# Biological Basis of Nocturnal Enuresis

**An assay for partial fulfillment for master degree of neuropsychiatry**

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**LIST OF ABREVIATIONS:**

**ADHD :** Attention Deficit Hyperactivity

**ADH :** Antidiuretic hormone

**ANP :** Atrial Natriuretic Peptide

**AVP :** Arginine Vasopressin

**CFC :** Chronic Functional Constipation

**CPAP :** Continuous Positive Airway Pressure

**DDAVP**: 1-desamino-8-D-arginine vasopressin

**EEG :** Electro-Encephalogram

**IgE :** Immunoglobulin E

**MNE :**Monosymptomatic Nocturnal Enuresis

**NE :** Nocturnal Enuresis

**non-REM sleep :** non rapid eye movement sleep

**OSA :** Obstructive Sleep Apnoea

**PNE :** Primary Nocturnal Enuresis

**PPNE :** Persistent Primary Nocturnal Enuresis

**PSQ :** Peadiatric Sleep Questionnaire

**REM sleep :** rapid eye movement sleep

**SBO :** Presence of spina bifida occulta

**SDB :** Sleep Disordered-Breathing

**SNE:** Secondary Nocturnal Enuresis

**SSRI:**serotonin-selective reuptake inhibitor

**UTI :**Urinary Tract Infection

**VUR :** vesicoureteral reflux

# INTRODUCTION

Nocturnal enuresis is a common problem that can be troubling for children and their families (Carolyn. 2003).

It can be classified as primary or secondary and monosymptomatic or polysymptomatic. Primary nocturnal enuresis is the presence of nocturnal urinary incontinence since birth, whereas secondary nocturnal enuresis is the development of nocturnal urinary incontinence after the patient has been “dry” at night for a minimum of 6 consecutive months. Polysymptomatic nocturnal enuresis is associated with any one of the following symptoms: severe urgency, urge incontinence, or a staccato voiding pattern. In monosymptomatic nocturnal enuresis, no other voiding abnormalities are present (Douglas et al.1996).

Because of normal maturational delay within the neurourologic system, primary nocturnal enuresis should not be diagnosed until the child is 5 years of age (Douglas et al.1996).

It is estimated to affect 5 to 7 million US children  6 years of age. Yearly, the spontaneous rate of resolution for nocturnal enuresis is 15%. There are few population-based studies to date concerning the natural resolution of diurnal or polysymptomatic nocturnal enuresis. In 0.5% it persists into adulthood (Wadie et al.2004, Amanda Williams 2005).

Nocturnal enuresis has several possible causes, including genetic inheritance (Loyes et al.2002), reduced bladder capacity (Douglas et al. 1996), sleep disorders (Tryggve et al.2006), a relative lack of ADH (AbdEl Fatah.2009, Maria Vella 2006),  psychologic abnormalities (Gregory Fritz et al.2004), neurologic dysfunction (Freitag et al.2006),  bacteriuria (Abdel-Latif et al.2006), constipation

(Lane et al.2005) & airways obstruction with snoring (Stone et al.2008). Diet & drinks containing methylxanthines , such as tea, coffee, cola and chocolate, can aggravate the situation by their diuretic action. Other risk factors that predispose to nocturnal enuresis is to be expected in those with global developmental delay, with or without an associated syndrome such as Down's syndrome (Touchette et al.2005).

Even without gross developmental delay, there is more likely to be persistent bed wetting in children with delayed developmental milestones (Alexander Von Gontard et al. 2006), premature delivery or behavioural disorders such as hyperactivity or inattention deficits (Ubeda Sansano et al. 2005). There is no evidence that early potty training prevents bedwetting (Gregory Fritz et al.2004).

For the vast majority of children, the presence of diurnal and nocturnal enuresis is a source of shame and embarrassment. It profoundly affects the child's life socially, emotionally, and behaviorally and also impacts the everyday life of his/her family (CFN and Wong. 2004).

A thorough assessment of the patient's voiding history is of major importance in the management of the condition. Whether the patient has monosymptomatic or polysymptomatic nocturnal enuresis must be determined (Gregory Fritz et al.2004).

Treatment options include pharmacotherapy,behavioral modification with an alarm system, or a combination of these modalities In order for treatment to be successful, the physician, patient, and patient's parents must be involved in the decision-making process (Carolyn Thiedke. 2003).

Some may use alternative medicine such as hypnosis, psychotherapy, acupuncture and chiropractic however a Cochrane review found poor evidence to support them as each case was supported by single small trials (Gregory Fritz et al.2004).

