

CME CASE PRESENTATION

Nocturia and Night-Time Incontinence

David R. Staskin, MD

Associate Professor of Urology
Director, Female Urology and Male Voiding Dysfunction
St. Elizabeth's Medical Center
Tufts University School of Medicine, Boston, MA

Disclosure record for David R. Staskin, M.D.
Last reviewed/edited this information on January 10, 2011.
Uroplasty: Consultant or Advisor; American Medical Systems:
Consultant or Advisor; Astellas: Consultant or Advisor;
Pfizer: Consultant or Advisor; Glaxo: Consultant or Advisor;
Allergan: Consultant or Advisor

LEARNING OBJECTIVES:

1. Discuss the definitions of Nocturia and Night-Time Incontinence (N & NTI);
2. Identify the etiology and pathophysiology of N and NTI;
3. Evaluate the symptoms of N and NTI and the differential diagnosis for these symptoms; and
4. Describe appropriate treatment strategies for N and NTI into daily practice.



UNT | HEALTH SCIENCE CENTER

PHYSICIAN ACCREDITATION STATEMENT

The University of North Texas Health Science Center at Fort Worth Office of Professional and Continuing Education is accredited by the American Osteopathic Association to award continuing medical education to physicians.

The University of North Texas Health Science Center at Fort Worth Office of Professional and Continuing Education is accredited by the American Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

PHYSICIAN CREDIT STATEMENT

The University of North Texas Health Science Center has requested that the AOA Council on Continuing Medical Education approve this program for 1 hour of AOA Category 2B CME credits. Approval is currently pending.

The University of North Texas Health Science Center at Fort Worth designates this enduring material for a maximum of 1 *AMA PRA Category 1 Credit(s)*[™].

Physicians should claim only the credit commensurate with the extent of their participation in the activity.

A 67 Y/O MALE PRESENTS WITH THE COMPLAINT of night-time voiding, awakening several times (2-4) at night to void. He admits to frequency and urgency but denies incontinence with urgency. He is post robotic radical prostatectomy and admits to drops of leakage with a hard cough or significant exertion during exercise.

QUESTION 1: What is the definition of nocturia?

Nocturia

- A. is the complaint that the individual has to wake 3 or more times to void.
- B. effects the quality of sleep.
- C. is more common in men.
- D. is associated with stress urinary incontinence.
- E. A and B

DISCUSSION OF QUESTION ONE

The correct answer is B.

Nocturia is defined as waking one or more times per night and defined as such affects approximately 50% of the adult population. However, studies support the fact that few patients are bothered by waking just once per night but that with an increase in nocturia frequency to >2 voids per night, the bother caused by the condition increases, along with negative effects on QoL and daytime functioning.

Previous definitions that have been used, included ≥ 2 voids or ≥ 3 voids per night. For a night-time void to be counted as a nocturia episode, sleep must precede and follow the voiding episodes. Patients with nocturia can be categorized according to the presence of sleep disorders, decreased functional bladder capacity, and/or excessive urine production.

Nocturia is also reported to be one of the most bothersome of lower urinary tract symptoms (LUTS). It negatively affects quality of life from fatigue due to sleep deprivation resulting in decreased productivity at work and low energy levels during the day. It is the most prevalent of LUTS in the general community, is as common in women as it is in men, and affects a significant proportion of younger as well as older people. Elderly patients are likely to be exposed to serious health

risks as there is an increased chance of traumatic injury through falling from 10 to 21% with ≥ 2 voids per night.

Clinical recommendations concerning evaluation and treatment of nocturia should be understood as an adequate initial clinical approach, but are not strongly evidence-based as the definition has not been agreed upon by researchers or regulatory agencies.

