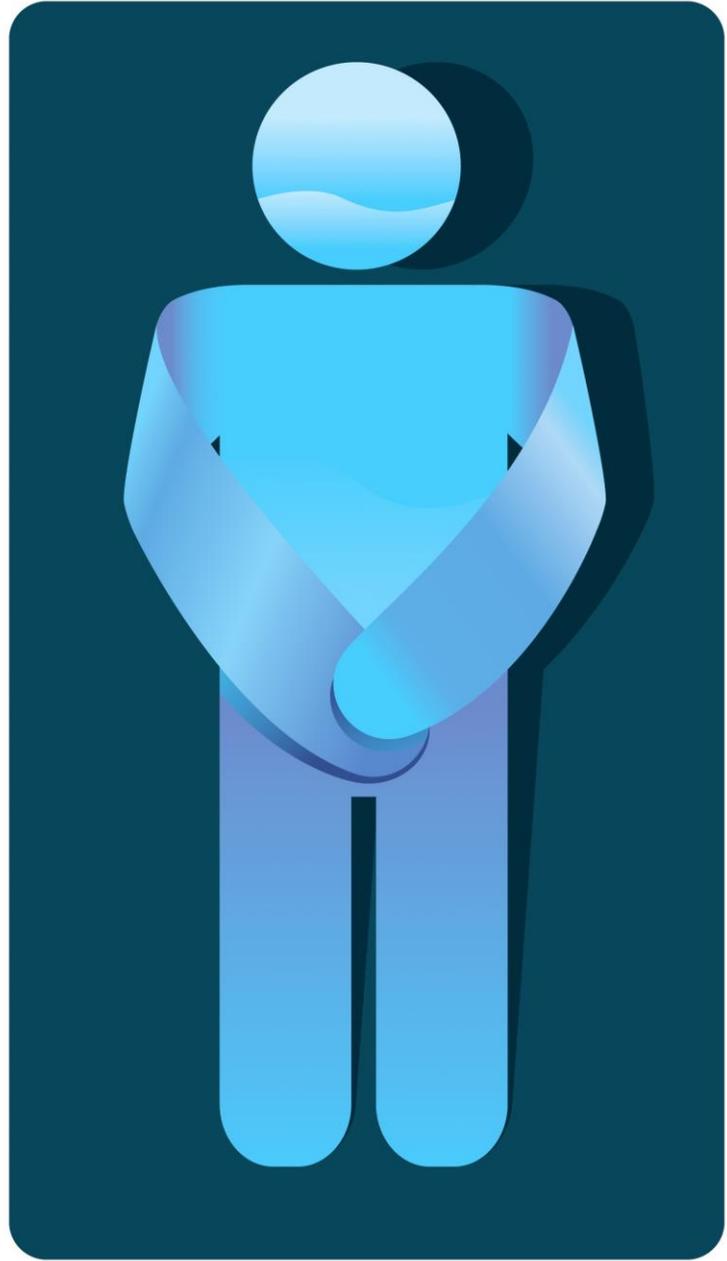


# Bladder Dysfunction in Parkinson's Disease

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# Outline

- Incontinence in the general population
  - Prevalence
  - Types of incontinence
  - Causes
  - Evaluation
  - Treatment
- Bladder symptoms in Parkinson's disease
  - Causes
  - Assessment
  - Treatment

# Age

- 3.5% of women ages 20 to 29; 33% of women ages 54 - 79; 38% of women over 80 (Wu et al., 2014).
- 4.8% of men ages 19 to 44; 11.2% of men ages 45 - 64; 21.1% of men over the age of 65

# Incontinence and Quality of Life

- Associated with lower quality of life
- Negative impact on caregivers (Gotoh et al. 2009).
- Tendency to alter daily routine: work less hours during the day. Avoid going far from home.
- Greater affect on emotional and social wellbeing on men than in women (Tennstedt et al. 2010).
- Men are half as likely as women to get help.

