $\beta_3$  receptors thereby **facilitating the detrusor relaxation mechanisms**.

## Is this clinically relevant???..... The Side Effect Profile

Probably the main difference is not going to be in the outcome for OAB symptoms. The main difference will be in the side effect profile. Any drug that alters the activation of sympathetic and parasympathetic nerves will often do so not just in the LUT, but in multiple areas of the body.

### The Antimuscarinic Side Effects

The antimuscarinics worked by blocking parasympathetic muscarinic receptors. Parasympathetics normally also cause production of saliva, production of lubrication to the eye, colonic peristalsis etc

The side effects of antimuscarinics were therefore dry eyes, dry mouth, constipation, dizziness etc.

### The $\beta_3$ -AR Agonist Side Effects

The  $\beta_3$  Agonists work by enhancing sympathetic actions. Therefore, the side effects will be enhancement of normal sympathetic mechanisms. These include increasing blood pressure, headache, nasopharyngitis (cold like symptoms such as runny nose etc), dizziness and nausea.

## Main Clinical Relevance for Physiotherapists

There will soon be a new drug on the market for OAB. This new class of drugs will have different side effects and different precautions. They work via a very different mechanism to the anti-muscarinics. Being aware of this option is important when working with the multidisciplinary team and being able to support our patients in understanding all the options available to them to manage their urinary disorders.

**NEXT PAGE..... QUICK SUMMARY OF THE MAIN POINTS ABOUT MIRABEGRON .....**

## Mirabegron – Summary

**Public Name**

**Myrbetriq**

**Company**

Astellas

**Appearance:**

Tablet - oval  
Light Brown / Yellow  
Not scored (cannot be broken)  
Astellas Logo and either “325” or “355” printed.



**Dosage:**

25mg / 50mg x 1 daily with or without food  
1. start with 25mg and then increase to 50mg if needed  
2. active ingredient is slow release so only once daily

**Time to Full Benefit:**

~8 weeks

**Duration of Treatment**

Not curative (needs long term use)



**Efficacy**

3 x High Quality Randomised Controlled Trials

**Contra-Indications**

None

**Main Warnings**

Risk of increasing blood pressure in people with uncontrolled hypertension  
  
Risk of urinary retention in patients with either bladder outlet obstruction or those already taking an Antimuscarinic.

**Pregnancy / BF:**

There are no adequate studies at this time on Mirabegrons effects during pregnancy in humans. In animals there were no toxicities / adverse effects at 6x the standard 50mg equivalent dose. Bone changes and decreased fetal body weight were seen when levels 14-22x the standard dose were used.  
  
No human trials. Mirabegron has been found in the milk of rats at concentrations twice that of maternal plasma levels. It is therefore predicted that Mirabegron is excreted in breastmilk and so not advised during BF.



## IN THE NEWS

### What research has recently been published?

Outlined below are some major points from research recently published online. Most of these articles are prior to official publication in their respective journals – but have been released ahead of print online. The dates are therefore often the online publication date.

Please note – the bold underlined statement is the major point relevant to physio not the title of the articles. Links to the abstracts are provided.

#### BIRTH AND THE PF

##### **COCHRANE REVIEW on PFMT for PREVENTION OF URINARY AND FAECAL INCONTINENCE POST BIRTH**

A new Cochrane review of PFMT for Urinary and faecal incontinence postpartum was published in 2012. Twenty-two trials involving 8485 women (4231 PFMT, 4254 controls) met the inclusion criteria and contributed to the analysis.

- Pregnant women without prior urinary incontinence who are randomised to intensive antenatal PFMT are less likely than women randomised to no PFMT or usual antenatal care to report urinary incontinence up to six months after delivery (about 30% less; risk ratio (RR) 0.71, 95% CI 0.54 to 0.95, combined result of 5 trials).
- Postnatal women with persistent urinary incontinence (treatment) three months after delivery and who received PFMT were less likely than women who did not receive treatment or received usual postnatal care to report urinary incontinence 12 months after delivery (about 40% less; RR 0.60, 95% CI 0.35 to 1.03, combined result of 3 trials). It seemed that the more intensive the programme the greater the treatment effect.

