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Review

Andreas Vesalius' understanding of pulmonary ventilation

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ABSTRACT

The historical evolution of understanding of the mechanical aspects of respiration is not well recorded. That the anatomist Andreas Vesalius (1515–1564) first recorded many of these mechanics in *De Humani Corporis Fabrica Libri Septem* has received little attention. We searched a digital copy of *De Fabrica* (1543) and its English translation as provided by Richardson and Carman (1998–2009) for references to aspects of pulmonary ventilation. We found that Vesalius grasped the essentials of tidal and forced respiration. He recognized that atmospheric pressure carried air into the lungs, approximately 100 years before Borelli did. He described an *in vivo* experiment of breathing, some 120 years before John Mayow produced his artificial model. He reported on positive pressure ventilation through a tracheotomy and on its life-saving effect, some 100 years before Robert Hook did. In publicly recording his insights over 450 years ago, Vesalius laid a firm basis for our understanding of the physiology of respiration and the management of its disorders.

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1. Introduction

The historical evolution of the concepts regarding the chemical aspects of respiration has been amply documented (Perkins, 1964) but relatively little has been written on the development of our understanding of the mechanical aspects of respiration (Otis, 1986). The "father of physiology" Erasistratus (±304 BC) accepted the diaphragm as the only muscle of breathing and Galen (129–200–216) already recognized that the intercostal muscles and some accessory respiratory muscles are also involved (Otis, 1986). Still, it was the anatomist Andreas Vesalius (1515–1564) who first recorded many of the mechanical details and structures of breathing that we currently know, in his epoch-making *De Humani Corporis Fabrica Libri Septem* (*De Fabrica*). (Vesalius, 1998).

So far, Vesalius' records have received little attention because the anatomical illustrations rather than the text of *De Fabrica* got all

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attention in the majority of commentaries on this work (Elkhadem et al., 1993; Lambert, 1936; West, 2012a). Consequently, Vesalius' understanding of negative intrapleural pressure was still ignored in 2002 (Aboud and Verghese, 2002). In Vesalius' time this may have been explained by the novelty of illustrating anatomical texts whereas (Elkhadem et al., 1993), in our time, it may have resulted from difficulty of handling the Latin language (Lambert, 1936; Richardson and Carman, 1994). This excuse to disregard Vesalius' text no longer prevails since the completion, in 2009, of an excellent English translation of the entire text of *De Fabrica* by the classicist Richardson and the anatomist Carman.

Vesalius' instructions for a spectacular *in vivo* demonstration of pulmonary movements in a breathing dog inspired us to study de rest of *De Fabrica* to assess to what extent he understood the physiology of ventilation mechanics. To commemorate Vesalius' 500th anniversary, we report on this assessment.

2. Methodology

During normal tidal breathing, inspiration starts with contraction of the diaphragm and the external intercostal muscles to increase the size of the thorax. Subsequently, the negative pressure in pleura increases, the alveolar volume increases, and the intra-alveolar pressure decreases. The resulting gradient relative to atmospheric pressure causes air to enter the lungs. During this process pulmonary elastic recoil forces increase (Chandrasekhar, 2016; West, 2012b). Once the active inspiratory muscle contractions are stopped, these elastic recoil forces cause the intra-alveolar pressure to increase above atmospheric pressure and the lungs to partially collapse by expiration. Hence, normal tidal expiration is passive because no muscles need to contract to produce it. Accessory inspiratory muscles are brought into action for forced inspiration. Of these, the scalenus muscles are the first to start contracting and the sternocleidomastoid, trapezium and other muscles are gradually brought into action. Contraction of the abdominal (rectus abdominis, internal and external obliques, and transversus abdominis) and internal intercostal muscles for expiration is always accessory.

The intrathoracic parts of the trachea and the bronchi narrow during expiration and widens during inspiration. Their cartilage support prevents them from total collapse. Still, flow rates may not be increased by forced expiration for most of the expiratory phase because the resulting increasing positive pressure in the thorax compresses the airway to a level that decreased airway size counters the increased force to expire (Chandrasekhar, 2016; West, 2012b).

We searched the text of Vesalius' Books I—The Bones and Cartilages, II—The Ligaments and Muscles, and VI—The Heart and Associated Organs of *De Fabrica* for references to these aspects of the respiratory physiology. For this inventory we used the digital copy of the first print of *De Fabrica* (1543) (Vesalius, 1998) and its English translation as provided by Richardson and Carman (Richardson and Carman, 1998, 1999, 2009).

