Teaching the effects of gravity and intravascular and alveolar pressures on the distribution of pulmonary blood flow using a classic paper by West et al.

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Levitzky, Michael G. Teaching the effects of gravity and intravascular and alveolar pressures on the distribution of pulmonary blood flow using a classic paper by West et al. Adv Physiol Educ 30: 5–8, 2006; doi:10.1152/advan.00051.2005.—“Distribution of blood flow in isolated lung; relation to vascular and alveolar pressures” by J. B. West, C. T. Dollery, and A. Naimark (J Appl Physiol 19: 713–724, 1964) is a classic paper, although it has not yet been included in the Essays on the American Physiological Society Classic Papers Project (http://www.the-aps.org/publications/classics/). This is the paper that originally described the “zones of the lung.” The final figure in the paper, which synthesizes the results and discussion, is now seen in most textbooks of physiology or respiratory physiology. The paper is also a model of clear, concise writing. The paper and its final figure can be used to teach or review a number of physiological concepts. These include the effects of gravity on pulmonary blood flow and pulmonary vascular resistance; recruitment and distention of pulmonary vessels; the importance of the transmural pressure on the diameter of collapsible distensible vessels; the Starling resistor; the interplay of the pulmonary artery, pulmonary vein, and alveolar pressures; and the vascular waterfall. In addition, the figure can be used to generate discovery learning and discussion of several physiological or pathophysiological effects on pulmonary vascular resistance and the distribution of pulmonary blood flow.

When I was asked if I would submit a manuscript for the Advances in Physiology Education Using Classic Papers to Teach Physiology series, the first paper that I considered was “Distribution of blood flow in isolated lung; relation to vascular and alveolar pressures” by J. B. West, C. T. Dollery, and A. Naimark [J Appl Physiol 19: 713–724, 1964 (8)]. It is the classic “zones of the lung” paper. Because I give at least eight lectures a year about pulmonary blood flow to medical students; graduate students; anesthesiology residents; pulmonary, trauma surgery, and neonatology fellows; nurse anesthesia and respiratory therapy students; and pulmonologists; I refer to this paper constantly. Each time I discuss it, I point out that in addition to the importance of the concepts presented and the elegance of the methods used, the paper is a model of clear, concise writing. Although few of the people I teach will read the original paper in its entirety, I do go through most of the figures in the paper in my usual presentation. I encourage graduate students to read the original paper.

I consulted the list of papers that have been presented in the Essays on the American Physiological Society (APS) Classic Papers (http://www.the-aps.org/publications/classics/), part of the APS Legacy Project (http://www.the-aps.org/publications/legacy/), and I was surprised to learn that this important paper was not on the list. I was relieved to hear from the editor of this series that the reason that it is not included is that Dr. West served on the committee that selected the papers and did not feel it was appropriate to include one of his own.

The paper investigates the relationships of pulmonary artery pressure, pulmonary vein pressure, and alveolar pressure as they affect the distribution of pulmonary blood flow in an isolated lung. Gravity influences intravascular pressures, so it is implicit in the discussion. As West noted in his review of the history of the research on pulmonary blood flow and gas exchange, the differences in blood flow from the upper to lower regions of the lung “were first recognized when it was found that the rate of removal of inhaled oxygen-15 labeled carbon dioxide was much slower from the apex of the upright lung than from the base” (5). I therefore start the discussion of the “zones of the lung” with a figure showing blood flow increasing with distance down the upright lung. I always point out that this was first noticed in experiments using human subjects (7). In the interest of honesty (one of my long-term goals), I must confess that the figure I show is from a much later paper (2) that used radioactive xenon, not carbon dioxide. This figure, which shows the regional perfusion in human subjects at the total lung capacity, is basically the same one used by West in his textbook (6). This leads directly to Fig. 1 (Fig. 3C in the original) of the “zones” paper, showing a very similar figure but this time obtained from an isolated perfused dog lung and also using radioactive xenon. The lung was ventilated with negative pressure. (The slides I show, now scanned into Powerpoint, were originally from a set of Dr. West’s slides made available to physiology teachers through the APS. I bought them a little more than 30 years ago!)

This raises the important teaching point of why blood flow increases with distance down the lung. Students have little difficulty understanding that because of gravity, the blood pressure in pulmonary vessels increases with distance down the lung. They know that the pressure at the bottom of a column of liquid increases with the height of the column (the pressure equals the product of gravity, the density of the liquid, and the height of the column; usually referred to as Pascal’s Law), but the increasing pressure doesn’t explain the increasing flow; the pulmonary arterial and pulmonary venous pressures increase by the same amount with distance down the lung—the “driving pressure” is the same. The blood flow increases because of characteristics of the pulmonary circulation: the greater intravascular pressures lead to more recruitment and distention of vessels (discussed with the students before the discussion of the zones), so the resistance to blood flow...
flow decreases with distance down the lung. If increasing blood pressure with vertical distance due to gravity increased blood flow in the systemic circulation, most of the cardiac output would flow to a standing person’s feet. That doesn’t happen because the systemic arterial system has muscular arterioles to control local resistance to blood flow, and recruitment and distention don’t play a role. It does, however, explain why blood pools in the distensible veins of a standing person’s lower extremities.

