



# Clinical manifestations and diagnostic evaluation of benign prostatic hyperplasia

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# INTRODUCTION

Benign prostatic hyperplasia (BPH) is a histologic diagnosis that refers to the proliferation of glandular epithelial tissue, smooth muscle, and connective tissue within the prostatic transition zone. BPH is ubiquitous in the aging male, with worldwide autopsy-proven histological prevalence starting at age 40 to 45 years, reaching 60 percent at age 60, and 80 percent at age 80 [1].

BPH can be asymptomatic, in which case it does not require treatment. However, BPH may lead to an enlargement of the prostate (benign prostatic enlargement [BPE]) and result in lower urinary tract symptoms (LUTS) due to obstruction at the level of the bladder neck.

LUTS can be caused by a variety of conditions. In the discussion below, LUTS/BPH will be used to indicate LUTS attributed to BPH, in accordance with the American Urological Association (AUA) BPH clinical guidelines. This topic will review the clinical manifestations and diagnostic evaluation of LUTS/BPH.

The epidemiology and pathophysiology of BPH, medical and surgical treatment of BPH, incontinence, other causes of LUTS, and nocturia are presented separately.

- (See "Epidemiology and pathophysiology of benign prostatic hyperplasia" and "Lower urinary tract symptoms in males" and "Nocturia: Clinical presentation, evaluation, and management in adults" and "Urinary incontinence in men".)
- (See "Medical treatment of benign prostatic hyperplasia".)

- (See "Surgical treatment of benign prostatic hyperplasia (BPH)".)
- (See "Epidemiology and pathophysiology of benign prostatic hyperplasia" and "Lower urinary tract symptoms in males" and "Nocturia: Clinical presentation, evaluation, and management in adults" and "Urinary incontinence in men".)
- (See "Epidemiology and pathophysiology of benign prostatic hyperplasia" and "Lower urinary tract symptoms in males" and "Nocturia: Clinical presentation, evaluation, and management in adults" and "Urinary incontinence in men".)
- (See "Epidemiology and pathophysiology of benign prostatic hyperplasia" and "Lower urinary tract symptoms in males" and "Nocturia: Clinical presentation, evaluation, and management in adults" and "Urinary incontinence in men".)

#### TERMINOLOGY

The acronym BPH (benign prostatic hyperplasia) is often incorrectly assumed to represent benign prostatic hypertrophy, which is an archaic term describing an increase in cell size rather than cell number. BPH results in benign prostatic enlargement (BPE) in some but not all men. This enlargement can, in turn, lead to benign prostatic obstruction (BPO) and bladder outlet obstruction (BOO). While BPH alone does not require treatment, BPE and BPO are often associated with lower urinary tract symptoms (LUTS), which may require treatment.

#### **CLINICAL MANIFESTATIONS**

**Clinical presentation** — Benign prostatic hyperplasia (BPH) can be asymptomatic, and the correlation between symptoms and the presence of prostatic enlargement on physical examination or transrectal ultrasonographic assessment is poor.

When symptomatic, BPH presents with lower urinary tract symptoms (LUTS). Typical manifestations of LUTS/BPH include [2]:

- Storage (irritative) symptoms Urinary frequency, urgency, nocturia and incontinence
- Voiding symptoms Slow urinary stream, straining to void, urinary intermittency (stream starting and stopping during micturition) or hesitancy, splitting of the voiding stream, and terminal dribbling

Storage symptoms are often more bothersome than voiding symptoms. Symptom severity (most often graded as mild, moderate, or severe) motivates patients to seek BPH-related treatment [3].

Physical examination findings include a non-tender, enlarged prostate on digital rectal examination (DRE). The size of the prostate on examination does not correlate well with symptom severity.

There are no typical laboratory or imaging findings, except that BPH is associated with higher levels of prostate-specific antigen (PSA), produced by benign prostatic tissue.

**Natural history** — Symptoms tend to progress gradually over a period of years, especially in older patients; however, they may improve spontaneously in a minority of patients [4-8].

