

Urinary incontinence

The symptoms of urinary incontinence cause great distress in elderly women and those around them. A recent cohort study suggests that it may affect over one-fifth of people aged over 85 years, however this may be an underestimate.¹ In this article we will explore the pathophysiology of urinary incontinence and also look at the management options available for patients.

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Urinary incontinence poses a challenge for doctors in both primary and secondary care to provide the most suitable management appropriate for the patient's symptoms. There are a number of underlying causes which show differential responses to the available therapies. One of the most important factors is to determine the reversible pathologies as quickly and effectively as possible to limit distress. It is also important to understand that urinary incontinence may be part of a more serious underlying illness. The overall physical and psychological effects can be profound.²

Epidemiology

The prevalence of urinary incontinence in elderly women is highly variable. This is due to differences in populations, presentation and response to management. In addition, many people delay seeking medical help for these problems for fear of embarrassment and general lack of awareness of it being a

treatable condition.³ It has been suggested that one in 10 women will have symptoms of urinary incontinence at some point during their lives.⁴ In elderly women the rates of incontinence can be anywhere between 17–42%.⁵ Another study found that in post-menopausal women, with an average age of 67 years, 56% reported symptoms of urinary incontinence at least once weekly.⁶ The number of pharmacological agents available for the treatment of urinary incontinence are, therefore, also increasing.⁷

Pathophysiology

Male and female urethras differ significantly. The female urethra is shorter in length and has a lower external sphincter pressure.

Micturition involves the interplay of a number of pathways. The nervous pathways innervating the bladder and its sphincters include sympathetic, parasympathetic and somatic nerve fibers.

The sympathetic component supplying the bladder and

internal sphincter arises from the tenth thoracic to the second lumbar spinal cord segment (T11–L2). Sympathetic stimulation is via the hypogastric nerve, which suppresses contraction of the detrusor (active during bladder filling). The parasympathetic component originates from the “micturition center” located in the S2–S4 region of the sacral cord. Parasympathetic stimulation is via the pelvic nerve and causes contraction of the detrusor (active during bladder emptying).

The internal urethral sphincter is composed of smooth muscle and is under the control of the autonomic nervous system. The external sphincter is composed of striated muscle and is under voluntary control, innervated by the pudendal nerve. Finally the somatic component, via the pudendal nerve, arises from the motor neurons originating from S2–S4.

When the bladder fills to a volume of 150ml, you will feel the sense to void. Fullness is reached between 350–500mls, this is when you feel the urge to void. A learned reflex prevents you from

Box 1: Pharmacological causes of incontinence

Medication class	Effect
ACE inhibitors	If they cause a cough, this can lead to stress incontinence
Alpha-agonists	Cause urinary retention
Alpha-antagonists	Relaxation of smooth muscle of bladder neck
Anti-cholinergics	Relaxation of bladder smooth muscle causing retention
Beta-agonists	Urinary retention
Calcium channel blockers	Urinary retention
Diuretics	Increase urine production (increase excretion of NaCl and water)
Tricyclic antidepressants	Urinary retention
Sedatives	Urinary retention and sedation (reduced perception of the need to urinate)

voiding in a socially unacceptable situation (efferent stimulation from the brain inhibits parasympathetic stimulation of the detrusor muscle causing contraction of the bladder).⁸

The voiding response requires a coordinated response. As the bladder gets to voiding capacity the bladder stretch receptors are activated and the supraspinal centres block stimulation by the hypogastric and pudendal nerves. This causes relaxation of external urethral sphincter and removes the sympathetic inhibition on the parasympathetic nerves. The parasympathetic cell bodies within the cord are activated and release acetylcholine causing muscle contraction.⁹

Types of incontinence

The International Continence Society defines urinary incontinence as “the complaint of any involuntary leakage of urine”.¹⁰ The three recognised causes of urinary incontinence are as follows.

