SPECIAL ARTICLE

The Travels of a Pulmonologist Through the Upper Airway

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Introduction

When I first heard that the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) wanted me to give the 2003 Manuel Tapia lecture, my initial reaction was a feeling of pride. But this was, however, immediately overwhelmed by a second emotion: panic. Whatever could I talk about to justify such an honor?

In the days that followed I turned the question over in my mind, compiling a mental inventory of all the articles I had written (and contributed to) over the last 25 years. While I was still trying to come to grips with an answer and the question still nagged at the back of my mind against the hubbub of my daily round, I realized, not without surprise, that I could identify two constants in my clinical research. Firstly, that I had changed the subject of my research every 4 or 5 years; and secondly, that most of my research has involved—directly or indirectly, slightly or to a considerable degree, either as a principal focus or tangentially—an anatomical structure that strictly speaking lies outside the field of pulmonology: the upper airway.

And so I decided to give the Manuel Tapia Lecture as a review of my personal contribution to clinical research in pulmonology, but focusing on the topics that emphasize the role of the upper airway in respiratory physiology and respiratory disease.

The Upper Airway

Anatomy books define the upper airway as the portion of the respiratory tract situated above the trachea (or the larynx). Traditionally, the upper airway is the preserve of the otorhinolaryngologist, with the pulmonologist taking charge of everything from the larynx down.

The nasal pyramid is the distal origin of the upper airway. Extending dorsally by way of the nares, this space is in fact made up of 2 high, narrow passages, 1 to the left and 1 to the right, which run from the anterior face to the center of the head under the base of the skull. These 2 passages are separated by the nasal septum, a straight but irregular wall. The cavity is also partially separated into 3 vertical zones by the nasal conchae, which define the superior, middle, and inferior meatus. The nasal cavity communicates with the paranasal sinuses through their orifices in the lateral walls: the frontal sinuses in front and above, the maxillary sinuses 1 on each side, the ethmoidal cells in the upper middle position, and the sphenoid sinuses above and at the back.

At the point where they pass under the base of the skull, the nasal passages open out into a single tube, the pharynx, which makes a 90º turn and then continues downwards. The posterior wall of the pharynx lies against the cervical vertebrae, the lateral walls are formed by the thin sheaths of the pharyngeal muscles, and the anterior pharyngeal wall—below the nasal cavity—is the posterior wall of the mouth. This last is formed by the superposition of the soft palate, which hangs from the posterior edge of the floor of the nasal cavity (formed by the hard palate), and the tongue. The tongue is a complex, purely muscular structure. One end is anchored into a bone (a mobile bone, the mandible), the midsection has a floating point of insertion (in the hyoid bone, the position of which depends on the balance of the forces of all the muscles attached to it), and finally the muscular tip is not fixed anywhere and has viscoelastic properties that allow it to project into space in all directions, and even extend forward outside of the head. In this respect, the tongue is the equivalent of an elephant's trunk. The tongue has, therefore, three sections: the horizontal portion, which forms the floor of the mouth; the vertical portion, which forms the anterior wall of the oropharynx and the hypopharynx; and a third portion, which fills the virtual cavity of the closed mouth.

At the root of the tongue, a cartilaginous structure—the epiglottis—is supported by the anterior wall of the hypopharynx. Below the epiglottis, the thyroarytenoid ligaments give rise to the larynx in front of the arytenoid cartilage, and to the pharynx outside and behind the airway.

The Measurement of Lung Volume

Total lung capacity was traditionally measured by the dilution method, that is, by helium dilution or nitrogen washout. In 1956, Dubois et al[1] described the

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plethysmographic method, which was much more rapid and tended to replace the earlier dilution method. The advantages of plethysmography were that it measured total lung capacity (rather than solely the volume in direct communication with the main airway) and that it made possible repeated measurements in the same patient, thereby reducing the risk of error.

The use of body plethysmography in patients experiencing acute bronchial asthma attacks led to the observation of surprisingly large swings in total lung capacity over short periods of time, with increases in total lung capacity of 1 or 2[1] during spontaneous acute asthma attacks (and even during provoked attacks). Such increases disappeared a few minutes after the attack was over.[2-4]

The basic premise of the plethysmographic method is that, during the panting maneuver against a closed shutter, mouth pressure accurately represents alveolar pressure because pressure at all points of a closed system will equalize. However, the changes in total lung capacity recorded were so large as to be unrealistic, making it seem possible that they might be due to a methodological error. We decided to find out if this was the case.