##### LINKS:

1. <http://summaries.cochrane.org/CD007471/pelvic-floor-muscle-training-for-prevention-and-treatment-of-urinary-and-faecal-incontinence-in-pregnant-women-and-women-who-have-recently-given-birth>
2. <http://www.ncbi.nlm.nih.gov/pubmed/23616292>

##### **10min PFMT in a standard 60min exercise class during pregnancy significantly reduces incidence of UI**

Pelaez et al found that 95.2% women who completed 10min of PFMT 3 times per week for at least 22 weeks of their pregnancy as part of a standard 60min exercise class had no urinary incontinence compared to 60.7% of a control group. The exercise group had no formal assessment of ability to perform a correct contraction.

<http://www.ncbi.nlm.nih.gov/pubmed/23389863>

##### **At 2 Years Post Birth – UI rates are similar between LSCS and Vaginal Birth??**

Barbosa et al 2013 compared 220 women who had undergone either an elective caesarean section or vaginal birth. At 2 years post birth the urinary incontinence rates were 18.9% and 17% respectively. The primary risk factor for UI at 2 years post birth was weight gain during pregnancy and gestational urinary incontinence. Pre-Pregnancy BMI <25 and normal pelvic floor muscle function was protective. <http://www.ncbi.nlm.nih.gov/pubmed/23657511>

Taryn's Note: this study is purely on the "RATE" of urinary incontinence, not the severity.



## OVERACTIVE BLADDER

### **Bladder Training (Australian Version - urge suppression) improves symptoms of Idiopathic Overactive Bladder**

**Lee et al 2013** finds that a bladder training program involving a combination of refraining from going to the bathroom, ceasing current activity and performing 5-6 PFM contractions led to a significant improvement in frequency, nocturia and urgency. Bladder diary reports also showed significant improvement in maximum voided volume after Rx.

<http://www.ncbi.nlm.nih.gov/pubmed/23610706>

### **In men with nocturia already treated by an $\alpha$ -adrenergic antagonist, addition of Behavioural therapy was more effective than adding Antimuscarinic therapy**

**Johnson et al 2013** found that addition of behaviour therapy reduced Nocturia by 1/night whereas addition of Antimuscarinic therapy only reduced Nocturia by 0.5/night in men already being treated with an  $\alpha$ -adrenergic antagonist. <http://www.ncbi.nlm.nih.gov/pubmed/23448285>

### **E-STIM Studies**

#### **Sacral TENS much more effective than Tibial nerve TENS for OAB in children.**

**Barroso et al 2013** n = 37 children treated with sacral TENS, n = 22 children treated with posterior tibial nerve stim. 70% of children with OAB in the sacral stim group showed complete resolution of symptoms, whereas only 9% showed complete resolution with Tibial nerve stimulation. However, the small numbers meant that the data did not reach statistical significance. <http://www.ncbi.nlm.nih.gov/pubmed/23422257>

Taryn's Note: The above study seems to be very significant and one where statistics fail to represent the reality. The p-value came out as 0.55 (not statistically significant). There is obviously a large difference in the two groups, but due to small numbers you can't definitely rule out the possibility of chance (ie a high p-value).

#### **Both Tibial nerve stim and Vaginal e-stim are effective for OAB, but significantly more women who receive 20min 3/week vaginal e-stim regard themselves as cured compared to 1/week tibial nerve e-stim.**

**Ugurlucan et al 2013** <http://www.karger.com/Article/FullText/343756>

#### **Systematic Review states that most clinical trials show that electrostimulation is effective in the treatment of OAB but better quality trials are needed.**

**Jerez-Roig et al 2012** <http://www.ncbi.nlm.nih.gov/pubmed/23246103>

#### **Surface electrical stimulation near the clitoris to stimulate the dorsal clitoral nerve leads to significant improvements in bladder capacities and voided volume in subjects with neurogenic detrusor overactivity.**

**Opisso et al 2012** <http://www.ncbi.nlm.nih.gov/pubmed/23281007>

**Women with combined urgency/frequency symptoms and overactive pelvic floor /PF spasm have an average 67% improvement in symptoms after 6 weeks of vaginal e-stim and biofeedback retraining.**

**Bendana et al 2009** showed that 1 week sessions of transvaginal e-stim and biofeedback gave an average of 67% improvement in symptoms after 6 weeks. In addition, at the 12 week follow up (6 weeks after completion of treatment) this improvement increased to 75%. E-stim occurred at 5-10Hz, 20Hz and 200Hz depending on tolerability. <http://www.ncbi.nlm.nih.gov/pubmed/19579410>