# AIM OF THE WORK

The aim of this work is to provide a review regarding the biological basis of nocturnal enuresis and the new lines of therapy to control this problem and to improve the quality of life of these patients.

# ANATOMY

The essential foundation for understanding any disease process is a firm concept of the underlying anatomy and physiology of the system involved (www.continence-foundation.org.uk).

## THE URINARY BLADDER:

The urinary bladder is a reservoir; it varies in size, shape, position and relations, according to its content and the state of neighbouring viscera. When empty, it lies entirely in the lesser pelvis but as it distends it expands anterosuperiorly into the abdominal cavity. When empty, it is somewhat tetrahedral and has a base (fundus), neck, apex, a superior and two inferolateral surfaces**.** The base (fundus) of the bladder is triangular and posteroinferior. In females it is closely related to the anterior vaginal wall (Fig.1) in males it is related to the rectum although it is separated from it above by the rectovesical pouch and below by the seminal vesicle and vas deferens on each side . In a triangular area between the vasa deferentia, the bladder and rectum are separated only by rectovesical fascia, commonly known as Denonvillier's fascia. The inferior part of this area may be obliterated by approximation of the ampullae of the vas deferens above the prostate (Jonathan Glass.2004).

The neck is the lowest region and is also the most fixed. It is three to four centimeters (3-4 cm) behind the lower part of the symphysis pubis (Fi g. 2), which is a little above the plane of the inferior aperture of the lesser pelvis. The bladder neck is the internal urethral orifice and alters little in position with varying conditions of the bladder and rectum. In males the neck rests on, and is in direct

continuity with, the base of the prostate; in females it is related to the pelvic fascia, which surrounds the upper urethra (Griffiths et al. 2005).

The vesical apex in both sexes faces towards the upper part of the symphysis pubis. The median umbilical ligament ascends behind the anterior abdominal wall from the apex to the umbilicus, covered by peritoneum to form the median umbilical fold. The triangular superior surface is bounded by lateral borders from the apex to the ureteric entrances and by a posterior border, which joins them. In males the superior surface is completely covered by peritoneum, which extends slightly onto the base and continues posteriorly into the rectovesical pouch and anteriorly into the median umbilical fold. It is in contact with the sigmoid colon and the terminal coils of the ileum. In females the superior surface is largely covered by peritoneum, which is reflected posteriorly onto the uterus at the level of the internal os (i.e. the junction of the uterine body and cervix), to form the vesicouterine pouch. The posterior part of the superior surface, devoid of peritoneum, is separated from the supravaginal cervix by fibroareolar tissue. In males, each inferolateral surface is separated anteriorly from the pubis and puboprostatic ligaments by the (potential) retropubic space. In females the relations are similar, except that the pubovesical ligaments replace the puboprostatic ligaments. The inferolateral surfaces are not covered by peritoneum (Zhang et al. 2005).