We decided to use esophageal rather than mouth pressure to measure alveolar pressure.[5] As long as there are no major changes in lung capacity (which is the case during panting against a closed shutter), changes in esophageal pressure should be a real and direct reflection of the changes in alveolar pressure. The frequency response results obtained using an esophageal balloon catheter were not as good as those obtained by measuring mouth pressure, but seemed acceptable up to a frequency of 5 Hz. In patients having a spontaneous or provoked asthma attack, we demonstrated that in airway obstruction the changes in mouth pressure during plethysmographic measurement of lung volumes were smaller than the changes in esophageal pressure measured at the same time. Moreover, a phase delay between the two signals was observed in the mouth pressure-plethysmographic volume curve but not in the esophageal pressure-plethysmographic volume curve. The differences between the two pressure types disappeared when the airway obstruction disappeared.

In light of these findings we advanced the hypothesis that during the panting maneuver against a closed shutter not only would the gas in the lungs be compressed and decompressed with equalized pressure throughout the closed system, but that there would also be movement of gas between the alveoli and the mouth. This movement would be made possible by the existence of the upper airway, especially the pharynx, and in part by the mouth itself. In effect, given that they are plastic rather than rigid, these structures can swell and shrink, thereby allowing a certain flow of gas between the mouth and the alveoli. In a healthy individual without airway obstruction this "internal flow" does not give rise to a loss of pressure since airway resistance is very low. Conversely, in an asthmatic patient with very high airway resistance, the "internal" flow through the resistance would lead to a loss of pressure. This would give rise to mouth pressure lower than alveolar pressure so that the plethysmographic method (which uses mouth pressure) would exaggerate the lung volume measurement. The radical changes in total lung capacity would, therefore, represent technical errors rather than real changes. An electrical model in which the upper airway was represented by a parallel impedance led us to believe that this might in fact be the case.

In order to confirm this hypothesis, we created an experimental model of acute airflow obstruction by inflating a small balloon in the trachea of healthy volunteers.[6] We then repeated this maneuver in the same volunteers but this time with a rigid upper airway (the volunteers had been intubated with semi-rigid intubation tubes). In the first part of the experiment the changes in mouth pressure were smaller than the changes in esophageal pressure (so that lung volumes were exaggerated by the classic plethysmographic method), while in the second part of the experiment no differences were observed between the changes in mouth and esophageal pressure, so that lung volumes were measured correctly.

Then, to confirm that the plasticity of the upper airway was such that, during panting against a closed shutter, it would assure a sufficient flow of gas to cause a noticeable loss of pressure, we used cineradiography to study healthy panting volunteers and directly measured gas flow in the isolated upper airway of cadavers.[7] These experiments confirmed that "internal" flows as large as 150 mL/s can occur, and that the upper airway can change in diameter in a proportion of 1 to 2 during panting maneuvers against a closed shutter; the size change was greater in the transverse axis (80%) than in the anteroposterior axis (50%).

We were eventually able to demonstrate that the underestimation of alveolar pressure was dependent on panting frequency, and that underestimation increased with an increase in panting frequency.[8] In that study we were also able to ascertain that reducing the panting frequency to 1 Hz reduced the underestimation to practically zero.

Laryngeal Wheezing and Pseudoasthma

In a case we reported in 1983—a patient diagnosed with severe bronchial asthma resistant to corticosteroids who was suffering from iatrogenic Cushing's syndrome—diagnostic studies of the patient's lung function tests led us to the conclusion that she was not suffering from bronchial asthma, but rather that she "fabricated" acute episodes of dyspnea accompanied by wheezing which she produced using the glottis.[9] A physiological saline solution challenge provoked acute dyspnea and wheezing when the patient was told the solution contained histamine intended to trigger an attack. The upper airway mechanics used by the patient to produce wheezing involved breathing near residual

volume such that tidal flows were maximal; wheezing was produced with adduction of the vocal cords to narrow the glottal opening. Cases of pseudoasthma fabricated using the glottis (during expiration, inspiration, or during both phases of the respiratory cycle) have been confirmed by other authors in subsequent publications.