REFERENCES:

1. Van Kerrebroeck P, Abrams P, Chaikin D, et al. The standardisation of terminology in nocturia: Report from the Standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn* 2002;21:179-83.
2. Fiske J, ScarperoHM,XueX, et al. Degree of bother caused by nocturia in women. *Neurourol Urodyn* 2004;23:130-3.
3. Chapple CR, Batista J, Berges R, et al. The impact of nocturia in patients with LUTS/BPH: Need for new recommendations. *Eur Urol Suppl* 2007;5:12-8.
4. Yu HJ, Chen FY, Huang PC, et al. Impact of nocturia on symptom-specific quality of life among community-dwelling adults aged 40 years and older. *Urology* 2006;67:713-8.
5. Irwin DE, Milsom I, Hunskaar S, et al. Population-based survey of urinary incontinence, overactive bladder, and other lower urinary tract symptoms in five countries: Results of the EPIC study. *Eur Urol* 2006;50:1306-15.
6. Yu HJ, Chen J, Lai MK, et al. High prevalence of voiding symptoms in Taiwanese women. *Br J Urol* 1998;82:520-3.
7. Jolleys JV, Donovan JL, Nanchahal K, et al. Urinary symptoms in the community: How bothersome are they? *Br J Urol* 1994;74:551-5.
8. Fiske J, ScarperoHM,XueX, et al. Degree of bother caused by nocturia in women. *Neurourol Urodyn* 2004;23:130-3.
9. Chapple CR, Batista J, Berges R, et al. The impact of nocturia in patients with LUTS/BPH: Need for new recommendations. *Eur Urol Suppl* 2007;5:12-8.
10. Asplund R. Nocturia: Consequences for sleep and daytime activities and associated risks. *Eur Urol Suppl* 2005;3:24-32.
11. Hernandez C, Estivill E, Prieto M, et al. Nocturia in Spanish patients with lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH). *Curr Med Res Opin* 2008;24:1033-8.
12. Van Kerrebroeck P, Abrams P, Chaikin D, et al. The standardisation of terminology in nocturia: Report from the Standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn* 2002;21:179-83.
13. Kujubu DA, Abofse SR. Evaluation of nocturia in the elderly. *Permanente J* 2007;11:37-9.
14. Weiss JP, Weinberg AC, Blaivas JG. New aspects of the classification of nocturia. *Curr Urol Rep* 2008;9:362-7.

NOCTURIA IS ASSOCIATED with Overactive Bladder (urgency, usually with frequency, with or without urgency incontinence and nocturia which is a function of the associated decreased bladder capacity. Stress (or effort) urinary incontinence is not associated with nocturia.

QUESTION 2: Nocturia may be associated with:

- A. Sleep disorders (eg., environmental, behavioral, medical)
- B. Increased nocturnal urinary production (eg., polydipsia, polyuria, fluid overload, hormonal)
- C. Decreased bladder capacity (eg., detrusor overactivity/abnormal bladder sensation)
- D. All of the above

DISCUSSION OF QUESTION TWO

The correct answer is D.

A frequent contributor to nocturia is nocturnal polyuria. NP is an overproduction of urine at night (defined as a urinary output greater than 20% of the daily total in young individuals and greater than 33% in older individuals), believed to be due to inadequate secretion of the antidiuretic hormone arginine vasopressin at night. A state of altered hemodynamics is an important factor in the etiology of NP.

A variety of etiological factors have been identified to contribute to increased nocturia, including nocturnal polyuria, sleep disturbances, and diminished bladder capacity. (Table I)

REFERENCES:

1. Van Kerrebroeck P, Abrams P, Chaikin D, et al. The standardisation of terminology in nocturia: Report from the Standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn* 2002;21:179–83.
 2. Weiss JP, Blaivas JG, Jones M, Wang JT, Guan Z, 037 Study Group (2007) Age related pathogenesis of nocturia in patients with overactive bladder. *J Urol* 178:548–551

TABLE 1.

CAUSE	UNDERLYING CAUSE
Poor sleep pattern	Mental or physical ill health
LUT dysfunction	Incomplete voiding BOO Detrusor under-activity Bladder overactivity Bladder hypersensitivity
Excessive fluid output	Primary polydipsia Drugs; diuretics, alcohol, caffeine Circadian changes to arginine vasopressin secretion Diabetes insipidus, mellitus Hypercalcaemia

A 47 Y/O FEMALE C/O FREQUENCY, urgency, and nocturia x3-4 and urgency incontinence episodes on the way to the bathroom. She awakens with a desire to void, and a strong sensation of urgency occurs “when her feet hit the floor”. The symptoms are daytime and night time. There is no other GU history except an occasional urinary tract infection responding to routine short course antibiotic therapy. Of note, the patient reports a constant thirst for water and carries a water bottle – from which she sips during the office visit. The patient is G2P2A2 with an emergency hysterectomy for uncontrolled post-partum bleeding. There is a history of manic depressive illness. There is no cardiac or pulmonary history and no history of hypertension. There is a history of polypharmacy drug abuse 10 years ago resolved with inpatient treatment. The patient is currently on lithium and with improvement of her bipolar symptoms. U/A is negative.

