INTRODUCTION

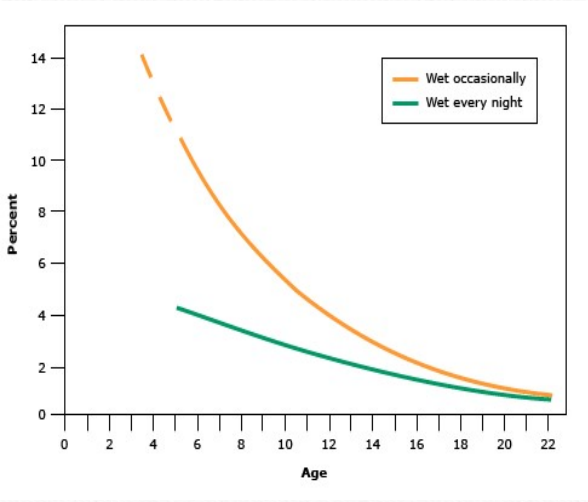
Enuresis

- Enuresis (or synonymous with intermittent nocturnal incontinence) refers to discrete episodes of urinary incontinence during sleep in children ≥5 years of age .
- A: **monosymptomatic**
- B: **non-monosymptomatic forms**

Monosymptomatic enuresis

- Enuresis in children without any other lower urinary tract symptoms and without a history of bladder dysfunction.
- A: **primary** ➡ Children who have never achieved a satisfactory period of nighttime dryness. 80%
- B: **secondary forms** ➡ Children who develop enuresis after a dry period of at least six months.
- It is ascribed to an unusually stressful event (eg, caregiver , divorce, birth of a sibling) at a time of vulnerability in a child's life.

EPIDEMIOLOGY AND NATURAL HISTORY



The prevalence varies according to age

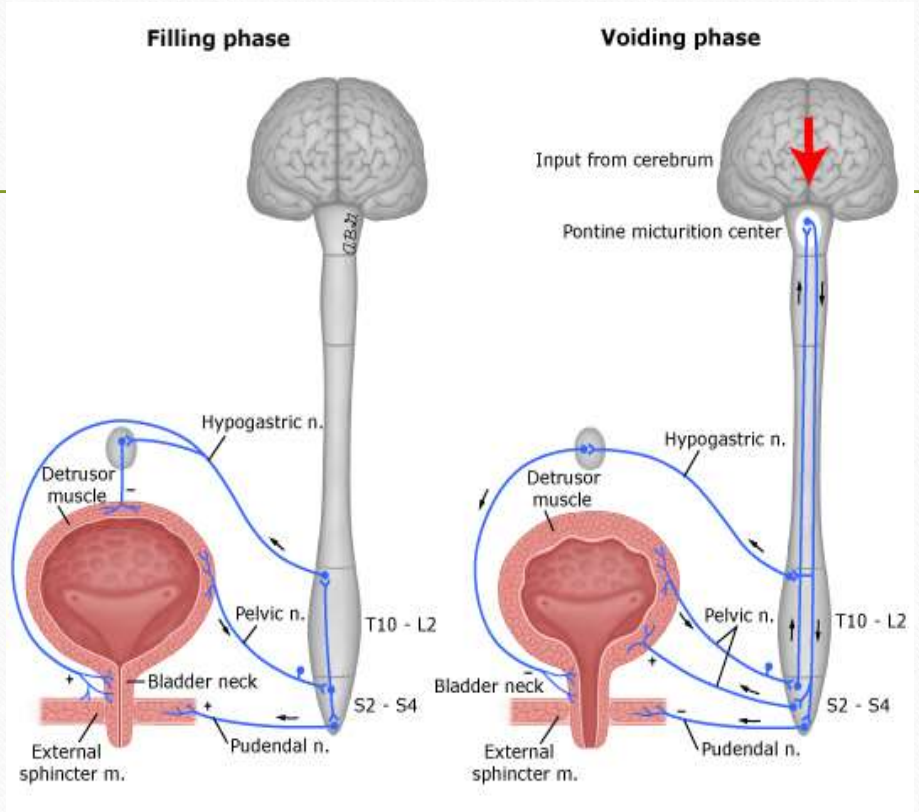
- 5 years – 15 percent
- 6 years – 13 percent
- 7 years – 10 percent
- 8 years – 7 percent
- 10 years – 5 percent
- 12 to 14 years – 2 to 3 percent
- ≥15 years – 1 to 2 percent
- **twice as common among boys as girls**. It resolves spontaneously at a rate of approximately 15 percent per year . The longer the enuresis persists, the lower the probability that it will spontaneously resolve