Stress incontinence

Stress incontinence is involuntary leakage of urine caused by an increase in intra-abdominal pressure (eg. sneezing or coughing) causing the pressure within the bladder to exceed that in the urethra.¹¹ The most common causes include pelvic floor injury sustained

during child birth, pelvic surgery and a hysterectomy.¹²

Urge incontinence

Urge incontinence is caused by a failure of the micturition centres to inhibit contractions of the bladder, causing involuntary leakage of urine. This can also be referred to as hyperactive or irritable bladder.¹³

Mixed incontinence

Mixed incontinence is caused by a combination of both urgency and exertion.¹⁰

Overactive bladder syndrome

Overactive bladder syndrome (OAB) is defined by the International Continence Society

Box 2. Side effects

Pharmacological agent	Side effects
Oxybutynin	Constipation, blurred vision, dry mouth, drowsiness, cognitive impairment
Duloxetine	Nausea, vomiting, dyspepsia, GI disturbance, reduced appetite, weight changes, dry mouth, palpitations

as “urinary urgency, usually accompanied by frequency and nocturia, with or without urgency incontinence, in the absence of urinary tract infection or any other pathologies.”¹⁴ One study estimates the prevalence of OAB could be as high as 34%.¹⁵

Causes of incontinence

An easy way to remember the common causes of urinary incontinence is from the well known mnemonic DIAPERS.¹⁶

- D Delirium, dementia, diabetes
- I Infection, inflammation
- A Atrophy of the vaginal tissues
- P Pharmacological (see Box 1), psychological
- E Excessive urinary output
- R Restricted mobility
- S Stool impaction, sacral nerve root pathology, surgery.

One study concluded that Caucasian women, ranging between 70–79 years of age, had a two-fold greater prevalence of incontinence occurring at least one weekly than women of Afro-Caribbean origin. Risk factors predisposing to stress and urge incontinence included white race, oral oestrogen use, and arthritis. Other factors, specifically associated with urge incontinence included insulin dependent diabetes, depression, older age, and poor physical mobility particularly affecting the lower limbs. Chronic obstructive lung conditions and a high BMI were specifically associated with stress incontinence.¹⁷

History and examination

One study defined it as “at least one episode of objectively proven inappropriate loss of urine, regardless of amount”.¹⁸ The main points to be covered in the history include:

- Symptoms of frequency, urgency, hesitancy, slow urinary stream
- Urinary leakage on coughing, sneezing, exertion

BYETTA® (exenatide)

ABBREVIATED PRESCRIBING INFORMATION

Presentation Exenatide solution for injection in a pre-filled pen. Each dose contains 5 micrograms (µg) in 20 microlitres, or 10µg in 40 microlitres. Also contains metacresol.

Uses Byetta is indicated for treatment of Type 2 diabetes mellitus in combination with metformin, sulphonylureas, thiazolidinediones, or combinations of metformin and a sulphonylurea or metformin and a thiazolidinedione in adults who have not achieved adequate glycaemic control on maximally tolerated doses of these oral therapies. It is also indicated as adjunctive therapy to basal insulin, with or without metformin and/or pioglitazone, in adults who have not achieved adequate glycaemic control with these agents.

Dosage and Administration Initiate at 5µg exenatide per dose, administered twice daily (BD), for at least one month. The dose can then be increased to 10µg BD. Doses higher than 10µg BD are not recommended. Byetta can be administered at any time within the 60-minute period before the morning and evening meal (or two main meals of the day, approximately 6 hours or more apart). Byetta should not be administered after a meal. If an injection is missed, the treatment should be continued with the next scheduled dose. Each dose should be administered as a subcutaneous injection in the thigh, abdomen, or upper arm. Byetta and basal insulin must be administered as two separate injections. When Byetta is added to existing metformin and/or pioglitazone therapy, the current doses of these agents can be continued as no increased risk of hypoglycaemia is anticipated. When Byetta is added to sulphonylurea or basal insulin, the doses of sulphonylurea or basal insulin should be evaluated and a reduction in dose considered to reduce the risk of hypoglycaemia. Blood glucose self-monitoring may be necessary to adjust the dose of sulphonylureas or basal insulin. **Elderly:** Byetta should be used with caution, and dose escalation from 5µg to 10µg should proceed conservatively in patients >70 years. **Renal or hepatic impairment:** No dosage adjustment is necessary in patients with mild renal impairment (creatinine clearance 50-80ml/min) or hepatic impairment. In patients with moderate renal impairment (creatinine clearance 30-50ml/min), dose escalation from 5µg to 10µg should proceed conservatively. Not recommended for use in patients with end-stage renal disease or severe renal impairment (creatinine clearance <30ml/min). **Paediatric population:** The safety and effectiveness of exenatide have not been established in patients under 18 years of age.