QUESTION 3: Initial evaluation of this patient should not include:

- A. Electrolytes, glucose, serum osmolarity, urine analysis
- B. Voiding diary with voided volumes
- C. Water deprivation test
- D. Cystoscopy
- E. A, B and C

QUESTION 4: The serum sodium osmolarity is significantly elevated with water restriction – the most likely diagnosis is:

- A. Overactive bladder
- B. Psychiatric sleep disorder
- C. Psychogenic water drinking
- D. Diabetes insipidus
- E. A and C

DISCUSSION OF QUESTION THREE AND FOUR

3. *The correct answer is E.*

4. *The correct answer is D.*

Diabetes insipidus (DI) is a condition characterized by excessive thirst and excretion of large amounts of severely diluted urine, with reduction of fluid intake having no effect on the latter. There are several different types of DI, each with a different cause. The most common type in humans is central DI, caused by a

deficiency of arginine vasopressin (AVP), also known as antidiuretic hormone (ADH). The second common type of DI is nephrogenic diabetes insipidus, which is caused by an insensitivity of the kidneys to ADH. It can also be an iatrogenic artifact of drug use such as Lithium.

In order to distinguish DI from other causes of excess urination, blood glucose levels, bicarbonate levels, and calcium levels need to be tested. Measurement of blood electrolytes can reveal a high sodium level (hypernatremia as dehydration develops). Urinalysis demonstrates a dilute urine with a low specific gravity. Urine osmolarity and electrolyte levels are typically low.

Habit drinking (in its severest form termed psychogenic polydipsia) is the most common imitator of diabetes insipidus at all ages. While many adult cases in the medical literature are associated with mental disorders, most patients with habit polydipsia have no other detectable disease. The distinction is made during the water deprivation test, as some degree of urinary concentration Lithium-induced nephrogenic DI may be effectively managed with the administration of amiloride, a potassium-sparing diuretic often used in conjunction with thiazide or loop diuretics. Clinicians have been aware of lithium toxicity for many years and traditionally have administered thiazide diuretics for Lithium-induced polyuria and nephrogenic diabetes insipidus. However, recently amiloride has been shown to be a successful treatment for this condition.

QUESTION 5: Following correction of her Lithium-induced nephrogenic DI the patient continues to complain of urgency and urgency incontinence. The appropriate therapy would be:

- A. Addition of an antimuscarinic
- B. CT scan to rule out central DI
- C. An alpha agonist agent to increase sphincter tone
- D. Cystoscopy

DISCUSSION OF QUESTION FIVE

The correct answer is A.

The patient has overactive bladder in addition to her DI. Appropriate treatment for OAB would be the institution of an antimuscarinic agent.

A 72 Y/O MALE PRESENTS WITH SYMPTOMS of nocturia X 4-5. In addition the patient complains of persistent daytime and nighttime urgency and frequency and an impaired urinary stream with some post voiding dribbling. During the day, the patient is able to toilet but at night significant urgency may precipitate an incontinence episode on the way to the bathroom.

PMH: obesity, CAD, PVD and mild CHF TIA without residual. COPD and sleep apnea, diabetes mellitus (poorly controlled).

SH: married, retired machinist, and likes to watch sports on TV at night. Drinks “a few beers” with “chips or pretzels” while watching the game. Prior cigarette smoker (~75pk-yrs) now smokes an occasional cigar.

MEDS: digoxin, furosemide, insulin, metformin, ASA, doxazosin

PE: ht: 5'7" wt: 265 BP: 160/110 PE: S4, rales at bases with wheezes, distended abdomen, enlarged prostate without nodules, peripheral edema +3 bilaterally (@2PM exam)

LAB: BUN/Cr (22 / 1.4) U/A: +10rbc/hpf, 0-1 wbc, glucose +2, protein – trace, HA1c 8.1.

