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REVIEW

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The multiple inert gas elimination technique (MIGET)

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Abstract This brief review centers on the multiple inert gas elimination technique (MIGET). This technique, developed in the 1970s, measures the pulmonary exchange of a set of six different inert gases dissolved together in saline (or dextrose) and infused intravenously. It then uses those measurements to compute the distribution of ventilation/perfusion ratios that best explains the exchange of the six gases simultaneously. MIGET is based on the very same mass-conservation principles underlying the classic work of Rahn and Fenn and of Riley and coworkers in the 1950s, which defines the relationship between the ventilation/perfusion ratio and the alveolar and capillary partial pressures of any gas. After a brief history of MIGET, its principles are laid out, its information content is explained, and its limitations are described. It is noted that in addition to quantifying ventilation/perfusion inequality and pulmonary shunting, MIGET can identify and quantify diffusion limitation of O_2 exchange, when present, as well as explain the contributions of extrapulmonary influences such as inspired O_2 concentration, ventilation, cardiac output, Hb concentration/P_{50}, body temperature and acid/base state on arterial oxygenation. An overview of the technical details of implementing MIGET is given, and the review ends with potential future applications.

Keywords Ventilation/perfusion inequality · Shunt · Alveolar–capillary diffusion limitation · Hypoxemia · Hypercapnia · Inert gases

Introduction

Most patients cared for in the ICU have inefficient pulmonary gas exchange, causing hypoxemia and requiring increased inspired O_2 levels to sustain O_2 availability to tissues. Most medical students know that hypoxemia may be caused by one or more of four different physiological processes [1]: (1) Hypoventilation, (2) diffusion limitation, (3) ventilation/perfusion inequality, and (4) shunt (right to left). Most residents know that hypoxemia can be assessed by any of five common parameters: (1) arterial PO_2 (and PCO_2) itself, (2) arterial PO_2/FIO_2 ratio, (3) alveolar–arterial PO_2 difference, (4) venous admixture (also termed physiological shunt), and (5) physiological dead space. Most intensivists know that these several parameters, while readily available and clinically useful, offer quite limited information and are open to misinterpretation when the underlying assumptions and requirements are not met. For the most part, the four causes of hypoxemia are difficult to distinguish in any given patient using these tools. Intensivists also know that in addition to the above four causes of hypoxemia, so-called extrapulmonary factors can greatly modulate arterial PO_2. These factors are, in addition to FIO_2, total ventilation, cardiac output, metabolic rate, Hb concentration, Hb P_{50}, body temperature, and acid/base status.

The multiple inert gas elimination technique (MIGET) [2–5] was introduced in the early 1970s as a way to overcome many of the limitations imposed by the classical methods mentioned above. This short review will

discuss the MIGET in terms of its history, its theoretical basis, its implementation, and its future, in that order.

A brief history of the MIGET

In the late 1940s, 1950s and early 1960s, prior to the availability of digital computation, three groups of investigators developed the modern foundations of pulmonary gas exchange. Rahn and Fenn published their remarkable graphical analysis of the relationship between PO_2, PCO_2, and the ventilation perfusion ratio, $\dot{V}A/\dot{Q}$ [6]; Riley and coworkers developed the concepts of quantifying gas exchange disturbances by calculating venous admixture and physiological dead space [7, 8], and Briscoe and King added to this new scientific domain by exploring the relationship between ventilation/perfusion inequality and diffusion limitation of O_2 transport in the lung [9, 10].

The foundation of all of their efforts was one simple principle: steady-state gas exchange in the lung obeyed mass-conservation principles. Simple mass-conservation equations for O_2 (and CO_2) were written down for both disappearance of O_2 from alveolar gas and its subsequent appearance in the pulmonary capillary blood. This led to the famous ventilation/perfusion equation, approximated for O_2 as follows:

$$\dot{V}A/\dot{Q} = 8.63 \times [Cc'O_2 - CvO_2]/[PIO_2 - PAO_2] \quad (1)$$

and for CO_2:

$$\dot{V}A/\dot{Q} = 8.63 \times [CvCO_2 - Cc'CO_2]/[PACO_2]. \quad (2)$$

Here, Cc′ and Cv represent end-capillary and mixed venous concentrations (ml/dl) while PI and PA represent inspired and alveolar partial pressures (mmHg). Note that 7.5 mmHg = 1 kP. The constant 8.63 reconciles the units and conventional conditions of expression (O_2 and CO_2 concentrations in ml/dl, STPD; $\dot{V}A$ in l/min, BTPS, $\dot{Q}$ in l/min. Its value is actually given by $0.01 \times 760 \times [(273 + T)/273]$, where 760 is standard barometric pressure in mmHg (101.3 kP) and T is body temperature in °C, assumed here to be 37.

