

Breathing Life into Pulmonary Physiology

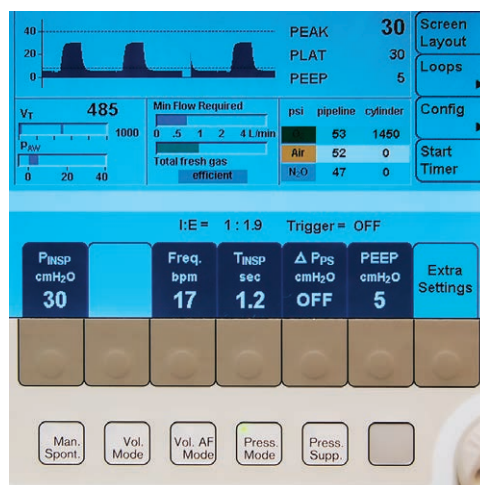
How Age and Body Weight Impair Oxygenation

Jeffrey Thiboutot, M.D., M.H.S., Robert H. Brown, M.D., M.P.H.

In the words of the famous H. L. Mencken, one of the most influential writers of the last century, “For every complex problem there is an answer that is clear, simple, and wrong.” Impaired arterial oxygenation is a complex problem. While one solution to impaired oxygenation is to increase the inspired oxygen, that is not necessarily the correct solution. As we parse out the various factors that cause worsening oxygenation, we get closer to understanding the reasons and thus closer to more accurate solutions.

As advances in anesthetic and surgical techniques have progressed over the past few decades, we continue to perform more surgeries on patients who previously were thought to be at too high a risk. Two determinants of worsening outcomes for patients undergoing anesthesia are old age and obesity. Traditionally, increased age is commonly associated with increasing comorbidities, and obesity is associated with obstructive sleep apnea and atelectasis, all of which portend to poorer anesthesia outcomes. Beyond these superficial assessments, there is much to be learned about what is happening physiologically during anesthesia as it relates to these determinants. In the current issue of the journal, Hedenstierna *et al.* studied the pathophysiologic effects of increased age and body weight on impaired oxygenation during anesthesia.¹

Caring for patients with obesity and morbid obesity has become a regular part of everyday practice. It is estimated that worldwide, by 2025, global obesity will surpass 18% of men and 21% of women,² with even greater rates in high-income countries. Similarly, it is expected that by 2030, the number



“[R]ecruitment maneuvers may still be useful in overweight (and obese) patients to reduce atelectasis...[but not] in elderly patients... [where] one should consider increasing lung volume, such as through the use of positive end-expiratory pressure...”

of people worldwide aged 60 yr and over will rise by nearly 56% to nearly 1.6 billion people.³ With advances in areas such as transplant, oncologic, laparoscopic, and robotic surgeries, more procedures are safely being performed in the elderly.⁴⁻⁶ As these obese and elderly patients will respond differently to our approaches and treatments, a better understanding of the physiologic alterations induced by aging and weight is needed to best care for these populations.

The healthy lung comprises a heterogeneous distribution of various proportions of ventilation (\dot{V}) and perfusion (\dot{Q}). This is commonly assessed by their ratio \dot{V}/\dot{Q} , which is highest at the apices and decreases toward the bases. Shunt is an abnormal physiologic phenomenon that is at the extreme end of the \dot{V}/\dot{Q} spectrum (no \dot{V} , all \dot{Q}). Both areas of low \dot{V}/\dot{Q} and of shunt can lead to oxygen impairment. Until recently, there have been limited studies of the effects of anesthesia on \dot{V}/\dot{Q} and oxygen impairment. One method to assess ventilation and \dot{V}/\dot{Q} defects is the multiple inert gas elimination technique (MIGET). MIGET uses infused inert gases with different solubilities and measures systemic and pulmonary artery concentrations as well as mixed expired concentrations of these inert gases to calculate \dot{V}/\dot{Q} .⁷

In this issue, Hedenstierna *et al.* capitalized on MIGET technology to assess if \dot{V}/\dot{Q} differences exist in healthy patients (American Society of Anesthesiologists class I) undergoing anesthesia.¹ MIGET, computed tomography scans of the chest, and P_{aO_2} measurements were performed in healthy patients across varying ages and body weights both in the awake and anesthetized states to assess the drivers of impaired

Image: J. P. Rathmell.

This editorial accompanies the article on p. 46.

Accepted for publication February 28, 2019. From the Department of Medicine (J.T., R.H.B.), Department of Anesthesiology and Critical Care Medicine (R.H.B.), Department of Environmental Health and Engineering (R.H.B.), and Department of Radiology (R.H.B.), Johns Hopkins University, Baltimore, Maryland.