Figure 2 (Fig. 4 in the original) from the paper shows that at reduced pulmonary artery pressure, above the point at which pulmonary artery pressure is equal to alveolar pressure, there is no blood flow. As already discussed, the intravascular pressure decreases with distance up the lung, so there may be a point at which the pressure inside the vessels equals the alveolar pressure. Above that point, the pressure outside the pulmonary capillaries must be greater than the pressure inside them because it is greater than pulmonary artery pressure. Having already discussed (usually in a previous lecture) the importance of the transmural pressure difference in determining flow through a collapsible vessel, another important teaching point, students can easily see that the vessels must be collapsed. (I often facetiously say that I should have thought of this myself, but I was in high school at the time and I was thinking about what high school boys think about instead.) Figure 3 (Fig. 6 in the original) from the paper shows that with high pulmonary artery pressure, the blood flow decreased with distance up the lung, but there “was still considerable blood flow at the top of the lung.” Figure 4 (Fig. 7 in the original) shows that increasing alveolar pressure moved the level of the lung at which blood flow ceases farther down the lung. In Fig. 4A, alveolar pressure is +6 cmH₂O, and blood flow ceases at about 12 cm from the bottom of the lung. In Fig. 4B, alveolar pressure is −5 cmH₂O, and blood flow occurs to the top of the lung. At this point, we have gravity, pulmonary artery pressure, and alveolar pressure in our discussion of the distribution of pulmonary blood flow; only venous pressure remains to be considered. Figure 5A (Fig. 8A in the original) from the paper shows the relationship between pulmonary venous pressure and alveolar pressure on the vertical distribution of blood flow. As in previous figures, blood flow decreases with distance up the lung, but the slope of the line relating distance up the lung to blood flow changes abruptly at the point at which the pulmonary venous pressure is equal to the alveolar pressure. When the venous pressure was raised (by raising the venous outflow reservoir) high enough that it exceeded alveolar pressure even in the uppermost part of the lung, as in Fig. 5B (Fig. 8B in the original), there was no point at which the slope of the relationship changed abruptly. The reason that the slope of the line relating blood flow to distance up the lung theoretically
changes abruptly at the point at which pulmonary venous pressure is equal to alveolar pressure. The point at which alveolar pressure is the effective downstream pressure in determining blood flow. Because alveolar pressure exceeds pulmonary venous pressure, the driving pressure for blood flow is therefore pulmonary artery pressure minus alveolar pressure. The slope changes because when pulmonary venous pressure is the downstream pressure, as already noted, upstream and downstream pressures both increase by the same amount with distance down the lung; the driving pressure is constant. When alveolar pressure is the downstream pressure, at any instant it is constant at all levels of the lung. That means that the driving pressure increases with distance down the lung because the upstream pressure increases with distance down the lung but the downstream pressure doesn’t change.

Figure 6 (Fig. 11 in the original) is the classic diagram that summarizes how the relationships among pulmonary artery pressure, pulmonary vein pressure, and alveolar pressure (and gravity) affect blood flow in different parts of the lung. It is reproduced in most of the textbooks of physiology or respiratory physiology. The right side of Fig. 6 is Fig. 5A turned on its side (and reversed right to left). The left side of Fig. 6 divides the lung into three regions, or zones. Inside the outline of the lung is a picture of a Starling resistor model of a blood vessel for each of the three regions or zones, and next to it is the relationship of the three pressures in that zone. In the top region (zone 1), alveolar pressure is greater than pulmonary artery pressure; the vessel is collapsed, and there is no blood flow. In the bottom region (zone 3), pulmonary artery pressure is greater than pulmonary vein pressure, and both exceed alveolar pressure. The vessel is open, and the model shows it as somewhat distended; the driving pressure for blood flow is pulmonary artery pressure minus pulmonary vein pressure. In the middle region (zone 2), pulmonary artery pressure is greater than alveolar pressure, but alveolar pressure is greater than pulmonary vein pressure. The vessel is partly collapsed at the venous end, and the driving pressure for blood flow is pulmonary artery pressure minus alveolar pressure.