What do these equations tell us? That local alveolar PO_2 (and PCO_2) is uniquely set by the local $\dot{V}A/\dot{Q}$ ratio – for a given set of "boundary conditions" (the inspired and venous blood composition and the particulars of the O_2 and CO_2 dissociation curves).

These rather simple equations are tantalizingly hard to actually solve – that is, to come up with the actual PO_2 for any $\dot{V}A/\dot{Q}$ ratio – because the dissociation curve is so complex. The principles apply to all gases, however, and if gas exchange is examined for a gas whose transport in blood is only by physically dissolving, the above equations become much simpler.

Suppose such a gas (we shall call it an inert gas) is being eliminated from the body (just as is CO_2). Equation 2 applies and looks like this:

$$\dot{V}A/\dot{Q} = 8.63 \times \text{solubility} \times [Pv_{IG} - Pc'_{IG}]/[PA_{IG}] \quad (3)$$

[because concentration = solubility × partial pressure (Henry's Law)]. Using this nomenclature, solubility is the ratio of concentration to partial pressure, and is usually expressed in ml (of the gas dissolved in blood) per dl (of blood) per mmHg partial pressure (of the gas in blood). Now, if we assume that diffusion equilibration for an inert gas is complete, $Pc'_{IG} = PA_{IG}$. Dropping the subscript IG and recognizing that λ, the blood–gas partition coefficient of the inert gas, =8.63 × solubility, we have:

$$\dot{V}A/\dot{Q} = \lambda \times [Pv - PA]/[PA]. \quad (4)$$

Note that λ, in words, is the ratio of concentrations of the gas in blood and (alveolar) gas, at equilibrium. Equation 4 can be rearranged as follows:

$$PA/Pv = \lambda/[\lambda + \dot{V}A/\dot{Q}] = Pc'/Pv. \quad (5)$$

This equation says that for an inert gas being eliminated from the blood by the lung, the fraction that is *not* eliminated (i.e., the fraction that is retained in the end-capillary blood, Pc′/Pv) is a simple function of the partition coefficient (λ) and the $\dot{V}A/\dot{Q}$ ratio.

The point of this exercise is to show that Eq. 5, which turns out to be the complete foundation of the MIGET, is nothing more than the ventilation/perfusion equation of mass conservation applied to an inert gas. Seymour Kety [11] and then Leon Farhi and his colleagues [12, 13] used this equation extensively to understand inert gas exchange in the lung, and Farhi et al. went on to propose a method for characterizing the lung as a two-compartment distribution of ventilation and blood flow using measured PA/Pv ratios for three gases forced to exchange across the lungs [13].

Before moving to MIGET itself, another advance must be mentioned: Lenfant and coworkers developed an approach to use the pattern of arterial PO_2 response to increasing FIO_2 to calculate a continuous distribution of ventilation and blood flow [14, 15]. While an approach based on PO_2 has some attraction, there were too many concerns to support its widespread use. However, it laid the groundwork for the concept of (essentially) continuous $\dot{V}A/\dot{Q}$ distributions as the "holy grail" of gas exchange research.

Theoretical basis of the MIGET

Returning to inert gases, Eq. 5 is the basis of MIGET. It reflects precisely the same physiological principles of mass conservation as for O_2 and CO_2.

How does it work?

Suppose we introduce a foreign inert gas into the body by venous infusion of a solution of that gas, and we measure retention as measured from an arterial blood sample as the ratio Pa/Pv (arterial to mixed venous inert gas partial pressure ratio, termed R). Further suppose the lung is perfectly homogeneous. We have:

$$R = \lambda/[\lambda + \dot{V}A/\dot{Q}]. \quad (6)$$

where $\dot{V}A/\dot{Q}$ is the ratio of alveolar ventilation to cardiac output.