The natural history of LUTS/BPH progression was described in the Health Professionals Followup Study [4]. In this cohort of 9628 men who initially reported moderate LUTS, about onequarter progressed to severe LUTS over a mean follow-up of 5.9 years, and progression rates rose steeply as men aged.

**Complications** — Potential complications of untreated BPH include acute urinary retention. In addition, chronic obstruction and failure to completely empty the bladder of urine can increase the risk of urinary tract infections (UTIs), bladder stones, formation of bladder diverticuli, and renal damage.

BPH is not a risk factor for prostate cancer. BPH occurs primarily in the central or transitional zone of the prostate, whereas prostate cancer originates primarily in the peripheral part of the gland. An analysis from the placebo arm of the Prostate Cancer Prevention Trial, where routine biopsies were performed, did not find an association between BPH and prostate cancer [9].

#### **DIFFERENTIAL DIAGNOSIS**

Many other urologic conditions can present with lower urinary tract symptoms (LUTS). Before concluding that LUTS is related to benign prostatic hyperplasia (BPH), other disorders that can cause these symptoms should be excluded by history, physical examination, and selected laboratory and urologic tests. (See 'Evaluation' below.)

Other causes of LUTS are described in detail elsewhere. (See "Lower urinary tract symptoms in males" and "Lower urinary tract symptoms in males", section on 'Etiologies of LUTS'.)

Briefly, other causes include:

• **Urologic causes of obstruction** – Urethral stricture, bladder neck contracture, and prostate cancer. (See "Strictures of the adult male urethra", section on 'Clinical

manifestations' and "Clinical presentation and diagnosis of prostate cancer", section on 'Clinical presentation'.)

- Other urologic conditions Urinary infections and bladder cancer. (See "Acute simple cystitis in adult males", section on 'Clinical manifestations' and "Acute bacterial prostatitis", section on 'Clinical manifestations'.)
- **Non-urologic conditions** Other medical conditions can either coexist with BPH causing worsening of urologic symptoms, or mimic BPH:
  - Cardiovascular disease Heart failure, peripheral vascular disease, or cardiac dysfunction associated with peripheral edema may worsen LUTS due to fluid shifts inducing diuresis [10]. Diuretic use can also cause or exacerbate urinary symptoms.
  - Neurologic disease Patients with Parkinson disease or a history of stroke frequently develop voiding dysfunction. Normal micturition requires a complex interplay of the bladder outlet, bladder, and regulatory spinal cord centers, and neurologic events may affect detrusor function and stability. Neurologic conditions may add to the complexity of diagnosis and affect therapeutic options.
  - Endocrine disease Longstanding, poorly controlled diabetes mellitus leads to decreased bladder sensation, decreased detrusor contractility, and incomplete bladder emptying. Furthermore, increased filtration of glucose in the urine leads to an osmotic diuresis and obligate polyuria, thereby worsening LUTS due to increased urine production. Recognizing this common relationship in LUTS is critical to controlling symptoms.
  - Polydipsia the obligate diuresis from polydipsia may cause urinary symptoms which mimic those of LUTS/BPH. Information about the fluid type and timing of intake relative to symptom onset, the use of a voiding diary, and the lack of obstructive symptoms are helpful in uncovering this relationship.

#### **EVALUATION**

The evaluation of lower urinary tract symptoms (LUTS)/benign prostatic hyperplasia (BPH) should include a detailed medical history and focused physical examination, which should include a brief neurologic screen, abdominal examination, and genitourinary examination including digital rectal examination (DRE). A small number of laboratory tests are needed to exclude other etiologies.

The specific goals for the patient should be defined as part of the evaluation. If symptoms are not significantly bothersome or not impacting the patient's health, or if the patient does not want treatment, no further evaluation is recommended. This approach is recommended by the American Urological Association (AUA) BPH clinical guidelines [11,12] and is a priority of the AUA Choosing Wisely Program [13]. Such patients are unlikely to experience significant health problems in the future due to their condition and can be seen again if necessary.