PSA 3.5ng/ml

QUESTION 6: The first intervention should be:

- A. Review of habits, co-morbidities and medications
- B. Assess cardiac status/treatment of peripheral edema
- C. Evaluation/control of sleep apnea
- D. Improved diabetic control
- E. Other

DISCUSSION OF QUESTION SIX

The correct answer is E.

This patient (especially with smoking history) should be evaluated for microscopic hematuria to rule out malignancy. The source of hematuria may be the upper urinary tract (renal or ureters), or the lower urinary tract (bladder, prostatic urethra, urethra). A bladder malignancy may be responsible for irritative (urgency, frequency) voiding symptoms. A benign source (urinary tract stone, benign prostatic enlargement may also be the source).

QUESTION 7: The urological consultation reveals an enlarged moderately obstructing prostate and a small bladder stone which is removed endoscopically. The patient declined surgical intervention for prostatic obstruction and an alpha-reductase inhibitor was added to the doxazosin. The urology note indicates a post voiding residual of 150ccs. The next intervention should be:

- A. Review of habits, co-morbidities and medications
- B. Bladder diary with voided volumes
- C. Assessment and improved control of hypertension, diabetes, peripheral edema, sleep apnea
- D. Smoking cessation and weight loss counseling
- E. All of the above

DISCUSSION OF QUESTION SEVEN

The correct answer is E.

QUESTION 8: Over the next 2 months, the patient stops smoking cigars (his wife thanks you), limits himself to one beer at night (he likes watching baseball and it is winter), and begins an exercise program (brisk-walking with the dog in AM and PM for an extra 45 minutes (the dog thanks you). His voiding diary revealed 40 percent of his urine output between 11:30 pm and 6:30 am. His sleep evaluation revealed significant periods of sleep apnea. After adjustment of his diabetes and hypertension regimen his HA1c is now 7.4 and BP: 140/85. His nocturia has decreased to +/- 3-4 per night but is still bothersome (his wife still complains of his snoring and frequent trips to the bathroom).

The next step is:

- A. Sleep clinic evaluation for CPAP
- B. Increase lasix
- C. Adjust hypertension meds
- D. Referral back to urologist for reassessment
- E. A, B and C

DISCUSSION OF QUESTION EIGHT

The correct answer is E.

Move lasix to afternoon, change to alpha blocker with less alpha1b to address peripheral edema and add an additional hypertension med.

QUESTION 9: Six months following the initial visit the patient presents with nocturia +/-2-3. He reports less urgency and frequency during the day and less urgency at night with less post-void dribbling (his wife thanks you again). He has lost 28 lbs (wt. 237lb). He has been utilizing his CPAP and taking his lasix at 4PM and elevating his legs during the day when reading or watching TV. He limits himself to 1-2 “lite beers” while watching the game with no snacks. He notices he might get up one additional time if he drinks 2 beers. On exam his BP is 135/80 and peripheral edema +1-2 (4PM). He has not seen the urologist but his pre-visit labs show that his PSA is now 2.0 and HbA1c 7.3. He feels “better”.

The next intervention is:

- A. The patient is happy – no more intervention for nocturia
- B. The patient should see the urologist in f/u for a check of residual urine and to discuss further intervention for BPH
- C. Consider an antimuscarinic agent for urgency and frequency if PVR is <50cc.
- D. Encourage patient to remain compliant with behavioral interventions and medications
- E. B, C and D

DISCUSSION OF QUESTION NINE

The correct answer is E.

QUESTION 10: The patient returns 6 months after minimally invasive therapy for his BPH and 1 year following his initial visit. His nocturia is 2 per night. His residual urine is now 50 cc. The urologist started the patient on a low dose anticholinergic agent for persistent frequency and urgency which has improved and has discontinued the alpha blocker for BPH (the patient remains on the alpha reductase inhibitor). His weight is 207 lbs, BP: 135/80 HbA1c is on 7.1 U insulin. The patient continues to exercise and follow his medical regimen. He has moved from sleeping on the couch to the bedroom and inquires about a PDE-5 inhibitor (no comment from the wife).