# Risk Factors

- Multiple pregnancies and births
  - Prostate disease
  - Obesity - strongest risk factor in women
  - Diabetes
  - History of frequent urinary tract infections
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- Age
  - Depression
  - Constipation
  - Neurological disease

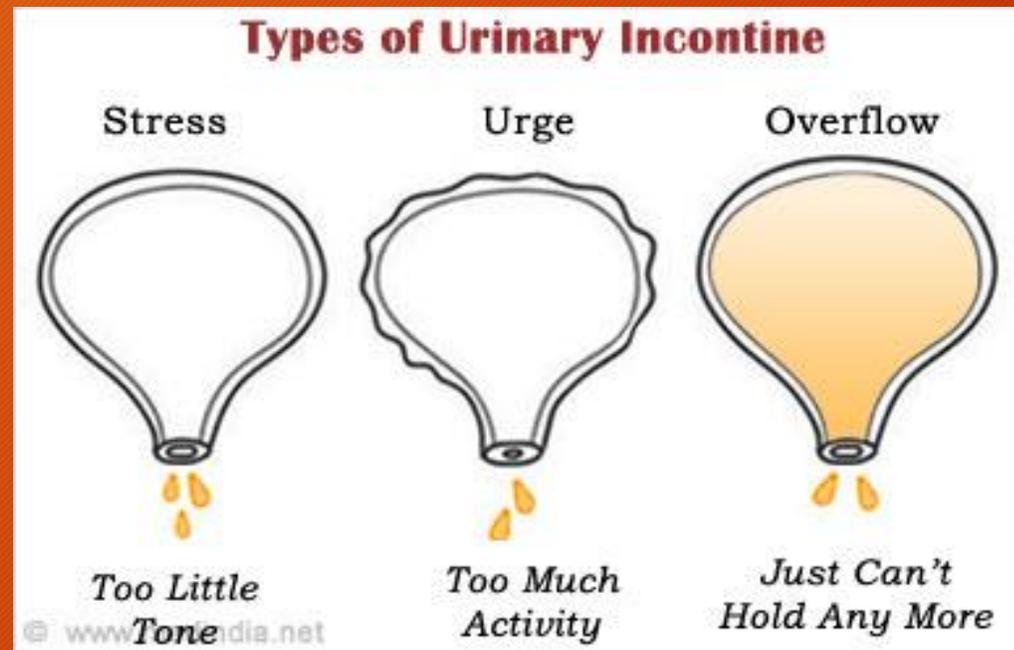
# Screening questions

- Do you leak urine unintentionally?
- Do you leak urine on the way to the bathroom?
- Do you leak urine with laughing or sneezing or coughing or exertion?

# Types of Incontinence

- Stress incontinence - leakage caused by activity, sneezing or coughing.
- Urge incontinence - leakage following sudden urge to urinate without being able to control that urge.
- Overflow incontinence - leakage caused by 'overflow' of urine from an overly full bladder because of not completely emptying the bladder.
- Mixed incontinence - typically a combination of both urge and stress incontinence. Most common type in women.