**History** — The history should include evaluation of storage (irritative) symptoms (frequency, urgency, and nocturia) and voiding symptoms (slow or decreased force urinary stream, straining to void, intermittency, hesitancy, splitting of the voiding stream), and post-void dribbling. This information is useful to estimate the impact and severity of initial symptoms.

Symptoms of hematuria, incontinence, or urinary retention should prompt urology referral. (See 'Indications for urology referral' below.)

Other historical features to elicit include:

- History of urethral trauma, urethritis, or urethral instrumentation that could lead to urethral stricture
- Gross hematuria or pain in the bladder region, which may be suggestive of a bladder calculi or cancer
- Underlying neurologic disease, which might indicate a neurogenic bladder
- Cigarette smoking, which is a risk factor for bladder cancer
- Treatment with drugs or over-the-counter agents that can impair bladder contractility (eg, anticholinergic agents) or increase outflow resistance (eg, sympathomimetic agents)
- The temporal relationship between the onset and severity of LUTS and medication use (ie, diuretics for hypertension or congestive heart failure)

A detailed description of the initial evaluation of a patients with LUTS is provided separately. (See "Lower urinary tract symptoms in males", section on 'Initial patient evaluation'.)

**Voiding diary** — A well-kept voiding diary or frequency-volume chart is usually obtained in patients who have nocturia as a predominant symptom, but it can be useful in other patients as well. It can provide information on the patient's total daily voided volume, daily urinary frequency, nocturnal fraction of voiding urine, and functional bladder capacity. It also provides information on fluid intake, incontinent episodes, use of incontinence pads, and/or defecation frequency. Data are typically recorded for three days to create a more representative sample of typical fluid management [14]. Frequency-volume charts are discussed in detail separately. (See "Nocturia: Clinical presentation, evaluation, and management in adults", section on 'Frequencyvolume chart'.) In patients with nocturia, the voiding diary can provide evidence of nocturnal polyuria, which occurs when >33 percent of the daily urine output is expelled during nighttime hours. Nocturnal polyuria should prompt a search for secondary causes, and is discussed in detail elsewhere. (See "Nocturia: Clinical presentation, evaluation, and management in adults", section on 'Nocturnal polyuria'.)

**Physical examination** — The physical examination should include DRE in addition to evaluation of the abdomen, pelvis, perineum. A motor and sensory evaluation of the pelvis and lower limbs should be performed. Given the complexity of the motor and neurologic interplay involved in pelvic health and bladder maintenance, any abnormal finding should prompt further inquiry. A more extensive neurologic examination is indicated for patients with possible neurogenic lower urinary tract dysfunction.

DRE should be performed to estimate prostate size. A normal prostate is approximately the size of a walnut (between 7 to 16 grams, with an average of 11 grams) and firm and nontender. Although DRE is not a precise tool for measuring prostate volume [15-17], serial exams are useful to follow prostate size, and the examination can identify other abnormalities:

- An exquisitely tender prostate gland may reflect the presence of prostatitis
- The presence of asymmetry or nodules raises suspicion for malignancy (see "Clinical presentation and diagnosis of prostate cancer")
- The presence of decreased sphincter tone or absence of perineal sensation may suggest a neurologic etiology

**Laboratory tests** — We obtain urinalysis in all patients being evaluated for BPH/LUTS. The purpose is to identify pyuria, glucosuria, proteinuria, ketonuria, or bacteriuria, which may be signs of alternative diagnoses and thus warrant further evaluation. Although mild hematuria may occur with BPH, the finding of hematuria requires further evaluation for other genitourinary disorders such as cancer of the prostate or bladder, especially in older men. (See "Etiology and evaluation of hematuria in adults", section on 'Initial evaluation'.)

