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CME MOC

# Cleveland Clinic Journal of Medicine

## Why is obstructive sleep apnea of special interest to a rheumatologist?

## Oral lichen planus

## Stiff hands in a patient with poorly controlled type 1 diabetes

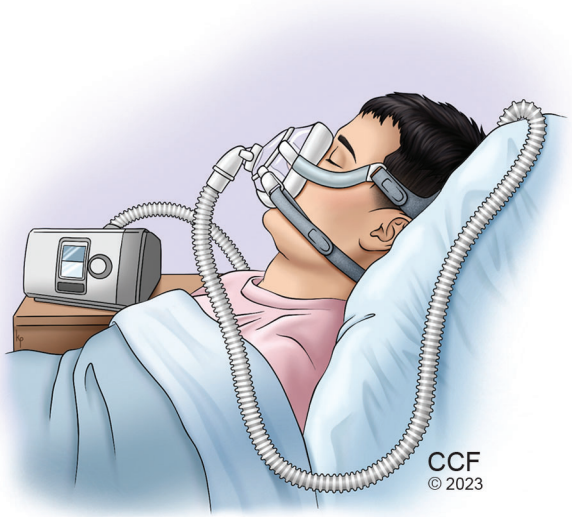
## Should patients take blood pressure medications in the evening to enhance cardiovascular benefit?

## Hey, Doc: Could the 2023–2024 cold and flu season finally be the calm after the storm?

## The drop of a pin: Accidental ingestion of a sharp foreign body

## Contemporary surgical and procedural management of benign prostatic hyperplasia

## Treatments for obstructive sleep apnea: CPAP and beyond



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# Table of Contents



CONTINUED ON PAGE 711

## Upcoming Features

- Grading the current consumer-grade wearable cardiac monitors
- When to consider SGLT-2 inhibitors in patients with acute decompensated heart failure?

CONTINUED FROM PAGE 709

# Why I, as a rheumatologist, am happy to make the diagnosis of obstructive sleep apnea

In this issue of the *Journal*, Aboussouan and his multidisciplinary coauthors[1] review available treatment options for patients with obstructive sleep apnea (OSA) and discuss the relative benefits. The cardiovascular morbidities associated with OSA are well known. But why should a rheumatologist have special interest in this disorder? The answer lies in 2 major reasons patients are referred for a rheumatology consultation: fatigue and inflammation.

The fatigue part seems obvious. People who don't sleep well are fatigued, although those with severe OSA, if carefully questioned, describe symptoms of sleepiness instead of or in addition to "fatigue." Recognizing and implementing effective therapy for OSA will reduce sleepiness and, often, fatigue. While fatigue frequently accompanies inflammation and will likely not abate unless the inflammation is treated, patients with noninflammatory pain may also experience fatigue and sleep disorders. The pain-sleep relationship is complex and bidirectional. Chronic pain can disrupt effective sleep, and patients with disrupted sleep often experience pain and amplified discomfort with various forms of sensory stimulation. Fibromyalgia is the exemplar of the latter.

In addressing fibromyalgia, many of us try to correct the sleep disorder. But this is hard to accomplish. In my experience, behavioral sleep approaches have limited success in these patients, as do pharmacologic efforts to treat the sleep disturbance and pain. Interestingly, OSA seems to be prevalent in patients with fibromyalgia.[2] Since OSA has a reasonable chance of responding to treatment, it is worth questioning patients (and their partners) about the symptoms of this disorder and having a low threshold to order a formal sleep study. I have seen benefits in reducing patient symptoms using this approach, and in rare cases, a patient may report resolution of fibromyalgia after successful remediation of their OSA.[3]

The link between OSA and inflammation is more biologically intriguing but still not well understood, and its clinical significance is not yet clear. Successful treatment of OSA with positive airway pressure has been shown to reduce elevated C-reactive protein levels.[4] Patients with OSA have higher serum urate levels, and some studies have indicated they also have a higher likelihood of having gout,[5,6] though it is not certain what proportion of this increased risk is attributable to comorbidities in OSA such as obesity and diabetes.[7] The authors of a study of 30 patients with moderate-severe OSA suggested that continuous positive airway pressure can elicit a modest reduction in the serum urate level.[8] But there have been no large studies on a potential benefit of effective OSA therapy in the management of patients with gout.

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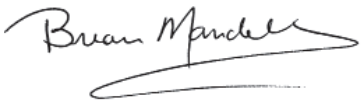
Thus, whenever I make the diagnosis of OSA, I also have the possibility of reversing a sleep disorder that may be amplifying a patient's pain, as well as potentially reducing their systemic inflammation.

As 2023 draws to a close, we at the *Journal* take this opportunity to thank our peer reviewers and authors who have devoted hours of effort to help us present practical and timely educational articles. We send our sincere wishes for a healthy and hopefully kinder and more peaceful 2024 to them—and to you, our readers.



Brian F. Mandell, MD, PhD
Editor in Chief

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### DECEMBER

**ADVANCES IN THE TREATMENT PARADIGM OF MYELOID MALIGNANCIES: FROM BIOLOGY TO CLINICAL PRACTICE**
December 8
San Diego, CA

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March 7–10
Miami Beach, FL

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### APRIL

**THYROID SUMMIT 2024: ADVANCES IN THYROIDOLOGY**
April 11
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### MAY

**DIABETES DAY**
May 2
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**CARDIOVASCULAR DISEASE AND MODIFIABLE CARDIOMETABOLIC RISK FACTORS: CURRENT AND EMERGING THERAPIES**
May 3
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**CLEVELAND CLINIC ULTRASOUND COURSE: INTEGRATING POCUS INTO YOUR PRACTICE**
May 8–11
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May 29–31
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### JUNE

**SHAPING THE MANAGEMENT OF PARKINSON DISEASE**
June 8–9
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June 10–14
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### AUGUST

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# Oral lichen planus

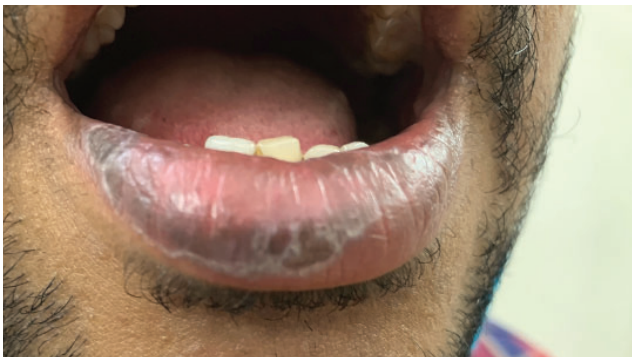

**Figure 1.** Well-defined violaceous plaque on the lower lip.

A 36-year-old male presented with lesions over the lips and the left buccal mucosa for the past 6 months. The lesions were associated with pain and a burning sensation, aggravated by spicy foods. He had no history of skin disorders, local trauma, dental procedures, smoking, or alcohol consumption. He was not on any medications and had no history of drug reactions.

## WORKUP AND DIAGNOSIS

Clinical examination revealed a nonindurated, well-defined, violaceous plaque with a white, lacy appearance on the lower lip (**Figure 1**) and the left buccal mucosa (**Figure 2**). There was no involvement of the skin, nails, or genital mucosa.

The differential diagnoses included lichen planus, oral candidiasis, oral lichenoid reaction, and leukoplakia. Potassium hydroxide microscopic study of the lesions was negative for oral candidiasis. Biopsy study of the buccal mucosal lesions showed wedge-shaped hypergranulosis and a dermal, lichenoid, lymphocytic, inflammatory infiltrate, admixed with melanophages

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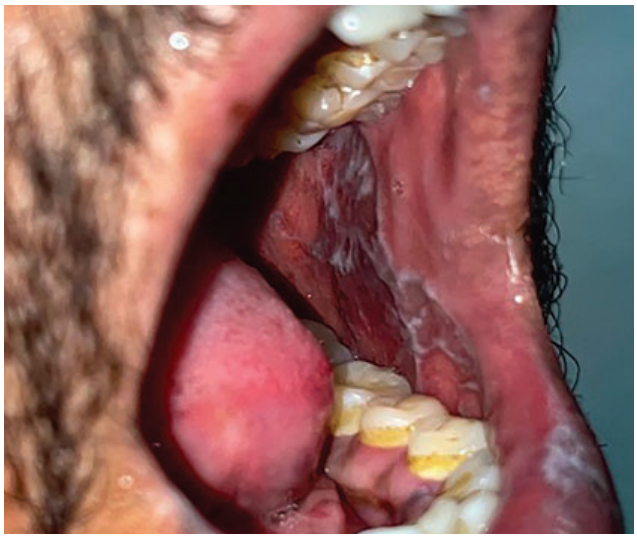

**Figure 2.** Violaceous plaque with whitish lacy streaks in the left buccal mucosa.

(ie, macrophages containing melanin). Hepatitis C serology was nonreactive.

Based on the classical nonindurated reticular plaques with the pathognomonic Wickham striae, absence of a preceding drug-intake history, negative potassium hydroxide study, and histopathologic findings, a diagnosis of oral reticular lichen planus was made, and the patient was started on topical steroids, which brought improvement of the lesions.

## ORAL LICHENOID LESIONS

Lichen planus is a chronic immune-mediated inflammatory disorder affecting the skin, scalp, nails, and mucosa. Oral lichen planus involving the buccal mucosa, gingiva, and tongue affects 1% to 2% of the world's population.[1] It is considered a multifactorial disease with risk factors including medications, dental materials, and viral infections such as hepatitis C.[2]

Oral lichen planus classically presents as 6 types: reticular, atrophic, papular, bullous, plaque, and erosive-ulcerative. The reticular type is often asymptomatic, and the presence of interlacing white streaks suggestive of Wickham striae is pathognomonic.[3] The differential diagnoses for this type include candidiasis, leukoplakia, and lichenoid reactions.[3]

Oral candidiasis presents with whitish erythematous plaques on the buccal mucosa, tongue, or palate and can be confirmed by potassium hydroxide study, which was negative in our patient.

Leukoplakia is a premalignant condition that presents as whitish indurated plaques in the buccal mucosa. Diagnosis is usually based on the findings of squamous hyperplasia with or without dysplasia.

Oral lichenoid contact reactions typically involve the buccal mucosa and lateral borders of the tongue, with the lesions located adjacent to the offending allergen. The most common culprits are dental amalgam, dental acrylics, cobalt, and nickel.[3] Diagnosis is made by a positive patch test and improvement after discontinuation of the allergen.

Oral lichenoid drug reactions have been reported with medications such as nonsteroidal anti-inflammatory drugs, antihypertensives (angiotensin-converting enzyme inhibitors, beta-blockers, diuretics), penicillamine, antimalarials, sulfonylureas, gold salts, and antiretrovirals for human immunodeficiency virus.[3] Resolution of lesions is noted on discontinuation of the drug.

## TREATMENT OPTIONS

The primary goal of management is symptom relief. Nonpharmacologic measures include maintenance of oral hygiene, smoking cessation, alcohol avoidance, and dietary restrictions including spicy acidic foods, citrus fruits, crispy or salty foods, crusted bread, and caffeinated drinks.

Twice-daily application of topical corticosteroids in the form of orabase gel or mouth rinse over a period of 1 to 2 months is the preferred treatment for oral lichen planus. Commonly used steroids include triamcinolone acetonide 0.1% gel and clobetasol propionate 0.05%.

Intralesional injection of triamcinolone acetonide in concentrations of 10 to 20 mg/mL is helpful in persistent oral lichen planus.[3]

Systemic corticosteroids like methylprednisolone or prednisolone (1–1.5 mg/kg daily) may be indicated in patients unresponsive to topical steroids.[3] Other medications such as topical calcineurin inhibitors, oral retinoids, hydroxychloroquine, mycophenolate mofetil, and oral and topical cyclosporine have also been used in the treatment of oral lichen planus.[2]

Oral lichen planus, especially the erosive type, is a potentially premalignant disorder with a higher risk of progression to squamous cell carcinoma and necessitates periodic follow-up.[4]

## DISCLOSURES

The authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

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# Stiff hands in a man with type 1 diabetes

A 23-year-old man with type 1 diabetes presented with stiffness in both hands that had progressively worsened over the previous 6 months. He had trouble completely flexing or extending the small joints of his hands, resulting in the inability to make a fist or place his hands flat on a surface.

On examination, his skin looked waxy, yellowish, and hard. He was unable to press the palmar surfaces of the interphalangeal joints together, despite maximal effort, thus demonstrating the prayer sign (**Figure 1**). He did not have a history of pain, paresthesia, or early morning stiffness.

He had no palpable nodular or cord-like swelling on the palmar aspect or preferential involvement of the medial 2 fingers, as seen in Dupuytren contracture. Tinel and Phalen tests were negative, nor was there any tingling or numbness in any of the fingers, ruling out carpal tunnel syndrome. There were no signs of sclerodactyly, loss of finger-pad contour, Raynaud phenomenon, or associated digital tip ulcers or scars suggestive of systemic sclerosis.

The patient's glycemic management was poor, as evidenced by a recent hemoglobin A1c of 7.2% (reference range 4% to 5.7%). He was on injectable insulin for the past 6 years, with frequent dose titrations because of poor control.

Funduscopy showed severe nonproliferative diabetic retinopathy in the right eye and proliferative diabetic retinopathy in the left eye. Urine tests did not show any microalbuminuria. A diagnosis of diabetic cheiroarthropathy was made based on the patient's inability to completely extend or flex the small joints of his hand, along with the waxy and yellowish thickening of his palmar skin.

The patient was advised to begin physiotherapy and increase his dosage of both long-acting and regular insulin. However, after 6 weeks, no improvement in his hand stiffness was observed. He was advised to continue physiotherapy and injectable insulin. He was thereafter lost to follow-up.