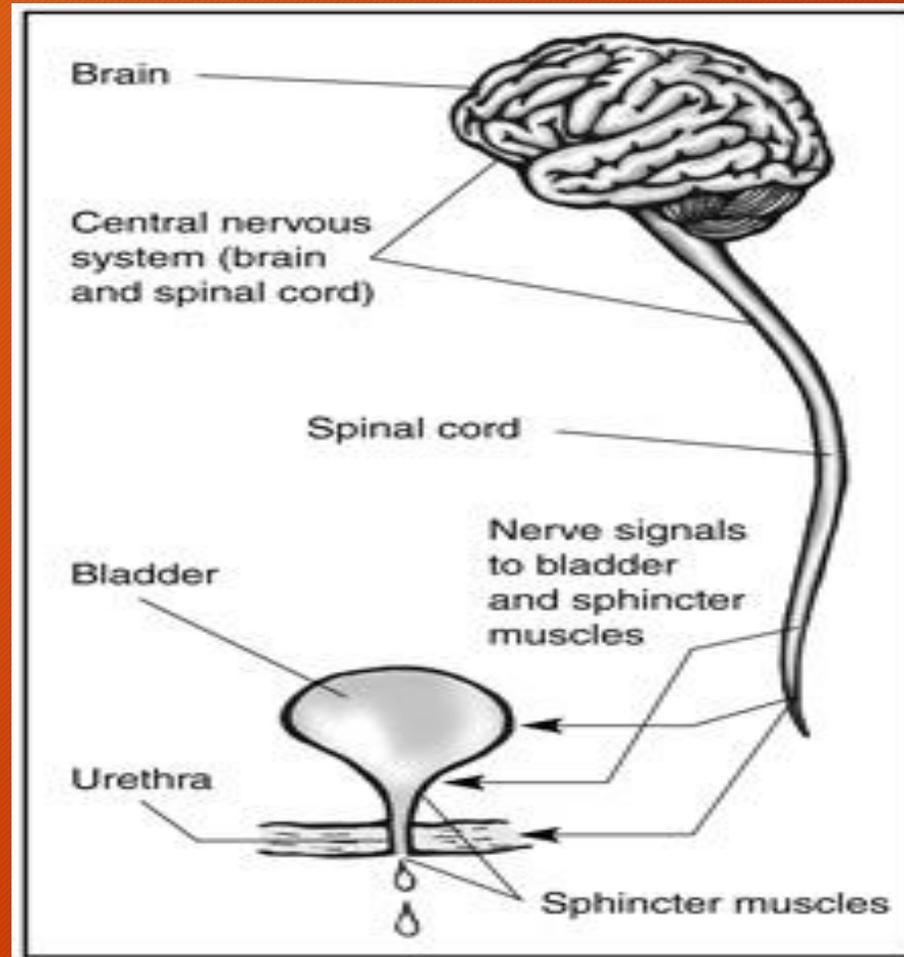
# Types of Incontinence



# Mechanism

- Stress incontinence causes
  - Prostate surgery can damage the urethral sphincter.
  - In women this often happens as a result of childbirth which causes loss of pelvic floor support.
  - It can also be related to obesity, chronic cough or chronic high impact activity.

# Mechanisms ctd



# Mechanism ctd

- Urge incontinence or “overactive bladder” is difficult to sort out.
  - Most common type in men.
  - Most common type in Parkinson’s disease.
  - Faulty signals from the bladder to the brain as is seen in nerve problems. This is common in diabetes.
  - Inability of the brain or spinal cord to control bladder contractions. Very common in various neurological conditions such as spinal cord injury, multiple sclerosis, Parkinson’s disease.
  - Can come from the bladder muscle itself being overactive which happens with aging.

# Mechanism ctd

- Overflow incontinence is leakage or dribbling when the bladder has not completely emptied.
  - Bladder is Underactive as opposed to urge incontinence which happens with bladder Overactivity.
  - Age related.
  - Nerve problems (neuropathy) such as with diabetes, vitamin b12 deficiency, alcoholism or with damage to the spinal nerve roots as is commonly seen with lower back spinal stenosis.
  - Also can come from things that compress the urethra such as tumors, fibroids, vaginal prolapse, prostate enlargement.

# Mechanisms ctd

- Smoking
- Alcohol and caffeine intake
- Severe constipation and stool impaction
- Urinary tract infection
- Cognitive impairment
- Normal Pressure Hydrocephalus
- Cancer (e.g. bladder cancer)

# Evaluation

- Take a good history
  - Classify the type of incontinence (urge vs. overflow vs. stress).
  - Are there other symptoms such as pain, fever, bleeding, sudden onset?
  - Medications - diuretics, memory medications, caffeine, nicotine.
  - Diary - timing of the incontinence, does it occur with heavy fluid intake, what is the maximum time in between voiding. Most places use a 3 day diary but a 24 hour diary is more easy for compliance purposes.
  - Bowel function
  - Sexual function
  - History of prostate problems
  - Impact on quality of life - this can guide treatment as it can target the most disruptive symptoms.