Copyright © 2019, the American Society of Anesthesiologists, Inc. All Rights Reserved. Anesthesiology 2019; 131:7–9. DOI: 10.1097/ALN.0000000000002710

oxygenation under anesthesia. In this study, increased oxygen impairment was associated with older age and increased body mass index in the anesthetized patients. MIGET revealed that areas of low \dot{V}/\dot{Q} increased with age, but had no association with body mass index. Shunt, on the other hand, followed a quadratic distribution with a peak at age 45 yr, and increased linearly with body mass index. Areas of low \dot{V}/\dot{Q} became more important drivers of impaired oxygenation than shunt in the elderly adults. The explanation for the increased shunt with high body weights is fairly intuitive (and confirmed by computed tomography findings). Higher body weights caused increased areas of atelectasis in the dependent portions of the lungs, through which blood is shunted, leading to impaired oxygenation. In addition, in the supine position, the size of these dependent portions of the lungs increases, further worsening atelectasis and shunt. However, what is most interesting was their finding that the peak effects of shunt occurred at age 45 yr. The authors hypothesized that these areas of low \dot{V}/\dot{Q} may actually be preventing atelectasis. If one has existing areas of low \dot{V}/\dot{Q} before anesthesia, during preoxygenation with higher fractional inspired oxygen tension (FiO_2 , 0.8 to 1), the nitrogen existing at the alveoli will not have enough time to be washed out. Then, after the induction of anesthesia, when FiO_2 is reduced, in areas of low ventilation, the oxygen will still be absorbed, but the larger amount of remaining nitrogen will act to stent open the alveoli. This theory has been supported by previous studies.^{8–10}

The work did have several limitations. This was a retrospective study that used previously acquired data from eight studies performed at two sites with slightly differing population demographics, general anesthetic choices, and respiratory settings. Also, the studies were only performed on healthy (American Society of Anesthesiologists class I) patients. Whether comorbidities will affect these findings remains to be determined. In addition, only nonobese (body mass index less than 30 kg/m²) subjects were studied. While there are no obvious reasons why the relationship between weight and impaired oxygenation should be different in obese (or morbidly obese) individuals compared to simply overweight ones, further studies including these populations should be performed. It is currently leap of faith, albeit small, to extrapolate these findings to obese patients. Another limitation is that while MIGET measurements can give an overall estimate of \dot{V}/\dot{Q} , it has no spatial resolution, so the sites of mismatch within the lungs cannot be identified. Unfortunately, this technique is not amenable to clinical practice and will remain as only a research tool.

So how do these findings affect clinical practice? One size may not fit all. While recruitment maneuvers may still be useful in overweight (and obese) patients to reduce atelectasis, recruitment maneuvers in elderly patients may not be helpful, as their oxygenation impairment may be driven by low \dot{V}/\dot{Q} , not atelectasis (shunt). As suggested by the authors, in the elderly patients where low \dot{V}/\dot{Q} will be the cause of the impaired oxygenation, one should consider

increasing lung volume, such as through the use of positive end-expiratory pressure to stabilize the airways and decreasing expiratory flow rates to keep airways open. While these findings are provocative and may lead to alternative interventions for different groups of patients with impaired oxygenation, they should be verified in the populations of interest, ideally through randomized controlled trials.

Research Support

Research reported in this publication was supported by the National Heart, Lung, and Blood Institute of the National Institutes of Health (Bethesda, Maryland) under award Nos. RO1HL121788 and F32HL144121. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Competing Interests

The authors are not supported by, nor maintain any financial interest in, any commercial activity that may be associated with the topic of this article.

