Complete Summary

GUIDELINE TITLE

Practice parameter for the assessment and treatment of children and adolescents with enuresis.

BIBLIOGRAPHIC SOURCE(S)

Fritz G, Rockney R, Bernet W, Arnold V, Beitchman J, Benson RS, Bukstein O, Kinlan J, McClellan J, Rue D, Shaw JA, Stock S, Kroeger Ptakowski K. Practice parameter for the assessment and treatment of children and adolescents with enuresis. J Am Acad Child Adolesc Psychiatry 2004 Dec;43(12):1540-50. [42 references] PubMed

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GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- December 04, 2007, Desmopressin Acetate (DDAVP, DDVP, Minirin, & Stimate): New information has been added to the existing boxed warning in Desmopressin's prescribing information about potential increased risk for severe hyponatremia and seizures.
- May 2, 2007, Antidepressant drugs: Update to the existing black box warning on the prescribing information on all antidepressant medications to include warnings about the increased risks of suicidal thinking and behavior in young adults ages 18 to 24 years old during the first one to two months of treatment.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Enuresis

GUIDELINE CATEGORY

Evaluation
Management
Treatment

CLINICAL SPECIALTY

Neurology
Pediatrics
Psychiatry
Sleep Medicine
Urology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide recommendations for the assessment and treatment of children and adolescents with enuresis

TARGET POPULATION

Children and adolescents with enuresis

INTERVENTIONS AND PRACTICES CONSIDERED

Assessment

1. Interview both parents and child
2. Obtain medical history

3. Physical examination with notation on the following abnormalities:
    - Enlarged adenoids or tonsils
    - Bladder distension
    - Fecal impaction
    - Genital abnormalities
    - Spinal cord anomaly
    - Neurologic signs
4. Routine laboratory tests including:
    - Urinalysis
    - Urine culture
5. Invasive laboratory tests as needed
6. First-morning urine specific gravity test
7. A two-week baseline record of wet and dry nights

Management/Treatment

1. Specialist referral and treatment when necessary (i.e., urologic referral and treatment)
2. Psychotherapy
3. Crisis intervention
4. Family therapy
5. Supportive approaches
    - Education
    - Demystification
    - Ensuring parents do not punish the child
    - Journal keeping
    - Fluid restriction
    - Night awakening
6. Conditioning therapy
    - Use of an alarm
7. Pharmacological therapy
    - Imipramine
    - Desmopressin acetate (DDAVP)
8. Monitoring during pharmacological therapy
    - Pretreatment electrocardiogram (imipramine)
    - Assessment of imipramine serum levels
    - Monitoring of serum electrolyte levels (desmopressin acetate)
9. Bladder stretching exercises (considered, but not recommended)
10. Hypnotherapy (considered, but not recommended)
11. Dietary manipulation (considered, but not recommended)
12. Desensitization to allergens (considered, but not recommended.

MAJOR OUTCOMES CONSIDERED

- Frequency of wetting episodes
- Relapse rate
- Antidiuretic hormone (ADH) levels

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

This practice parameter is based on an extensive review published as a chapter by the primary authors and used with permission. The existing world literature for the past 50 years was considered in the preparation of this parameter to place the problem in context and to provide a historical perspective. To ensure an up-to-date list of references, a Medline search covering the period 1997-1999 was conducted in January 2000. The search yielded 144 articles through the use of "enuresis" as the text word. More than 350 references were reviewed; 50 of the most relevant are included in the bibliography of this document.

NUMBER OF SOURCE DOCUMENTS

50

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review
Review of Published Meta-Analyses

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Each recommendation is identified as falling into one of the following categories of endorsement, indicated by an abbreviation in brackets following the statement.

These categories indicate the degree of importance or certainty of each recommendation.

[**MS**] "Minimal Standards" are recommendations that are based on substantial empirical evidence (such as well-controlled, double-blind trials) or overwhelming clinical consensus. Minimal standards are expected to apply more than 95% of the time (i.e., in almost all cases). When the practitioner does not follow this standard of care in a particular case, the medical record should indicate the reason.