Figure 1 (upper panel) shows R (calculated from Eq. 6) plotted against the $\dot{V}A/\dot{Q}$ ratio for gases of different λ. It shows that for any gas, R falls as $\dot{V}A/\dot{Q}$ ratio rises. Look at a gas with $\lambda = 0.01$ as an example: When $\dot{V}A/\dot{Q}$ is less than about 0.001, the gas is essentially fully retained in the blood. At even lower $\dot{V}A/\dot{Q}$ ratios, retention therefore does not change and this gas cannot discriminate between $\dot{V}A/\dot{Q}$ ratios of, say, 0.001 and any lower value. Similarly, elimination is essentially complete at $\dot{V}A/\dot{Q}$ ratios of 0.1 or higher, and this gas will not discriminate among $\dot{V}A/\dot{Q}$ ratios higher than 0.1. However, in the range 0.001 to 0.1, retention of this gas is very sensitive to $\dot{V}A/\dot{Q}$ ratio, and is thus a good gas to use to identify alveoli with $\dot{V}A/\dot{Q}$ ratios in that range. Similar arguments apply to all other gases.

Figure 1 (lower panel) plots exactly the same data, but this time retention is plotted against λ, not $\dot{V}A/\dot{Q}$. The message here is that a gas of a particular λ is best suited to identifying alveoli whose $\dot{V}A/\dot{Q}$ ratios approximate the value of λ. For $\dot{V}A/\dot{Q}$ ratios 10 times (or more) lower than λ, retention is essentially complete, and is essentially zero when $\dot{V}A/\dot{Q}$ is 10 times (or more) higher than λ. Thus, if several inert gases (whose λ vary over several decades) are exchanged simultaneously and their retentions measured, we have the potential to determine what kinds of $\dot{V}A/\dot{Q}$ regions are present in any given lung.

Figure 2 captures this concept more clearly with three examples: the upper panel represents a perfectly homogeneous lung (with $\dot{V}A/\dot{Q}$ ratio = 1), the middle panel a lung with 50% of its blood flow perfusing a region whose $\dot{V}A/\dot{Q}$ ratio is low, at 0.01 (the remaining 50% perfusing normal regions), and the lower panel a lung with 50% of its blood flow perfusing completely unventilated regions (i.e., shunt, $\dot{V}A/\dot{Q} = 0$). In each, the arterial retention values that would result for six different inert gases (named in the upper panel) are shown by the solid circles. The end-capillary/mixed venous ratios associated with each of the contributing regions are shown by the dashed lines in each case. It is clear that the shape and position of these "retention–solubility" curves vary widely according to the particular pattern of $\dot{V}A/\dot{Q}$ regions present. What this means is that from the measured pattern of retentions of such a set of six gases, it is possible to deduce the underlying pattern of