Contra-indications Hypersensitivity to the active substance or to any of the excipients.

Warnings and Special Precautions Do not use in patients with Type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. Must not be administered by intravenous or intramuscular injection. Not recommended for use in patients with end-stage renal disease or severe renal impairment (creatinine clearance <30ml/min). Clinical experience in patients with moderate renal impairment is very limited. There have been rare, spontaneously reported events of altered renal function, including increased serum creatinine, renal impairment, worsened chronic renal failure, and acute renal failure, sometimes requiring haemodialysis. Some of these events occurred in patients receiving medicinal products known to affect renal function/hydration status, including angiotensin converting enzymes inhibitors, angiotensin-II antagonists, non-steroidal anti-inflammatory medicinal products, and diuretics. Not recommended in patients with severe gastro-intestinal disease. There have been rare, spontaneously reported events of acute pancreatitis. Patients should be informed of the characteristic symptom of acute pancreatitis: persistent, severe abdominal pain. Resolution of pancreatitis has been observed with supportive treatment but very rare cases of necrotising or hemorrhagic pancreatitis and/or death have been reported. If pancreatitis is suspected, Byetta and other potentially suspect medicinal products should be discontinued. Treatment with Byetta should not be resumed after pancreatitis has been diagnosed. The concurrent use of Byetta with D-phenylalanine derivatives (meglitinides), alpha-glucosidase inhibitors, dipeptidyl peptidase-4 inhibitors, or other GLP-1 receptor agonists has not been studied and cannot be recommended. Experience in patients with BMI ≤25 is limited. Weight loss greater than 1.5 kg per week has been observed in approximately 5% of clinical trial patients treated with exenatide. Weight loss of this rate may have harmful consequences. When Byetta was used in combination with a sulphonylurea, the incidence of hypoglycaemia was increased over that of placebo in combination with a sulphonylurea. To reduce the risk of hypoglycaemia

associated with the use of a sulphonylurea, reduction in the dose of sulphonylurea should be considered.

Interactions Patients receiving orally administered medicinal products of either a narrow therapeutic ratio or that require careful clinical monitoring should be followed closely. If such medicinal products are to be administered with food, they should be taken with a meal when Byetta is not administered. Oral medicinal products that are dependent on threshold concentrations for efficacy should be taken at least 1 hour before Byetta injection. Gastro-resistant formulations containing substances sensitive for degradation in the stomach, such as proton pump inhibitors, should be taken at least 1 hour before or more than 4 hours after Byetta injection. **Digoxin, lisinopril, and warfarin:** A delay in T_{max} of about 2 hours was observed when digoxin, lisinopril, or warfarin was administered 30 minutes after exenatide. No clinically relevant effects on C_{max} or AUC were observed. Increased INR has been reported during concomitant use of warfarin and Byetta. INR should be closely monitored during initiation and dose increase of Byetta therapy in patients on warfarin and/or cumarol derivatives. **HMG CoA reductase inhibitor:** Lovastatin AUC and C_{max} were decreased and T_{max} was delayed when Byetta (10µg BD) was administered concomitantly with a single dose of lovastatin (40mg). Concomitant use of Byetta and HMG CoA reductase inhibitors was not associated with consistent changes in lipid profiles. Lipid profiles should be monitored regularly.

Fertility, Pregnancy, and Lactation Byetta should not be used during pregnancy and the use of insulin is recommended. Byetta should not be used if breast-feeding.

Driving, etc No studies on the effects on the ability to drive and use machines have been performed. When Byetta is used in combination with a sulphonylurea or a basal insulin, avoid hypoglycaemia while driving and using machines.