Non-monosymptomatic enuresis

Defined as enuresis in children with other lower urinary tract symptoms, including

1. Consistently increased (≥8 times/day) or decreased (≤3 times/day) voiding frequency
2. Daytime incontinence
3. Urgency
4. Hesitancy (difficulty initiating voiding)
5. Straining (application of abdominal pressure to initiate and maintain voiding)
6. A weak stream
7. Intermittency (micturition occurs in several discrete spurts)
8. Holding maneuvers (strategies used to postpone voiding)
9. A feeling of incomplete emptying
10. Postmicturition dribble
11. Genital or lower urinary tract pain
12. Bladder dysfunction
13. Bowel and bladder dysfunction

- Normal bladder function depends upon a complex interrelationship between autonomic and somatic nerves, which are integrated at various sites in the **spinal cord**, **brainstem**, **midbrain**, and **higher cortical center**.
- During the first three years of life, bladder capacity increases disproportionately relative to body surface area. By four years of age, most children void five to six times per day.
- The child first **becomes aware of bladder filling**, then develops the **ability to suppress detrusor contractions voluntarily** and, finally, learns to coordinate sphincter and detrusor function. These skills usually are achieved, at least during the day, by approximately four years of age. Nighttime bladder control is achieved months to years after daytime control but is not expected until five to seven years of age.


Filling phase
Voiding phase
Input from cerebrum
Pontine micturition center
Hypogastric n.
Detrusor muscle
Pelvic n.
T10 - L2
S2 - S4
Bladder neck
External sphincter m.
Pudendal n.

PATHOGENESIS

- Nocturnal enuresis occurs **when the child does not wake to void** .
- this may result from one or a combination of several related factors:
- **maturational delay**
- **genetic factors**
- **nocturnal polyuria**
- **disturbed sleep**
- **small bladder capacity**
- **detrusor overactivity**. **Psychological and behavioral abnormalities appear to be a result, rather than a cause, of enuresis .**

- **Maturational delay**: An increased incidence of delayed language and gross motor development and slowed motor performance among children with enuresis.
- **Genetic factors**: a genetic tendency toward nocturnal enuresis. concordance among monozygotic twins is almost twice that among dizygotic twins . one parent has a history of prolonged nighttime wetting, approximately 50 percent of the offspring are affected; when both parents have a history, approximately 75 percent of offspring are affected .On the other hand, when neither parent has a history of nocturnal enuresis, only 15 percent of offspring are affected.
- **Nocturnal polyuria and antidiuretic hormone**: Mechanisms for increased nighttime urine output may include
- 1)increased fluid intake before bedtime
- 2)reduced response to antidiuretic hormone (ADH)
- 3) decreased secretion of ADH .In children who do not have enuresis, urine output decreases during the night because the secretion of ADH and other regulatory hormones follows a circadian pattern, with increased secretion at night .
- **Disturbed sleep** : Excessively deep sleep also appears to contribute to nocturnal enuresis in adolescents and adults.

- **Small bladder capacity:** At birth, bladder volume is approximately 60 mL (2 ounces)
- That increases approximately 30 mL (1 ounce) per year until 10 years of age.
- Normal bladder capacity = age+ 2 in years, until 10 years of age. Children with nocturnal enuresis, have a smaller bladder capacity than age-matched children who do not have nocturnal enuresis

- **Detrusor overactivity:** Although detrusor abnormalities are more frequently associated with daytime urinary incontinence, detrusor overactivity should be considered in children with refractory monosymptomatic nocturnal enuresis.

