It is well accepted that many organs in the human body no longer provide evolutionary advantage and appear to be lacking known function. These include the appendix, most body hair, wisdom teeth, male nipples, and external ear muscles, to name just a few. Even worse, many such organs, such as the appendix or wisdom teeth, can be the source of serious pain and medical problems. In this perspective, it is suggested that airway smooth muscle falls into this category—that of an organ with no essential physiologic function that can lead to serious medical problems.

The function of smooth muscle in the airway wall has been speculated on for many years, but when looked at closely from a functional perspective, there really seems to be no need for airway smooth muscle. Indeed, most of the proposed reasons for presence of airway smooth muscle have not been based on experimental validation. In a recent discussion, Seow and Fredberg (1) commented that there is no known disease entity or physiologic deficit associated with loss of airway smooth muscle. They further suggested that perhaps airway smooth muscle was a vestigial remnant of its common embryologic origin with the gastrointestinal system, having no modern function. This conjecture, however, is in stark contrast to much classical thinking. In his extensive review article (2), Macklin could not imagine that such a system was there for no physiologic purpose, stating that “Organized as it is, into a very complex system, this muscle would seem of the utmost functional importance—in fact quite indispensable in respiration.”

In this discussion, we consider the validity of 10 possible roles for airway smooth muscle that have appeared in the literature over the past 125 years. The emphasis will not be on whether smooth muscle is indispensable in respiration, but rather whether it is needed at all. These possible roles consist of the following: (1) peristalsis to assist exhalation, (2) peristalsis to assist mucus propulsion, (3) peristaltic contraction in the fetal lung to generate fluid pressure, (4) promoting lymphatic and venous flow, (5) ventilation/perfusion matching, (6) protecting the peripheral lung, (7) protecting airway structure, (8) stabilizing airways, (9) enhancing the effectiveness of cough, and (10) optimizing anatomic dead space volume.

**PERISTALSIS TO ASSIST EXHALATION**

The several imagined functions of airway peristalsis were speculations based largely on the common embryologic origin of the airway tree and the gastrointestinal tract, where peristalsis and its neural control is a clearly essential property. Active contraction of bronchial smooth musculature that might contribute to exhalation was emphasized by Miller (3). His anatomic analysis of airway smooth muscle showed a three-dimensional geodesic arrangement analogous to a “lazy tongs” device for mechanical extensions in the axial direction. He also suggested an expiratory wave of peristaltic smooth muscle contraction starting from the periphery to aid in exhalation. This concept of bronchi aiding exhalation was endorsed later by Macklin (2), who stated that “it seems not so much to infer that the bronchial musculature is an essential in respiration, for it is involved in both the opening and the closing of the pulmonary bellows.” This concept continues to linger to this day with a recent suggestion that respiratory-related bronchial rhythmic constriction can facilitate gas exchange in the dog (4). However, the magnitude of such an effect, if it exists, must be quite small and of little physiologic significance. Gas exchange in the lung can be performed quite well with fully relaxed airway smooth muscle.

**PERISTALTIC CONTRACTION IN THE FETAL LUNG TO GENERATE FLUID PRESSURE**

A potential role for rhythmically contracting airway smooth muscle in fetal lung development has been suggested in a recent study (9). These investigators observed peristaltic-like contractions in airways in fetal rabbit and pig lung explants. They suggested that such contractions might contribute to fetal lung growth, particularly airway differentiation and branching. Al-
though their work clearly shows the capacity for fetal airway smooth muscle contraction, it is still not clear that this plays an essential role in lung development. In addition, the proposed peristaltic wave needed for this function would be in the periph-
eral direction, opposite to what was proposed as necessary by the early anatomists for exhalation and mucus clearance. Al-
though the role of lung liquid pressure and fetal lung stretch from lung fluid secretion is well documented (10, 11), why the airways might need active smooth muscle to counteract this luminal pressure is not clear. It would therefore seem that the effect of peristaltic fetal airway smooth muscle contraction would at best be contributory to the normal pressure generated by fluid secretion. In an air-filled postnatal lung, of course, it could have no function.

PROMOTING LYMPHATIC AND VENOUS FLOW

In the original Handbook of Physiology chapter on airway smooth muscle, Krahl speculates that “it may be surmised that this effect of bronchial musculature on venous and lymphatic channels must play an important role in propelling the vascular fluids toward the hilus of the lung” (12). He based this creative speculation on histologic observations indicating enlarged ves-
sels around contracted airways. However, for such airway smooth muscle contraction to serve as an effective pump, not only would it have to occur in a rhythmic fashion, but also it would require valves to direct the flow. Unfortunately, there are no valves, nor is there evidence of such rhythmic strong airway smooth muscle contractions in vivo. Furthermore, even if such rhythmicity were important, interstitial pressure variations that occur with normal ventilation would likely be more than suffi-
cient (13).