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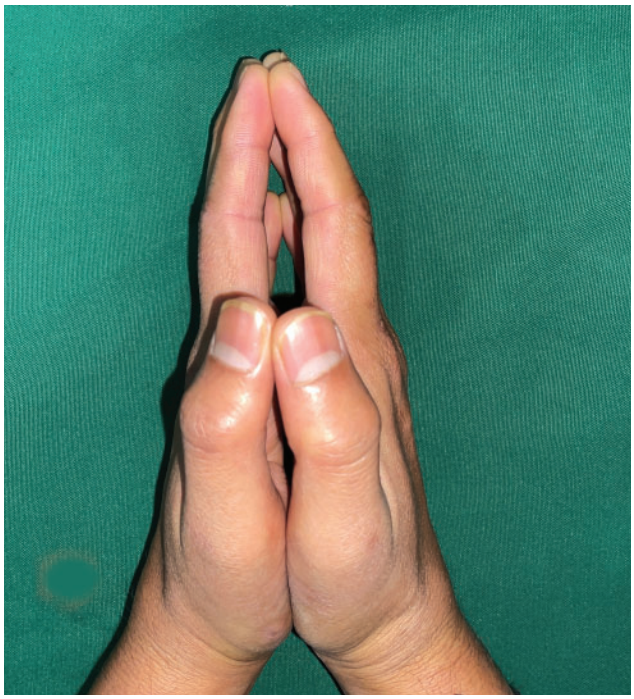

**Figure 1.** The prayer sign in diabetic cheiroarthopathy, ie, the inability to completely press the palmar aspect of interphalangeal joints together despite maximal effort.

## DIABETIC CHEIROARTHROPATHY

Diabetic cheiroarthropathy is a recognized complication of type 1 and type 2 diabetes. It is known to occur in 18.3% to 28.5% of patients with diabetes[1,2] and is more common in those with type 1 diabetes.[3] Increased

blood glucose leads to glycosylation and cross-linking of collagen, hindering its degradation and resulting in tight, waxy skin over the hands. An association between the severity of joint mobility restriction and the presence of diabetes-related microvascular complications has been reported.[1] Our patient also had associated diabetic retinopathy but no nephropathy.

## DIFFERENTIAL DIAGNOSIS OF STIFF HANDS

Dupytren contracture mimics diabetic cheiroarthropathy and has been reported in 16% to 42% of patients with diabetes.[4,5] It involves thickening of the palmar aponeurosis, leading to the formation of nodules and flexion contractures, commonly affecting the fourth finger. However, in our patient, limited joint mobility was observed in all four fingers, without the presence of taut fibrotic bands.

Flexor tenosynovitis is another condition that mimics diabetes-related cheiroarthropathy,[6] but it differs in that the contracture is not fixed and can be released, which produces a distinct snap.[2]

Magnetic resonance imaging has revealed thickening of the flexor tendon sheaths,[7] but this finding is nonspecific and should be interpreted within the appropriate clinical context.

## TREATMENT RECOMMENDATIONS

The primary focus of treatment lies in improving glycemic control and implementing physical therapy. There have been reports suggesting symptom relief, improved joint mobility, and overall improvement with these interventions.[8] Unfortunately, in our patient, significant improvement was not observed. Symptom-targeted therapies like anti-inflammatory drugs, analgesics, and intralesional corticosteroids have also been used, but their effectiveness is limited. Improving glycemic control remains the cornerstone of management to prevent further progression and irreversible disability.[9]

Limited joint mobility, or diabetic cheiroarthropathy,[6] is a commonly occurring but often overlooked complication in patients with diabetes. This is important to recognize not only because of its potential to cause severe disability, but also because it is often associated with diabetes-related microvascular complications.

## DISCLOSURES

The authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

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ONE MINUTE CONSULT

BRIEF ANSWERS TO SPECIFIC CLINICAL QUESTIONS

# Q: Should my patients take their blood pressure medications in the evening to enhance cardiovascular benefit?

**A:** No. Although the cardiovascular benefits of controlled blood pressure (BP) are clear,[1] current evidence is insufficient to recommend routinely dosing antihypertensive medications in the evening as opposed to morning for cardiovascular benefit. However, hypotension carries its own risks regardless of the time of day. Clinicians should employ shared decision-making with patients to individualize dosing practices based on risk factors and preferences.

## SCENARIO 1: ELEVATED BP IN THE MORNING

*A patient with primary hypertension and coronary artery disease takes antihypertensive medications in the morning. The BP is well controlled throughout the day, but the patient reports that it is elevated in the morning. The physician considers switching the patient to an evening dosing regimen for cardiovascular benefit.*

BP follows a diurnal rhythm, generally lower at night (nocturnal dipping) and increasing in the morning. Because morning BP surges have been associated with cardiovascular events,[2] it follows that administration of antihypertensive medications in the evening might confer cardiovascular protection.

Patients with hypertension can be subdivided based on the nocturnal dipping pattern in systolic BP observed on 24-hour ambulatory monitoring:

- Extreme "dippers": a drop greater than 20%
- Dippers: a drop from 10% to 20%
- Nondippers: a drop less than 10%
- Reverse or inverted dippers: no change or an increase in nocturnal systolic BP.[3]

There is evidence that nondippers are at higher risk for adverse cardiovascular events. Therefore, it makes sense that evening dosing might induce dipping in the nondipper phenotype.

Hermida et al examined this hypothesis in 2 major studies[4,5]:

- The MAPEC trial[4] (Monitorización Ambulatoria Para Predicción de Eventos Cardiovasculares [Ambulatory Blood Pressure Monitoring for Prediction of Cardiovascular Events]) included 2,156 patients with untreated or resistant hypertension. Patients were instructed to take BP medications at bedtime or on awakening. The primary end point, a composite of all-cause mortality and cardiovascular events, was significantly lower in the bedtime group, with a hazard ratio (HR) of 0.39 (95% confidence interval [CI] 0.29–0.51, $P < .001$).[4]
- The Hygia Chronotherapy Trial[5] examined the risk of cardiovascular disease in patients taking BP medications at bedtime compared with on awakening. The primary outcome was a composite end point consisting of cardiovascular disease-related death, myocardial infarction, coronary revascularization, heart failure, or stroke. As with the MAPEC trial, the bedtime-dosing group had a significantly better outcome, with a reported HR of 0.55 (95% CI 0.50–0.61, $P < .001$).[5]

These results seemed to favor bedtime dosing of antihypertensive medications, but the improbable effect size led others to question the methodology

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(problematic randomization), results (no independent adjudication of cardiovascular events), and conclusions.[6] In response, the HARMONY trial[7] (Hellenic-Anglo Research Into Morning or Night Antihypertensive Drug Delivery) in 2018 randomized patients to morning or evening antihypertensive dosing and utilized a crossover design over 12 weeks. Clinic and 24-hour ambulatory BPs were compared, and no difference was detected between groups.[7]

In 2022, Mackenzie et al[8] published the results of the TIME study (Treatment in Morning vs Evening), which included more than 21,000 patients randomized to once-daily dosing of medications, daytime vs evening. Patients were followed for a median of 5.2 years. The primary outcome examined was a composite score including hospitalization for nonfatal myocardial infarction or stroke and vascular death. The primary end point was seen in 3.4% of patients in the evening dosing group and in 3.7% of patients in the morning dosing group (HR 0.95; 95% CI 0.83–1.10; $P = 0.53$). The authors concluded that patients should take their antihypertensive medications when convenient and when they experience the fewest side effects.[8]

## SCENARIO 2: RISK OF FALLS AND WORSENING GLAUCOMA

*A 67-year-old woman with a history of glaucoma, hypertension, and type 2 diabetes mellitus presents to establish care. Her BP is uncontrolled, and she reports that she forgets to take her medications in the morning because of her fluctuating schedule. She had been told to avoid taking BP medications in the evening, when she routinely takes the rest of her medications, to minimize the risk of falls and worsening glaucoma.*

Fall risk is a major concern with dosing of nocturnal antihypertensive medications. After older studies linked low BP (systolic BP < 120 mm Hg) to an increased risk of falls,[9] many clinicians avoided prescribing evening antihypertensive medications to prevent orthostatic symptoms in the morning and to minimize fall risk. More recent data that examined intensive BP control (systolic BP < 120 mm Hg) showed a possible increased risk of syncope but not of falls.[10] The TIME study[8] (Treatment in Morning vs Evening) examined dizziness, falls, and fractures as secondary end points. Patients in the evening-dosing group reported fewer falls than their morning-dosing counterparts. The number of fractures reported was similar in both groups. The morning-dosing group reported more events of dizziness or lightheadedness.[8]

Another concern with nocturnal dosing of antihypertensive drugs is glaucoma, a debilitating disease worldwide. Nocturnal decreases in systemic BP have been postulated to lead to decreased ocular perfusion pressure, which may lessen blood flow to the optic nerve and perpetuate glaucomatous damage.[11] Studies have yielded equivocal results, but evidence is mounting that both high and low BP are associated with an increased risk of glaucoma. A meta-analysis found that a fall in nocturnal BP is a risk factor for worsening glaucomatous damage and visual field loss,[12] suggesting that evening dosing of antihypertensive medications may be inadvisable in patients with glaucoma who have a pronounced nocturnal BP dip. However, the available data are not robust enough to yield practice guidelines. Shared decision-making is key, given the potential risk of glaucoma progression with lower nocturnal BP.

Regarding the 67-year-old patient in scenario 2, her comorbidities including glaucoma suggest a need for shared decision-making to weigh the potential risks of worsening her glaucoma with nocturnal dosing of BP medications against the risk of compromising adherence if morning dosing is recommended.

## BOTTOM LINE: TAKE AS DIRECTED

Current evidence does not suggest any benefit with evening vs morning antihypertensive medication dosing. The cardiovascular outcomes and overall side effects appear to be similar. Patients who take their medications in the evening do not appear to have an increased risk of falls or fractures, but they also do not appear to have better cardiovascular outcomes. The focus should be to achieve BP control and facilitate adherence, regardless of the timing of antihypertensive medications.

It is unclear whether nondippers and reverse dippers, or even patients with early morning BP surges, would have better cardiovascular outcomes with a regimen that includes nocturnal medication dosing. Data are lacking in these subgroups of patients, and identifying them remains a challenge given the limited use of ambulatory BP monitoring.

For most patients with hypertension, the act of taking the medication as directed has more significance than the timing.

## DISCLOSURES

Dr. Mehdi has disclosed teaching and speaking for AstraZeneca and work as advisor or review panel participant for Fresenius. The other authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

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COMMENTARY

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# Hey, Doc: Could the 2023–2024 cold and flu season finally be the calm after the storm?

The 2023–2024 cold and flu season is the first in history in which we're armed with vaccines against the 3 currently most common viral respiratory pathogens: influenza, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, the causative agent for coronavirus 2019 [COVID-19]), and respiratory syncytial virus (RSV). So, while the 2022–2023 season was viewed as a "tripledemic" or a "perfect storm,"[1] now, a year later, with these 3 vaccines, we are in a much better place.

In addition, home antigen testing kits for COVID-19 have been widely available for the last 2 years, and in February 2023 the US Food and Drug Administration (FDA) approved a combined influenza and COVID-19 home antigen detection test.[2] There are reasons for pursuing a specific laboratory diagnosis for viral upper respiratory tract infections: symptoms and signs have low diagnostic specificity, outcomes of antiviral treatment are better with early diagnosis, and, just as important, we need to be good stewards of antibacterial drugs. This is especially important with wider use of telemedicine and easy access to antibiotics on demand.[3] Recently, an FDA panel voted that although nasal decongestants decrease nasal airway resistance, they provide only temporary symptom relief.[4]

Despite cumulative data showing that RSV, influenza, and COVID-19 have similar disease severity among hospitalized adults age 60 and older,[5] and despite recent data showing long-term symptoms not only after COVID-19 but also after other acute respiratory viral infections,[6] vaccine coverage remains suboptimal, and vaccine hesitancy is widespread, including among pregnant women.[7]

Here, I will answer important "Hey, Doc" questions our patients have about the currently available influenza, COVID-19, and RSV vaccines.

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### *Hey, Doc: Why do I have to keep getting the flu shot every year?*

Shift happens. Pardon the pun: genetic shift is a sudden, relatively large change in the virus's genome, as opposed to genetic drift, which is the expected, gradual accumulation of small changes. This virus keeps drifting every year, but occasionally it shifts, precipitating pandemics and thus keeping us searching for the Holy Grail, a universal flu vaccine that would be good once and for all. Even though vaccinated people shed more virus than unvaccinated people, hospitalization and mortality rates are lower in vaccinated people.[8]

### *Is there anything new about the flu shot this year (other than shifting)?*

Well, yes. I recall you were always trying to weasel out of getting your flu shot because you're allergic to eggs. For several years, the US Centers for Disease Control and Prevention (CDC) considered severe egg allergy a relative contraindication for receiving an egg-based influenza vaccine. This year, enough data have accumulated showing that people with egg allergies can receive any flu vaccine, egg-based or non-egg-based.[9]

### *Why must the CDC keep guessing every year how good the flu shot is going to be?*

*Guessing* is not the right word. The CDC predicts influenza vaccine effectiveness based on circulating flu serotypes at the time the vaccine is manufactured.

Most influenza vaccines are produced using embryonated hen's eggs. Sialic acid receptors on the surface of human and avian cells are the binding sites for influenza virus. Differences between the human and avian sialic acid receptors may select for mutated viral variants that

are better adapted for propagation in eggs. While this enhances affinity for avian cells, it unfortunately may reduce the vaccine's match to circulating viruses by 7% to 21%, and consequently reduce vaccine effectiveness by 4% to 16%.[10] In comparison, antigenic drift reduces vaccine match to circulating viruses by 8% to 24%, and reduces vaccine effectiveness by 5% to 20%.