Other studies are not performed routinely but may be useful in certain circumstances:

- A urine culture is not needed unless there is other evidence to suggest a urinary tract infection (UTI; ie, dysuria in the setting of pyuria or bacteriuria on urinalysis).
- Serum creatinine is not needed unless there is evidence to suggest renal impairment (ie, high post-void residual [PVR]) (see 'Post-void residual volume measurement' below). A high serum creatinine may be the result of bladder outlet obstruction (BOO) or underlying renal disease. If the serum creatinine concentration is high, renal ultrasonography is indicated

to assess for the presence of upper-tract hydronephrosis. (See "Clinical manifestations and diagnosis of urinary tract obstruction (UTO) and hydronephrosis".)

Prostate-specific antigen (PSA) testing is not needed for diagnosis but can be used as a proxy for prostate volume when considering the use of a 5-alpha reductase inhibitor (5ARI). These medications are only useful in men whose prostates are above 35 grams, which correlates with a PSA >1.5 ng/dL [18,19]. In addition, a PSA should be measured prior to initiation of treatment with 5ARI, as such treatment may lower PSA levels (typically by 0.5 ng/dL) and influence future prostate cancer screening [20]. (See "Screening for prostate cancer", section on 'Correction for 5-alpha reductase inhibitor'.)

The use of PSA testing for prostate cancer screening is discussed elsewhere. (See "Screening for prostate cancer", section on 'Screening with prostate-specific antigen'.)

The routine use of urine cytology in the setting of LUTS and a normal urinalysis should be avoided.

**Symptom questionnaires** — Validated questionnaires should be utilized to measure symptom severity, symptom bother and to document response to medical or surgical therapies. The most commonly used are the AUA Symptom Index (AUA-SI) and the International Prostate Symptom Score (IPSS). One of these should be obtained at each visit [21] ( table 1). These indices are described in detail elsewhere. (See "Lower urinary tract symptoms in males", section on 'International Prostate Symptom Score'.)

**Post-void residual volume measurement** — We obtain a measurement of PVR volume in all patients presenting with LUTS/BPH symptoms to evaluate for retention as recommended by expert groups [11,22]. The PVR can be measured with the aid of a bedside "bladder scanner," which utilizes ultrasonography to estimate the bladder's volume, or by use of a straight catheter following the conclusion of a spontaneous void. Bladder palpation is not a reliable method for estimating PVR.

Moderate to severe LUTS is associated with an increased incidence of acute urinary retention [23]. Normal men have less than 12 mL of residual urine, but most urologists are not concerned unless the PVR volume is greater than 250 mL. Management of acute urinary retention is discussed separately. (See "Acute urinary retention".)

There is significant interpersonal variability in PVR measurements, and their greatest value is in changes over time. Increasing PVR may indicate treatment failure or provide indication for surgical intervention. A high baseline PVR indicates a higher likelihood of symptomatic deterioration over time [18,24].

#### Additional tests for selected patients

**Prostate imaging** — Transrectal ultrasound is not needed for diagnosis. It is indicated only when the treatment choice of LUTS/BPH is dependent on total prostate volume, as in the use of 5ARIs, or in the choice of certain surgical techniques. It is important to remember that size of the prostate gland does not correlate with the degree of obstruction nor with the presence or severity of LUTS.

The routine use of computed tomography (CT) or magnetic resonance imaging (MRI) for the sole purpose of LUTS/BPH is discouraged, although the repurposing of cross sectional and mid-sagittal images done for other indications can be useful when the treatment choice of LUTS/BPH is dependent on total prostate volume [11].

**Cystoscopy** — Cystoscopy or, more correctly stated, urethrocystoscopy is not needed in the routine assessment of LUTS/BPH [20]. It should be considered in men with a history suggestive of a urethral stricture or bladder neck contracture. In addition, urologists also routinely perform urethrocystoscopy to assist in planning surgical treatment of men with BPH.