The next intervention is:

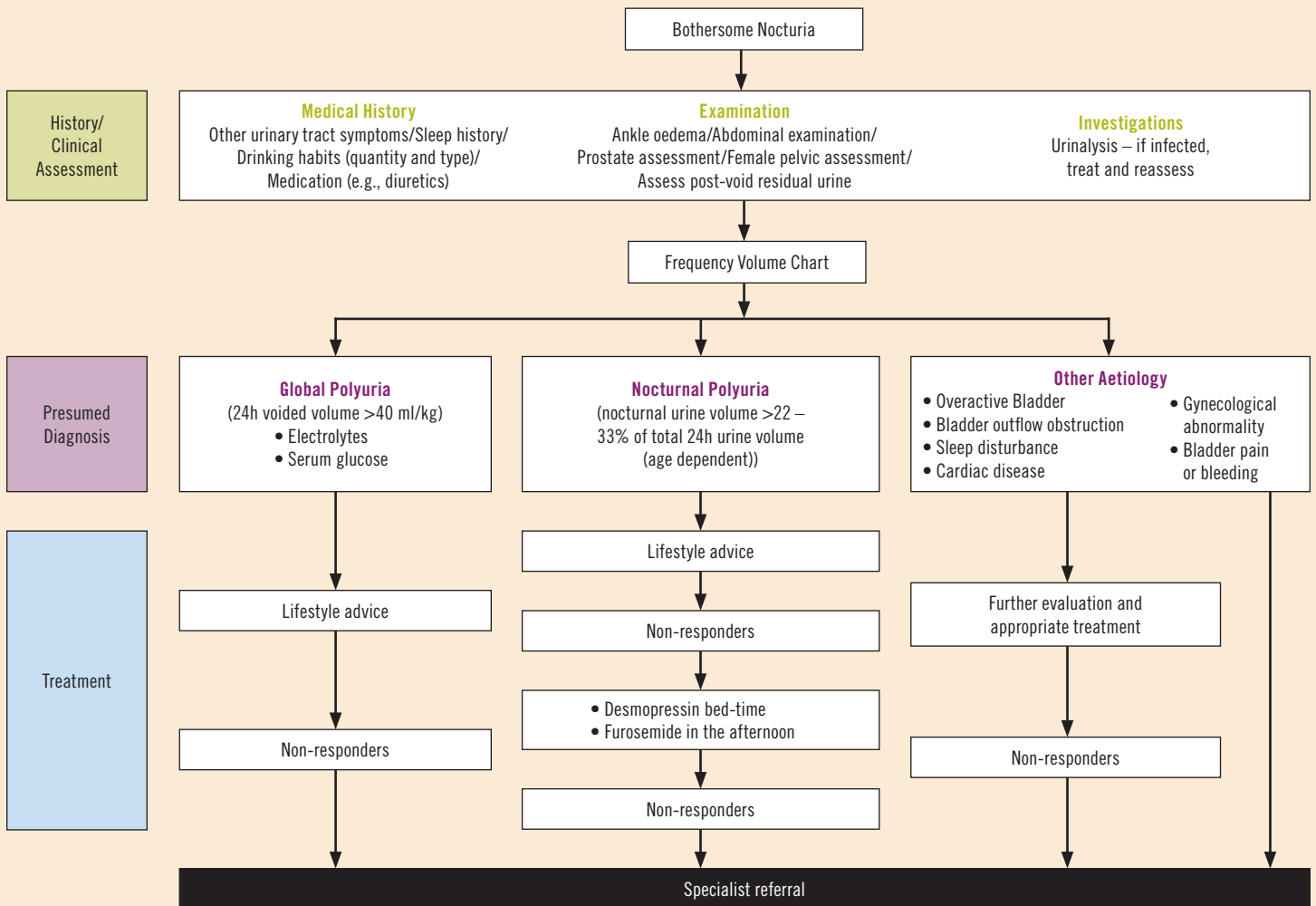
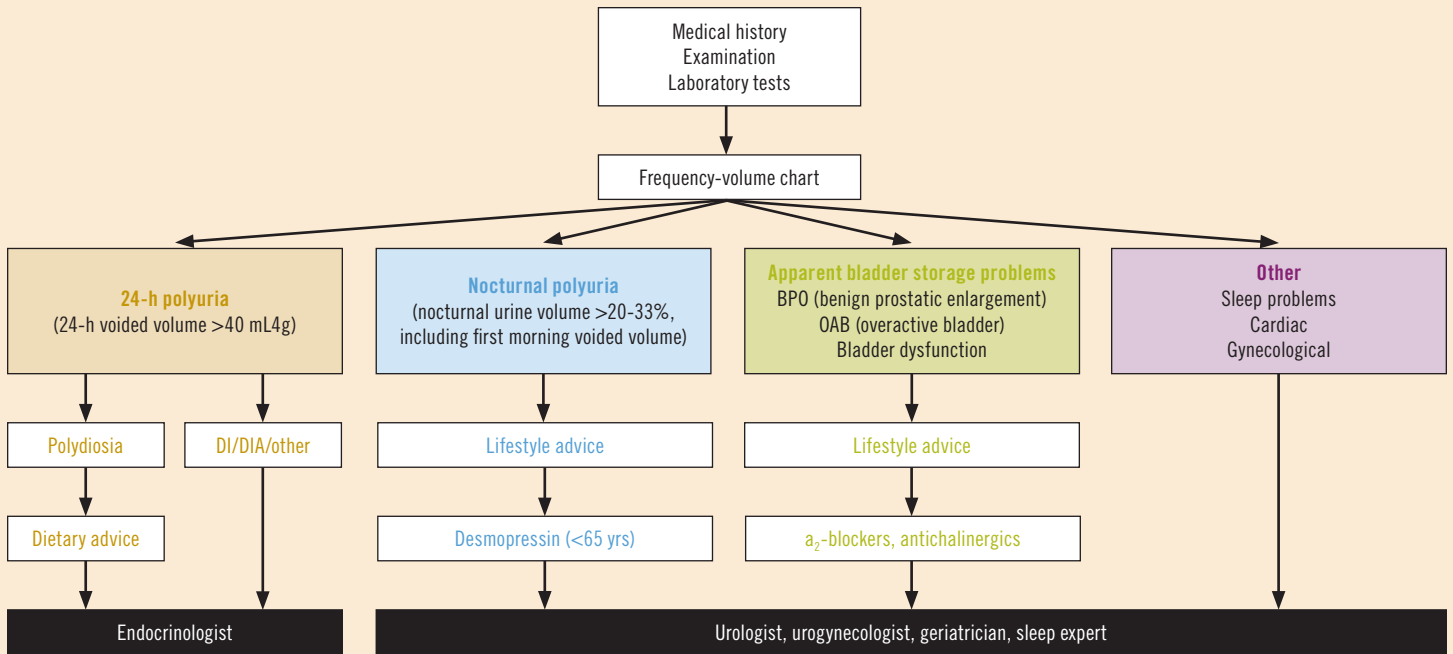
- A. The patient is happy and no additional therapy is indicated/diet counseling
- B. Labs per disease panels and medication review
- C. Yearly psa, u/a and residual urine with urologist
- D. Re-evaluate CPAP as indicated
- E. All of the above