[**CG**] "Clinical Guidelines" are recommendations that are based on empirical evidence (such as open trials, case studies) and/or strong clinical consensus. Clinical guidelines apply approximately 75% of the time. These practices should always be considered by the clinician, but there are exceptions to their application.

[**OP**] "Options" are practices that are acceptable, but not required. There may be insufficient empirical evidence to support recommending these practices as minimal standards or clinical guidelines. In some cases they may be the perfect thing to do, but in other cases they should be avoided. If possible, the practice parameter will explain the pros and cons of these options.

[**NE**] "Not endorsed" refers to practices that are known to be ineffective or contraindicated.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

This parameter was made available to the entire American Academy of Child and Adolescent Psychiatry (AACAP) membership for review in September 2001 and was approved by the AACAP Council in June 2002. It is available to AACAP members on the World Wide Web (www.aacap.org) and appears in a future supplement to the JAACAP.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Recommendations are identified as falling into one of four categories of endorsement. These categories, which are defined at the end of the "Major Recommendations" field, indicate the degree of importance or certainty of each recommendation.

Definitions

Enuresis is defined in the Diagnostic and Statistical Manual of Mental Disorders - Fourth Edition - text revision (DSM-IV-TR) as the repeated voiding of urine into the bed or clothes at least twice a week for at least 3 consecutive months in a child who is at least 5 years of age. The DSM-IV-TR definition also considers a child to be enuretic if the frequency or duration is less but there is associated distress or functional impairment. *Nocturnal enuresis* refers to voiding during sleep; *diurnal enuresis* defines wetting while awake. *Primary enuresis* occurs in children who have never been consistently dry through the night, while *secondary enuresis* refers to the resumption of wetting after at least 6 months of dryness.

Etiology and Clinical Presentation

There is a clear genetic component to enuresis. Compared with a 15% incidence of enuresis in children from nonenuretic families, 44% and 77% of children were enuretic when one or both parents, respectively, were themselves enuretic. Data are accumulating that link foci on two chromosomes with enuresis.

Sleep studies have demonstrated a random pattern of wetting that occurs in all stages of sleep in proportion to the amount of time spent in each stage. A subgroup of enuretic patients has been identified in whom there is no arousal to bladder distension and an unusual pattern of uninhibited bladder contractions prior to the enuretic episode. The dysfunctional arousal system during sleep may be a key etiologic factor for this subgroup of children. One specific sleep disorder, sleep apnea stemming from upper airway obstruction, has been associated with enuresis.

Developmental immaturity, including motor and language milestones, is relevant in the etiology of enuresis for some children, although the mechanism is unknown.

Identifiable psychological factors are clearly contributory in a minority of children with enuresis. These children are most frequently secondary enuretics who have experienced a stress, such as parental divorce, school trauma, sexual abuse, or hospitalization; their enuresis is a regressive symptom in response to the stress or trauma. Psychological factors can also be seen as etiologically central in the rare instance in which family disorganization or neglect has resulted in there never having been a reasonable effort made at toilet training. Other signs of neglect are usually evident in these cases.

Assessment

When enuresis is identified, either as the chief complaint or as an incidental part of an evaluation for another problem, the psychiatric assessment must be expanded to include enuresis-specific elements [**MS**]. In every instance both the parents and the child should be interviewed, and sensitivity to the emotional consequences of the symptom should be high. The enuresis-specific history should explore every aspect of urinary incontinence, with thorough review of the genitourinary and neurologic systems [**MS**]. A thorough physical examination is essential; enlarged adenoids or tonsils, bladder distension, fecal impaction, genital abnormalities, spinal cord anomaly, and neurologic signs should be noted [**MS**]. Routine laboratory tests need only include urinalysis and possibly urine culture;

more invasive tests are pursued only with specific indications [**CG**]. First-morning specific gravity may be helpful in predicting who will respond to desmopressin acetate (DDAVP) treatments [**OP**]. A 2-week baseline record of wet and dry nights is useful [**CG**].