**Dynamic testing** — Additional urodynamic tests, which are typically performed by urologists, can be useful adjuncts in the evaluation of LUTS in some patients. Uroflowmetry is an office-based procedure that can help support the diagnosis of BPH by documenting obstruction; flow rates of <10 mL/s have shown a specificity of 70 percent, a positive predictive value of 70 percent, and a sensitivity of 47 percent for obstruction [25]. If the patient's condition is not suggestive of obstruction (eg, peak urinary flow [ $Q_{max}$ ] >10 mL/sec), pressure flow studies (PFS), which are invasive (requiring use of a small gauge urodynamic catheter) but more conclusive as to the cause of the symptoms, should be considered. PFS are useful in such cases because empiric interventions are at risk of failure in the absence of obstruction. PFS can also be used in the evaluation of patients whose clinical manifestations are atypical or when there is reason to suspect an alternative diagnosis (ie, neurogenic bladder from Parkinsonism). The use of these tests in the evaluation of LUTS are discussed in detail elsewhere. (See "Lower urinary tract symptoms in males", section on 'Uroflowmetry' and "Lower urinary tract symptoms in males", section on 'Pressure-flow studies and urodynamics'.)

#### DIAGNOSIS

The diagnosis of lower urinary tract symptoms (LUTS)/benign prostatic hyperplasia (BPH) is established by the presence of storage, voiding, and/or irritative urinary symptoms in the

absence of history, examination or laboratory findings suggesting of non-BPH causes of LUTS. (See 'Differential diagnosis' above.)

The diagnosis does not require histologic confirmation. A prostate biopsy is only warranted if there is concern about prostate cancer such as an asymmetric or nodular gland on digital rectal examination (DRE) or an increased or rising prostate-specific antigen (PSA) level.

### INDICATIONS FOR UROLOGY REFERRAL

Referral to a urological specialist may be appropriate for patients with any of the following:

- Severe symptoms or pain
- Men < 45 years old
- Abnormality on digital rectal examination
- Hematuria
- Elevated prostate-specific antigen (PSA)
- Dysuria as a possible symptom of bladder cancer
- Incontinence
- Neurologic disease known to impact lower urinary tract symptoms (LUTS)
- Urinary retention (post-void residual [PVR] urine volume >250 mL, or a palpable bladder)
- Suspicion of other urological disease

#### **INFORMATION FOR PATIENTS**

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5<sup>th</sup> to 6<sup>th</sup> grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10<sup>th</sup> to 12<sup>th</sup> grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Benign prostatic hyperplasia (enlarged prostate) (The Basics)")
- Beyond the Basics topics (see "Patient education: Benign prostatic hyperplasia (BPH) (Beyond the Basics)")

# SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Benign prostatic hyperplasia".)

# SUMMARY AND RECOMMENDATIONS

- Clinical manifestations Most men will develop benign prostatic hyperplasia (BPH), which can be associated with lower urinary tract symptoms (LUTS). The common clinical manifestations of LUTS/BPH include storage symptoms (increased daytime frequency, nocturia, urgency, and urinary incontinence) and voiding symptoms (slow urinary stream, splitting or spraying of the urinary stream, intermittent urinary stream, hesitancy, straining to void). Symptoms vary in severity over time and do not correlate well with prostate size or physiologic abnormalities. (See 'Clinical manifestations' above.)
- **Determining need for treatment** It is important to assess the severity and health impact of LUTS suspected to be caused by BPH. Men who have minimally bothersome symptoms generally do not need further evaluation or treatment. (See 'Evaluation' above.)
- **History and physical examination** The presumptive diagnosis of LUTS/BPH is established by the presence of storage and voiding symptoms in the absence of a history suggesting non-BPH causes of LUTS. The presence of a symmetrically enlarged, smooth, non-tender prostate on physical examination supports the diagnosis. (See 'History' above and 'Physical examination' above and 'Diagnosis' above.)
- **Differential diagnosis** Other potential causes of LUTS include urethral stricture, bladder neck contracture, prostate cancer (less common), urinary tract infection (UTI) and acute prostatitis, neurogenic bladder, bladder calculi, and bladder cancer (less common).
- **Evaluation** The evaluation of BPH/LUTS is intended to rule out other potential causes. (See 'Differential diagnosis' above and "Lower urinary tract symptoms in males", section on