OTHER CAUSES OF NOCTURNAL ENURESIS

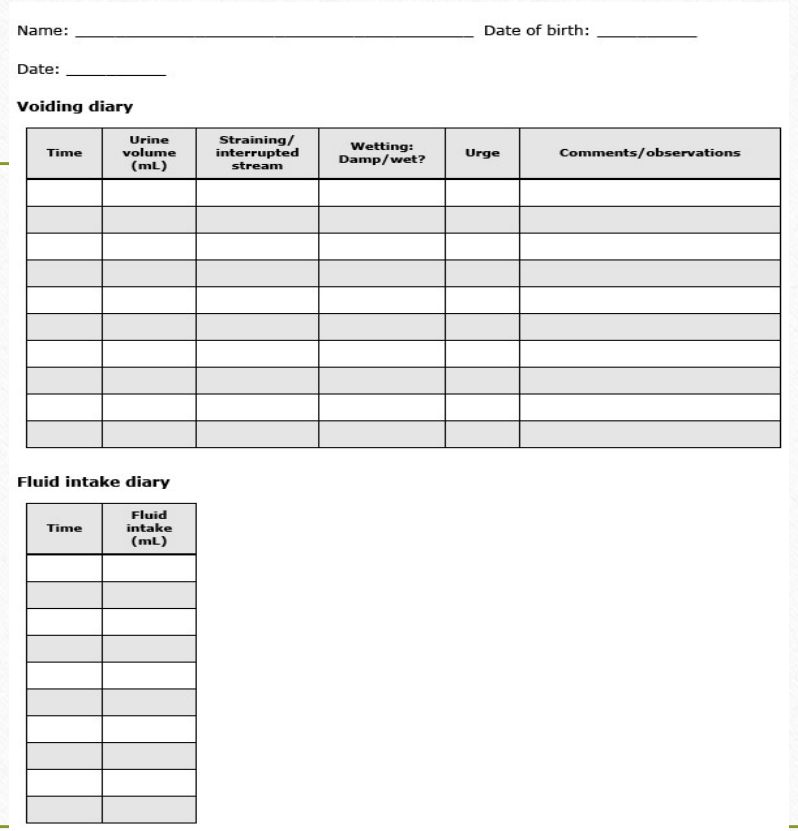
- Bladder dysfunction
- Urinary tract infection
- Chronic kidney disease
- Posterior urethral valves AND Ectopic ureter in girls
- Fecal incontinence or constipation
- Sickle cell disease
- Seizures
- Diabetes mellitus AND Diabetes insipidus
- Spinal dysraphism
- Obstructive sleep apnea
- Pinworms
- Primary polydipsia

History

- Daytime wetting or lower urinary tract symptoms
- Whether the child ever had a prolonged period of dryness
- Frequency and trend of nocturnal enuresis
- Fluid intake diary
- Stooling history and history of soiling
- Determination of which interventions the caregivers have tried and whether they were successful.
- Medical history
- Family history of nocturnal enuresis.
- Social history
- Assessment of how the problem has affected the child and family
- Developmental and behavioral histories and developmental-behavioral screening questionnaires

voiding diary

- Timing of daytime voids
- Volume of voided urine (to estimate bladder capacity)
- Lower urinary tract symptoms



Name: _____ Date of birth: _____

Date: _____

Voiding diary

Time	Urine volume (mL)	Straining/ interrupted stream	Wetting: Damp/wet?	Urge	Comments/observations

Fluid intake diary

Time	Fluid intake (mL)

Your name _____ Started on Date _____

Date	Time	Measured amount of urine	Did you have leakage, yes or no?	Approximate amount of leakage	Time you went to bed/got up, drank coffee or soda, any other comments

Physical examination

- **The physical examination of the child with primary monosymptomatic nocturnal enuresis usually is normal.**
- Poor growth and/or hypertension
- Tonsillar hypertrophy or "adenoid facies
- Detection of wetness in the undergarments is a sign of daytime incontinence
- Palpation of stool in the abdomen suggests constipation or fecal incontinence
- Perianal excoriation or vulvovaginitis may indicate pinworm infection
- Detection of incomplete bladder emptying
- Abnormalities of the lumbosacral spine

Imaging for select patients

- Ultrasonography
- renal sonogram and voiding cystourethrogram
- UA and seldom uc

PRETREATMENT EVALUATION

- Include assessment for causes of nocturnal enuresis that may require additional evaluation and/or treatment
- **(diabetes mellitus, obstructive sleep apnea, constipation, bladder dysfunction)**
- It is difficult to successfully treat enuresis if **coexistent constipation** is not addressed. When evaluating for constipation, it may be helpful to ask about soiling in addition to the usual questions about bowel habits.

WHEN TO INITIATE MANAGEMENT

- **The timing of initiation of treatment ⟹ varies from child to child.**
  The major determinants are :
- 1)whether the child and caregivers view the enuresis as a problem
- 2) how strongly motivated they are to participate in a treatment program.
- 3) The age at which enuresis is considered to be a "problem" varies from family to family.