The Soft Palate and Oronasal Respiration

Certain patients with severe chronic obstructive lung disease try to combat exertional dyspnea with pursed-lips breathing. What seems curious is that, without using a noseclip or holding the nares closed with their fingers, these patients can direct the whole expiratory flow via the mouth and prevent any air from passing through the nose. Using spirometry and cineradiographic studies, we demonstrated that this was due to the position of the soft palate, which is raised until it comes into contact with the posterior pharyngeal wall completely occluding the passage between the nasopharynx and the oropharynx so that the whole expiratory flow is redirected through the mouth. In effect, when the soft palate rises it also opens the posterior entrance to the oral cavity.[10] This method of partitioning the respiratory flow between the mouth and the nose is not only applicable to pursed-lips breathing but is also activated whenever—the mouth being open—air can pass through either the nose, the mouth, or simultaneously through both passages. It is the soft palate that regulates oronasal partitioning, either by moving closer to the tongue or by moving away from the tongue and closer to the posterior pharyngeal wall in a rising movement.[11]

The same mechanism comes into play in infants and explains how they are able to breathe through the mouth during nasal occlusion. Pediatric literature previously maintained that infants were unable to breathe through their mouths because of the raised position of the infant epiglottis. We demonstrated that this was not the case and that, a few moments after nasal occlusion, the infants, whether awake or asleep, opened their lips, raised the soft palate opening the oropharyngeal passage, and breathed through their mouths.[13] We also demonstrated that this protective mechanism was intact in infants at risk for sudden infant death syndrome.

Finally, we studied the role of the soft palate in the mechanism of tobacco smoke inhalation in chronic cigarette and pipe smokers, and in nonsmokers who were asked to "smoke" a cigarette.[14] We discovered that the nonsmokers inhaled the smoke directly (holding the cigarette between slightly parted lips) and kept the soft palate in a high and posterior position. Therefore their inspiration exercised its aspiratory effect directly through the cigarette, drawing smoke and air directly into the lower respiratory tract, where it immediately causing coughing. The chronic cigarette smokers, on the other hand, began by sucking a bolus of smoke into the oral cavity closed at the back by the juxtaposition of the base of the tongue and the soft palate. This maneuver is followed by a resting period (during which the smoke cools and certain suspended solid elements are deposited), and only after this does the soft palate separate from the base of the tongue and adopt a raised and posterior position, allowing the smoker to breathe air in through pursed lips and inhale the bolus of smoke into the lower airway.

Chronic pipe smokers, never inhale the smoke into their lungs; the oropharyngeal passage remains closed by the apposition of the base of the tongue and the soft palate. The horizontal portion of the tongue acts as a piston inside the oral cavity sucking boluses of smoke from the bowl of the pipe, and expelling them through lips opened slightly around the stem of the pipe. Meanwhile the pipe smoker breathes continuously through the nose, so that the bolus of smoke is never taken into the lungs. Pipe smokers who have previously been cigarette smokers do not perfectly control this mechanism and inhale some of the smoke.

The Pharynx and Sleep

It was research into snoring, in which the soft palate plays a major role, that brought me to the world of sleep and sleep apnea syndrome.[15] We demonstrated that head position—flexed or extended—influenced airway resistance because of its effect on the pharynx.[16] We ascertained that upper airway surgery, whether nasal or pharyngeal (tonsillectomy, uvulopalatopharyngoplasty), was not an effective treatment for sleep apnea (and this was one of the first articles to raise doubts about the effectiveness of otorhinolaryngological surgery in the treatment of sleep apnea).[17] We analyzed the mechanics of snoring in simple snorers and in patients with sleep apnea and observed that the snoring of the simple snorer is associated with airflow limitation while in apneic patients the snoring occurred when the airflow limitation disappeared. The pressure-flow curve of the former is clockwise while that of the latter is counterclockwise.[18]

The most cited of my contributions to the literature of this field is a study of the shape and dimensions of the pharynx.[19] Until that time it had been believed that the pharynx of patients with sleep apnea was much narrower than that of individuals who did not suffer from this disorder. Taking advantage of the advent of the first magnetic resonance machine, we studied healthy subjects, simple snorers, and patients with sleep apnea. The patients had to weigh less than 150 kg, which was the maximum weight supported by the magnetic resonance machine table.