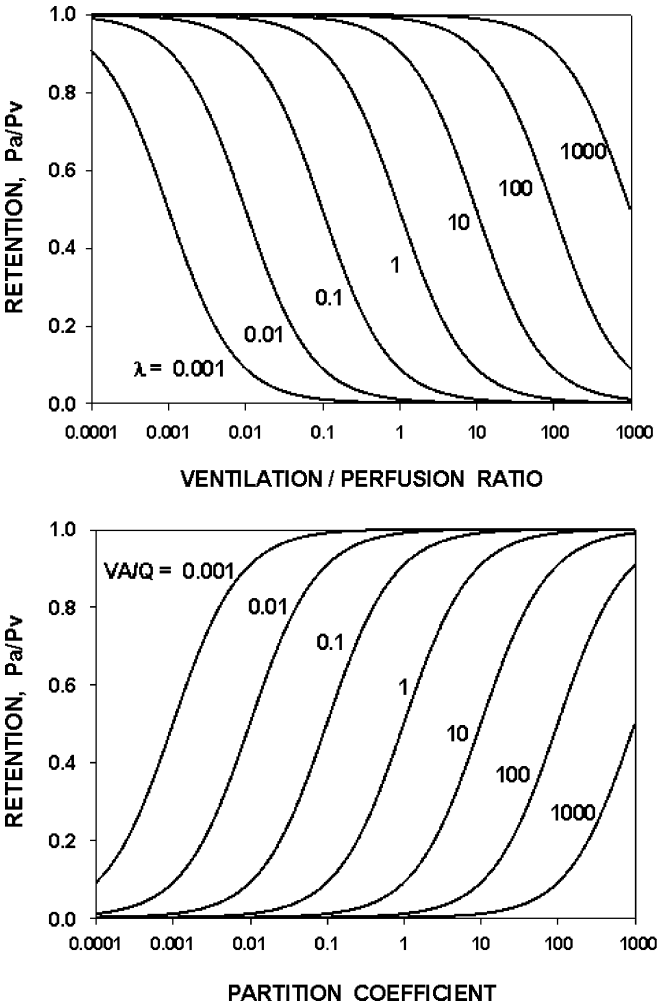

Fig. 1 *Upper panel:* Inert gas retention (as defined in, and computed from, Eq. 5) as a function of the ventilation/perfusion ratio ($\dot{V}A/\dot{Q}$). Each line reflects a gas of indicated partition coefficient, λ. While retention falls as $\dot{V}A/\dot{Q}$ increases, and is higher for more soluble gases at any given $\dot{V}A/\dot{Q}$ ratio, the key point is that a given gas is sensitive to $\dot{V}A/\dot{Q}$ in only a fairly narrow range (from $\dot{V}A/\dot{Q} = 10\times$ lower to $10\times$ higher than λ for that gas). *Lower panel:* Identical data as for upper panel, but now plotting retention against λ (defining the retention/solubility relationship) for lung regions of indicated $\dot{V}A/\dot{Q}$. The major point is that a gas of given λ is most sensitive to $\dot{V}A/\dot{Q}$ ratios from $10\times$ lower to $10\times$ higher than its λ

distribution of $\dot{V}A/\dot{Q}$ ratios. The mathematics underlying this relationship is somewhat complex and cannot be laid out in such a brief review as this, but has been presented on several occasions [5, 16–18]. It entails searching for the distribution of blood flow and ventilation that best fits, according to least-squares principles, the measured set of retentions of the six gases. It is conceptually similar to a simple two-variable linear regression between a set of two variables, X and Y, where the slope and intercept of a straight line are found that best fit the paired (X,Y) data by minimizing the sum of squares between the