V˙/Q˙ MATCHING

One might think that the potential need for airway smooth muscle to optimize V˙/Q˙ matching is a modern idea. However, almost a century ago, Keith (14) suggested that airway muscle contraction not only might affect the distribution of ventilation but also that the decreased alveolar pressure on inspiration distal to a narrowed airway might dilate the capillaries and increase perfusion. Of course, we now know that the simultaneous de-
crease pleural pressure would largely prevent such vascular dil-
ation, and even if it did not, such an increased perfusion with a decreased ventilation would not serve any teleologic advantage. V˙/Q˙ could potentially be affected by the local CO₂ concentration, as low CO₂ is known to contract airway smooth muscle, and elevated CO₂ may cause relaxation. However, the sensitivity of airways to CO₂ reductions in the normal range is quite low, having little effect till it falls to less than 2% (15). Although this may possibly occur with hyperventilation or with local vascular obstruction, it does not seem to be an essential function of normal living. Indeed, even in the most extreme situation of complete obstruction of left or right main pulmonary artery, ventilation to the obstructed lung was only reduced by approxi-
ately 25% (16). Such an experimental observation is consistent with the understanding that resting ventilation distribution is largely controlled by regional lung distensibility rather than air-
way resistance (17). Thus, a need for airway smooth muscle to regulate airway resistance seems even less relevant in this regard. Nevertheless, at least one study measuring nitrogen washout in normal subjects has suggested that loss normal vagal tone promotes ventilation heterogeneity (18). These results may have been partially related to the loss of elastic recoil after atropine, but perhaps more importantly, there is no indication that such ventilation changes would be linked to similar changes in perfu-
sion. Thus, it is even possible that V˙/Q˙ distribution could have improved after atropine, an idea supported by results showing a more uniform apex to base ventilation distribution (and hence a poorer match with perfusion distribution) after methacholine challenge (19). Furthermore, in another study in asymptomatic subjects with asthma, the distribution of ventilation was found to be unaffected by relaxation of spontaneous tone with isopro-
terenol (20).

PROTECTING THE PERIPHERAL LUNG

Noxious particles or gases are known to have the capacity to either directly or indirectly lead to airway smooth muscle con-
traction (21–23). Thus, the question naturally arises whether this constriction might serve some protective function, having evolved to prevent further penetration to the already exposed airway (24). Although such speculation may seem superficially reasonable, when viewed in the context of the living organism, it quickly breaks down. To maintain life, one must continue to ventilate, and thus, a uniform constriction limiting peripheral ventilation of all airways would not be possible for very long. If the insult were local, then there could be reduced ventilation to that region. However, such a reduction in ventilation to one region would lead to significantly altered ventilation and deposi-
tion to the rest of the lung (25). In fact, Macklem and colleagues have concluded that a redistribution of ventilation would likely lead to a more peripheral deposition in the unconstricted region (26), thereby negating any beneficial effect of the original protec-
tive function.

PROTECTING AIRWAY STRUCTURE

There has been some recent discussion hypothesizing that normal airway tone is required to protect the airway from overdis-
tension that might occur with normal breathing. Without normal airway tone, the airway may become distorted, promoting fibro-
proliferative pathology (27). Although there is no experimental evidence directly testing such a hypothesis, it seems that the airway structure itself is built to inherently resist overdistension. As shown by James and colleagues (28), the basement membrane provides a relatively nondistensible natural limit that can be used to compare airway size. Computed tomographic imaging has also shown this natural limit to exist in vivo when there is no airway tone (29), and thus, unless breathing near this elastic limit leads to airway inflammation, this proposed role of airway smooth muscle seems unlikely.