Undesirable Effects *Very common:* Hypoglycaemia, nausea, diarrhoea, vomiting. *Common:* Decreased appetite, headache, dizziness, dyspepsia, abdominal pain, gastro-oesophageal reflux disease, abdominal distension, hyperhidrosis, feeling jittery, asthenia, injection site reactions, weight decreased. *Rare:* Anaphylactic reaction, dehydration, generally associated with nausea, vomiting and/or diarrhoea (some reports associated with elevation of serum creatinine), acute pancreatitis, altered renal function. *Frequency not known:* INR ratio increased with concomitant warfarin (some reports associated with bleeding). Patients may develop anti-exenatide antibodies following treatment with Byetta. These patients tend to have more injection site reactions (eg, skin redness, itching). *For full details of these and other side-effects, please see the Summary of Product Characteristics, which is available at <http://emc.medicines.org.uk/>.*

Legal Category POM

Marketing Authorisation Numbers

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£68.24 per pack of 5µg (1 pen), £68.24 per pack of 10µg (1 pen)

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Adverse events should be reported. Reporting forms and further information can be found at: www.mhra.gov.uk/yellowcard. Adverse events and product complaints should also be reported to Lilly: please call Lilly UK on 01256 315 000.

References

1. BYETTA Summary of Product Characteristics. March 2012.
2. Buse JB, Bergenstal RM, Glass LC, et al. *Ann Intern Med*. 2011;154:103-112.
3. Douek IF, Gale EAM. *Medical Education Partnership*. 2001:80-89.



- Is there any haematuria (red flag sign)
 - Constipation, faecal incontinence
 - Determine daily fluid intake (specify intake of caffeine)
 - Other medical history: history of stroke (high prevalence of urinary incontinence in patients who have had a stroke)¹⁹, diabetes mellitus, Parkinson's disease
 - Previous surgical procedures relating to abdominal/pelvis
 - Drug history (Box 1)
 - Psychological impact of illness (how are the symptoms impacting on the quality of life).^{1,10,17}
- When examining the patient a general examination of all systems should be carried out. There should however, be particular focus on palpating for abdominal masses and tenderness. You should ask the patient to cough, to look for stress leakage. A neurological examination assessing tone, power, coordination and sensation should be done. A rectal examination should be done to assess peri-anal sensation, sphincter tone and for impaction. In female patients you should examine for vaginal atrophy and prolapse. Urinalysis should be carried out at the bedside.²⁰

Investigations

A bladder diary logging frequency and volume should be kept by the patient and brought to clinic to assess the severity of symptoms. This information should be documented over a minimum period of three days according to NICE guidelines.¹ The urine

should be sent for culture, microscopy and sensitivity if there are leucocytes and nitrites on the urine dip.¹ Routine blood tests looking for markers of inflammation, infection, renal function and also blood glucose should be sent. A urinary tract infection, if found, can be treated with antibiotics and may resolve the problem.²⁰ The volume of urine that remains in the bladder post voiding (post-void residual volume) should be measured.²¹

Indications of referral for specialist investigations such as:^{1,22}

- Failure of conservative and medical management
- Pelvic and/or abdominal mass
- Prolapse of pelvic organs
- Micro/macrosopic haematuria
- Neuropathy.

Management

Before deciding what management option is more suitable for the patient, it is important to determine the underlying cause. Not all patients require pharmacological therapy or even surgical management.

Conservative

Simple measures such as reducing daily fluid intake, particularly of caffeinated drinks, can help a great deal in some cases. If the patient has a high BMI, lifestyle advice and introducing measures to decrease weight may help.^{17,23} One clinical trial found that behavioural training is effective and acceptable for management of urge incontinence. It was found to be more effective than drug therapies such as oxybutynin.²⁴ Pelvic floor exercises with regular

physiotherapy has also proven to be effective, particularly with stress or mixed incontinence.²⁵ One clinical trial showed that there was great improvement in those women with stress incontinence who engaged with physiotherapy over a four-week period and there was complete resolution in over two-thirds of women.²⁶