Egg adaptation does not occur with the cell culture flu vaccine, making it about 10% more effective than egg-based vaccines.[11] While we cannot control viral antigenic drift or shift, we can avoid the reduction in vaccine match and effectiveness resulting from egg adaptation by avoiding egg-based vaccine production.

### *Does the CDC really know how good this year's flu shot will be?*

Yes. The 2023 Southern Hemisphere seasonal influenza vaccine, which included influenza antigenic serotypes similar to those targeted by the 2023–2024 Northern Hemisphere influenza vaccine formulation, reduced the risk for influenza-associated hospitalizations by 52%.[12]

### *Can you look at your crystal ball to tell me what to expect for next year's flu shot?*

No crystal ball is needed. The World Health Organization provided an update on September 29, 2023, indicating that the B/Yamagata lineage antigen (1 of the 2 influenza B serotypes in the current quadrivalent influenza vaccine) will no longer be needed.[13] So, we may be back to a trivalent vaccine next year, rather than the current quadrivalent one.

### *Is COVID-19 still bad out there?*

Because many of us have had COVID-19 at least once by now, and most of us have received at least 1 dose of the COVID-19 vaccine, disease severity has fortunately decreased. However, COVID-19 continues to circulate year-round in the United States and Europe, with hospitalizations and deaths peaking in November through April.[14] Recent data from the United States showed that between January and August 2023, adults age 65 and older, particularly those with multiple underlying conditions, accounted for almost two-thirds of COVID-19-related hospitalizations, and fewer than a quarter of them had received the bivalent COVID-19 vaccine recommended during that period.[15]

COVID-19 vaccines prevented an estimated 1.5 million hospitalizations and 200,000 deaths during the first 10 months they were available.[16] Vaccine effectiveness of 3 doses of the first-generation COVID-19 messenger RNA (mRNA) vaccines during the omicron BA.4/BA.5 sublineage-predominant periods was 68% for 4 months after vaccination but decreased to 36% after that.[17]

### *Is there a way to detect COVID-19, perhaps in the air we breathe, before things get out of hand again?*

Funny you should ask. The concentration of SARS-CoV-2 in wastewater appeared to predict COVID-19 cases and hospitalizations in the United States, with the maximum sensitivity (93%) and specificity (82%) at a concentration of 51% relative to the peak in January 2022.[18]

### *I've already had 5 COVID-19 shots and I have no clue what to call them anymore! Monovalent, bivalent, primary series, boosters? My head is spinning. What are you calling them this year?*

My head is spinning too!

SARS-CoV-2 is changing much more quickly than the influenza virus. Remember, we first had the wild type, then delta, then omicron. The current updated omicron XBB.1.5-adapted monovalent vaccine generates immune response against multiple XBB-related sublineage variants, including XBB.1.5, XBB.1.16, XBB.2.3, and EG.5.1 (Eris), which continue to dominate globally, and it is recommended for everyone 6 months of age and older.[19] This updated COVID-19 vaccine is not a booster, and it aims to further improve protection against severe illness and hospitalization.

The number of recommended doses depends on multiple factors, including receipt of prior COVID-19 vaccines, age, and underlying immunosuppressed states (**Table 1**).[20] The CDC recommends delaying receipt of the updated vaccine for 3 months after being diagnosed with COVID-19 infection.

### *I read online that the mRNA COVID-19 vaccine can change my genetic makeup. What's up with that?*

Don't believe everything you read online. There are mRNA vaccines for other indications that have been studied for more than half a century, and they cannot change our genetic makeup (ie, our DNA, deoxyribonucleic acid) stored in the cell nucleus.[21] Human mRNA carries DNA-encoded information from the cell nucleus to the cytoplasmic ribosomes, which translate this information into amino acids, the building blocks of proteins. Once human mRNA completes its job, it rapidly degrades.

Similarly, synthetic mRNA vaccines expose human cells to COVID-19 spike protein, stimulating them to mount a protective immune response in the event of future exposure to SARS-CoV-2. This synthetic mRNA rapidly degrades after entering the human body.

**TABLE 1**
**Guidance for the 2023–2024 COVID-19 vaccines for people age 12 and older**

| Immune status | Vaccines received previously | What to give now |
|---|---|---|
| **Not moderately or severely immunocompromised** | None | 1 dose of Moderna, or<br>2 doses of Novavax, or<br>1 dose of Pfizer |
| | 1 or more doses of any messenger RNA vaccine, or<br>1 or more doses of Novavax or Jannssen, including in combination with any original monovalent or bivalent COVID-19 vaccine doses | 1 dose of Moderna, or<br>1 dose of Novavax, or<br>1 dose of Pfizer |
| **Moderately or severely immunocompromised** | None | 3 doses of Moderna, or<br>2 doses of Novavax, or<br>3 doses of Pfizer |
| | 1 dose of any Moderna | 2 doses of Moderna |
| | 2 doses of any Moderna | 1 dose of Moderna |
| | 1 dose of any Pfizer | 2 doses of Pfizer |
| | 2 doses of any Pfizer | 1 dose of Pfizer |
| | 3 or more doses of any messenger RNA vaccine, or<br>1 or more doses of Novavax or Jannssen, including in combination with any original monovalent or bivalent COVID-19 vaccine doses | 1 dose of Moderna, or<br>1 dose of Novavax, or<br>1 dose of Pfizer |

Adapted from reference 20.

***Should even my 13-year-old grandson, who is healthy as a horse and is on his school's football team, take the COVID-19 shot? I heard it can affect his heart.***

Yes, he should, to protect himself as well as to protect you! More studies are showing that cardiac complications such as myocarditis are much more common after COVID-19 infection than after receiving COVID-19 vaccine.[22]

***What is the US government doing to tackle COVID-19 vaccine disparities among racial minorities, particularly after discontinuing the government-funded vaccination program?***

Thank you for bringing up the elephant in the room. COVID-19 vaccine disparities in the United States remain a problem, even in vulnerable populations such as residents of long-term care facilities[23] and pregnant women.[24] One thing is clear: not only do healthcare providers' recommendations to receive the COVID-19 vaccine positively impact patients' decisions, on-site administration of this and other indicated vaccines further increases vaccination rates.[25]

In September 2023, the US Department of Health and Human Services launched the Bridge Access Program to safeguard free COVID-19 vaccination for 25 to 30 million uninsured and underinsured adults.[26]

***Is it true that a drug approved for treatment of COVID-19 is named after one of the Marvel Comics Avengers? Can it actually increase the spread of altered virus and thus further prolong the pandemic?***

You're partially right. Molnupiravir is named after Mjölnir, the hammer of the Norse god Thor. Molnupiravir induces viral genomic mutations, impairing viral replication and reducing viral load. And patients in whom SARS-CoV-2 infection is not completely eradicated can—possibly unknowingly—transmit this mutated virus to other people.[27] The clinical impact of infection with a molnupiravir-associated mutated virus is yet to be determined.

***Please tell me we'll never go back to the 'lockdown' and universal masking days!***

I hate to disappoint you, but I'm afraid I cannot say that. So-called nonpharmaceutical interventions are what carried us through this pandemic: social-distancing measures (including stay-at-home orders, physical distancing, and restrictions on gathering size and room occupancy), masking (particularly with higher quality

masks [respirators] in healthcare settings), testing, contact tracing and isolating (of infected people as well as their contacts), travel restrictions and controls across international borders, and environmental controls (such as enhanced ventilation and air treatment to remove infectious virus[28]), together with widespread, effective vaccination.

### *Is long COVID really the bogeyman? How scared should I be?*

We are learning more and more about long COVID. You should not be scared if you're protecting yourself by following the nonpharmaceutical interventions we talked about and by staying up to date on your COVID-19 vaccinations.

About 7% of US adults who had COVID-19 develop long COVID.[29] Women are about 1.5 times more likely than men to develop long COVID. The highest rate is in adults ages 35 to 49 compared with other age groups. Hispanic people are disproportionately affected, with a rate more than 3 times higher than in Asian people. Adults living in rural areas are more likely to develop long COVID than adults living in large central metropolitan areas. Adults with family incomes at 400% or more of the federal poverty level are less likely to develop long COVID.

Researchers from the University of Oxford in the United Kingdom performed serial brain magnetic resonance imaging and cognitive tests in 401 people with mild COVID-19 and 384 without COVID-19, ages 51 to 81.[30] Patients with COVID-19 had greater reduction in gray matter thickness and tissue contrast in the orbitofrontal cortex and parahippocampal gyrus, greater changes in markers of tissue damage in regions that are functionally connected to the primary olfactory cortex, greater reduction in global brain size, and greater cognitive decline. These degenerative or neuroinflammatory changes involving the limbic cortex may have resulted from spread of the infection through olfactory pathways, or from the loss of sensory input due to anosmia. So it's unclear whether these changes are the chicken or the egg. Time will tell whether they are reversible.

### *What about the new RSV vaccine? I thought only kids get this virus.*

Far from the truth. RSV sickens as many older adults as influenza does. Of the people that RSV infection sends to the hospital, most are age 75 or older, reside in long-term care facilities, or have underlying obesity, chronic obstructive pulmonary disease, or congestive heart failure.[31] In 2023, after several decades of research, the FDA approved 2 RSV vaccines for adults age 60 and older.[32]

Adults ages 70 to 79, particularly those with underlying chronic lung and heart disease, benefit most from this vaccine, which decreases the incidence and severity of infection.[33] No data are available describing the effect of the RSV vaccine on infectivity. RSV vaccine development started in the 1960s. Real-world experience with RSV vaccines remains to be seen.

### *My niece is pregnant. Should she get all these shots now or wait until she delivers the baby?*

Several studies over the last decade demonstrated the protective effect of influenza vaccination during pregnancy for newborns and infants 6 months and younger.[34] More recently, similar studies demonstrated similar protective effects of COVID-19 vaccination during pregnancy.[35] The good news is that the new RSV vaccine is also approved for pregnant persons at 32 to 36 weeks of gestation to prevent RSV-associated bronchiolitis in their newborns and infants up to 6 months after they are born.[36]

We can now nickname the influenza, COVID-19, and RSV vaccines the "mighty trio," protecting those youngsters with yet-immature immune systems who would not mount protective responses to these vaccines.

### *I'm 61 years old, so I'm not a kid, but I'm also not that old! Did I hear you correctly that you want me to take 3 shots today?*

Yes. While I understand that nobody is eager to take yet another shot for the cold and flu season, experts advise that these shots can be coadministered.[37] Unfortunately, combined vaccines against any of these viruses will not be available for the current season.[38]

## DISCLOSURES

The author reports no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

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# The drop of a pin: Accidental ingestion of a sharp foreign body

A 36-year-old female presented to the emergency department following foreign body ingestion. Thirty minutes before arrival to the emergency department, while fitting her husband's clothing, she had accidentally swallowed a tailor's pin (**Figure 1**).

Presenting symptoms included a mild sore throat and nonradiating abdominal pain described as "soreness" and "pressure" located left of the umbilicus. She denied fever, chills, cough, wheezing, shortness of breath, choking sensation, chest pain, nausea, vomiting, hematemesis, coffee-ground emesis, hematochezia, melena, inability to swallow saliva, dysphagia, regurgitation, diarrhea, or constipation.

The patient's medical history was insignificant with no surgical or noteworthy family history. She noted occasional use of alcohol and no use of tobacco, illicit drugs, anticoagulants, antiplatelets, or nonsteroidal anti-inflammatory drugs. She lived in a house with her husband and worked as a chemist. At initial presentation, her vital signs included the following:

- Blood pressure 143/89 mm Hg
- Pulse 71 beats per minute
- Temperature 97.9°F (36.6°C)
- Respiratory rate 16 breaths per minute
- Oxygen saturation 99% on room air
- Body mass index 26 kg/m$^2$.

On physical examination, the patient was alert and oriented to person, place, and time, looked comfortable, and was not in acute distress. There were no obvious signs of bleeding from the mouth or upper airway, no scleral icterus. Her lungs were clear to auscultation, she had a regular heart rate and rhythm without murmurs, rubs, or gallops, and no crepitus on palpation of neck and chest. Her abdominal exam was soft, nontender, nondistended, without guarding or rebound tenderness, and exhibited positive bowel sounds.

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**Figure 1.** Example of a tailor's pin.

Initial laboratory results were all within normal limits, including complete blood cell count, comprehensive metabolic panel, and liver enzyme tests.

## NEXT STEPS: IMAGING

**1** What radiologic test would you obtain next?

- ☐ Computed tomography (CT)
- ☐ Barium esophagography
- ☐ Magnetic resonance imaging of abdomen
- ☐ Abdominal radiography

Foreign body ingestion is common among pediatric and adult populations, more frequent in the former, and foreign bodies can further be categorized as food and nonfood.[1] Nonfood foreign body ingestion, a true foreign body ingestion, is more commonly seen in incarcerated adults and adults with psychiatric comorbidities.[1–4] Although there are multiple radiologic tests for providers to order, biplane radiographic imaging is the preferred choice following foreign body ingestion.[1,4]

Abdominal radiographic imaging can confirm presence of the foreign body as well as the location, size, and shape of the object and is standard practice for management of foreign bodies based on American Society for Gastrointestinal Endoscopy guidelines.[1] Furthermore, both chest and abdominal radiography are used to evaluate for foreign body aspiration and signs of free air that suggest perforation.[1] This is important because insufflation of air into the upper gastrointestinal tract via endoscopy can increase perforation size and delay life-saving surgery.

Nonetheless, radiographic imaging does have limitations. Certain animal bones may not be visualized on radiography, such as fish or chicken bones. Furthermore, radiolucent materials such as plastic, glass, wood, and thin radiopaque metals may not be visualized. Although CT could assess foreign bodies, it is expensive and may not locate the aforementioned, radiolucent materials.[1] If indicated, three-dimensional reconstruction could be used to improve detection; however, radiographic imaging should be used first.[5] Any imaging that uses contrast, such as barium esophagogram, should not be performed as it may increase the risk of aspiration and decrease visualization of the foreign body during endoscopy.[1] Lastly, magnetic resonance imaging is not recommended in this patient owing to the ingestion of a metal foreign body. Therefore, abdominal radiography is the imaging test of choice in this patient.

