Voluntary forced deflation of the lungs may cause further forced expiratory efforts, which we termed “deflation cough” in an article in this issue of CHEST (see page 690). Deflation cough is a rare example of a positive feedback reflex response, a neural stimulus increasing its own degree of activity. These responses have rarely developed in evolution because they would be explosive, unless there was a self-limiting mechanism.

The best respiratory example is the Head paradoxical reflex (HPR). Usually, inflation of the lungs inhibits the diaphragm by a vagal reflex, the well-known Breuer-Hering inflation reflex, because of slowly adapting pulmonary stretch receptors (SARs). Head showed that if this reflex is blocked by partial vagal cooling, inflation of the lungs paradoxically activates the diaphragm, hence HPR. In quiet breathing with normal vagi, HPR is manifested when the lungs tend to collapse and become less compliant; this sensitizes pulmonary rapidly adapting receptors (RARs). The increased sensor discharge augments the inspiratory activity of the brainstem respiratory center. The ensuing deep inspiration, a sigh or augmented breath, further distends the lungs, opening any collapsed areas and increasing their compliance, which reduces the stimulus to discharge in the RARs. This self-limiting mechanism switches off the reflex. This paradoxical reflex also augments the first breaths of newborn babies.

With deflation cough, a voluntary forced deflation of the lungs to residual volume (RV), augments (paradoxically) the existing expiratory drive with further brief, but strong (and ineffective), expiratory efforts (deflation cough). To provoke deflation cough, the subject needs to squeeze air out of his or her lungs as much as possible, for example, during an FVC or slow vital capacity (SVC) assessment performed according the American Thoracic Society/European Respiratory Society guidelines. A maximal expiration lasting at least 6 s is most often effective in evoking deflation cough in sensitive subjects. In our experience, the expiration does not need to be forced but does need to be maximal, and an SVC maneuver works as well as an FVC. Additionally, the magnitude of the preparatory inspiration that is crucial for reliable FVC and SVC measurements has no impact on the possibility of evoking deflation cough. Indeed, a few observations show that expiration can be started from virtually any lung volume, the critical aspect being only the maximal expiratory effort.

Gastroesophageal reflux (GER) is an essential component of deflation cough, but probably by sensitizing...
the reflex from lung receptors as GER does for other types of cough from the lungs. GER alone has never been shown to cause expiratory efforts.

What is the self-limiting process? Deflation cough occurs when the lungs are fully deflated to RV. RARs respond to lung volume changes and not to external pressure. Further deflation attempts below RV would not provide extra RAR stimulation; even with strong expiratory efforts, this is impossible because the receptors and the reflex are switched off.

But Head made another important observation that introduces another paradox. Inflation of the lungs of open-chest rabbits with normal vagi inhibits the diaphragm, that is, the Breuer-Hering inflation reflex mediated by SARs as just described. But in these rabbits, deflation activates the diaphragm (the Breuer-Hering deflation reflex), which is the opposite of our findings that forced deflation causes expiratory efforts. Head showed that the inflation (inhibitory) and deflation (excitatory) diaphragm responses involve two separate vagal pathways. The inspiratory activation on deflation in closed-chest animals was greater than the inspiratory activation that occurred on cutting the vagus nerves. The latter would promote inspiration by abolishing the inspiration-inhibitory activity of inflation sensors (SARs), so deflation must activate a new group of sensors, now thought to be the RARs, which have no or little tonic activity to be affected by vagotomy.

We suggest that the RARs are responsible for both paradoxical reflexes (those described by Head and us) and for Head’s deflation response. They are rapidly adapting, have myelinated afferent fibers, are stimulated by both inflations and deflations, and have short conductance latencies (about 20 milliseconds)—all properties required by the experimental results. Sensors responsible for cough (starting with an inspiration) have mainly C-fiber afferent nerves, giving a long latency (about 500 milliseconds). Deflation cough resembles the expiration reflex from the lower airways.

The problem is how can the same sensors cause inspiration in one case (HPR and augmented breaths) and expiratory activity in the other (deflation cough)? The answer may be that the reflex respiratory response depends on the phase of breathing. There is accumulating evidence of this for airway receptors. The same brief mechanical or electrical stimulus to the trachea will cause a cough starting with an inspiration if the stimulus is in the inspiratory phase and an expiration reflex to start with an expiration if it is in the expiratory phase. With Head’s experiments, lung deflation in open-chest animals applies when the respiratory center is in the inspiratory phase (caused by the switch off of the Breuer-Hering inflation reflex), whereas in our experiments the center is in a voluntarily induced expiratory phase.

Positive feedback probably applies to many expulsive processes (defecation, urination, vomiting, coughing, childbirth). When in progress, these events seem to be self-promoting—a kind of positive feedback. They are terminated when the expulsion is complete and the positive feedback ended. A positive feedback mechanism may contribute to more efficient airway clearance by two distinct and interactive mechanisms. First, it may promote the sequence of compressions and expulsions that occur at progressively lower lung volumes within a cough bout; in turn, this phenomenon would favor progression of secretions and debris from more peripheral airways into the larger ones as lung volume is decreased. Second, according to equal pressure point theory, dynamic airway compression caused by the repeated expulsive efforts of a cough bout are accompanied by the development of significant radial wall acceleration that is believed to contribute significantly to the shaking out of secretions. In the absence of experimental evidence, this consideration must be speculative.

Finally, deflation cough was reported in only 43 of 1,720 patients (2.5%) who performed routine SVC/FVCs. These tests are performed with nearly all patients who attend respiratory clinics. Whether a more prolonged expiratory effort also would eventually provoke deflation cough in those who failed to do so during a conventional FVC or SVC maneuver remains to be established. However, preliminary evidence from our lung function laboratory seems to suggest that if the deflation cough is present, it ensues within the time frame of a conventional lung emptying maneuver. We suggest that observation of deflation cough should be included in future tests, if necessary with encouragement to breathe out a bit more. These larger studies would show whether deflation cough has diagnostic value and significance, particularly in its relationship to GER.

We suggest that there are four lung reflexes that can affect breathing. The Breuer-Hering inflation and deflation reflexes mediated by SARs and HPR and our paradoxical reflex mediated by RARs, leaving out irritant-induced cough, but that is another story. We also suggest (with Dr Fontana dissenting) that “the Fontana paradoxical reflex” should be added to the literature, and this commentary should be its first (and possibly last) listing in PubMed.

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