ues than did their nonsmoking counterparts. This may also be explained by a similar hypothesis that subjects with higher lung volumes are more likely to tolerate the acute effects of cigarette smoke and then go on to become long-term smokers. The missing piece in this intriguing puzzle is what determines the adverse effects of smoking that are observed in only about 20% of long-term smokers.

There is no doubt about the epidemiologic and clinical evidence that smokers have a chronic cough, and we need to explain this in the context of the observations by Dicpinigaitis. A proportion of long-term smokers will develop mucus hypersecretion (i.e., chronic bronchitis), which is a stimulus for the RARs. Long-term cigarette smoking causes neutrophilic inflammation in vulnerable smokers that sensitizes cough-sensitive nerves by the release of sensory neuroneptides and the direct stimulation of the nerves/receptors. In addition, emphysematous damage to the parenchyma may damage the inhibitory parenchymal pulmonary C-fibers. While cough and bronchoconstriction exist as independent reflexes, bronchoconstriction induced by cigarette smoke also may stimulate cough. This presupposes that smokers with a chronic cough have a sensitized cough reflex in response to conventional cough challenge testing. Surprisingly, this has not been well-studied, as most cough challenge studies exclude smokers.

Many more resources must be devoted to cough research so that we can, in particular, decipher the black box that controls the cough reflex. The observation in the current study suggests that there is a lot more to be learned from cough challenge testing in humans and about the influence of factors such as smoking. Definitive studies that investigate the cough reflex in smokers with and without COPD and/or asymptomatic cough compared to control subjects will help us to understand the reflex and the effects of cigarette smoke on the cough reflex. This also may shed some light on why some smokers are predisposed to lung disease from smoking. Meticulous attention to detail and standardized challenge procedures, such as those defined for bronchial challenge testing, is critical to make these observations more meaningful.

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Continuous Positive Airway Pressure
By Nose or Mouth?

Treatment of obstructive sleep apnea with continuous positive airway pressure (CPAP) is less than ideal, not because the concept is incorrect but because the delivery is cumbersome and patients find it difficult to adapt to its use. Apart from being anchored to a mask, tubing, and a potentially noisy pressure-generating device, there may be nasal discomfort, nasal congestion, nasal obstruction, claustrophobia, the feeling of either overventilated or underventilated, and mouth and mask leaks that make acceptance and adherence with nasal CPAP difficult for many patients. Several approaches1–4 have had some success in overcoming the disadvantages of CPAP including heated humidification, chin straps, treatment of nasal congestion both pharmacologically and surgically, use of hypnotics, different types of interfaces such as nasal cannulas, or a full-face mask (also called an oronasal mask). Despite these approaches, adherence and acceptance are less than ideal.5

An alternative that would avoid nasal congestion and obstruction and potentially would lessen the claustrophobic feeling from a confining mask would be to deliver CPAP through the mouth. However, although there are at least two devices available in the United States that permit oral CPAP, a search of
that the airway mechanics are similar during oral and CPAP. Furthermore, although the study suggests possibility of sex differences in response to oral
larly if higher pressures are required), and the potential that the flexibility of the soft tissues of the mouth such as the cheeks may produce discom-
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Smith et al have made a small but important step forward in validating that oral CPAP is a potentially viable method of treating patients with obstructive sleep apnea. This preliminary study of seven subjects (five men and two women) addresses a focused and relevant question. Does the use of an oral interface to deliver CPAP produce equivalent pressure-flow curves of the upper airway, indicating that nasal and oral CPAP are potentially therapeutically equivalent? Although it might seem intuitive that “splinting” the airway with pressure from the nose or mouth would lead to similar results, the differing anatomy and geometry of the oral route vs the nasal route raised the possibility that differing pressures would be required. The data from this small sample suggest that there are not marked differences in the pressure required to keep the airway from collapsing and to maintain airway patency without flow limitation (ie, without continued partial upper airway obstruction) during tidal breathing. The authors also allowed subjects to sleep with the oral device without the nose clip, which was used during pressure-flow curve measurements. There was no apparent loss of effectiveness (pressure-flow curves were not measured) of oral CPAP. Of note, the pressure that eliminated flow limitation in this group of subjects with severe obstructive sleep apnea averaged 11 cm H2O.