### Findings on imaging

Ninety minutes after ingestion, initial biplane chest radiography did not identify a foreign body or signs concerning for perforation, such as free air or mediastinal air. Her abdominal radiography 2 hours after ingestion showed a foreign body measuring 18 mm in the left upper quadrant, likely in the stomach. No free air was noted, and shortly thereafter, 3 hours after ingestion, the gastroenterology team was consulted for further evaluation.

## NEXT STEPS: TREATMENT

**2** What is the most appropriate endoscopic timing for the ingested foreign body in this patient?

- ☐ Emergent endoscopy
- ☐ Urgent endoscopy
- ☐ Nonurgent endoscopy
- ☐ Monitor clinically

Endoscopy is commonly performed in foreign body ingestion.[1,6] However, depending on the age and clinical condition of the patient and type of foreign object ingested, endoscopy timing may be emergent, urgent, or nonurgent[1] with different endoscopic tools used to help retrieve the foreign body including forceps, nets, and snares.[1,6]

Emergent endoscopy is defined as immediate, within 6 hours of ingestion, and is indicated for complete esophageal obstruction, disk batteries in the esophagus, or sharp-pointed objects in the esophagus.[1,7,8] Emergent endoscopy is especially important for complete esophageal obstruction owing to risk of aspiration from the inability to manage secretions and chest discomfort.[7–10] Disk batteries are critical to remove owing to potential risk of liquefactive necrosis increasing the risk of esophageal perforation.[1,11] It is important to retrieve button batteries as soon as possible, as they are considered an emergency in the pediatric population and an urgent case in the adult population.[1] Lastly, sharp-pointed objects include animal bones (such as fish), dental bridgework, and needles, and when found in the esophagus, increase the risk of esophageal perforation, thereby indicating emergent endoscopy.[8,12]

Urgent endoscopy is defined as taking place within 24 hours of ingestion. It is indicated for esophageal food impaction without complete obstruction, esophageal foreign objects that are not sharp-pointed, sharp-pointed objects in the stomach or duodenum, objects greater than 6 cm in length at or above the proximal duodenum, and magnets within endoscopic reach.[1] Because incomplete obstruction of esophageal food impaction has a decreased risk of aspiration compared with complete obstruction, endoscopy can be deferred for 24 hours. Furthermore, esophageal foreign objects that are not sharp-pointed can also be deferred up to 24 hours.[1] Sharp-pointed objects in the stomach and duodenum must be endoscopically retrieved within 24 hours as the narrow lumen and fixed position of the duodenum makes maneuvering more difficult.[1,13]

Nonurgent endoscopy typically occurs within 48 hours and is most appropriate for foreign objects such as coins in the esophagus, objects in the stomach with a diameter greater than 2.5 cm, and disk and cylindrical batteries that are in the stomach of patients without signs of gastrointestinal injury.[1] Coins in the esophagus can be observed for 12 to 24 hours before endoscopic removal in asymptomatic patients. If symptomatic, endoscopic removal is recommended.[1,14] Foreign objects in the stomach that are greater than 2.5 cm in diameter are recommended to be removed within 24 hours because the chance of passage across the pylorus is less likely when the diameter is more than 2.5 cm.[1,13,14] Lastly, disk and cylindrical batteries

in the stomach without signs of gastrointestinal injury can be observed for up to 48 hours before endoscopic removal. Once the battery passes the duodenum, 85% pass through the body within 3 days. An abdominal radiograph is recommended every 3 to 4 days to assess progression through the body.[1]

Conservative management is appropriate in asymptomatic patients with gastric foreign objects that do not meet the emergent, urgent, or nonurgent criteria.[1] Because such foreign bodies can take up to 4 weeks to pass, these patients can resume their regular diet, monitor their stool for foreign body passage, and obtain weekly abdominal radiographic imaging.[1] If a foreign body distal to the duodenum does not migrate after 1 week and can be retrieved endoscopically, endoscopic removal is recommended. If the foreign body cannot be removed endoscopically, surgical consultation is recommended.[1,13]

Lastly, magnets within endoscopic reach should be retrieved within 24 hours because magnets that trap bowel tissue between another magnet or metal foreign body can cause pressure and bowel wall necrosis increasing the risk of obstruction, fistula formation, and perforation.[1,15] If the magnet cannot be endoscopically reached, close monitoring and surgical consultation is recommended if the magnet fails to migrate.[1]

## CASE CONTINUED

Because our patient had a sharp-pointed object observed in the left upper quadrant of the abdominal radiograph, suggesting the tailor's pin was in the stomach, the most appropriate next step in management was urgent endoscopy. About 5 hours after ingestion, gastroenterology clinicians performed an upper endoscopy using a flexible adult esophagogastroduodenoscopy scope with no sign of the tailor's pin up to the third portion of the duodenum. Consequently, the esophagogastroduodenoscope was exchanged for a flexible pediatric colonoscope to perform a push enteroscopy in efforts to locate the pin. Unfortunately, no pin was found up to the proximal jejunum.

**3** What is the next best step in management?

- ☐ Proceed with colonoscopy
- ☐ Computed tomography
- ☐ Consult surgery
- ☐ Serial abdominal radiography
- ☐ Capsule endoscopy

If a sharp-pointed foreign body cannot be retrieved endoscopically, daily radiographs should be performed to track the migration through the gastrointestinal tract.[1,4,13] Laxatives may expedite passage through the gastrointestinal tract and can be used to decrease transit time if initial endoscopy is unsuccessful.[1] If a sharp-pointed object fails to progress in 3 days, surgical consultation is recommended.[13]

While sharp-pointed objects that enter the stomach often pass through the remainder of the gastrointestinal tract, complications can occur.[1] Indications for immediate surgical intervention include development of complications such as obstruction or perforation.

Lastly, although CT can locate the foreign body, abdominal radiography can also do this, although abdominal radiography is less expensive and exposes the patient to less radiation.

## ENTEROSCOPY: EXAMINATION OF THE SMALL INTESTINE

There are multiple endoscopic techniques that can be used to examine the small intestines and retrieve foreign bodies.[16] Upper endoscopes commonly used in esophagogastroduodenoscopy are first used to retrieve foreign bodies in the esophagus, stomach, and duodenum. Although some upper endoscopes can reach the jejunum, this rarely occurs. Therefore, the upper endoscope is exchanged for a colonoscope, which is longer, wider, and stiffer and is passed orally and pushed to its maximum distance ("push enteroscopy").

Pediatric colonoscopes can reach 45 to 60 cm from the ligament of Treitz, whereas dedicated enteroscopes can reach 25 to 80 cm from the ligament of Treitz.[16] However, the colonoscope and endoscope are used to advance as far as possible until looping limits the ability to progress. Therefore, device-assisted enteroscopy, including single- and double-balloon enteroscopy and spiral enteroscopy, was designed to improve reach into the small intestine by pleating the small bowel while propelling the scope for greater insertion depth as the balloon expands. The scope can be passed anterograde via the mouth to reach the ileum, or retrograde via the rectum to reach the ileum.

In contrast to balloon-assisted enteroscopy, spiral enteroscopy, a simpler and faster technique, does not use a balloon; it is designed to pleat the small intestine by spiraling clockwise with its spiral ridged overtube.[16]

Single-balloon enteroscopy can reach 133 to 270 cm for anterograde and 73 to 199 cm for retrograde examination, double-balloon enteroscopy can reach 220 to 360 cm anterograde and 124 to 183 cm retrograde, and spiral enteroscopy can reach 175 to 262 cm anterograde.[16]

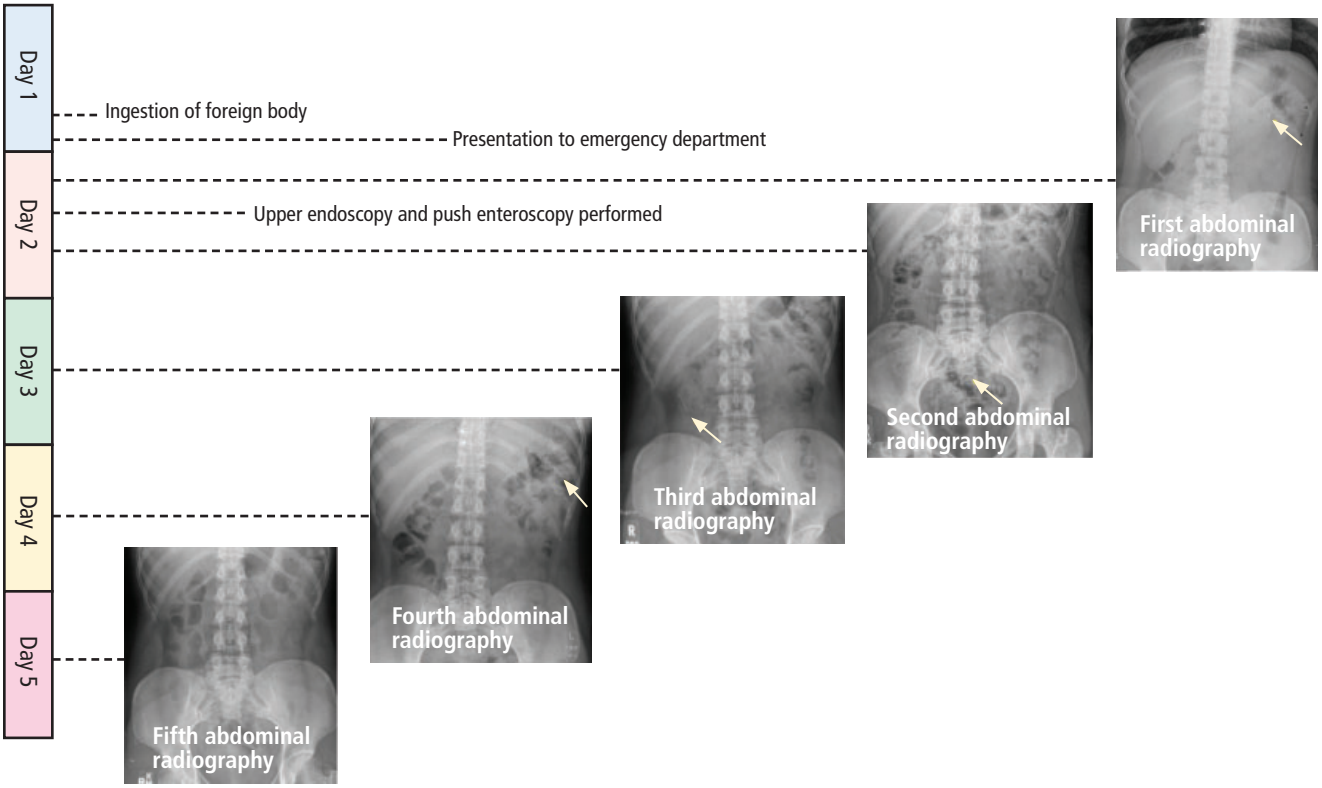


**Figure 2.** Timeline of foreign body ingestion, endoscopy, and abdominal radiography.

A new balloon-assisted device that allows "on-demand" enteroscopy involves passing a balloon through the endoscope or colonoscope working channel.[16] As in balloon enteroscopy, it also helps pleat the small intestine shorter by anchoring the balloon to the small intestine and pulling the scope toward the balloon distally. It can reach 120 to 190 cm anterograde and 89 to 110 cm retrograde. Device-assisted enteroscopy is more expensive than push enteroscopy.

Lastly, intraoperative enteroscopy can be considered. Intraoperative enteroscopy is performed in the operating room with a surgical team.[16] After obtaining access via laparoscopy or laparotomy, the surgeon pleats segments of the intestine while pushing the enteroscope into the small intestine. However, this is the most invasive technique available. Intraoperative enteroscopy can reach up to the ileocecal valve.

Foreign bodies in the colon and terminal ileum may be retrieved using either adult or pediatric colonoscopes in a retrograde approach.[16,17] However, these colonoscopes can only reach a few centimeters into the terminal ileum. Therefore, single- and double-balloon enteroscopes can be inserted retrograde to assess the ileum.

## CASE CONTINUED

Colonoscopy and capsule endoscopy were not appropriate for our patient as she did not complete bowel preparation, and the exact location of the foreign body was not specifically known. Because endoscopic retrieval failed and the object was presumed to have already passed distal to the proximal jejunum, and because the patient did not have complaints indicating obstruction or perforation, the decision was made to manage conservatively with daily serial outpatient abdominal radiography for 3 days (**Figure 2**). It was determined that if the object did not pass after 3 days or if she developed acute symptoms such as increased abdominal pain, nausea, or fever concerning for obstruction or perforation, hospital admission and CT scan of her abdomen and pelvis would be performed with immediate surgical consultation. She was advised to return to the emergency department immediately if any of the concerning symptoms occurred.

About 18 hours after ingestion, she underwent repeat abdominal radiography following endoscopy that had taken place earlier in the morning. The foreign body was visualized over the superior pelvis.

Shortly after the radiology report, the patient was called to provide an update as well as assess for any symptoms. She denied any pain and felt well.

About 42 hours after ingestion, she completed her third abdominal radiography following endoscopy. The foreign body now appeared over the right upper quadrant. Again, the patient was called to review radiography results and to assess for any symptoms. She denied abdominal pain, fever, chills, sweats, hematochezia, or melena stool. She endorsed 3 soft bowel movements that same day as well as some bilateral rib soreness, but otherwise noted no complaints.