DISCUSSION OF QUESTION TEN

The correct answer is E.

REFERENCES:

1. van Kerrebroeck, P., Abrams, P., Chaikin, D. et al. The standardisation of terminology in nocturia: report from the standardisation sub-committee of the International Continence Society. *Neurourol Urodyn* 2002, 21: 179-83.
2. Jolleys, J.V., Donovan, J.L., Nanchahal, K., Peters, T.J., Abrams, P. Urinary symptoms in the community: how bothersome are they? *Br J Urol* 1994, 74(5): 551-5.
3. Swithinbank, L.V., Donovan, J., Shepherd, A.M., Abrams, P. Female urinary symptoms: just how much “bother” are they? *Neurourol Urodyn* 1997, 16(5): 431-2. (Abst 59a).
4. Kobelt, G., Borgstrom, F., Mattiasson, A. Productivity, vitality and utility in a group of healthy professionally active individuals with nocturia. *BJU Int* 2003, 91(3): 190-5.
5. Van Dijk, L., Kooij, D.G., Schellevis, F.G. Nocturia in the Dutch adult population. *BJU Int* 2002, 90(7): 644-8.
6. Avery, K., Hashim, H., Gardener, N., Abrams, P., Donovan, J., Abraham, L. Development and psychometric testing of the ICIQ-Nocturia module as presented at the joint meeting of the International Continence Society and the International Urogynecological Association, 2004 as a read-by-title abstract (Abst 595).
7. Andersson, K.E., Appell, R., Cardozo, L. et al. Chapter 14: Pharmacological treatment of urinary incontinence. In: *Incontinence: 3rd International Consultation on Incontinence*, June 26-29, 2004. P. Abrams, L. Cardozo, S. Khoury and A. Wein (Eds.). 2005 edition. Health Publication Ltd.: Plymouth 2005, pp. 859-4.
8. Pederson, P.A., Johansen, P.B. Prophylactic treatment of adult nocturia with bumetanide. *Br J Urol* 1988, 62(2): 145-7.
9. Reynard, J.M., Cannon, A., Yang, Q., Abrams, P. A novel therapy for nocturnal polyuria: a double-blind randomized trial of frusemide against placebo. *Br J Urol* 1998, 81(2): 215-8.
10. Mattiasson, A., Abrams, P., Van Kerrebroeck, P., Walter, S., Weiss, J. Efficacy of desmopressin in the treatment of nocturia: a double-blind placebo-controlled study in men. *BJU Int* 2002, 89(9): 855-62.
11. Lose, G., Alling-Moller, L., Jennum, P. Nocturia in women. *Am J Obstet Gynecol* 2001, 185(2): 514-21.



ACTIVITY TITLE:	Nocturia and Night-Time Incontinence
DATES VALID:	August 17, 2011 – August 17, 2012
CREDITS AVAILABLE:	1 Category 2B, AOA; 1 Category 1 <i>AMA PRA</i> ™

INSTRUCTIONS: Please complete this form and return it to the address or fax number below.

PLEASE PRINT CLEARLY	FULL NAME:		DEGREE(S):	
	Last 4 digits of SSN: (for tracking)		or AOA Number: (if applicable)	
	MAILING ADDRESS:			
	PHONE:		FAX:	
	E-MAIL:			

QUESTION RESPONSES					
Q#	A	B	C	D	E
1	(A)	(B)	(C)	(D)	(E)
2	(A)	(B)	(C)	(D)	
3	(A)	(B)	(C)	(D)	(E)
4	(A)	(B)	(C)	(D)	(E)
5	(A)	(B)	(C)	(D)	
6	(A)	(B)	(C)	(D)	(E)
7	(A)	(B)	(C)	(D)	(E)
8	(A)	(B)	(C)	(D)	(E)
9	(A)	(B)	(C)	(D)	(E)
10	(A)	(B)	(C)	(D)	(E)

ONLINE:
www.RegisterWithUNT.com

MAIL TO:
UNTHSC/PACE Office
3500 Camp Bowie Blvd
Fort Worth, TX 76107

OR FAX TO:
817-735-2598

Your certificate will be mailed within three weeks of receipt.

PROGRAM EVALUATION						
Scale:		P=Poor	F=Fair	G=Good	VG=Very Good	E=Excellent
LEARNING OBJECTIVES						P F G VG E
1	Discuss the definitions of Nocturia and Night-Time Incontinence (N & NTI).	(1)	(2)	(3)	(4)	(5)
2	Identify the etiology and pathophysiology of N and NTI.	(1)	(2)	(3)	(4)	(5)
3	Evaluate the symptoms of N and NTI and the differential diagnosis for these symptoms.	(1)	(2)	(3)	(4)	(5)
4	Describe appropriate treatment strategies for N and NTI into daily practice.	(1)	(2)	(3)	(4)	(5)
CONTENT						P F G VG E
5	To what extent this activity is fair and balanced.	(1)	(2)	(3)	(4)	(5)
6	Likelihood that you will implement change in your practice based on information from this activity.	(1)	(2)	(3)	(4)	(5)
7	Your OVERALL rating of this activity.	(1)	(2)	(3)	(4)	(5)
PRACTICE						P F G VG E
12	How will you use the information presented to improve the care of your patients?					

SIGNATURE

DATE