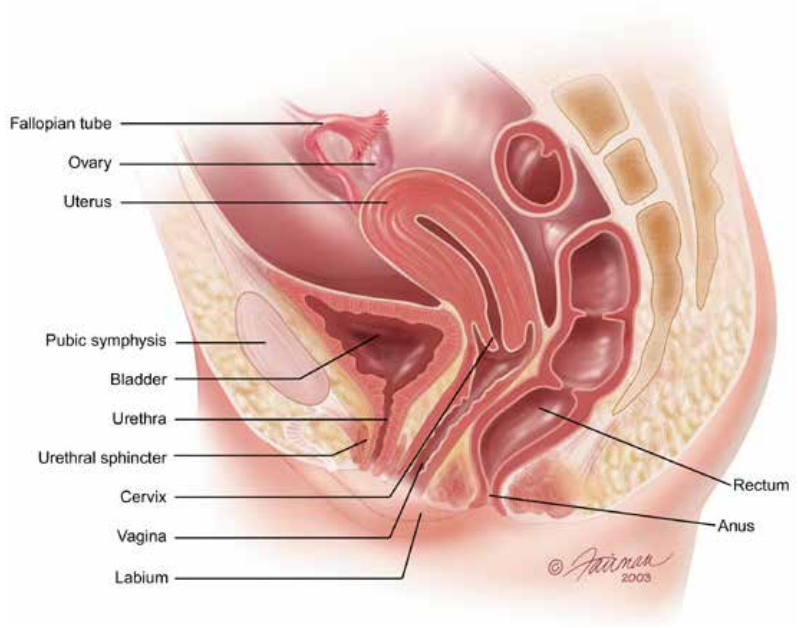


**Figure 1 Female urinary bladder (www.coloplast.com)**

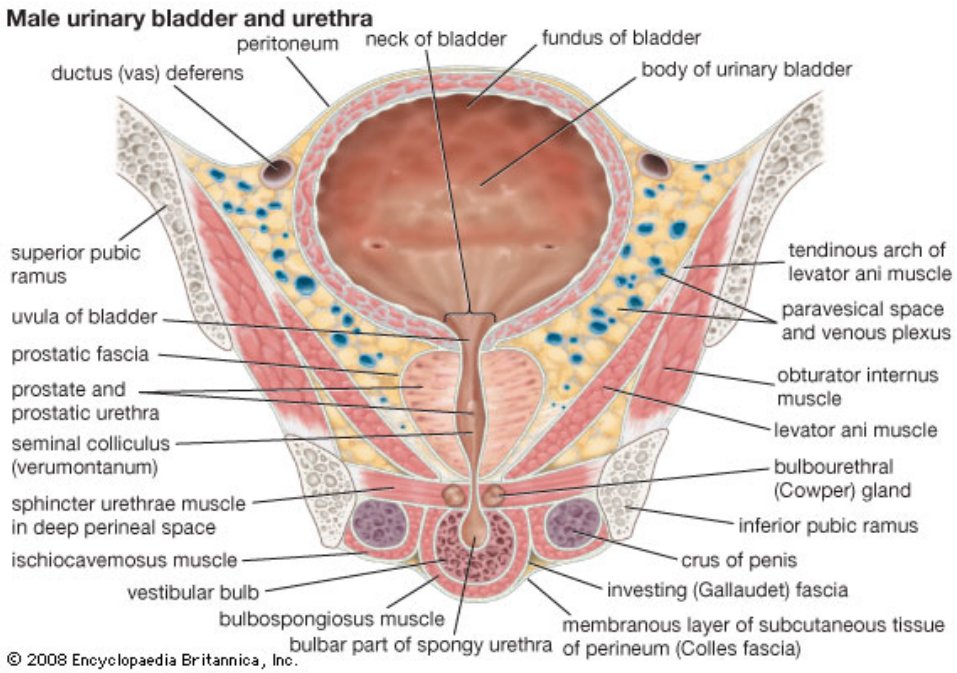


**Figure 2 Male urinary bladder ( www.britannica.com)**

## BLADDER INTERIOR (Fig. 3)

### *TRIGONE*

The smooth muscle of the trigone consists of two distinct layers, sometimes termed the superficial and deep trigonal muscles. The latter is composed of muscle cells, indistinguishable from those of the detrusor, and is simply the posteroinferior portion of the detrusor muscle proper. Confusion might be avoided if the term deep trigonal muscle was abandoned in favour of the more accurate term trigonal detrusor muscle. The superficial trigonal muscle represents a morphologically distinct component of the trigone, which, unlike the detrusor, is composed of relatively small diameter muscle bundles continuous proximally with those of the intramural ureters. The superficial trigonal muscle is relatively thin but is generally described as becoming thickened along its superior border to form the interureteric crest. Similar thickenings occur along the lateral edges of the superficial trigone. In both sexes the superficial trigone muscle becomes continuous with the smooth muscle of the proximal urethra, and extends in the male along the urethral crest as far as the openings of the ejaculatory ducts (Griffiths et al. 2005).

### *TOW URETERIC ORIFICES*

The slit-like ureteric orifices are placed at the posterolateral trigonal angles. In empty bladders they are tow and half centimeter apart, and tow and half centimeter from the internal urethral orifice; in distension these measurements may be doubled (Jonathan Glass.2004).

***INTERNAL URETHRAL ORIFICE***

The internal urethral orifice is sited at the trigonal apex, the lowest part of the bladder, and is usually somewhat crescentic in section. There is often an elevation immediately behind it in adult males (particularly past middle age) which is caused by the median prostatic lobe, sometimes known as the uvula of the bladder (Delancey and Ashton-Miller 2004).

**THE FEMALE URETHRA:**

Is shorter and wider than male urethra. It's surrounded by the urethral sphincter in the deep pouch (Klutke and Siegel.1995).

**THE MALE URETHRA:**

It has three parts: prostatic urethra, membranous urethra, spongy (penile) urethra is its narrowest part (Jonathan Glass.2004).