About 66 hours after ingestion, she completed additional abdominal radiography showing that the tailor's pin was located in the left upper quadrant. She again reported no symptoms. Although the guidelines recommend surgical consultation for retained sharp-pointed foreign object after 3 days of observation and the patient failed to pass the tailor's pin on day 4, it was decided to observe for 1 more day and add a laxative to help expedite foreign body passage as the patient was asymptomatic and the foreign body was advancing every day. She was prescribed 2 L of polyethylene glycol to help expulse the foreign body.

About 90 hours after ingestion, the patient reported passing the pin. She received confirmatory abdominal radiography reporting no foreign body.

## CASE MANAGEMENT

Urgent endoscopic management within 24 hours is indicated for ingested sharp-pointed foreign bodies that appear to be in the stomach or duodenum at presentation.[1] However, if endoscopy can be performed within 4 hours of foreign body ingestion, endoscopy is also recommended as expedited foreign body removal avoids admissions, repeat radiography, and potential complications. If endoscopic retrieval of the foreign body fails, conservative management with serial abdominal radiography for 3 days is appropriate, and supplementation with bowel preparation can be offered to assist passage of the foreign body.[1,13] If a sharp-pointed foreign body fails to progress within the aforementioned timeframe or if the patient develops symptoms of perforation, then CT with surgical consultation is recommended. In this case, the decision to proceed with endoscopic evaluation early was made to increase the chance of foreign body retrieval within the proximal gastrointestinal tract.

## TAKE-HOME POINTS

- Complications of foreign body ingestion may be severe and include perforation, obstruction, and aortoesophageal fistula and tracheoesophageal fistula formation.[10,15]
- Timing of endoscopy for ingested foreign objects is dependent on the clinical condition of the patient; the size, shape, content, and anatomic location of the ingested object; and the time since ingestion.[1] Based on these details, the patient may qualify for emergent, urgent, or nonurgent endoscopy, or expectant management.
- If endoscopic retrieval of a sharp-pointed foreign body fails, conservative management may be appropriate with daily abdominal radiography for 3 days.[13]

## DISCLOSURES

The authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

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# Contemporary surgical and procedural management of benign prostatic hyperplasia

## ABSTRACT

Interventions for benign prostatic hyperplasia have evolved from transurethral resection of the prostate and simple prostatectomy to a myriad of office-based and operating-room procedures. The contemporary approach involves matching the right procedure to the right patient, choosing on the basis of prostate characteristics, patient preference, and urologist expertise. This review details currently available and guideline-backed surgical and procedural treatments.

## KEY POINTS

Symptoms of benign prostate hyperplasia can be related to prostate size or shape, or both. Certain surgeries and procedures are better suited for certain sizes and shapes of prostates.

For patients who prefer an in-office procedure or wish to avoid sexual function-related side effects such as retrograde ejaculation, the minimally invasive surgical procedures are excellent choices.

For patients with a larger prostate, holmium laser enucleation and simple prostatectomy are the definitive options and can provide durable results.

For those who wish to avoid a postoperative catheter, the prostatic urethral lift procedure or a temporarily implanted nitinol device may be a good option.

Interventions for benign prostatic hyperplasia have advanced in the last 30 to 40 years and now include laser procedures, robotic surgery, and office-based minimally invasive surgeries. Historically, transurethral resection of the prostate was the main endoscopic treatment and is still widely used, but it usually causes adverse effects on sexual function, primarily retrograde ejaculation.

Many of the newer treatments remove prostatic tissue more effectively and cause fewer adverse effects than transurethral resection. For instance, holmium laser enucleation of the prostate and photoselective vaporization of the prostate are approximately as clinically effective as transurethral resection but entail less bleeding risk and shorter hospitalization time, recovery time, and catheterization time. Water vapor thermal therapy and prostatic urethral lift, which are both office-based minimally invasive surgical treatments, can be done without general anesthesia and hospitalization.

This review details the operative indications, efficacy, advantages, disadvantages, and complications of various procedures to treat benign prostatic hyperplasia, including the risks of retrograde ejaculation, erectile dysfunction, and urinary incontinence. It does not cover prostate artery embolization, which is still considered experimental, and medical treatment will be covered in a future review.

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**TABLE 1**
**Office-based procedures for benign prostatic hyperplasia, compared with transurethral resection**

| Treatment | Transurethral resection of the prostate | Prostatic urethral lift procedure | Water vapor thermal therapy | Temporarily inserted nitinol device |
|---|---|---|---|---|
| **Surgery type** | Cystoscopic electric excision | Cystoscopic placement of sutures to open the urethra | Cystoscopic application of steam to ablate the prostate | Cystoscopic placement of a temporary urethral stent |
| **Operative setting** | Operating room | Office | Office | Office |
| **Anesthesia** | General or spinal | Local, sometimes with sedation | Local, sometimes with sedation | Local, sometimes with sedation |
| **Ideal prostate size** | ≤ 80 cc (sometimes a bit larger) | ≤ 80 cc with no median lobe enlargement | ≤ 80 cc (sometimes a bit larger) | < 75 cc, with no median lobe enlargement |
| **Contraindications** | Anticoagulation<br>Elevated bleeding risk<br>Narrow urethra | Large median lobe<br>High bladder neck<br>Allergy to implant | Fibrotic gland (due to prior procedure for prostatic hyperplasia or radiation) | Large median lobe<br>Larger gland<br>Fibrotic gland |
| **Advantages** | Historical gold standard<br>Widely accessible | Preserves sexual function | Preserves sexual function | Preserves sexual function |
| **Postoperative catheter time** | 1–3 days | None (some cases) | 3–7 days | None |
| **Durability** | Good | Poor | Good | Unknown |
| **Erectile dysfunction** | Uncommon | None | None | None |
| **Unique complications** | Electrolyte abnormalities (transurethral resection syndrome) | Expected retreatment<br>Bladder stones | Transient retention from prostate edema | Dislodgement or migration |

## TRANSURETHRAL RESECTION OF THE PROSTATE: THE GOLD STANDARD

During transurethral resection, an electrified wire loop is introduced through a scope to shave away the inner portion of the prostate, expanding the prostatic urethral channel and relieving obstruction. First performed in the 1940s, it is so effective that it remains the gold standard with which other procedures for benign prostatic hyperplasia are compared (**Table 1**).

This procedure is generally done in the operating room with the patient under general or spinal anesthesia. Patients can be discharged home the day of surgery with a Foley catheter or a few days after surgery without a catheter, depending on surgeon preference and clinical situation. The catheter is typically removed on postoperative day 1 to 3.

**Efficacy.** Of the available treatments, transurethral resection has the most robust and rigorous long-term data. At least three-fourths of patients report their voiding symptoms as "better" or "much better" afterward and have a lower (ie, improved) International Prostate Symptom Score and American Urological Association Symptom Index.[1] Objectively, maximum urinary flow rate, postvoid residual bladder volume, and other measures of urodynamic function also significantly improve after this surgery, and these improvements have been found to persist up to 12 years.[2]

Because transurethral resection removes prostatic tissue, the prostate-specific antigen level decreases afterward, and the degree to which it falls depends on both the extent (thoroughness) of resection and the histologic (glandular or stromal) makeup of the tissue removed.

**Contraindications.** Transurethral resection of the prostate is unsuitable for patients who cannot discontinue anticoagulation for surgery.

**Complications.** The main complications of transurethral resection include hemorrhage requiring a blood transfusion (occurring in 2% of cases in a meta-analysis),[3] stress urinary incontinence or permanent lifelong leakage associated with increased abdominal pressure (0.6% or less), postoperative urinary retention (4.5%–6.8%), need for retreatment (0.5%), temporary postoperative dysuria and urinary urgency (0%–38%), urethral stricture (4.1%), and transurethral resection syndrome, ie, acute dilutional hyponatremia (0.8%).[3–5]

Transurethral resection syndrome typically presents with neurologic symptoms of confusion, nausea, vomiting, hypertension, vision changes, and bradycardia. The incidence of this complication has drastically fallen since the introduction of bipolar electrodes for the procedure, which enabled the use of iso-osmolar irrigant (normal saline). Additionally, using bipolar electrodes poses a lower risk of hemorrhage, as the technology facilitates better hemostasis.

Regarding sexual dysfunction, retrograde ejaculation is the main risk and occurs in about two-thirds to three-fourths of patients.[6,7] Some physicians tell their patients to expect it with near certainty. The risk is lower if only parts of the prostate are removed and certain areas are preserved.[8,9] The effects of transurethral resection on erectile function vary, as some studies show it may improve sexual function, while others have shown it can impair erections if the resection is too extensive and perforates the capsule or extends into or beyond the peripheral zone of the prostate (near the neurovascular bundles that facilitate erection).[10,11]

**Bottom line.** Overall, transurethral resection of the prostate has withstood the test of time. Like any surgical procedure, it can have excellent outcomes if done by an experienced surgeon.

## MINIMALLY INVASIVE SURGICAL TREATMENTS

Minimally invasive treatment options for benign prostatic hyperplasia include the prostatic urethral lift procedure, water vapor thermal therapy, and temporary implantation of a nitinol device (**Table 1**).

### Prostatic urethral lift

The prostatic urethral lift procedure (using the UroLift system) is minimally invasive and unique in that it relieves obstruction by mechanically separating and compressing prostatic tissue instead of ablating or resecting it. Through a cystoscope, stainless steel and nitinol anchors are placed in the prostate and connected by permanent sutures. The implants hold the lateral prostatic lobes apart, similar to how curtain ties keep drapes separated beside a window, creating an open channel in the prostatic urethra.

**Advantages.** Studies show essentially no new ejaculatory or erectile dysfunction or urinary incontinence after prostatic urethral lift.[12,13] The implants typically do not encrust or form bladder stones, and they typically epithelialize within 12 months.[14] The implants do not affect the prostate-specific antigen level and are benign unless a known allergy exists.[12]

The primary advantages of this procedure are that it can be performed in the office with local anesthesia, it preserves sexual function, and some patients do not need a catheter after the procedure.[15]

**Efficacy.** In a randomized trial comparing urethral lift vs a sham procedure, at 12 months, men who underwent the real procedure had significant improvements in American Urological Association Symptom Index (decreasing from 22 on a scale of 35 before the procedure, to 11.1 after) and maximum urinary flow rate (a gain of 4.4 mL/sec at 12 months, sustained at 4.0 mL/sec at 60 months).[14] In a head-to-head comparison with transurethral resection of the prostate, the success rate was lower with the lift procedure, and the retreatment rate was higher, 11% vs 6% at 2 years.[16] However, all of the patients who underwent the lift procedure maintained ejaculatory function compared with 34% in the transurethral resection group.[16]

**Contraindications.** Prostates with an enlarged median lobe or prostate volume greater than 80 cc are not well suited for this treatment, which highlights the importance of diagnostic cystourethroscopy and prostate imaging (ultrasonography or cross-sectional imaging) to determine candidacy for the procedure.

**Complications** are generally temporary and include dysuria (in 25%–53%), hematuria (16%–75%), pelvic pain (3.7%–19.3%), and need for postprocedural catheterization (20%–100%).[17] In addition, malpositioned implants can lead to bladder irritation or growth of bladder stones. Although the growth of stones is rare, they almost always require another surgical procedure to manage.[18]

**Bottom line.** While the prostatic urethral lift procedure is an excellent option to preserve sexual function, its long-term durability is unknown, and the lack of tissue removal will likely lead those who undergo it to ultimately require some form of subsequent treatment.

### Water vapor thermal therapy

Water vapor thermal therapy (with the Rezūm system) uses steam to ablate prostatic tissue. Through a

specialized scope, the surgeon inserts a small needle to inject water vapor into the transitional zone (lateral and median lobes) of the prostate in up to 15 different sites for up to 9 seconds each. The steam diffuses throughout the prostatic tissue but does not cross the surgical capsule into the peripheral zone. It induces localized cell death and tissue necrosis. Over the next 4 to 6 weeks, the ablated tissue shrinks, enlarging the prostatic lumen.

Because this treatment ablates tissue, the prostate-specific antigen level decreases once inflammation from the procedure resolves. The initial injection of steam often causes prostatic edema, so an indwelling Foley catheter or intermittent catheterization is required for a few days postoperatively.

**Advantages.** The primary advantages of water vapor thermal therapy are that it can be performed in the office under local anesthesia, it generally preserves ejaculatory function, and it can be used in prostates with a median lobe.

**Efficacy.** In a randomized trial,[19] water vapor thermal therapy produced significant improvements in symptoms, maximum flow, and quality of life at 12 months. This persisted to 2 years compared with sham treatment, with a 51% reduction in International Prostate Symptom Scores, 4.2-mL/sec improvement in maximum flow, and 50% improvement in quality-of-life scores. These results did not differ in patients with an enlarged median lobe. Ejaculatory bother scores were 31% better at 1 year, and de novo erectile dysfunction was not observed.[19] However, in another study, 4 (2.9%) of 136 men reported ejaculatory dysfunction, which is less than with transurethral resection but more than with prostatic urethral lift.[20]

**Contraindications.** Previous radiation treatment or fibrosis of the prostate (due to a prior procedure for benign prostatic hyperplasia) are relative contraindications for this procedure.

**Complications** of water vapor thermal therapy include dysuria, hematuria, urinary frequency and urgency, hematospermia, and urinary tract infection.[19,21] These symptoms are typically mild to moderate and resolve within 3 weeks.

**Bottom line.** Overall, water vapor thermal therapy is an effective minimally invasive surgical treatment that eliminates hyperplastic tissue, although with a delayed time to effect. It can be easily performed in the office, it usually preserves ejaculatory function, and it achieves durable results in a variety of prostate sizes and configurations.

## TEMPORARILY IMPLANTED NITINOL DEVICE

The iTind device, a temporarily implanted nitinol device, is a newer minimally invasive surgical treatment and one of a growing number of devices inserted into the prostatic urethra. When placed, the wirelike device springs open like a stent in the prostatic channel. It is left in place for only 5 to 7 days before it is removed in the office. While it is in, the struts of the device compress the urethral wall, induce tissue ischemia, and cause tissue remodeling and erosions or incisions into the prostate at the 12, 5, and 7 o'clock positions, effectively performing a transurethral incision of the prostate and improving urine flow.