Correspondence

Address correspondence to Dr. Thiboutot: Jthibou1@jhmi.edu

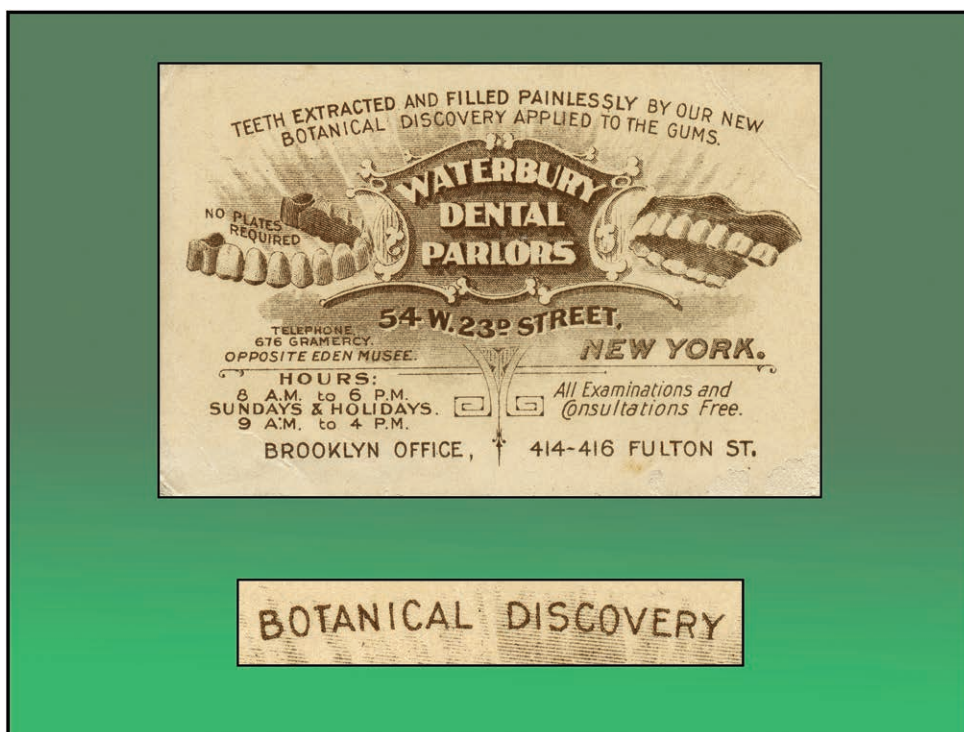
References

1. Hedenstierna G, Tokics L, Scaramuzzo G, Rothen HU, Edmark L, Öhrvik J: Oxygenation impairment during anesthesia: Influence of age and body weight. *ANESTHESIOLOGY* 2019; 131:46–57
2. (NCD-RisC) NRFC: Trends in adult body-mass index in 200 countries from 1975 to 2014: A pooled analysis of 1698 population-based measurement studies with 19.2 million participants. *Lancet* 2016; 387:1377–96
3. United Nations DoEaSA, Population Division. World Population Ageing 2015. *ST/ESA/SER.A/390*. New York, United Nations, 2015
4. Ceccarelli G, Andolfi E, Biancafarina A, Rocca A, Amato M, Milone M, Scricciolo M, Frezza B, Miranda E, De Prizio M, Fontani A: Robot-assisted surgery in elderly and very elderly population: Our experience in oncologic and general surgery with literature review. *Aging Clin Exp Res* 2017; 29(suppl 1):55–63
5. Segall L, Nistor I, Pascual J, Mucsi I, Guirado L, Higgins R, Van Laecke S, Oberbauer R, Van Biesen W, Abramowicz D, Gavrilovici C, Farrington K, Covic A: Criteria for and appropriateness of renal transplantation in elderly patients with end-stage renal disease: A literature review and position statement on behalf of the European Renal Association-European Dialysis and Transplant Association Descartes Working Group and European Renal Best Practice. *Transplantation* 2016; 100:e55–65

6. Otake A, Sasase A, Suzuki A, Takahashi K, Sasamoto N, Miyoshi Y, Shioji M, Yamamoto Y, Adachi K: Assessment of age-specific safety of laparoscopic surgery in elderly patients with ovarian tumors. *J Obstet Gynaecol Res* 2016; 42:297–301
7. Mélot C: Contribution of multiple inert gas elimination technique to pulmonary medicine. 5. Ventilation-perfusion relationships in acute respiratory failure. *Thorax* 1994; 49:1251–8
8. Edmark L, Kostova-Aherdan K, Enlund M, Hedenstierna G: Optimal oxygen concentration during induction of general anesthesia. *ANESTHESIOLOGY* 2003; 98:28–33
9. Sum Ping SJ, Makary LF, Van Hal MD: Factors influencing oxygen store during denitrogenation in the healthy patient. *J Clin Anesth* 2009; 21:183–9
10. Rothen HU, Sporre B, Engberg G, Wegenius G, Reber A, Hedenstierna G: Prevention of atelectasis during general anaesthesia. *Lancet* 1995; 345:1387–91

ANESTHESIOLOGY REFLECTIONS FROM THE WOOD LIBRARY-MUSEUM

Numbing a World of Hurt: T. D. Waterbury Cruises from Cocaine to Carbolic Acid



Following the discovery of cocaine's local anesthetic properties, some entrepreneurs began concocting their own proprietary compounds of topical and injectable cocaine, thereby sidestepping the expense of cocaine-laden nostrums and patent medicines. Neither a dentist nor a pharmacist, businessman Thomas D. Waterbury (1866 to 1921) launched his namesake dental chain by 1897 with a "New Botanical Discovery" (*lower*) that was compounded with something not-so-new: cocaine. His Waterbury Dental Parlors (*upper*) in Brooklyn and then Manhattan were successful enough to fund a 2-yr cruise around the world with his wife. Weeks after the global tour ended, Mr. Waterbury confirmed his business affairs were in order and that none of the 40 dentists working for him knew the formulation of his "New Botanical Discovery." Turning from venal to phenol, he checked himself into the Hotel McAlpin and committed suicide by drinking carbolic acid. (Copyright © the American Society of Anesthesiologists' Wood Library-Museum of Anesthesiology.)

George S. Bause, M.D., M.P.H., Honorary Curator and Laureate of the History of Anesthesia, Wood Library-Museum of Anesthesiology, Schaumburg, Illinois, and Clinical Associate Professor, Case Western Reserve University, Cleveland, Ohio. UJYC@aol.com.