## PROLAPSE

**Women with prolapse have altered genital sensation and this is not improved after prolapse surgery.**

**North et al 2013** <http://www.ncbi.nlm.nih.gov/pubmed/23240799>

## STRESS INCONTINENCE

**Abdominal Bulging leads to a 12-18cmH2O reduction in urethral pressure**

**Sapsford et al 2013** <http://www.ncbi.nlm.nih.gov/pubmed/23192396>

**Double Blind, Randomised Controlled trial shows that Transvaginal Electrical Stimulation + SEMG Biofeedback leads to statistically significant reductions in SUI and increased PF mm strength when compared to placebo vaginal stimulation.**

**Terlikowski et al 2013** participants underwent 2 sessions per day for 8 weeks. Rx group had better outcomes for 24hour pad test, mm strength, QOL. <http://www.ncbi.nlm.nih.gov/pubmed/23443345>

## HORMONES AND THE PELVIC FLOOR

**Women with Polycystic Ovary Syndrome and Hyperandrogenism have reduced rates of Urinary Incontinence but no difference in pelvic floor strength**

**Antonio et al 2013** compared women with hyperandrogenism and PCOS to a control group of women with a normal menstrual cycle. Women with PCOS/Hyperandrogenism had no difference in pelvic floor strength as assessed by vaginal manometry but had no incidence of urinary incontinence. The rate of urinary incontinence in menstruating controls was 18.6%. <http://www.ncbi.nlm.nih.gov/pubmed/23575700>

Taryn's Comment: This study is consistent with other studies indicating that the risk of incontinence increases with release of oestrogen possibly due to the softening effect on the pubocervical fascia → urethral hypermobility and lack of urethral co-aptation during increased intra-abdominal pressure.

## GENERAL PF / PFMT

**Most women can contract their pelvic floor correctly on verbal instruction!!**

**Henderson et al 2013** found that 85% of women with POP, or SUI, or neither POP/SUI can contract their Pelvic Floor correctly on the first attempt. However this percentage reduces to 69% in women with both POP/SUI.

<http://www.ncbi.nlm.nih.gov/pubmed/23321652>

## **Pelvic Dimensions are correlated with Levator Ani defects and Prolapse**

**Berger et al 2013** found that women with levator ani defects have a sacrococcygeal to pubis distance 3mm shorter than women without levator ani defects. In women with severe levator ani defects and prolapse the distance was 5mm shorter. Shorter sacrococcygeal to pubis length combined with forceps is a major risk factor for levator trauma.

<http://www.ncbi.nlm.nih.gov/pubmed/23306771>

## **Less than half of all women referred for PFMT by urologists / gynaecologists complete their PFMT program**

**Tibaek and Dehlendorff 2013** <http://www.ncbi.nlm.nih.gov/pubmed/23291858>

## **65% of women with UI have improvement in QOL after PFMT and the benefit is not affected by age**

**Fan et al 2013** n = 372 women with UI practiced PFMT for ~10months. Over 65% recorded improvement in symptoms and quality of life. Age was not associated with a difference in response.

<http://www.ncbi.nlm.nih.gov/pubmed/23551071>

## **Provision of 1-to-1 PFMT Plus a self-Instruction manual provides greater improvements in POP Symptoms than a self-instruction manual alone.**

**Kashyap et al 2013** <http://www.ncbi.nlm.nih.gov/pubmed/23332657>

## **PFMT changes not only strength and co-ordination but structural measures of the pelvic floor –**

**Madill et al 2013** have found that 12/52 of PFMT in women 60 years and older leads to a reduction in anorectal angle and a higher urethra-vesical angle (bladder neck) both at rest and on straining. Participants were also able to activate their PF more rapidly and with more repetitions. <http://www.ncbi.nlm.nih.gov/pubmed/23359286>

## **Women who undergo Biofeedback in addition to their PFMT for UI are 25% less likely to say they are not improved, but this could be related simply to more health professional contact.**

**Herderschee et al 2013 – COCHRANE REVIEW** <http://www.ncbi.nlm.nih.gov/pubmed/23239361>

## **OVERACTIVE PELVIC FLOOR / PAIN DISORDERS**

### **Rape Victims are More Likely to Suffer from Hypertonic Pelvic Floor**

**Postma et al 2013** compared 89 young women 18-25yrs who were victims of rape during adolescents to 114 non-rape controls. Three years post-treatment for post-traumatic stress disorder the rape victims were still 2.4 times more likely to have sexual dysfunction (lubrication problems and pain) and 2.7 times more likely to have pelvic floor dysfunction

(provoked vulvodynia, LUT dysfunction and irritable bowel syndrome).