3. Results

3.1. *Vesalius' instructions for* in vivo *demonstration of pulmonary movements*

Vesalius opened the very last chapter of *De Fabrica* entitled *Some Remarks on Vivisection*, by stating that it is *'appropriate that* [medical] *students should begin by dissecting the dead and then go on to inquire into the action and function of the parts by addressing a living animal'* (quote on p. 263) (Figs. 1 and 2) (Richardson and Carman, 2009). But beware, *'for there is no point in trying vivisection unless one is a skilled dissector of the dead'* (quote on p. 265) (Richardson and Carman, 2009). Among many other *in vivo* experiments (Perkins, 1964), he described the visualization of the moving lung by two different approaches (Figs. 3 and 4). For the first approach "*in order to see the natural movement of the lung as it follows the thorax, cut away the cartilages of two or three middle ribs on one side, make incisions along the intervals between these ribs, and break off each rib by bending it outward. This makes an area through which you can inspect the lung on the undamaged side; for the membranes that partition the thorax in dogs are quite transparent and it is easy to examine through them the part of the lung that is still following the movement of the thorax and, after piercing carefully through the membranes, to see how this part of the lung as well ceases to move*" (quote on p. 269) (Richardson and Carman, 2009).

Alternatively, if he "*decided to follow my more difficult procedure*", Vesalius made *'in one side of the thorax .[.]. a longitudinal incision down to the rib bones roughly at the point where the bones turn into cartilage. Then I make transverse incisions along the rib bones,* so *creating an area over which I can denude the bones of the muscles that lie upon them; and then .[.]. I go to two of the intercostal intervals and remove the intercostal muscles in them from the tunic that undergirds the ribs, so that, using my hands alone, I can pull away half of the rib between these intervals from the tunic that undergirds the ribs, break it away from its cartilage, and bend it downwards to the side; this reveals the large cavity of the tunic that undergirds the ribs, which being transparent shows clearly the movement of the lung' (quote on p. 271–2)* (Richardson and Carman, 2009). Only after some 120 more years, did John Mayow produce an artificial model of this *in vivo* experiment (Aboud and Verghese, 2002; Otis, 1986; Perkins, 1964).

3.2. *Vesalius' records on respiration*

On the physiology of respiration Vesalius opened with noting that '*respiration is performed by two contrary movements, a movement of distension and dilatation that draws in, and one of constriction that evacuates'* (quote on p. 283). (Richardson and Carman, 1999) He noted that '*it is therefore obvious the lung follows the movement of the chest by the power of the vacuum when the chest is either compressed or dilated, it was necessary that muscles moving the thorax be constructed in order to expand or contract it'* (quote on p. 283) (Richardson and Carman, 1999). By using the words *'vacui potissimum ui sequatur'* in the Latin original of this quote (on p. 287) (Vesalius, 1998) Vesalius showed to recognize that air is sucked in by the sub-atmospheric pressure that occurs in the lungs as the chest expands, approximately 100 years before Borelli did (Aboud and Verghese, 2002; Perkins, 1964).

By his vivisections he had shown the necessity of this vacuum between the lungs and thoracic wall by local resection of all layers of the thoracic wall while leaving the parietal pleura intact and subsequently inflicting a unilateral pneumothorax in the still breathing dog: *'now I pierce through this tunic in its turn and point out that the lung on this side collapses even though the thorax continues to move as before. In order to reveal this more clearly I detach several more rib bones from their cartilages and open as much as possible of this side of the thorax so that the other part of the lung (which is still in the chest cavity and, being undamaged, is still moving nicely along with the thorax) may be seen through the membranes that partition the thorax; and I then pierce through these membranes in their turn and show that this causes an immediate collapse of the lung'* (quote on p. 272) (Richardson and Carman, 2009).

Likewise, he showed his understanding of the physiological mechanics of the pressure gradients during respiration when he recorded that *'because of this* [respiratory] *function the rough artery* [trachea] *had to be made like a membranous channel, so it could easily collapse when empty and distend again when full: for something that is to be filled solely by avoidance of the vacuum and then emptied solely by the force of compression has to be capable of distending and*