# Evaluation ctd.

- Physical exam - all women with incontinence should receive a pelvic exam and all men should receive a prostate exam.
- Everyone with incontinence should receive a urine analysis.
- Kidney function should be checked in anyone with overflow incontinence as urine can back up into the kidneys and cause kidney swelling.

# Evaluaton ctd.

- Bladder stress test - can be used to assess whether stress incontinence is present. Patient is examined with a full bladder and asked to cough or bear down.
- Post void residual - the patient either is catheterized after voiding or receives an ultrasound to determine how much urine is left in the bladder. This is done mainly with overflow incontinence or when urinary retention is suspected. Anything over about a cup (or 200 ml) is abnormal.
- Urodynamic testing - not routinely used as it is invasive and expensive and rarely dictates treatment.

# Treatment

Stepwise approach! Start from the least invasive treatments and progress to the more invasive treatments as necessary.

- What causes can be changed? Offending medications? Urinary tract infection? Is there “functional problem” where the patient can’t get to the bathroom on time?
- What are the most bothersome symptoms? It is crucial to discuss the Goals of treatment and manage expectations!

# Treatment ctd

## Least invasive

- Lifestyle modifications
  - Weight loss
  - Dietary changes - cut back on alcohol, caffeine and carbonated beverages.
  - Cut back on excessive fluid intake but avoid dehydration!
  - Cut back on night time fluid intake if nocturia.
  - Smoking cessation

# Treatment ctd

## Behavioral treatment

- Pelvic floor (Kegel) exercises - more effective in women. Used in stress and urge incontinence mainly. Strengthening of pelvic floor muscles provides support around the urethra which can block bladder contractions. Biofeedback can be helpful if patients have trouble isolating these muscles.
- Bladder training - used mainly with urge incontinence. Use of a voiding diary is required. Patients then void at regular timed intervals using the shortest times demonstrated in the diaries that patients can go without voiding. Urgency episodes are dealt with by distraction and Kegel movements. Voiding intervals are gradually increased over the course of several weeks.

KEGEL EXERCISE



# Other non-medication treatments

- Pessaries
- Weighted vaginal cones
- Surgery - mainly for stress incontinence
- Pads
- Treatment of secondary causes of incontinence (e.g., spinal cord compression, UTI, pelvic floor tumors)

# Drugs

- Alpha blockers - Tamsulosin (Flomax), doxazosin (Cardura), terazosin (Hytrin), alfuzosin (Uroxatral). Used to treat urge and overflow incontinence in men with enlarged prostates. Side effects include orthostatic hypotension and dizziness.
- Anticholinergic drugs - Oxybutynin (Ditropan), tolterodine (Detrol), darifenacin (Enablex), solifenacin (Vesicare), fesoterodine (Toviaz), and trospium (Sanctura). Most common medications used to treat urge incontinence and overactive bladder in both men and women. Side effects include blurred vision, dry mouth, constipation, fast heart rate and confusion/hallucinations. Shouldn't take if have narrow angle glaucoma, severe constipation or if on memory drugs such as Aricept.

# Drugs ctd.

- Mirabegron (Myrbetriq) is now being used in patients with urge incontinence who can't tolerate anticholinergic medicine. Associated with less dry mouth and constipation. Can cause high blood pressure.
- Botox injections - weaken the bladder muscle. Helpful for urgency/urge incontinence which could be helpful in Parkinson's. Caution against patients with atypical Parkinsonism such as MSA because the problem there is often bladder Underactivity and could result in not being able to empty the bladder.

# Urinary symptoms and Parkinson's disease

- Studies have shown prevalences ranging from 27% to 85% for urinary symptoms in Parkinsons patients. (McDonald et al. 2016)
- Large discrepancy in prevalences is a reflection of the diversity of different Parkinson's populations. Some studies also probably accidentally include atypical parkinsonian patients where urinary symptoms are more common such as with MSA.
- The Priamo study (Barone et al., 2009) was quite thorough and probably has the most accurate estimate. Urinary symptom prevalence was around 57 %.