- **Nocturnal enuresis usually becomes a problem for children when it interferes with their ability to socialize with peers**.

Treatment probably should be delayed if it seems that the caregivers are more interested in treatment than the child and the child is unwilling or unable to assume some responsibility for the treatment program. The child must be highly motivated to participate in a treatment program that may take months to achieve successful results.

Important Point

- **1) management with education and motivational therapy in children younger than six years .**
- **2) age should not be the only criterion for initiation of active treatment**
  3) Enuresis as infrequent as once per month is associated with decreased self-esteem .
- **4) treatment can improve self-esteem, even if treatment is not completely successful.**

INDICATIONS FOR REFERRAL

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- **Monosymptomatic nocturnal enuresis usually can be managed by the primary care provider**

1) Suspicion of structural or anatomic abnormalities (refer to pediatric urologist).

2) Nonmonosymptomatic enuresis.

3) Developmental, attentional, or learning difficulties.

4) Behavioral or emotional problems.

5) Known or suspected physical or neurologic problems.

6) Caregivers who express anger, negativity, or blame toward the child; these caregivers may need additional support The possibility that the child is being **abused** should be considered if the caregivers report that the child is deliberately wetting the bed.

7) Refractory enuresis.

INITIAL MANAGEMENT

A) Treatment of coexisting conditions

- Constipation/Sleep disordered breathing/Attention deficit hyperactivity disorder

B) Establish goals and expectations

- Reducing the number of wet nights
- Reducing the impact of enuresis on the child and family
- Staying dry on particular occasions (eg, sleepover)
- Avoiding recurrence

C) Education and advice

- Surveys indicate that between one-fourth and one-third of caregivers punish their child for wetting the bed, and sometimes the punishment is physically abusive.

RECOMENDATION

- The child should attempt **to void a total of four to seven times per day**, including **just before going to bed**; if the child wakes at night, the caregivers should take the child to the toilet.
- **High-sugar and caffeine-based drinks** should be avoided in the evening hours.
- Restricting fluid intake in the evening may be helpful for some children but should be continued only if it is successful .
- drink 40 percent their total daily fluid in the morning (7 AM to 12 PM)
- 40 percent in the afternoon (12 PM to 5 PM)
- only 20 percent in the evening (after 5 PM)

Motivational therapy for select patients

- It is an appropriate initial therapy for nocturnal enuresis in children between **five and seven years** of age who do not wet the bed every night.
- **Initial rewards**

should be given for agreed-upon behavior (eg, going to the toilet before bedtime) rather than dryness .

- **Successively larger rewards**

agreed upon in advance, are given for longer adherence to agreed-upon behavior and, eventually, for longer periods of dryness .

ADDITION OF ACTIVE THERAPY

- Initial active therapies include Enuresis alarms and desmopressin.
- children with monosymptomatic nocturnal enuresis who have no improvement after three to six months of initial management if enuresis continues to be a problem for the child and family (is associated with diminished self-esteem, prevents the child from attending sleepovers).

Selecting active therapy

- **Alarms and desmopressin** are
- 1) effective
- 2) simpler than combination therapy
- 3) and have few serious adverse effects

Alarms For children :

- 1)who have enuresis more than twice per week
- 2) whom short-term improvement is not a priority enuresis
- 3) alarms have lower relapse rates
- 4) require a highly motivated child and family and a time commitment of at least three months

Desmopresin For children:

- 1) whom short-term improvement is a priority
- 2) who have nocturnal polyuria with normal daytime voided volumes
- 3) who have enuresis ≤2 times per week
- **Nocturnal polyuria ((nocturnal urine production greater than 130 percent of expected bladder capacity for age)) =**
- **30 x (age [in years] +1)**

Desmopressin rapidly **effective than alarms**

requires a **shorter time commitment**

less caregiver supervision

has a higher relapse rate

decreases nocturnal urine production

Desmopresin should not be used in children with hyponatremia or a history of hyponatremia

Enuresis alarm

Types of alarms

- work through **conditioning**: The child learns to wake or inhibit bladder contraction in response to the physiologic conditions present before wetting

1) **Enuresis alarms consist of a sensor** sensor is placed in the undergarments or on a bed pad