STABILIZING AIRWAYS

The notion that intraparenchymal airway smooth muscle con-
traction might stabilize the airways and prevent airway collapse seems to fly in the face of logical thought. If one contracts an airway in vitro (30, 31) or in vivo (32), the airway will continue to narrow until it is closed. This concept of contraction stabilizing airways seems to have originated from the work of Olsen and colleagues (33) and later supported by Coburn and colleagues (34). Olsen and colleagues studied both tracheal and bronchial segments in vitro. It is relatively easy to see how contraction of the trachealis could in fact protect the tracheal lumen from obstruction with external compression by limiting invagination of the tissue between the ends of the C-ring cartilage; however, even maximal contraction of the trachealis by itself would never lead to tracheal collapse. The situation with intraparenchymal bronchi, however, is quite different. Given the fact that large cartilaginous airways can close in vivo with sufficient methacho-
line (32), it is hard to imagine an excised airway remaining patent with 20 cm H₂O negative transmural pressure. Yet this is what
Olsen and colleagues showed in contracted bronchi. The only explanation that seems plausible is that their measurements of absolute volume in the bronchial segments were in error and that their airways were at much lower absolute volume than calculated. Indeed, more recent histologic measurements (35) do not support this concept that airway smooth muscle contraction protects or otherwise limits narrowing of intraparenchymal airways. At any transmural pressure, contracted airways were found to have smaller luminal areas than relaxed airways.

ENHANCING THE EFFECTIVENESS OF COUGH

Somewhat related to this possible ability of airway smooth muscle to stabilize airways is its potential role in optimizing airflow velocity to enhance coughing effectiveness (24, 36). It is well accepted that airway narrowing that occurs during coughing can increase velocity at the flow limiting segments, thereby augmenting clearance of mucus from the airway (37). This airway narrowing normally results from dynamic compression at specific sites along the airway tree. Thus, it may seem that airway smooth muscle could be activated to cause localized airway narrowing in anticipation of a cough, but there is little experimental evidence to support such a role (38). Although reflex bronchoconstriction and coughing occurs on inhalation of dust and irritant gases, the afferent receptors do not originate from intraparenchymal airways (39). Thus, were a large inhaled particle to deposit in a bronchus, there would not be a localized reflex bronchoconstriction to help expel it. In other pathologic situations such as bronchiectasis with enlarged airways, where coughing effectiveness is often impaired (40), contraction of smooth muscle is either not used or not effective in correcting this limitation. Furthermore, regional dynamics during coughing are quite complex, and too much airway narrowing must also lower the local regional flow. For this reason, Leith has suggested that bronchodilators may actually improve the effectiveness of coughing by increasing expiratory flow rates (36). Thus, an active role for airway smooth muscle in coughing presently seems quite uncertain.

OPTIMIZING ANATOMIC DEAD SPACE VOLUME

Macklin (2) and later von Hayek (41) thought that an important role of airway smooth muscle was to play an active role in regulating the volume of the anatomic dead space. The design of the lung is such that anatomic dead space must be small enough to allow adequate alveolar ventilation, yet not so small as to make the airways so narrow to make breathing difficult. This design compromise in the human lung was discussed in detail by Widdicombe (8), who calculated theoretical graphs to show how evolution has optimized the work of breathing, with a dead space of approximately 20% of the normal tidal volume and a breathing frequency of approximately 15 per minute. Is there any reason that it should be necessary to change this ratio? Were there some pathology that prevented taking normal tidal breaths, perhaps then it would be advantageous to decrease the dead space. At the other extreme, with heavy exercise, the tidal volume, and alveolar ventilation increase and with higher flow rates, the airway resistance may become limiting. Dilation of the airways in this situation might thus be advantageous. Although the work of breathing is clearly a function of dead space, the sensitivity to dead space changes is not very strong (8). While this function of active dead space regulation is indeed a legitimate reason for airway smooth muscle, it begs the question of how such a feedback system might be regulated. What is the sensor that determines that dead space needs to be altered? It would have to be an extraordinarily complex feedback system taking into consideration ventilation, work of breathing, blood gases, airway resistance, etc. Furthermore, simply breathing at higher mean lung volume during exercise would by itself tend to dilate the airways to near maximal size.

CONCLUSIONS

In summary, it thus seems clear that none of these potential functions of airway smooth muscle are essential to normal lung physiology. If airway smooth muscle were eliminated, then the airways might enlarge slightly, but there would be no other obvious physiologic consequence. The intrinsic elasticity of the airways would still allow the airway tree to distend with inspiration and relax with expiration. This review thus strongly supports the speculation that airway smooth muscle is indeed a vestigial organ (1), analogous to the appendix, which also has no known function, but can cause serious medical problems. Such being the case, if there were a way to treat airway smooth like an inflamed appendix, that is, to effectively cut it out, then asthma, like appendicitis, could be cured. Airway inflammation with associated secretions may still be present, but without an ability to translate inflammatory signals into airway smooth muscle contraction, dyspnea would be greatly minimized. Such procedures would obviously not involve surgical excision but may possibly involve pharmacologically targeting airway smooth muscle with a directed toxin, genetically impairing the contractile apparatus of airway smooth muscle, or physicochemical disruption of the airway wall. Future therapies directed to this goal may provide alternative and effective new treatments for asthma.

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