The pharynx was studied in transverse sections from the nasopharynx to the hypopharynx. Surprisingly it was observed that the surface of the pharyngeal cross sections was similar in the healthy subjects, the patients with sleep apnea, and in the simple snorers. There were even some apneic patients who had a larger pharynx than some healthy individuals. However, a medical student who was assisting us in the measurements (Yves

Thomas) was struck by a difference in the shape of the pharynx in the three groups studied: the pharynxes of the control group of non-snorers appeared to have a half-moon shape, with the long axis in the transverse plane, while the pharynxes of the snorers and the apneic patients were rounded or elongated from back to front. This finding was later confirmed by other authors.

We advanced the following hypothesis to explain these findings: a reduction of the transverse diameter of the pharynx (caused for example by fatty tissue deposits on the lateral pharyngeal walls) would cause a considerable increase in the airway resistance of the pharynx, since the transverse diameter is the longest axis of the pharynx. In order to compensate for this reduction in caliber, the main dilating muscle of the pharynx—the genioglossus—would be activated. This muscle pulls forwards from the anterior wall of the pharynx, thereby increasing anteroposterior diameter and reestablishing a normal, or even an increased, diameter, but producing an abnormal shape.

Various experimental findings supported this hypothesis: the electrical activity of the genioglossus is, in effect, greater in apneic patients[20]; cushions of fatty tissue are found on the anterolateral pharyngeal walls of apneic patients, whether or not the patient is obese[21]; and finally, the application of positive pressure to the upper airway produces an increase primarily in the transverse diameter of the pharynx, thereby re-establishing the organ's original normal shape.[22]

The Glottis and Noninvasive Ventilation

A few years after continuous positive airway pressure was first described as a treatment for sleep apnea, the concept of connecting to the airway by means of a nasal or facial mask in order to administer positive pressure began to be applied in other areas unrelated to sleep apnea. This concept became even more widely applied after the introduction of Bi-level positive pressure (Bipap) for the same purpose, Physicians started to offer patients requiring intubation and mechanical ventilation the alternative of mechanical ventilation without intubation thanks to what came to be known as "noninvasive" ventilation.[23] We were one of the first teams to use this technique in patients with restrictive defects secondary to neuromusculoskeletal disease.[24] One night, after starting this treatment in a myopathic patient with acute respiratory insufficiency, acidosis, and hypercapnia, we observed, and were intrigued by, episodes of complete apnea (that is, a total absence of chest movement) lasting between 20 and 40 seconds during which we observed that the volumetric respirator continued to insufflate the same tidal volume into the nasal mask. The appearance of a small oral leak did not provide a sufficient explanation for the phenomenon.

After verifying in 3 other patients that the events observed happened again, we postulated that they might be explained by complete closure of the glottis, probably secondary to hypocapnia caused by the mechanical ventilation.[25]

In a series of experiments in healthy volunteers, carried out both asleep and awake, we applied noninvasive mechanical ventilation with volumetric or barometric respirators in either assisted or controlled mode while continuously observing the glottis by way of a fiberoptic bronchoscope introduced through the nose.[26-32] In this way, we were able to confirm that our hypothesis was correct: the use of mechanical ventilation—owing to both mechanical effects and other carbon dioxide-dependent factors—provokes adduction of the vocal chords, which in certain situations totally closes the glottis and at other times can give rise to a progressive but incomplete closure followed by a progressive opening of the glottis. This gives rise to a periodic Cheyne-Stokes respiratory pattern. In effect, the adduction of the vocal chords forces part of the insufflated volume to remain in the pharynx or escape through the mouth, the esophagus, or between the mask and the patient´s skin without ever reaching the lower respiratory tract, that is, without participating in alveolar ventilation. Consequently, the proportion of effective tidal volume (and of minute ventilation) insufflated, which gives rise to effective tidal volume (and to effective minute ventilation), depends on the caliber of the glottis.

Using a iron lung, we were able to confirm in awake healthy volunteers that mechanical negative pressure ventilation did not cause glottic closure, and that, probably partly due to this fact, effective ventilation was much greater with negative pressure than with positive pressure for identical pressure levels.[33]

Conclusion

Following the course of many years and many different lines of research, this story recounts, from various different points of view, the successive visits of a pulmonologist with a certain knowledge of anatomy (the result of years of study) and of lung mechanics (the result of years of training) to the very edge of the field of respiratory medicine the frontier between pulmonology and otorhinolaryngology: the upper airway.

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