# Urinary symptoms in PD ctd

- In decreasing order of symptom prevalence (Fahn, Jancovic, 2007):
  - Nocturia
  - Frequency
  - Urgency
  - Urge incontinence
  - Hesitancy and bladder retention

# Urinary symptoms in PD ctd

- Urinary incontinence within one year of diagnosis suggests atypical parkinsonism or another cause unrelated to Parkinson's disease (Fahn & Jancovic, 2007)
- Again, MSA is often associated with not being able to empty the bladder and overflow incontinence whereas patients with PD have urgency related problems or just can't get to the bathroom on time. Also, urinary incontinence in PD Usually starts years after diagnosis.

# Urinary symptoms and PD ctd.

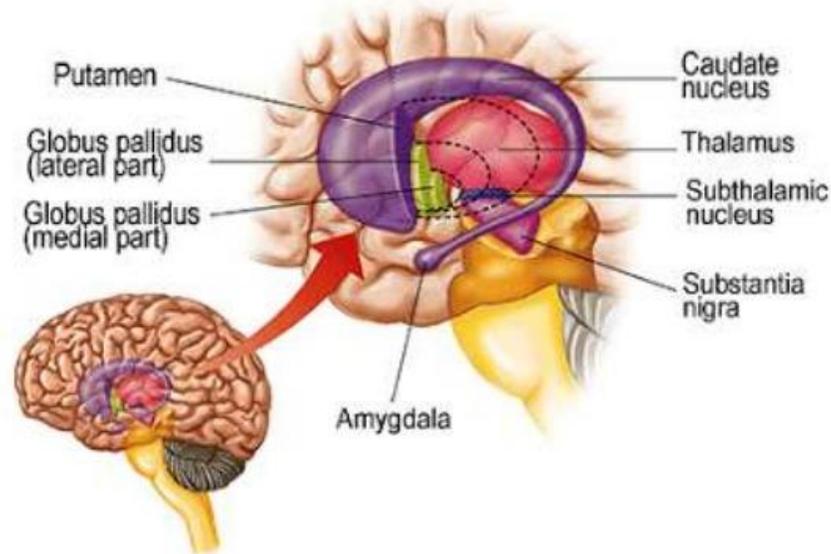
- It is unclear if the degree of urinary symptoms is associated with disease severity (McDonald et al, 2016).
- Some studies have shown that urinary symptoms (other than incontinence) in general don't occur until years after the diagnosis while other studies show patients have symptoms at the time of diagnosis and before. In my experience many patients can present with nocturia at the time of diagnosis unrelated to any other obvious cause. I also have patients who have urinary symptoms at the time of diagnosis related to other medical problems such as prostate issues and multiple births in my female patients.

# Urinary symptoms and PD ctd

- It is also variable as to what extent urinary symptoms affect quality of life.
- In general, urinary incontinence is the most bothersome symptom (McDonald et al. 2016).
- Some studies (Uchiyama et al. 2011) have found that urinary symptoms in early PD are not particularly bothersome or do not have a significant impact on quality of life.
- However, other studies have suggested that as PD progresses, urinary symptoms have a greater impact on quality of life, regardless of the symptom. That is, the same urinary symptom experienced later on in the PD course may be felt as more bothersome than when it is present early on in PD.

# Physiology of urinary symptoms in Parkinsons

## The Human Basal Ganglia



# Pathophysiology of urinary symptoms in Parkinson's disease

- The basal ganglia does contribute to control of urination and this is the control center in PD. Activation of D1 receptors causes inhibition of urination and activation of D2 receptors enhances micturition reflex. Parkinson's disease is thought to result in Underactivation of the D1 receptors thus causing failure to inhibit the urination reflex (McDonald et al. 2016).

# Pathophysiology of urination in PD ct.

- Studies looking at dopamine pathway imaging have shown more pronounced decreases in dopamine activity in PD patients with significant urinary problems compared to PD patients without significant problems. (Sakakibara et al. 2001).
- Deep brain stimulation in Parkinson's patients has shown improved bladder symptoms, particularly with regards to urinary urgency (Pietraszko et al. 2013).