Device placement can be done in the office with the patient under local anesthesia. No part of the device is left in place permanently, it does not require a postoperative catheter, and it preserves ejaculatory function.

**Efficacy.** Several single-arm studies show that this procedure significantly improves maximum urinary flow rate, symptoms, and quality of life at 1 to 2 years.[22,23] In one study, there was no new sexual dysfunction at 2 years.[24]

**Contraindications.** This device has not been studied in prostates larger than 60 cc, and in early studies it did not work well in patients with a large median lobe.[23] Many urologists believe that it is likely best suited for patients with tighter and smaller prostates that impede flow due to an elevated or constricted bladder neck and bladder-prostate junction.

**Bottom line.** The temporarily implanted nitinol device is a helpful addition to minimally invasive surgical treatments, offering novel advantages such as no postoperative catheterization and no permanent implants. However, long-term data on its durability and efficacy are lacking. Additionally, current indications for the procedure are limited to smaller prostates without enlargement of the median lobe. Time will tell if the induced tissue incisions and remodeling of the prostate are durable, and what role this procedure will have in managing benign prostatic hyperplasia.

## SURGICAL THERAPIES

Surgical therapies other than transurethral resection include photoselective vaporization, endoscopic laser enucleation, robotic or open simple prostatectomy, and robotically controlled water jet treatment (**Table 2**).

### Photoselective vaporization of the prostate

Photoselective vaporization of the prostate, another transurethral procedure, uses the 532-nm GreenLight laser device to open up the prostatic lumen. The light

**TABLE 2**
**Operating-room-based surgeries other than transurethral resection for benign prostatic hyperplasia**

| Treatment | Photoselective vaporization of prostate | Holmium laser enucleation of the prostate | Simple prostatectomy | Robotically controlled water jet treatment |
|---|---|---|---|---|
| **Surgery type** | Cystoscopic laser vaporization | Cystoscopic laser excision | Abdominal excision | Cystoscopic water jet ablation |
| **Operative setting** | Operating room | Operating room | Operating room | Operating room |
| **Anesthesia** | General or spinal | General or spinal | General or spinal | General or spinal |
| **Ideal prostate size** | ≤ 100 cc (sometimes a bit larger) | ≤ 250 cc | > 80 cc, with or without concomitant pathology, eg, bladder calculi, diverticula | ≤ 150 cc |
| **Contraindications** | Prior radiation | (Not available) | Anticoagulation<br>Elevated bleeding risk | Anticoagulation<br>Elevated bleeding risk |
| **Advantages** | Excellent hemostasis<br>Small caliber scope | Size-independent<br>Durable results | Done under vision (robotic)<br>Durable results | Preserves sexual function |
| **Postoperative catheter time** | 1 day | 1 day | 5–10 days | 1–5 days |
| **Durability** | Good | Excellent | Excellent | Unknown |
| **Erectile dysfunction** | Rare | Uncommon | Uncommon | None |
| **Unique complications** | Obstruction from sloughed tissue passage | Bladder injury from morcellator | Risks of surgical incision<br>Risks of intra-abdominal surgery | Unknown |

is absorbed by hemoglobin in prostatic cells, which heat up and lyse superficially while coagulating more deeply. As a result, the procedure is well suited for patients who are on therapeutic anticoagulation or are at higher risk of bleeding.

This procedure is typically done in the operating room with general or spinal anesthesia and with a small-caliber cystoscope, commonly as an outpatient or same-day surgery. A Foley catheter is generally left in place for 1 day afterward but can be kept in for longer as clinically indicated. As there is less prostate tissue afterward, the prostate-specific antigen level is expected to fall.

**Efficacy.** In a study in 139 men, photoselective vaporization of the prostate improved American Urological Association Symptom Index scores by 82%, maximum flow rate by 190%, and quality of life scores by 74%.[25] These improvements are durable, as evidenced by a low (6.8%) retreatment rate at 5 years in another report.[26] Complication rates and outcomes did not vary with anticoagulant use or prostate size over 80 cc.[27]

Direct comparisons with transurethral resection show that photoselective vaporization achieves equivalent outcomes with shorter hospital stays and catheterization time.[28,29] However, as noted previously, like any surgery or procedure, experience with the procedure is what drives excellent outcomes.

**Complications** of photoselective vaporization of the prostate are similar to those of transurethral resection, but are milder in some respects because the cystoscope is smaller in diameter. These include urethral stricture (2.8%), bladder neck contracture (4.4%), epididymitis (5%–7%), urinary tract infection (1%–20%), hemorrhage requiring blood transfusion (rare), prostatic capsular perforation (0.2%–1%), and need for

retreatment (1.7%–7%).[30–32] Transient postoperative dysuria and urinary urgency and frequency are expected during recovery as the coagulated tissue sloughs off and is passed with urination.

Several studies show this procedure either does not affect erectile function or may mildly improve it, while ejaculatory loss should be expected with a complete procedure.[33,34] However, as with transurethral resection, ejaculatory function can be maintained by removing only parts of the hyperplastic tissue as opposed to complete removal.[35,36]

**Bottom line.** In a number of practices, photoselective vaporization of the prostate has replaced transurethral resection of the prostate as the default option in light of its superior efficiency and flexibility.

### Anatomical endoscopic enucleation of the prostate using a holmium laser

Anatomical endoscopic enucleation of the prostate is a transurethral scope-based approach. An energy source, typically a laser, is used to incise the prostate to enable the surgeon to use mechanical force and the rigid scope to "peel out" or enucleate the hyperplastic tissue (transitional zone) along the surgical capsule, separating it from the peripheral zone of the prostate. This is like removing the inside of an orange (the prostatic tissue) and leaving the rind (the surgical capsule) intact. Once the prostatic lobes are freed, they are pushed into the bladder and morcellated (cut into smaller pieces) so they can be evacuated. The energy source is also used to maintain hemostasis throughout the procedure.

The oldest and best-studied of these procedures is holmium laser enucleation of the prostate, in which a holmium end-fire laser is the energy source. Holmium laser enucleation is a great advance in the surgical management of benign prostatic hyperplasia but has a steep learning curve, which has slowed its adoption and limited its widespread use. However, this is gradually changing as more urologists are becoming aware of its versatility.

Holmium laser enucleation can be used to treat very large prostates (> 120 cc), larger than is possible with transurethral resection or photosensitive vaporization. It is performed in the operating room with the patient under general or spinal anesthesia as a same-day or overnight-stay procedure. The Foley catheter is generally removed the day after surgery. Prostate tissue is removed, so the prostate-specific antigen level should decrease after the procedure.

**Efficacy.** In a series of 552 patients,[37] holmium laser enucleation of the prostate improved International Prostate Symptom Scores by 75% and maximum flow by 200% at 1 year, with a mean hospital stay of 1.5 days and average catheterization time of 1.4 days. Results are durable, with a 4.2% retreatment rate at 6 years.[38] In a randomized trial, compared with transurethral resection, holmium laser enucleation was associated with a shorter catheterization time (27.6 vs 43.4 hours), briefer hospitalization (53.3 vs 85.8 hours), and smaller drop in hemoglobin (1.3 vs 1.8 g/dL) despite a longer operative time (94.6 vs 73.8 min).[39] In a meta-analysis,[28] American Urological Association Symptom Index scores and maximum flow remained improved at 7 years with both procedures, again highlighting the effect of surgeon expertise with various procedures.

**Complications** of holmium laser enucleation of the prostate are similar to those of transurethral resection and photoselective vaporization and include capsular perforation, hemorrhage requiring blood transfusion, transient urinary urgency and dysuria, bladder neck contracture, and urethral stricture, all in low numbers that varied in different reports.[3,40–42] However, morcellator-related complications are specific to holmium laser enucleation of the prostate and can result in ureteral orifice injury, bladder perforation, and rarely, severe bladder damage that necessitates cystectomy and urinary diversion.[40,43,44]

Additionally, as the procedure entails mechanical dissection, stress on the urinary sphincter complex can result in transient stress urinary incontinence (in 10.7% in one series, improving with time in all but 0.7%).[40]

Retrograde ejaculation is to be expected after holmium laser enucleation, but not erectile dysfunction.[6,7]

**Bottom line.** Holmium laser enucleation of the prostate is a versatile treatment for a wide variety of prostate sizes and offers one of the most thorough removals of hyperplastic tissue available, explaining its excellent durability.

### Simple prostatectomy: Robotic or open approach

Historically, for prostates larger than 80 cc, open or laparoscopic robotic simple prostatectomy was the treatment of choice. These procedures involve a surgical incision and opening the prostate either from its anterior surface or through the bladder (after opening the bladder too). The surgeon then peels out the hyperplastic tissue (transitional zone) from within the peripheral zone of the prostate, similar to what is done in holmium laser enucleation of the prostate.

**Indications.** Simple prostatectomy is an excellent option for patients who have massively enlarged prostates or concomitant bladder diverticula, large bladder stones, or a contraindication to the dorsal lithotomy position.

Compared with transurethral resection or photoselective vaporization, simple prostatectomy has a neg-

ligible retreatment rate, as the prostatic hyperplastic tissue is completely removed.

Advances in robotic surgery have improved visualization of the operative field, reduced blood loss, enabled smaller incisions, shortened hospitalization, and improved recovery. Depending on the approach taken (extraperitoneal, transvesical, or transperitoneal), patients spend 1 to 3 days in the hospital and have a Foley catheter for 5 to 10 days after surgery. The new single-port robotic platform has enabled some surgeons to do prostatectomies as same-day surgeries and remove the catheter 3 days later.[45]

**Complications.** The overall rates of morbidity and mortality associated with simple prostatectomy have greatly improved over the years. The main complications are retrograde ejaculation, hemorrhage requiring blood transfusion (rare in modern series), stress incontinence (rare), erectile dysfunction, bladder neck contracture, and transient urinary urgency and frequency with urge incontinence, which is seen after many procedures for benign prostatic hyperplasia.[46–48]

**Advantages.** Whether performed open or robotically, simple prostatectomy is a definitive and durable treatment. Though holmium laser enucleation of the prostate can offer similar long-term outcomes without an incision, the "top-down" approach to the prostate used in simple prostatectomy does not put mechanical stress on the sphincter complex, and thus, transient stress incontinence is much less common than with holmium laser enucleation.[49–51]

### Robotically controlled water jet treatment

Robotically controlled water jet treatment with the Aquablation system is a new technique that is being more commonly adopted. It uses a robotically controlled high-velocity water jet to clear prostatic tissue (similar to a pressure washer) within a predefined area under real-time guidance with transrectal ultrasonography. The surgeon delineates the area of treatment, preserving the bladder neck, external sphincter, and ejaculatory region of the gland, making this a partial and not a complete treatment.

**Advantages.** This treatment preserves ejaculation (in 80%–90%), erections, and continence. It is performed with the patient under general or spinal anesthesia, can be done as an overnight-stay or same-day surgery, and can be done in prostate glands of varying sizes. In larger glands, multiple passes or treatment runs may be necessary, but these take only a few minutes each.

**Efficacy.** In a prospective, single-arm trial in 21 men, robotically controlled water jet treatment improved symptoms and maximum flow.[52]

**Complications.** Bleeding after tissue removal presents a challenge and requires surgeons to then use a transurethral resection scope to coagulate bleeding vessels and clear away a residual layer of hypertrophic tissue (similar to a very limited transurethral resection of the prostate) and any stubborn areas the water jet did not eliminate. Using a transurethral resection scope after the water jet treatment has enabled it to become a same-day procedure.

**Bottom line.** As robotically controlled water jet treatment is a new technique, long-term data are needed to evaluate its durability.

## THE RIGHT PROCEDURE FOR THE RIGHT PATIENT

We now have a range of options for treating benign prostatic hyperplasia and can choose among them based on prostate size and configuration, operative setting, expected side effects, and patient preferences and quality-of-life goals:

- For patients who prefer an in-office procedure or wish to avoid adverse effects on sexual function such as retrograde ejaculation, the minimally invasive surgical procedures are excellent choices.
- For patients with a larger prostate, holmium laser enucleation and simple prostatectomy are the definitive options and can provide durable results.
- For those who wish to avoid a postoperative catheter, the prostatic urethral lift procedure or a temporarily implanted nitinol device may be a good option.

Additionally, the consideration of a patient's specific anatomy before choosing a treatment option has led to a greater emphasis on preoperative imaging and endoscopic assessment with cystoscopy.

**Bottom line.** Most if not all available treatments for benign prostatic hyperplasia can deliver excellent outcomes. But as with any other surgery or procedure, the experience of the urologist with each specific treatment is an important factor for quality results. In the contemporary approach to benign prostatic hyperplasia, urologists must balance their skill with the various techniques with the patient's unique prostate anatomy, preferences, and quality-of-life goals to achieve optimal results for their patients.

## DISCLOSURES

Dr. Gill has disclosed consulting, work as advisor or review panel participant, and research as a co-investigator or site-lead for Boston Scientific and Urovant Sciences. The other authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

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REVIEW

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# Treatments for obstructive sleep apnea: CPAP and beyond

## ABSTRACT

Treatment options for obstructive sleep apnea include positive airway pressure and alternatives such as behavioral interventions, oral appliances, nasal expiratory positive airway pressure, negative pressure interventions, and surgical procedures. Certain drugs are also promising. An important aspect of the treatment includes troubleshooting the reasons for poor adherence to positive airway pressure treatment, discussing alternatives based either on individual preference or on phenotypic characterization of the sleep apnea, and managing expectations.

## KEY POINTS

As many as one-fourth of people age 30 to 70 may have obstructive sleep apnea, and the prevalence may be increasing.