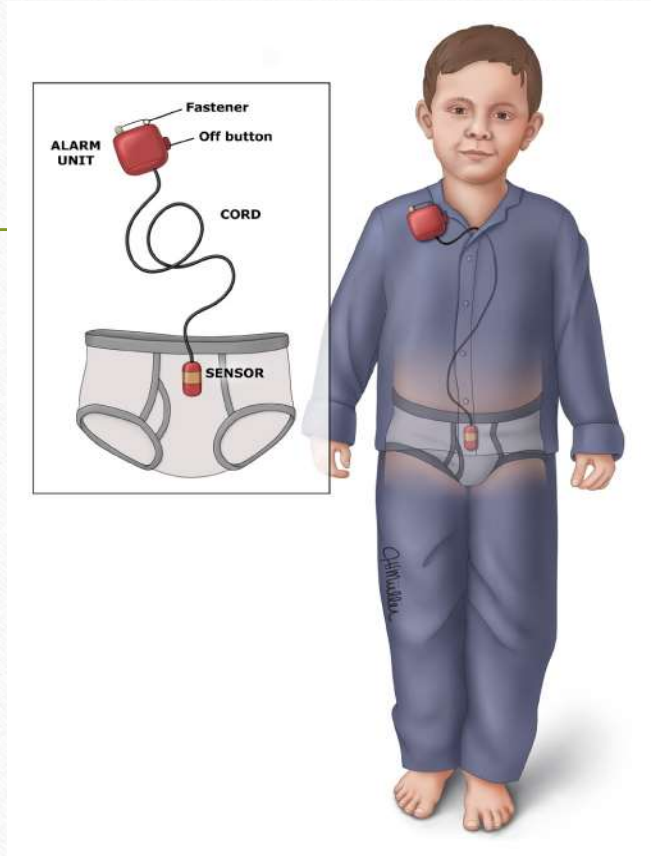
2) **an arousal device** arousal device is an auditory alarm and/or a vibrating belt or pager

- typically used in children ≥6 years of age
- should be demonstrated to the child and family before use.
- It must be used every night.
- The child is in charge of the alarm .
- Each night child should test the alarm
- Child should imagine in detail, for one to two minutes, the sequence of events

The sequence is as follows

- Child turns off the alarm, gets up, and finishes voiding in the toilet (**only the child should turn off the alarm**).
- The child's being fully awake and cognizant of what is happening is critical to the success of alarm therapy.
- The child returns to the bedroom.
- The child changes the bedding (with caregiver supervision) and clothing.
- Should be kept near the bed.
- The child wipes down the sensor (or replaces the sensor if it is disposable).
- The child resets the alarm and returns to sleep.

- A diary should be kept of wet and dry nights. Positive reinforcement should be provided for successful completion of the above sequence of events, waking and getting out bed to void, and for dry nights . Penalties (eg, the removal of a reward) for wetting episodes appear to be counterproductive.


Fastener
Off button
ALARM UNIT
CORD
SENSOR

Monitoring response

- The follow-up within one to two weeks of initiating .
- **If early signs of response**: Treatment should be continued for at least three months ,until the child has had at least 14 consecutive dry nights .
- After a three month trial, alarm therapy should be continued if the child has more dry nights per week than at baseline, even if they have not achieved ≥14 consecutive dry nights .
- Alternative interventions may be warranted if there has been no improvement after three months of alarm therapy.
- Therapy with the alarm can be reinitiated for relapse (≥2 wet nights per month).
- usually can achieve a rapid secondary response because of preconditioning during the initial treatment program.

Lack of early response

- For children who fail to demonstrate early signs of response we suggest either the addition of low dose desmopressin in addition to alarm therapy or discontinuation of the enuresis alarm with a plan for a subsequent trial in 6 to 12 months when the child is more mature.

Using desmopressin

I. Orally 60 minutes before bedtime . The dose is titrated to best effect; at the correct dose, the antienuretic effect is immediate. two formulation:

II. **Regular tablets** (the only formulation available in the United States; nasal spray is no longer available) – The initial dose is 0.2 mg; if necessary, it can be increased to 0.4 mg after seven days. The tablets can be crushed and mixed with a small amount of soft food (eg, applesauce, yogurt) or chewed.