# Assessment of urinary symptoms in PD

- Review of urinary symptoms should take place at routine follow up visits for Parkinson's disease.
- If indicated, a 3 day diary can be helpful to get a patter of what the urinary problem is like. This can help distinguish what type of issue is present such as urgency, overflow incontinence, stress incontinence.

# Assessment in PD ctd.

- Urinalysis should always be considered. Referral to urologist should always be considered. PSA testing should be considered if problems with urinary retention or overflow incontinence. Kidney ultrasound should also be done if signs of urinary retention as the kidneys can swell in severe instances.
- Any patient with sudden changes in urinary patterns should have urine analysis done that day. If worsening of PD symptoms is noticed suddenly, even without urinary symptoms, bladder infection is often present.

# Management of urinary symptoms in PD

## Behavioral management

- As mentioned earlier, bladder training is often the first treatment for frequency/urge incontinence. This has been looked at in PD. As high as 71% of patients have been shown to have at least a 50% reduction in symptoms and close to half of patients in one study showed a 100% decrease in incontinence episodes (Vaughen et al. 2011).

# Urinary symptom management in PD

## Dopaminergic medications

- There have been mixed results in studies looking at Parkinsons medication and treating urinary symptoms. Some studies (Aranda et al. 1993) have shown that medication such as Sinemet initially can worsen urgency symptoms. On the other hand, a study that patients initially had worse symptoms right after treatment but after 2 months had significant improvement in bladder capacity and urgency symptoms (Brusa et al. 2014). Also, Parkinsons medications probably help with functional urinary incontinence where patients have difficulty getting to the bathroom on time because of slowness and walking problems.

# Management of urinary symptoms in PD

## Anticholinergic Drugs

- Detrol and Vesicare for example
- Work by lowering stimulation to the bladder.
- This used to be the main treatment for urinary symptoms in PD. However, because of significant problems with confusion and memory and hallucinations, these are less popular.
- The newer meds in this class have less cognitive side effects but do have dry mouth and constipation. Vesicare for example was studied recently in PD. While it did not decrease urinary frequency, it did decrease incontinence episodes (Zesiewicz et al. 2015).

# Management of urinary symptoms in PD

## Beta-3 adrenergic agonists

- Mirabegron (Myrbetriq) is a newer form of bladder agent that relaxes the bladder muscle. It has not yet been formally studied in PD but has been studied in older patients and has been found to decrease frequency as well as incontinence (Khullar et al. 2012). The benefits were not huge but the medicine is less associated with cognitive effects.

# Management of urinary symptoms in PD

## Nocturia

- As mentioned above, Nocturia is the most common PD symptom with regards to urinary problems. Usually defined as 2 or more episodes needing to get up and urinate at night.
- Desmopressin has been studied in Parkinson's disease. Side effects most commonly include headache and low sodium. It has been associated with a significant decrease in nocturia but up to 30 percent of patients have had to stop the medication because of side effects (Giannantoni et al. 2014).

# Management of urinary symptoms in PD

## Enlarged Prostate

- Enlarged prostate (BPH) is common in many men with Parkinson's disease due to the age groups affected. Treatment of BPH with medications such as Cardura has been shown to result in significant improvement of urinary symptoms and quality of life in men with Parkinson's disease and urinary problems (Gomes et al., 2014).
- Prostatectomy is used to treat both BPH and prostate cancer. Patients with PD can be at greater risk for incontinence following the procedure. This risk has been shown to depend on the degree of sphincter control Before surgery (Staskin et al.2008).

# Management of urinary symptoms in PD

## Botulinum toxin

- Many studies have shown improvement in urinary symptoms following botulinum toxin injections to the bladder muscle, including improvement in incontinence, urge symptoms, urinary frequency, bladder capacity and in some cases, nocturia (Anderson et al. 2014; Giannantoni et al. 2011; Kulaksizoglu et al. 2010). However, there is a potentially serious side effect of not being able to empty the bladder. This can last for months and may require self-catheterization.

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