<http://www.ncbi.nlm.nih.gov/pubmed/23679151>

## **Vaginal Diazepam doesn't work**

**Crisp et al 2013** found that 10mg vaginal diazepam administered nightly over 4 weeks was not associated with any improvements in resting EMG or subjective outcomes when compared with placebo. Link:

<http://www.ncbi.nlm.nih.gov/pubmed/23681047>

## **Internal Manual therapy techniques are found to be most effective Physiotherapy technique for lifelong vaginismus**

**Reissing et al** found that internal manual therapy techniques were the most effective for vaginismus followed by patient education, dilatation exercises, and home exercises. <http://www.ncbi.nlm.nih.gov/pubmed/23470141>

Taryn's Note: this is a very small retrospective study. It should not be held with the same merit as an RCT.

## **PELVIC FLOOR SURGERY**

### **Long Term Outcomes after Abdominal Sacrocolpopexy**

**Nygaard et al 2013** by 7 years post op the anatomical POP recurrence rate was 22-27% and the symptomatic POP recurrence rate was 24-29%. Mesh erosion rate was 10.7%. Link: <http://www.ncbi.nlm.nih.gov/pubmed/23677313>

### **PFM Function Improves after Prolapse Surgery – as measured by EMG**

**Wang et al 2013** found that Max Voluntary Contraction and ability to perform repetitive short duration fast contractions was improved 3months post- prolapse surgery as measured by EMG. However, the PF function was still significantly reduced compared to non-prolapse controls. <http://www.ncbi.nlm.nih.gov/pubmed/23632801>

### **Women with Mixed Urinary Incontinence who have diagnosed Intrinsic Sphincter Deficiency Pre-Op are more likely to have their Urgency Incontinence cured by a Suburethral Tape Procedure.**

**Kassis et al 2013** found that 67% women with MUI related to ISD (VLPP<60cmH20 or MUP <20cmH20) had complete resolution of their frequency and urgency incontinence at 6-12/12 post-op compared to only 38% who had non-ISD-MUI. <http://www.ncbi.nlm.nih.gov/pubmed/23611929>

Taryn's Note: this is just another paper that I believe re-enforces the fact that some urge incontinence is actually urethral in origin. When there is an intrinsic urethral defect diagnosed in the presence of urgency symptoms, it is likely that a urethral treatment will work. When there is no intrinsic urethral diagnosis it is probably likely that the dysfunction is at the bladder level.

## Books, Apps and More.....

### **BOOK ANNOUNCEMENT!!!**

#### **THE NEW INTERNATIONAL CONSULTATION ON INCONTINENCE BOOK HAS BEEN RELEASED!**

For those of you who haven't heard of this book before you may wish to go back to the first newsletter of 2012 (it is on dropbox). I have done a review of how this book comes about in that newsletter.

But basically..... this is the encyclopedia of incontinence (urinary and anal), and an update is published about every 4 years.

The Book is 1,980pages and is written by

200 experts from around the world divided into 23 committees

They then get together and summarise all the recent research of the last 4 years.

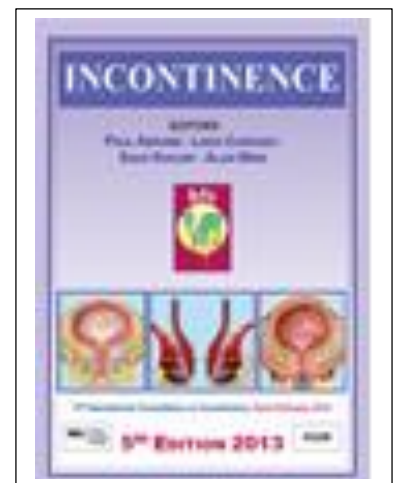
It is pitched at a very high level and so it is for the pelvic floor physio who wants the detail on everything and anything incontinence (anatomy, physiology, neurophysiology, diagnostic testing, conservative treatments, surgical treatments, future research plans etc, etc, etc)