Treatment

Treatment is based on the findings of the assessment. Positive findings on history, physical examination, or laboratory tests are indications for specific treatments. Daytime wetting, abnormal voiding (unusual posturing, discomfort, straining, or a poor urine stream), a history of urinary tract infections or evidence of infection on urinalysis or culture, and genital abnormalities are indications for urologic referral and treatment [**MS**]. A history of constipation, encopresis, or palpable stool impaction suggests mechanical pressure on the bladder. Disimpaction and treatment leading to a healthy bowel regimen will often eliminate the enuresis [**CG**]. Snoring and enlarged tonsils or adenoids may signal sleep apnea and indicate specific treatment. Surgical correction of upper airway obstruction has led to improvement or cure of enuresis [**CG**].

Psychosocial problems directly contributory to enuresis (as opposed to co-occurring with or resulting from the symptom) are relatively rare. Enuresis can be assumed to be of psychological origin when a previously dry child begins wetting during a period of stress (parental divorce, out-of-home placement, school trauma, abuse, hospitalization, etc.). At an early age, control struggles between parent and child may focus on urination patterns as a "battlefield"; this struggle serves to maintain the enuresis symptom as the child matures. In the uncommon instance in which family disorganization or neglect has resulted in a failure to toilet train the child, the symptom is seen to have psychosocial etiology. Individual psychotherapy, crisis intervention, and family therapy are specific psychological treatments applied on an individual basis [**CG**]. Effective treatment of the underlying psychological problem eliminates the enuresis in such cases.

When the history and physical examination do not suggest a specific etiology and the urinalysis results are completely normal, uncomplicated monosymptomatic primary nocturnal enuresis is treated with nonspecific approaches. Supportive approaches should always include education, demystification, and ensuring that parents do not punish the child for enuretic episodes [**MS**]. Journal keeping, fluid restriction, and night awakening may also fit in the category of nonspecific supportive approaches [**OP**].

Conditioning, using a modern, portable, battery-operated alarm - along with a written contract, thorough instruction, frequent monitoring, over-learning, and intermittent reinforcement before discontinuation --- makes this behavioral treatment highly effective as the first line of treatment with cooperative, motivated families [**MS**].

Two medications, imipramine and DDAVP, have proven efficacy in the treatment of enuresis [**OP**]. Imipramine in a single bedtime dose of 1 to 2.5 mg/kg has been used for many years if conditioning treatment fails or is not feasible. Many studies document 40% to 60% effectiveness, although the relapse rate is as high as 50%. The mechanism of action of imipramine in treating enuresis is unknown and not conclusively related to blood level. Because of the possibility of cardiac arrhythmia

associated with tricyclic antidepressants, including imipramine, a pretreatment electrocardiogram may be obtained to detect an underlying rhythm disorder (even though the highest dose used to treat enuresis is lower than the dose commonly used to treat depression).

DDAVP is a synthetic analog of the antidiuretic hormone (ADH) vasopressin, which decreases urine production at night when taken at bedtime. It is administered intranasally as a spray in doses of 10 to 40 micrograms (1-4 sprays) nightly; the lowest effective dose is determined empirically with each child. DDAVP is also available in 0.2-mg tablets applied in doses of 0.2 to 0.6 mg nightly. Water intoxication is a rare side effect but is serious enough to merit electrolyte monitoring if intercurrent illness complicates the picture during treatment [**CG**]. Studies of DDAVP have reported success rates of 10% to 65% and relapse rates as high as 80%. DDAVP can be prescribed for short periods, such as when the child is going to camp. Long-term administration has *not* been associated with depression of endogenous antidiuretic hormone secretion. The combination of DDAVP and a sustained-release anticholinergic agent may be more effective than DDAVP alone [**OP**].