Another study concluded that behavioural therapy has a number of advantages. There is the obvious absence of pharmacological side effects, and reduces costs and it can be done from home. Functional electrical stimulation has been shown to be effective in overactive bladder syndrome and can be used in combination with pelvic floor exercises.²⁷ In cases where conservative therapy has been proven to be unsuccessful then there is clear indication for the introduction of pharmacological agents.²⁸

Pharmacological

If conservative management fails then medical management has a role. This may be in combination with conservative management such as bladder training or pelvic floor exercises or it may be stand-alone therapy. Antimuscarinics are the main stay of pharmacological therapy for OAB. They work by blocking the muscarinic receptors on the bladder and therefore reducing detrusor and bladder muscle contractility.

There are several drugs in this class that can be used including tolterodine, trospium, propiverine, and solifenacin. NICE recommends offering oxybutynin as first line.²⁹ In addition to these, alpha-adrenergic agents can

be introduced. More recently duloxetine, a selective serotonin-noradrenaline reuptake inhibitor, has shown to be effective in stress urinary incontinence. The mechanism of action is thought to be through increasing pudendal nerve activity and sphincter muscle tone by inhibiting the reuptake of serotonin and noradrenaline.³⁰ There has to be a balance between the side effects (Box 2) caused by these agents and the relief they provide. The side effects can cause issues with compliance. Regular assessment of patient is required until an acceptable balance is achieved.

Postmenopausal women may suffer from urinary incontinence due to vaginal atrophy. In these patients intravaginal oestrogens may be offered.¹⁰

Neuromodulation is another management option for OAB and it is becoming increasingly popular in the NHS. There are two main types: sacral neuromodulation and percutaneous tibial nerve stimulation (PTNS).²⁵

Another increasingly used therapy is Botox. In those patients where pharmacological therapy in the form of antimuscarinics has failed, an injection of botulinum toxin into the wall of the bladder can be effective. This is only currently licensed for use in those patients with an overactive bladder.²⁵

Surgical

The surgical management of urinary incontinence depends on the underlying anatomical abnormality. A number of factors have to be taken into account before consideration of surgery.

The patient's existing health status and comorbidities, their age and any previous surgical procedures. Common conditions requiring surgery include, anterior vaginal prolapse (cystocele), rectocele and vaginal/vault prolapse.³¹ Where there is bladder neck insufficiency with an increase in urethra movement, sling procedures are commonly indicated. The gold standard operation of stress urinary incontinence remains the burch colposuspension. Where there is a non-mobile urethra but weakness at the bladder neck, transurethral injections of collagen is an option.³² A clam cystoplasty is the most common procedure for overactive bladder. This is when part of the bowel is attached to the bladder.²⁵

Summary

There is high prevalence of urinary incontinence in elderly females. Public awareness of the condition remains poor, resulting in late presentation to primary care and delay in further subsequent investigation and management. One study had shown that although one in 10 women experienced symptoms of moderate or severe incontinence, only about half had sought medical advice from the primary health care provider.³³ In some cases incontinence may not be managed appropriately and can be dismissed altogether as a minor symptom.

There has been great change in the attitude of physicians from years gone by. Urinary incontinence was regarded previously as part of the ageing process and was often poorly managed in primary and

secondary care. One paper describes how, less than 15% of medical notes recorded urinary incontinence as a medical problem in the 1980s.³⁴ There is still, however, a lot of scope for improvement.⁵ The Royal College of Physicians published findings from the National Audit of Continence Care 2010 and found that training relating to continence care was provided in less than 50% of hospitals and in only 40% of mental health services.³⁵

Concise history and examination is imperative in finding the underlying cause. Basic investigations can be carried out at the bed side, such as urinalysis, post-voiding residual volume and blood tests specifically looking at renal function, electrolytes and blood glucose levels. It is important to take into account any existing medical condition that the patient may have such as Parkinson's disease or diabetes mellitus. There are clear indications (persistent haematuria, pelvic organ prolapse, complication of prior surgery, frequent UTIs and no response to conservative or medical therapy) for specialist referral to a urologist should further, more detailed investigation be required.

Conflict of interest: none declared

References are included in online version at www.gmjjournal.co.uk