**This is the summary from the EAU Website:**

#### **Incontinence: Fifth Edition 2013**

Edited by Paul Abrams, Linda Cardozo, Saad Khoury and Alan Wein

*The International Consultation on Urological Diseases proudly presents the 5th Edition of its volume Incontinence, edited by Paul Abrams, Linda Cardozo, Saad Khoury and Alan Wein. This edition takes on board the results of the 5th International Consultation on Incontinence, held in Paris in February 2012. Two-hundred experts, divided into 23 committees presented the final drafts of their updated chapters, and received input from the wider audience for final adjustments. This method is a clear reflection of the ICUD's emphasis on consultation and consensus.*



**PURCHASE FROM THE EUROPEAN ASSOCIATION OF UROLOGY –**

<https://www.uroweb.org/publications/other-publications/>

**COST = 90 Euros plus postage**

## Useful APPS on the Market

**1. POP – Q (Pelvic Floor Institute)**    **Score:**    4.5/5 for clinical usefulness explaining POP    0/5 for PF anatomy

*(note this is a different app to POP\_Q by Bard)*

I must say that this **is the App I use most commonly in my clinic** and would recommend everyone to have who has an iPad. My patients love it because I can easily show them how the organs move in POP.

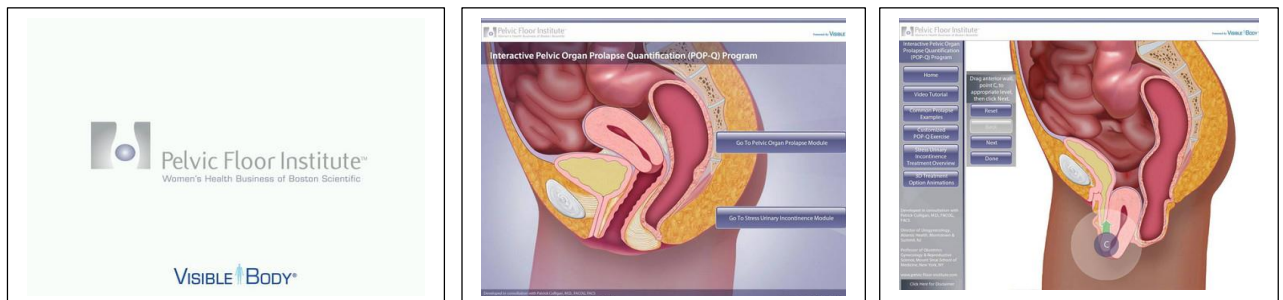
### Positives:

#### Section on “Common Prolapse Examples”

- Fantastic animation to show movement of each organ in prolapse

In this section you can quickly and easily choose whether you want a female pelvis with / without the uterus and then choose which compartment prolapse you want to demonstrate.

Forward and back arrows then allow you to show the bladder / uterus / rectum move downward pushing on the vaginal wall to various degrees.



- Good way to learn about the official POP-Q Assessment (Aa, Ba, Ap, Bp, C, D, TVL, etc)

If you find it hard to understand the POP-Q assessments performed by a doctor this can help you. You can put in a POP-Q assessment result given by a doctor and ask the App to show you the anatomy result. This can then be shown to your patient.

- Surgeries:

The app allows you to enter the patient's current prolapse anatomy, then tell the iPad the surgery they are having. It will create a PDF of the current anatomy, the surgery and the expected anatomical result. You can then email this to the patient or print it.

### Negative +++

The anatomy diagram does not show any of the fascia or muscles!!



**2. iUro:** **Score:** 4/5 for graphics, 3D PF anatomical animations! 0/5 for accuracy of voiceover!!

## Positives:

Great Section Called "How it Works" includes

- Fantastic 3D animation of the muscle and fascial anatomy of the pelvic floor: This animation is in the paid version of the app and gradually builds up all components of the pelvic floor including pubocervical fascia, rectovaginal fascia, uterosacrals, levator ani, obturator ani etc.

My Opinion:

*This short 2min animation is the best 3D animation of pelvic floor anatomy I have seen on the web. It is fantastic for getting your head around the interplay of the muscles and fascia. In terms of your own professional development on understanding pelvic floor fascial and muscular anatomy, probably worth the payment for the app on its own. It's quick, easy and 3D. BUT..... see the negative below!!!*

- Fantastic Animation showing expansion of the bladder as the bladder fills, contraction of the bladder during voiding, and compression of the bladder during coughing: Great for Patients!

## Negatives:

During the 3D anatomy animation the **VOICE OVER DOES NOT MATCH THE STRUCTURE** they are showing!!! The voiceover simply gives an instructional speech that bears no relevance to the structure they are highlighting at the time in the animation. Watch the animations without the voice over or you will get confused.