Bladder-stretching exercises to increase functional bladder capacity have been used without consistent evidence of effectiveness, and the effort not to void despite considerable urgency is unpleasant for both the child and the family [**NE**]. Despite anecdotal reports, there is no empirical evidence to suggest efficacy of hypnotherapy, dietary manipulation, and desensitization to allergens [**NE**].

Definitions:

[**MS**] "Minimal Standards" are recommendations that are based on substantial empirical evidence (such as well-controlled, double-blind trials) or overwhelming clinical consensus. Minimal standards are expected to apply more than 95% of the time (i.e., in almost all cases). When the practitioner does not follow this standard of care in a particular case, the medical record should indicate the reason.

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CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated. In general, the recommendations are based on evaluation of the scientific literature and relevant clinical consensus.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate assessment and treatment of children and adolescents with enuresis

POTENTIAL HARMS

- Recent reports of unexpected deaths due to cardiac arrhythmia in children taking imipramine or other tricyclic antidepressants suggest that a pretreatment electrocardiogram to determine an underlying rhythm disorder should be obtained, with periodic monitoring thereafter. Children usually tolerate the imipramine at low dosage levels and experience minimal anticholinergic or cardiovascular side effects.
- The most serious problem associated with imipramine is ingestion by the patient's younger siblings, leading to serious or fatal consequences.
- Desmopressin acetate (DDAVP) is a synthetic analog of the antidiuretic hormone (ADH) vasopressin, which decreases urine production at night when taken at bedtime. Water intoxication is a rare side effect but is serious enough to merit electrolyte monitoring if intercurrent illness complicates the picture during treatment.
- Headache, abdominal discomfort, nausea, and nasal congestion have been relatively rare side effects of desmopressin acetate.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This parameter is not intended to define the standard of care; nor should they be deemed inclusive of all proper methods of care or exclusive of other methods of care directed at obtaining the desired results. The ultimate judgment regarding the care of a patient must be made by the clinician in light of all the circumstances presented by the patient and his or her family, the diagnostic and treatment options available, and available resources. Given inevitable changes in scientific information and technology, this parameter will be reviewed periodically and updated when appropriate.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004

GUIDELINE DEVELOPER(S)

American Academy of Child and Adolescent Psychiatry - Medical Specialty Society

SOURCE(S) OF FUNDING

American Academy of Child and Adolescent Psychiatry

GUIDELINE COMMITTEE

Work Group on Quality Issues

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

This parameter was developed by: Gregory Fritz, M.D. and Randy Rockney, M.D.

Work Group on Quality Issues Members: William Bernet, M.D. (Chair); Valerie Arnold, M.D.; Joseph Beitchman, M.D.; R. Scott Benson, M.D.; Oscar Bukstein, M.D.; Joan Kinlan, M.D.; Jon McClellan, M.D.; David Rue, M.D.; Jon Shaw, M.D.; Saundra Stock, M.D.

AACAP Staff: Kristin Kroeger Ptakowski

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

As a matter of policy, some of the authors of this practice parameter are in active clinical practice and may have received income related to treatments discussed in this parameter. Some authors may be involved primarily in research or other academic endeavors and also may have received income related to treatments discussed in this parameter. To minimize the potential for this parameter to contain biased recommendations due to conflict of interest, the parameter was reviewed extensively by Work Group members, consultants, and Academy members; authors and reviewers were asked to base their recommendations on an objective evaluation of the available evidence. Authors and reviewers who believed that they might have a conflict of interest that would bias, or appear to bias, their work on this parameter were asked to notify the Academy.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format from the American Academy of Adolescent and Child Psychiatry (AACAP) Web site.

A CD-ROM containing all parameters is available for a fee. See the AACAP Publication Store for more information.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on April 1, 2005. This summary was updated by ECRI Institute on November 9, 2007, following the U.S. Food and Drug Administration advisory on Antidepressant drugs. This summary was

updated by ECRI Institute on December 7, 2007, following the U.S. Food and Drug Administration advisory on Desmopressin Acetate.

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