#### 'Initial patient evaluation'.)

- We suggest that a urinalysis be obtained in all patients being evaluated for LUTS/BPH. Abnormalities (eg, hematuria, pyuria, glycosuria) suggest potential alternative diagnoses that warrant further evaluation. (See 'Laboratory tests' above.)
- We obtain a measurement of post-void residual (PVR) volume in all patients presenting with LUTS/BPH symptoms to evaluate for retention. The PVR can be measured with the aid of a bedside "bladder scanner," which utilizes ultrasonography to estimate the bladder's volume, or by use of a straight catheter following the conclusion of a spontaneous void. (See 'Post-void residual volume measurement' above.)
- Men with a predominant symptom of nocturia should complete a voiding diary to evaluate for nocturnal polyuria (>33 percent of the daily urine output is expelled during nighttime hours). Nocturnal polyuria should prompt a search for secondary causes beyond BPH/LUTS. (See 'Voiding diary' above and "Nocturia: Clinical presentation, evaluation, and management in adults", section on 'Nocturnal polyuria'.)
- The diagnosis of BPH does not require histologic confirmation, and prostate biopsy is only warranted if there is a specific concern about prostate cancer. (See 'Diagnosis' above.)
- **Symptom assessment and monitoring** The American Urologic Association/International Prostate Symptom Score (AUA/IPSS) ( table 1) (assessing for frequency, nocturia, weak urinary stream, hesitancy, intermittence, incomplete emptying, and urgency) is useful for quantifying and monitoring BPH symptoms. (See 'Symptom questionnaires' above.)
- **Indications for urologic referral** Men with abnormal digital rectal examinations (DRE), hematuria, severe symptoms or pain, those under 45 years of age, an abnormal PSA, pain with urination (dysuria), a palpable bladder or urinary retention, incontinence, or neurologic disease known to impact LUTS (ie, Parkinsonism) should be referred to an urologist. (See 'Indications for urology referral' above.)

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#### **GRAPHICS**

# American Urological Association (AUA) urinary symptom score/International Prostate Symptom Score (IPSS)

Questions to be answered	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always
1. Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?	0	1	2	3	4	5
2. Over the past month, how often have you had to urinate again less than 2 hours after you finished urinating?	0	1	2	3	4	5
3. Over the past month, how often have you found you stopped and started again several times when	0	1	2	3	4	5

https://www.uptodate.com/contents/clinical-manifestations-and-diagnostic-evaluation-of-benign-prostatic-hyperplasia/print?search=bph&source=search\_result&sel... 14/17

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you urinated?						
4. Over the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5
5. Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5
6. Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5
7. Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?	0 (none)	1 (1 time)	2 (2 times)	3 (3 times)	4 (4 times)	5 (5 or more times)
				Sum of nu	mbers (AUA syn	nptom score):
Total score:						
0 to 7: Mild	symptoms					
8 to 10. Mo	dorato sympt	ome				

8 to 19: Moderate symptoms

20 to 35: Se	evere symptoms	5					
Quality of life due to urinary symptoms	Delighted	Pleased	Mostly satisfied	Mixed - about equally satisfied and unsatisfied	Mostly dissatisfied	Unhappy	T
If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that?	0	1	2	3	4	5	6

The AUA symptom score and the IPSS use the same questions and scale. The IPSS additionally includes the last disease-specific quality of life question.

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#### **Contributor Disclosures**

**Kevin T McVary, MD, FACS** Patent Holder: Thermal-Activated Penile Prosthesis [Erectile dysfunction]. Grant/Research/Clinical Trial Support: Boston Scientific [Benign prostatic hyperplasia];MedeonBio [Benign prostatic hyperplasia];Urovant [Overactive bladder]. Consultant/Advisory Boards: Antares[Voiding dysfunction];Boston Scientific [Benign prostatic hyperplasia]. All of the relevant financial relationships listed have been mitigated. **Michael P O'Leary, MD, MPH** No relevant financial relationship(s) with ineligible companies to disclose. **Jane Givens, MD, MSCE** No relevant financial relationship(s) with ineligible companies to disclose.

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