III. **Oral melt tablets :** The initial dose is 120 mcg; if necessary, it can be increased to 240 mcg after seven days.

IV. The trial should take place at least six weeks before camp.

Prevention of dilutional hyponatremia

1. The oral formulation of desmopressin should be used (the intranasal formulation is not indicated for enuresis because it was associated with increased risk of hyponatremic seizures).
2. Fluid intake should be limited to 6.75 ounces (200 mL) from one hour before to eight hours after administration
3. should be temporarily discontinued during episodes of fluid and/or electrolyte imbalance
4. It is not necessary to routinely measure weight, serum electrolytes, blood pressure, or urine osmolality.

Assessing response

- The response should be assessed within one to two weeks .
- Treatment should be continued for three months if there are signs of a response (eg, smaller wet patch
- When it is administered daily, desmopressin should be withheld for one week every three months to determine whether continued use is necessary or not.
- Lack of response within one to two weeks may be due to :
- reduced nocturnal bladder capacity (the most common reason for unresponsiveness)
- or persistent nocturnal polyuria (related to increased fluid intake in the evening, increased nocturnal solute excretion, or reduced pharmacodynamic effect of desmopressin) .

REFRACTORY ENURESIS

Lack of response to active intervention is defined by <50 percent improvement in baseline frequency of enuresis.

Referral to a specialist is warranted when children do not respond to an adequate trial of treatment with:

1) an enuresis alarm (**three months**)

2)desmopressin (**at a dose of 0.4 mg for regular tablets or 240 mcg for oral melt tablets**)

3)combination of alarm and desmopressin .

reasons for lack of response

- Overactive bladder
- Underlying disease (eg, diabetes mellitus)
- Incorrect or inconsistent use of alarm
- Occult constipation (ask about soiling in addition to the usual questions about bowel habits)
- Sleep apnea
- Social and emotional factors

Additional evaluation in refractory enuresis

- Abdominal/pelvic ultrasonography.
- Completion of a frequency volume chart.
- Evaluation for occult constipation with **abdominal radiographs** or a **trial of treatment for presumed constipation**.

Management

- It managed in consultation with a specialist (eg, developmental-behavioral pediatrician, behavioral psychologist, child psychiatrist, pediatric urologist).
- Following evaluation to exclude other causes of enuresis, management of refractory monosymptomatic nocturnal enuresis may include:

1) Periodic new trials of the enuresis alarm (with or without the addition of desmopressin).
2) Desmopressin alone
3) Desmopressin in combination with an anticholinergic agent.

- Given concerns about potential toxicity, tricyclic antidepressants (TCAs) usually are tried only after other interventions have been unsuccessful.
- prescribed by a specialist (**developmental-behavioral pediatrician, child psychiatrist, pediatric urologist**) .

TCAs

- stimulate vasopressin secretion and relax the detrusor muscle.
- Imipramine is the TCA that is most often used in the treatment
- other TCAs are effective.

Imipramine

- **Pretreatment evaluation** : **includes a thorough cardiac review of systems.**

❖Titration

- **administered orally one hour before bedtime.**
- **The initial dose is 10 to 25 mg; it may be increased by 25 mg if there is no response after one week (maximum dose 50 mg for children 6 to 12 years of age; maximum dose 75 mg for children ≥12 years of age)**
- The trial should take place at least six weeks before camp to titrate.

Monitoring response and follow-up

The response should be assessed after **one month**.

- If imipramine therapy is successful, the family should taper to the lowest effective dose. Approximately every three months, imipramine should be discontinued for at least two weeks to decrease the risk of tolerance .
- If there is no improvement after three months, imipramine should be gradually discontinued .

❖ **Adverse effects**: They are uncommon but may be serious. Approximately 5 percent of children treated with TCAs

❖ develop neurologic symptoms(, including nervousness, personality change, and disordered sleep.)

❖ The possibility of increased suicidality

❖ **cardiac conduction disturbances and myocardial depression,** particularly in cases of overdose.

OTHER INTERVENTIONS

- **Waking the child to urinate**
- **Bladder training**
- **Anticholinergic drugs**
- **Other drugs**indomethacin, phenmetrazine, amphetamine sulfate, ephedrine, atropine, furosemide, diclofenac, and chlorprothixene
- **Electrical stimulation therapy**
- **Complementary and alternative therapies(**hypnosis, psychotherapy, and acupuncture)

Thanks a lot
By : Dr Sepide Moallem