The discussion in the paper explains why the alveolar pressure is the effective downstream pressure in terms of a Starling resistor or a waterfall. [For a good brief biographical sketch of Ernest Henry Starling (1866–1927) and descriptions of some of his many important contributions to physiology, see http://www.whonamedit.com/doctor.cfm/1188.html.] These two explanations are not discussed in detail in the paper; the reader is referred to other two papers, one of which I also consider a classic. This paper, “Alveolar pressure, pulmonary venous pressure, and the vascular waterfall” by S. Permutt, B. Bromberger-Barnea, and H. N. Bane [Med Thorac 19: 239–260, 1962 (4)] relates the Starling resistor model to the pulmonary circulation. [Dr. Permutt described the background of the paper in a personal history (3) that is also very enjoyable reading. See also W. Mitzner’s essay on two classic APS papers by Dr. Permutt at http://www.the-aps.org/publications/classics/] This paper, published two years before the West et al. paper, begins with the following two statements:

1. Whenever pulmonary venous pressure is greater than alveolar pressure, flow is proportional to the difference between pulmonary artery pressure and pulmonary venous pressure, and changes in alveolar pressure have no influence on flow.

2. Whenever alveolar pressure is greater than pulmonary venous pressure, flow is proportional to the difference between pulmonary artery pressure and alveolar pressure, and changes in pulmonary venous pressure have no influence on flow.”

I often discuss with students (especially graduate students) why the Permutt paper isn’t better known. It looks a lot longer than the “zones” paper but it probably isn’t; it is in a single-column grid rather than a double-column grid. It is a little more difficult to read, but I think there are two greater reasons. One is Fig. 6 (Fig. 11 in the original) in the “zones” paper: it packages all the concepts in one picture, and it names the three potential regions zones 1, 2, and 3; the other reason is the journal in which it was published. Not only is it not an APS journal, it is in a journal that changed its name six years later: from Medicina Thoracalis to Respiration.

The Starling resistor is fairly easy for students to understand if they have already discussed the importance of the transmural pressure difference on the diameter of a collapsible/distensible
vessel. [A teaching point for some groups (graduate students in physiology or engineering students) is a discussion of what happens at the venous end of the vessels in zone 2. Are they open? Why are they open? Are they always open?] The vascular waterfall analogy requires explanation. If alveolar pressure exceeds pulmonary venous pressure and alveolar pressure is the effective downstream pressure, then venous pressure has no influence on pulmonary blood flow. This is analogous to a waterfall: the height of the waterfall does not influence the amount of water flowing over it.

Teaching points related to Fig. 6 (Fig. 11 in the original) therefore include:

1. The effect of gravity on the perfusion of the lung. Blood flow per unit volume increases with distance down the lung (or decreases with distance up the lung). This is a result of not only increasing intravascular pressure with distance down the lung but also decreased resistance to blood flow because of more recruitment and distention in response to the increased intravascular pressure.

2. The relationships of pulmonary artery pressure, pulmonary vein pressure, and alveolar pressures (the three zones). (This should be explained using the Starling resistor models inside the outline of the lung in each of the three zones.) There is no blood flow in zone 1 because alveolar pressure exceeds pulmonary artery pressure. In zone 3, pulmonary artery pressure is greater than pulmonary vein pressure, which is greater than alveolar pressure. The driving pressure for blood flow is pulmonary artery pressure minus pulmonary vein pressure, and the pressure difference does not change with distance down the lung. In zone 2, where pulmonary artery pressure is greater than alveolar pressure but alveolar pressure exceeds pulmonary vein pressure, alveolar pressure is the effective downstream pressure for blood flow. At any instant alveolar pressure is constant, so the driving pressure for blood flow increases with distance down the lung: the upstream pressure increases, but the downstream pressure remains the same. This change in the driving pressure explains the abrupt change of the slope of the line relating blood flow to distance down the lung.

3. The zones are physiological, not anatomic. The borders between zones can be moved by many physiological and pathophysiological alterations or conditions, including changes in body position; riding in a fast elevator; changes in right ventricular output; changes in pulmonary artery pressure, pulmonary vein pressure, and left atrial pressure; blood loss; changes in alveolar pressure; and positive pressure ventilation with or without positive end-expiratory pressure (PEEP). Zone 1 is alveolar dead space (it is ventilated but not perfused), and it does not contribute to gas exchange. During normal quiet breathing in a young healthy person with a normal cardiac output, pulmonary artery pressure, even in the uppermost regions of the lung, is greater than alveolar pressure, so there is no zone 1. However, blood loss or other causes of pulmonary hypotension, or positive pressure ventilation, especially with PEEP, can introduce zone 1 in a young, otherwise-healthy person and may increase it in older people or patients. Anything that increases the proportion of the lung in zone 1 decreases the surface area of the lung available for gas exchange.

Although gravity and the interactions among pulmonary artery pressure, pulmonary vein pressure, and alveolar pressure are not the only determinant of the regional distribution of pulmonary blood flow (1), they are important. Many of the clinical implications of these relationships were noted in the preceding paragraph. The classic and familiar figure from this paper provides a number of significant teaching points and opportunities for discovery learning (Table 1).

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**REFERENCES**