Patients should not expect continuous positive airway pressure (CPAP) therapy to help them lose weight. In fact, some patients gain weight on it.

Bariatric surgery may fail to control obstructive sleep apnea in over 20% of patients and may be associated with lower CPAP adherence.

Hypoglossal nerve stimulation is a newer surgical option for select patients who cannot use CPAP.

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Continuous positive airway pressure (CPAP) remains the gold standard treatment for obstructive sleep apnea, but it is not the only one. Alternative treatments may be better suited to some patients,[1] as this is a heterogeneous disorder with distinct clinical, polysomnographic, and physiologic phenotypes.[2,3]

Here, we review conservative, pressure-based, and surgical treatments for obstructive sleep apnea, including their indications, effectiveness, caveats, and the patients for whom they might be most effective.

## DIAGNOSIS BASED ON APNEA-HYPOPNEA INDEX

The American Academy of Sleep Medicine[4] bases the diagnosis of obstructive sleep apnea on the apnea-hypopnea index (AHI), ie, the number of obstructive respiratory events (apnea, hypopnea, or respiratory effort-related arousal) per hour of sleep, defined as one of the following:

- 15 or more events per hour, regardless of symptoms or comorbidities
- 5 or more events per hour with clinically significant symptoms (eg, daytime sleepiness, loud snoring, witnessed apneas, nocturnal awakenings with choking or gasping) or comorbidities (eg, hypertension, heart disease, diabetes, cognitive impairment).

The Wisconsin Sleep Cohort Study[5] reported that in the years 2007 to 2010, 26% of people age 30 to 70 had an AHI of at least 5, and about 10% had an AHI of at least 15

**TABLE 1**
**Conservative and medical treatments for obstructive sleep apnea**

| Treatment | Indications | Reduction in apnea-hypopnea index | Caveats | Possible predictors of success |
|---|---|---|---|---|
| **Weight loss**[7] | BMI ≥ 26 kg/m$^2$ | 26% per 10% weight loss | Weight loss and lifestyle changes difficult to maintain | Higher BMI, larger neck circumference |
| **Positional therapy**[13,14] | Positional sleep apnea | 7.4 fewer events per hour | 10% have sleep disturbance, back or chest discomfort | Positional obstructive sleep apnea, no obesity, lower AHI |
| **Drug therapy**[15,16] | No current labeling of specific drugs | Noradrenergic with antimuscarinic: 76% | Anticholinergic effects | Lower AHI and decreased collapsibility |
| | | Carbonic anhydrase inhibitors: 45% | Paresthesia, dyspepsia | High loop gain |
| **Oxygen therapy**[17,18,21] | Inability to tolerate positive airway pressure, failure of upper airway surgery | 72.5% in responders (25% of patients) | Prolongs apnea, increases risk of hypercarbia, no effect on blood pressure or excessive daytime sleepiness | High loop gain, decreased collapsibility, and increased pharyngeal compensation |
| **Oral appliances**[19,22] | Can be first-line, especially in mild to moderate obstructive sleep apnea | 56%; effective in 68% of patients after 2 years of treatment | Temporomandibular joint dysfunction, occlusion changes; requires manual dexterity | Retracted maxilla and mandible, narrow airway, short soft palate, positional obstructive sleep apnea, lower BMI, female, smaller neck circumference, lower AHI |
| **Myofunctional tongue stimulation**[20] | Alternative to CPAP, or adjunct to CPAP to improve adherence | 50% | Not recommended as standard treatment | Ineffective upper-airway dilator muscles |

AHI = apnea-hypopnea index; BMI = body mass index; CPAP = continuous positive airway pressure therapy

(representing moderate or severe obstructive sleep apnea), and that these were "substantial" increases compared with estimates from 1988 to 1994.

Untreated, obstructive sleep apnea causes daytime sleepiness in more than half of patients,[6] and increases the risk of motor vehicular accidents by 17%.[7] Long-term consequences include hypertension,[8] incident diabetes,[9] cardiovascular events,[10] and impairment in several domains of cognition, including attention, memory, and executive function.[11,12] Fortunately, the risks of these complications are modifiable with therapy.

## CONSERVATIVE TREATMENTS

Therapy usually includes weight loss, exercise, positional therapy, and alcohol avoidance as adjuncts to CPAP, while other conservative treatments can be alternatives to it (**Table 1**).[7,13–22]

### Weight loss

The body mass index is an important predictor of obstructive sleep apnea and figures prominently in prediction scales.[23] Conversely, in a longitudinal study, a 10% weight loss predicted a 26% decrease in AHI.[24] Weight loss decreases the collapsibility of the airway as measured by the pharyngeal critical closing pressure, with near-complete resolution of apnea when the pharyngeal critical closing pressure drops below –4 cm $H_2O$.[25]

**Lifestyle modifications.** In a large long-term randomized study in patients with obesity, diabetes, and sleep apnea, the rate of remission of obstructive sleep apnea at 10 years was 34.4% with intensive lifestyle interventions compared with 22.2% with diabetes support and education only.[26] The improvement in severity of obstructive sleep apnea was related to the change in body weight and to the original AHI.

**Bariatric surgery** can significantly improve obstructive sleep apnea, with rates of cure reported as 86%,[27] 57%,[28] and 45%.[29] However, in 1 study,[29] moderate or severe obstructive sleep apnea persisted in 20% of patients after surgery. In a randomized trial,[30] the reduction in AHI was not statistically significantly greater with gastric banding than with conventional weight loss, even though patients who underwent gastric banding lost more weight. Patients therefore need to be aware that bariatric surgery may not cure their obstructive sleep apnea, and this should be discussed before surgery.

CPAP adherence was poor after bariatric surgery in another study,[28] with patients using their machines on a median of only 49% of nights.[28]

**Glucagon-like peptide 1 receptor agonists** curb appetite and hunger, reduce food release from the stomach, promote postprandial fullness, and have been highly effective in promoting weight loss. They also decrease the AHI[31,32] by 6 episodes per hour more than with placebo in 1 study.[31] Two drugs in this class, liraglutide and semaglutide, are approved by the US Food and Drug Administration (FDA) for chronic weight management.[33] However, no drugs are approved specifically for treating obstructive sleep apnea (see discussion below).

### Exercise

Whether exercise alone improves sleep apnea is uncertain. In the Look AHEAD (Action for Health in Diabetes) study[26] of lifestyle interventions including exercise in patients with obesity and diabetes mellitus, the AHI decreased independently of weight change. Similarly, in a meta-analysis, exercise was found to improve obstructive sleep apnea despite minimal weight change.[34] In contrast, in another study in overweight adults with diabetes and sleep apnea, fitness did not change the obstructive sleep apnea severity after accounting for the weight change.[35]

Even so, we recommend exercise for patients with obstructive sleep apnea because it can favorably modify the associated cardiovascular risks.

### Positional sleep therapy

The AHI has been observed to be twice as high when people sleep on their back than when they sleep on their side.[13,36] The increase in AHI in the recumbent position was most prominent in people with less obesity and near-normal weight,[13] and patients with positional sleep apnea tended to have a lower body mass index and lower overall AHI than those with nonpositional sleep apnea.[37]

Positional therapy uses a variety of devices or garments to keep patients off of their back at night, such as pajama tops with a lump or a tennis ball sewn into the back. A Cochrane review[14] found no difference in the Epworth Sleepiness Scale score, quality of life, or sleep quality with positional therapy compared with CPAP. There were 6.4 fewer events per hour with CPAP, but adherence was 2.5 hours longer per night with positional therapy. Compared with scores in a control group, positional therapy improved the Epworth Sleepiness Scale score by 1.58 points (a difference that is not, however, considered clinically important), and reduced sleep apnea by 7.4 events per hour, but 10% of patients still had sleep disturbances and back or chest discomfort.[14]

### Alcohol avoidance

In meta-analyses, the prevalence of obstructive sleep apnea was 25% higher in people who consumed alcohol,[38] the duration of apnea was longer, and the nadir oxygen saturation was lower.[39,40] These effects may be mediated by a selective adverse effect of alcohol on airway dilator muscles, with depression of hypoglossal nerve or genioglossus muscle activity and without changes in breathing pattern, minute ventilation, or hypercapnic ventilatory response.[41,42]

The effect of alcohol on obstructive sleep apnea appears to be particularly pronounced in those with existing snoring or sleep apnea[39,40] and in men,[41] perhaps reflecting a potential protective effect of progesterone.[42]

### No approved pharmacologic therapy

No drug is currently approved or in common use for managing obstructive sleep apnea, and a Cochrane review from 2013 found insufficient evidence to recommend any drug for it.[43]

That said, the antidepressants protriptyline and fluoxetine were both found to reduce the number of events of apnea and hypopnea, in part from their expected effects of reducing rapid eye movement (REM) sleep, but also from a reduction in non-REM events.[44,45] However, the response was variable, and the drugs did not decrease the number of arousal or desaturation events.[45]

Carbonic anhydrase inhibitors such as acetazolamide, zonisamide, and topiramate can reduce the AHI (by 42% in a study of acetazolamide[15]) and improve sleep efficiency and oxygen saturation but not sleepiness.[15] The mechanism may relate to breathing stimulation and reduced ventilatory control sensitivity rather than to improvements in airway collapsibil-

ity. For instance, the reduction in the AHI correlates with the reduction in bicarbonate concentration[46] and with reduction in loop gain (ie, improving an exaggerated ventilatory response upon resumption of breathing following an obstructive event).[47] The AHI is particularly reduced when carbonic anhydrase inhibitors are combined with CPAP.[46] A European Respiratory Society guideline has a conditional recommendation based on low-quality evidence to use carbonic anhydrase inhibitors, but only in the context of a randomized control trial.[15]

A newer strategy is to counteract 2 mechanisms of pharyngeal hypotonia, namely loss of noradrenergic drive and active muscarinic inhibition,[48] using a combination of noradrenergic and antimuscarinic agents such as atomoxetine with oxybutynin,[48] reboxetine with oxybutynin,[49] or atomoxetine with fesoterodine.[50] While neither type of agent alone reduced the AHI, the combination can result in a greater than 50% short-term reduction in the AHI,[48,49] though the success may depend on targeting patients with a phenotype of milder upper airway collapsibility.[16,50] These combinations may be promising but are not currently available.

### Oxygen

Although oxygen is sometimes empirically prescribed as an alternative in patients unable or unwilling to use CPAP, its use for that purpose is not substantiated. In a meta-analysis of randomized controlled trials comparing CPAP and nocturnal oxygen, both interventions similarly improved nocturnal oxygen desaturation, but oxygen therapy prolonged the duration of sleep-disordered breathing events, may have promoted hypercapnia, and did not improve sleepiness.[17] Further, in patients with obstructive sleep apnea and cardiovascular disease or risk factors for it, oxygen supplementation did not reduce blood pressure, whereas CPAP did.[51]

These findings do not preclude the use of oxygen in patients who have specific endophenotypic traits of sleep apnea. For instance, a multivariable model identified the combination of increased loop gain plus decreased collapsibility or increased pharyngeal compensation as a predictor of a decrease in AHI with oxygen supplementation.[18]

### Oral appliances

Oral appliances can be an effective alternative for many patients with obstructive sleep apnea. These devices stabilize and advance the mandible anteriorly to open the airway, especially laterally in the velopharyngeal area.[52] An oral appliance can be a first-line therapy for mild to moderate obstructive sleep apnea and for severe obstructive sleep apnea when a patient cannot tolerate or refuses CPAP.[53]

When obstructive sleep apnea has been confirmed, the patient should be evaluated by a qualified dentist to determine candidacy for an oral appliance based on the health of dentition and existing dental work, relationship of the maxilla to the mandible, mandibular range of motion, and history of temporomandibular disorders.[54] The custom-fitted device places the mandible at a comfortable starting position as determined by the dentist and patient, and the device can then be calibrated based on subjective and objective responses within a range comfortable to the patient. When a patient achieves resolution of apnea symptoms, the referring clinician is notified and can confirm treatment efficacy.[54]

Treatment success with oral appliances can be measured in several ways, but often by a decrease in AHI of at least 50%. Using this metric, oral appliance therapy was effective in 68% of 172 patients after 2 years of treatment in one study.[19] In another study, the success rate was 69%, with success defined as at least a 50% reduction in AHI, coupled with an AHI of 10 or less.[55]

Multiple studies have shown that oral appliances can alleviate daytime sleepiness and mental fog, lower high blood pressure, and reduce the risk of cardiovascular-related deaths.[56–59]

Patients should be seen by a qualified dentist every 6 months for the first year of oral appliance therapy and then annually.[54] Follow-up is essential to monitor patients for any changes in sleep as well as any device-related side effects such as changes in occlusion or tooth position, jaw pain, temporomandibular joint disorders, and damage to existing dental work.[54]

### Myofunctional therapy

Myofunctional therapy consists of interventions such as electrical stimulation of the tongue,[60,61] speech therapy,[62,63] circular breathing, singing, or wind-instrument playing,[64,65] which strengthen the facial, tongue, oropharyngeal, or skeletal structures and enhance the neuromuscular compensatory mechanisms that counteract the anatomic mechanical loads contributing to airway narrowing.[66,67] A European task force did not recommend myofunctional therapy as a standard treatment of obstructive sleep apnea, based on limited and low-quality evidence.[15] However, it may have a role for patients seeking alternatives to more effective surgical or mechanical options.