While this is a promising start, many questions remain. Those include, among others, patient comfort with differing pressures, the obligatory need to keep the mouth sealed shut all night with the device, further examination of the position of the tongue that might potentially occlude the airway orifice on an individual basis, the possible need for heated or room-temperature humidification, the need for a nose clip to prevent nasal breathing or leakage on an individual basis, its use with an edentulous patient, the potential that the flexibility of the soft tissues of the mouth such as the cheeks may produce discomfort with distension from mouth pressure (particularly if higher pressures are required), and the possibility of sex differences in response to oral CPAP. Furthermore, although the study suggests that the airway mechanics are similar during oral and nasal CPAP during non-rapid eye movement sleep, only a select few measurements were made, and there is no description of whether body or head position or rapid eye movement (REM) sleep had any effect on the results. These conditions may potentially affect the results by putting pressure or stress on the mouth (head position), by relaxing the upper airway (REM sleep), or by increasing pressures to prevent airway collapse and maintain airway patency (head position, body position, or REM sleep). In addition, as with any occlusion of the mouth, there is the hypothetical possibility of the aspiration of stomach contents should the patient regurgitate during the night and not be able to expel the emesis through an occluded mouth. Of note, this is also a hypothetical possibility with a full-face mask but there are few if any documented cases of this occurrence.

Until there have been properly performed randomized and comparative trials—including attention to long-term maintenance of CPAP levels, adaptability to autotitrating CPAP systems, general sleep architecture, the durability of the oral mask, body and head position, airway characteristics and effectiveness during REM sleep, daytime sleepiness, other outcomes such as health status and ideally cardiovascular complications—the use of oral CPAP will remain experimental. To date, there is no published peer-reviewed documentation of the potential side effects and general therapeutic effectiveness of oral CPAP. If one decides to treat a patient with oral CPAP, there should be careful follow-up with close questioning of the patient and documentation regarding the safety and effectiveness of the treatment, including a provision for follow-up polysomnography. Whether patients will prefer oral CPAP is not known. For example, full-face masks are in use for patients, usually those who do not respond to nasal CPAP. However, there are data to suggest that patients generally prefer nasal CPAP and are more adherent to therapy when compared to the use of a full-face mask as the initial approach to treatment. Similarly, until studied, it is not clear whether oral or nasal CPAP would be preferred by the majority of patients.

One of the available devices is intriguing in that it combines mandibular advancement with the potential for oral CPAP. The mandibular advancement feature may modify the geometry of the airway so that it is hypothetically possible that this would lead to lower CPAP pressures than with the use of oral or nasal CPAP without mandibular advancement. This hypothesis should be tested since it is a common experience that tolerance declines in some patients with higher CPAP pressures.

In summary, nasal and oronasal CPAP treatment
are effective when tolerated. Unfortunately, many patients find CPAP difficult to tolerate and, even when tolerated, may have difficulty keeping the mask in place. Oral delivery may hypothetically benefit such patients as an alternative to the nasal and oronasal delivery of CPAP. Unfortunately, we have barely progressed beyond the hypothetical stage to a practical and documented understanding of the place, if any, for the oral delivery of CPAP. To state it another way, *caveat emptor* (buyer beware)!

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How Is HRV Measured?

In most clinical applications, HRV is analyzed by time and/or frequency domain methods. Time-domain analysis refers to statistics that are derived directly from the measurement of the normal-to-normal (N-N) intervals (ie, intervals between consecutive QRS complexes resulting from sinoatrial discharge) and statistics calculated from the differences between successive N-N intervals. Premature ectopic beats are ignored in these analyses. N-N interval-based measures are influenced both by short-term factors (eg, respiratory) and long-term factors (eg, circadian). The simplest variable to calculate is the SD of the N-N intervals (SDNN). SDNN reflects all the cyclic components (ie, short-term and long-term) that are responsible for variability in the period of recording. The SD of the averages of N-N intervals determined for each 5-min period during a 24-h recording (SDANN) is a measure that nullifies short-term variability within 5-min cycles and, therefore, is used to assess intermediate-term and long-term components of HRV. Short-term HRV can be evaluated using the mean of the SDNNs derived for each 5-min period for > 24 h. Alternatively, time domain variables that are based on comparisons of the lengths of adjacent cycles (eg, the square root of the mean squared differences of successive N-N intervals) can be used to evaluate short-term variation.

HRV analysis in the frequency domain is mathematically even more complex. Power spectral density analysis provides the basic information of how power (variance) distributes as a function of frequency. The