**TABLE 2**
**Airway pressure treatments for obstructive sleep apnea**

| Treatment | Indications | Reduction in apnea-hypopnea index | Caveats | Possible predictors of success |
|---|---|---|---|---|
| **Positive airway pressure**[73] | First-line treatment for mild obstructive sleep apnea with cardiovascular disease or excessive daytime sleepiness, and moderate to severe obstructive sleep apnea | 73% | Nasal irritation, dry mouth, sinus infection; weight loss should not be expected | Positional obstructive sleep apnea |
| **Nasal expiratory pressure**[70,74,75] | Mild to moderate obstructive sleep apnea | 70% | Difficulty exhaling, nasal discomfort, dry mouth, different effects between devices | Positional obstructive sleep apnea |
| **Intraoral negative pressure**[71] | Moderate to severe obstructive sleep apnea | 25% have at least a 50% reduction from baseline | Dental or oral tissue discomfort | Retropalatal airway collapse |
| **Negative external pressure**[72] | Moderate to severe obstructive sleep apnea | 75% | Skin irritation | Anteroposterior airway collapse |

In a systematic review, myofunctional therapy decreased the AHI by 50%, with improvement in oxygen saturation nadir, snoring, and daytime sleepiness.[20] One available electrical tongue-stimulation device (eXciteOSA) is FDA-approved for snoring and mild sleep apnea, and objectively improves snoring, sleepiness, sleep-related quality of life, and AHI (from 10.2 to 6.8 events per hour).[60,61]

An additional role for myofunctional therapy may be as an adjunct to CPAP to improve CPAP adherence,[68] with potential incremental benefits compared with CPAP alone.[69]

## AIRWAY PRESSURE THERAPY

Several types of machines prevent obstructive events by keeping the airway open (**Table 2**).[70–75]

### CPAP is the mainstay

CPAP is a first-line therapy for moderate or severe obstructive sleep apnea and for mild obstructive sleep apnea associated with comorbidities or cardiovascular risk factors. CPAP machines apply a positive pressure column of air to stent the upper airway and reduce the AHI, often to normal.[76]

CPAP is considered standard of care based on its effectiveness in improving blood pressure control, sleep-related quality of life, and daytime sleepiness, though its effects on cardiovascular risk and glycemic control are less well established.[77,78] Blood pressure is lowered even in patients with resistant hypertension.[79,80] There is conflicting evidence on the impact of CPAP therapy on cognition, with some studies demonstrating a signal toward a mild and transient improvement in executive and frontal lobe cognitive function solely in patients with severe obstructive sleep apnea.[81,82]

In mild symptomatic obstructive sleep apnea, CPAP is recommended if the patient has daytime sleepiness, in which case CPAP can improve quality of life.[83] In a patient with asymptomatic mild obstructive sleep apnea, the decision to use CPAP would be based on a discussion with the patient regarding the potential reduction in cardiovascular risk.

CPAP adherence, particularly in the first few weeks, can be predictive of long-term success with treatment. Insurance companies, including Medicare, require that patients use their CPAP machine for at least 4 hours on 70% of nights. Ideally, patients should use their device for the entire sleep period. Several factors can be addressed to improve patient comfort and compliance, including the type of mask, expiratory pressure relief, short-term use of hypnotics, cognitive behavioral therapy, and frequent contact with the healthcare team with continued education about the expected benefits. Poor CPAP adherence remains a concern, but adherence at 90 days and even

at 1 year was reported as about 75% in recent studies, which is significantly better than earlier data.[1,84]

Although CPAP is often touted as facilitating weight loss, there is considerable controversy on this topic, and larger well-conducted studies even suggest that it can cause weight gain as a side effect,[85–87] owing to a reduced sleep and wake metabolic rates and increased caloric intake.[88,89]

**Automatic or auto-titrating positive airway pressure** (APAP) is gaining popularity, as it allows one to prescribe a range of pressures that the device can use to stent the airway based on proprietary algorithms. The pressure range can also be adjusted in the outpatient setting according to compliance reports downloaded from the actual device.[90] Potential benefits of APAP include a lower overall cost with faster initiation of therapy since there is no need for a titration study. Titration studies are therefore becoming less common, though they are still useful to define an APAP pressure range, to meet insurance requirements, or to assist in the appropriate choice of device and pressure settings in more complex cases.

**Bilevel positive airway pressure** does not have clearly better adherence rates than CPAP but should be considered in patients with sleep-disordered breathing associated with daytime hypercapnia, sleep-related hypoventilation, mixed obstructive and central apnea events, or a high pressure requirement, or in those who cannot tolerate high expiratory pressures.[90]

### Nasal expiratory positive airway pressure devices

Nasal expiratory airway pressure (EPAP) devices are alternatives to CPAP for patients with moderate or mild obstructive sleep apnea. Those devices generate a resistance to expiratory flow and are secured to the nose through nasal inserts with optional headgear (Bongo Rx), or nasal pillows with headgear (OptiPillows, ULTepap). In contrast to CPAP, which provides a continuous pressure through both inspiration and expiration, the back pressure generated by EPAP is present only during expiration with minimal inspiratory resistance.[91] Some of these devices have FDA clearance for mild or moderate sleep apnea (Bongo Rx, ULTepap), and others for snoring only (Optipillows).

In an early study (in 1983), EPAP at 10 cm $H_2O$ reduced the number of apnea events, reduced the duration of these events, and improved nocturnal saturation.[92] In currently used devices, the back pressures generated depend on the flow rates, with significant differences in back pressures at similar flow rates between different devices, ranging from 1 to 14 cm $H_2O$.[91,93] In a randomized trial of EPAP vs sham therapy, the median AHI was reduced from 15.7 to 4.7 events per hour after 1 year.[70]

This intervention works across a range of severity of sleep apnea. Ideal candidates may be those with sleep-disordered breathing that has a positional component (worse when supine compared with lateral or prone).[94] However, a randomized trial found no benefit from EPAP in patients with moderate to severe sleep apnea who had discontinued CPAP.[95]

### Oral negative pressure therapy

This technique applies negative pressure through an intraoral interface held in place with a flange that fits between the teeth and the lips. The iNAP device is FDA-approved for sleep apnea of any severity. This device improves the retropalatal airway size by displacing the anterior-superior segment of the tongue forward and the soft palate anteriorly and superiorly.[96]

Oral negative pressure therapy may be more effective in sleep apnea with retropalatal collapse than with retroglossal airway collapse,[96] though this was not found in another study.[97] In a review of the intervention, only 25% to 37% of patients had at least a 50% reduction in the AHI and a residual AHI of 10 or less, and a substantial number of patients still had significant obstructive sleep apnea.[71] The baseline severity of sleep apnea did not correlate with success.[71]

### Negative external pressure

Continuous negative expiratory pressure is applied by an external silicone collar worn around the anterior neck where it provides negative pressure to open the airway by pulling away the soft tissue structures. As the collar does not cover any facial structures, patients may find it easier to acclimate and adhere to the therapy. The settings of the system are titrated similarly to those of CPAP by increasing the pressure enough to keep the airway open by overcoming the critical airway closing pressure.

In a pilot study, 9 (60%) of 15 patients had an "excellent" response to continuous negative external pressure therapy, defined as reducing the AHI to less than 5 events per hour (down from a baseline of 43.9.[72]

A newer device can vary the negative external pressure throughout the night and is available in various collar sizes and shapes. In a prospective, open-label trial of this device in 28 patients with moderate obstructive sleep apnea, 14 (50%) had an excellent response and 6 (21%) had a partial response (a decrease in AHI of at least 50% from baseline).[98]

These devices are currently undergoing randomized trials but are not used in practice.

**TABLE 3**
**Surgical treatments for obstructive sleep apnea**

| Treatment | Indications | Reduction in apnea-hypopnea index | Caveats | Possible predictors of success |
|---|---|---|---|---|
| **Hypoglossal nerve stimulation**[100–102] | Moderate to severe obstructive sleep apnea not tolerating CPAP; BMI < 40 kg/m$^2$; AHI 15–100 | 68% | Tongue weakness, infection, hematoma, pneumothorax | Anteroposterior collapse, female, lower BMI and AHI, higher arousal threshold |
| **Uvulopalato-pharyngoplasty**[99] | Excessive daytime sleepiness, AHI > 15 | 33%; with laser-assisted uvuloplasty, 18% | Velopharyngeal insufficiency, nasal regurgitation, foreign body sensation | Velopharyngeal/ retropharyngeal airway collapse |
| **Tongue reduction**[99] | Macroglossia | 34% (radiofrequency ablation) | Bleeding, tongue edema causing airway obstruction, wound infection | Large base of tongue, macroglossia |
| **Maxillo-mandibular advancement**[99] | Failure of other options, especially CPAP; can be a primary option with jaw deformities | 87% | Change in appearance, dental or facial numbness | Craniofacial deformities with retruded mandible |

AHI = apnea-hypopnea index; BMI = body mass index; CPAP = continuous positive airway pressure therapy

## SURGICAL OPTIONS

Surgery for obstructive sleep apnea (**Table 3**)[99–102] can be considered when a patient has not found success with other therapies. Most sleep surgeons perform drug-induced sleep endoscopy before considering sleep surgery. This procedure is performed with the patient sedated and asleep but spontaneously breathing. Areas of obstruction and collapse can be identified and surgeries to correct these findings can be contemplated.

### Uvulopalatopharyngoplasty

Surgery for obstructive sleep apnea began in earnest in the early 1980s, when Fujita[103] adapted a procedure used for snoring to treat patients with sleep apnea. Uvulopalatopharyngoplasty has been a mainstay of surgical treatment since that time, with variations and improvements over the years to make it more mucosal-sparing and to address lateral wall collapse.

Success rates vary, as each surgeon uses a slightly different technique. In a meta-analysis based on 15 observational studies (quality of evidence "very low"), the reduction in AHI was 33%.[99] However, over time, the AHI tends to drift back upward because of loosening of scar tissue or change in body weight.[104]

Laser-assisted uvulopalatoplasty, an alternative technique, was found to reduce the AHI by 18% in a meta-analysis of 2 randomized trials (level of evidence "low").[99]

### Tongue reduction

To try to improve the outcomes of uvulopalatopharyngoplasty, surgeons began addressing the tongue. Tongue reduction can be performed in several ways. A midline glossectomy removes an ellipse of tissue in the dorsal surface of the mid-tongue. Radiofrequency treatment can be performed with channeling within the tongue or with needle-tipped prongs to reduce the amount of tongue muscle.

In a meta-analysis of 8 observational studies (level of evidence "very low"), radiofrequency reduction of the tongue was associated with a 34% reduction in the AHI.[99]

Friedman et al[105] created a staging system based on physical findings such as modified Mallampati score (assessment of tongue size and shape vs the oropharngyeal opening) and tonsil size to predict success when performing uvulopalatopharyngoplasty with radiofrequency reduction of the tongue. Patients with a small tongue and large tonsils had the greatest success, while patients with a large tongue and small tonsils had the lowest success rates.[105]

### Hypoglossal nerve stimulation

The newest development in sleep surgery has been hypoglossal nerve stimulation. The only commercially available system (Inspire) in the United States was approved by the FDA in 2014 and has been steadily gaining acceptance since publication of the

Stimulation Therapy for Apnea Reduction trial.[100] The device consists of an implanted pulse generator, a stimulation lead, and a respiratory sensor lead. The pulse generator augments the neural input of the hypoglossal nerve to the genioglossus and geniohyoid muscles, thereby resulting in protrusion of the tongue forward with each sensed respiration.[106]

Indications approved by the FDA are as follows: adult age 22 or older; candidate must have tried CPAP without success, have an AHI between 15 and 100 events per hour (with no more than 25% of events being central or mixed apneas), and have a body mass index of 40 kg/m$^2$ or less. Also included are patients ages 18 to 21 with an AHI 15 to 100, and pediatric patients with Down syndrome ages 13 to 18 and an AHI 10 to 50 who have not been effectively treated with or who have a contraindication to adenotonsillectomy, and who have failed or cannot tolerate positive airway pressure therapy. Insurance coverage indications may be more restrictive..[102] For a patient to be considered a candidate for hypoglossal nerve stimulation, a drug-induced sleep endoscopy study is required and must show palatal collapse in an anterior-posterior pattern. Concentric collapse is a contraindication.[100] As experience and technology improve, the eligibility criteria will continue to change.

During the implant surgery, 3 incisions are enough to place the pulse generator and the 2 leads. The incisions are just below the jaw line and in the upper chest. The procedure is done on an outpatient basis, with the patient under general anesthesia. Once the optimal system settings are obtained through in-laboratory polysomnography, the device is activated by the patient only when going to bed.[106]

Hypoglossal nerve stimulation is associated with high adherence and durable benefits up to 5 years, consisting of improvements in the Epworth Sleepiness Scale score, patient-reported outcomes comparable with those of CPAP, and reduced AHI.[100,107–109]

Initial results showed a 68% reduction in AHI and a 66% success rate (defined as an AHI < 20 and at least a 50% reduction in AHI),[100] but with improved surgical technique and better understanding of device programming, success rates have improved to 75% to 80%.[110] Female sex, lower baseline body mass index, lower initial AHI, and high arousal threshold predict successful therapy.[108,110,111]

Studies of cardiovascular outcomes with hypoglossal nerve stimulation are ongoing.[112] Heart rate variability during sleep was noted to improve (decrease), and the improvement correlated with improvement in AHI.[113] In a study at Cleveland Clinic,[114] positive airway pressure therapy lowered diastolic and mean blood pressure more than hypoglossal nerve stimulation. In another study, although diastolic blood pressure declined by 3.7 mm Hg and mean arterial blood pressure declined by 3.7 mm Hg with hypoglossal nerve stimulation,[115] this improvement may be present only in the subset of patients with baseline high blood pressure.[114]

### Maxillomandibular advancement

Skeletal surgery can increase the volume of the airway. A combination of a LeFort 1 osteotomy with a bilateral sagittal split of the mandibular rami creates a larger "box" to give more room around the soft tissue contents of the airway. In 9 case series in 234 patients, this surgery was associated with an 87% reduction in AHI.[99] However, a study by Kezirian et al[116] found that 30 times more uvulopalatopharyngoplasty surgeries were performed compared with maxillomandibular advancements, suggesting that despite the excellent success rate of maxillomandibular advancement, patients are less accepting of the procedure.

## DISCLOSURES

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