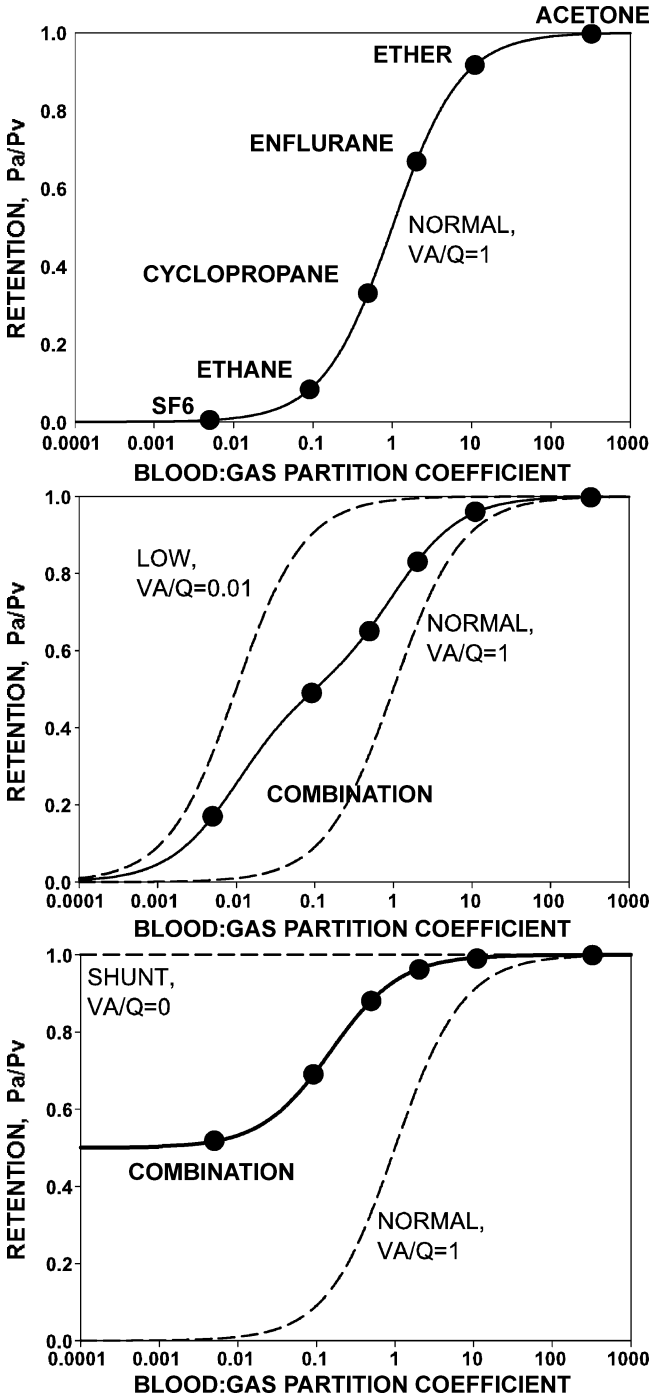

Fig. 2 Three examples of retention/solubility relationships. *Top panel:* Retention values expected in a normal lung, indicating the six inert gases commonly used in MIGET. Importantly, the six gases are chosen to sample the full extent of the curve. *Middle panel:* Retention/solubility curve in a lung with equally perfused regions of both normal and greatly reduced $\dot{V}A/\dot{Q}$ ratios. The shape and position are grossly different from the normal lung. *Bottom panel:* Retention/solubility curve in a lung with equally perfused regions of both normal and zero $\dot{V}A/\dot{Q}$ ratios. Note that when $\dot{V}A/\dot{Q} = 0$, this means an unventilated lung region, i.e., a shunt. The shape and position is grossly different from that in both the normal lung and the lung with low $\dot{V}A/\dot{Q}$ regions

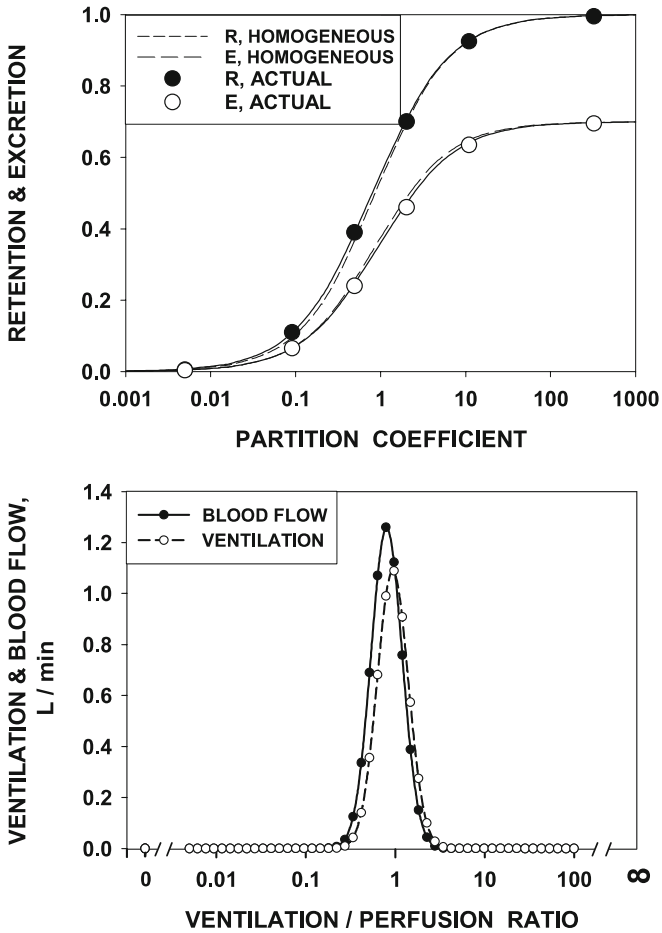

Fig. 3 Retention (and excretion)/solubility curves for a normal lung (*upper panel*) and corresponding distributions of ventilation and blood flow (*lower panel*). The range of $\dot{V}A/\dot{Q}$ in health is only about one decade ($\sim$0.3 to $\sim$3) as shown

actual Y values and those predicted from the regression equation.

Figure 2 is limited to arterial retention of the six gases, as would be measured from samples of arterial blood. It is also possible to measure the mixed expired concentrations of the same six gases at the same time, and we have called the ratio of mixed expired to mixed venous concentration excretion, E. Just as retention, R, reflects the pattern of allocation of blood flow to regions of different $\dot{V}A/\dot{Q}$ ratio, excretion reflects the pattern of distribution of ventilation to the same regions. In any given lung, the values of E and R for the lung as a whole must obey mass conservation, such that:

$$\dot{V}_{IG} = \dot{V}E \times E = \lambda \times \dot{Q}T \times [1 - R] \quad (7)$$

Here, $\dot{V}_{IG}$ is the volume of each inert gas eliminated per minute, $\dot{V}E$ is total minute ventilation and QT is total pulmonary blood flow (cardiac output). In addition, in any gas-exchange unit [i.e., a collection of alveoli in which PO_2 (and PCO_2) is uniform], local alveolar ventilation and

local blood flow define the $\dot{V}A/\dot{Q}$ ratio, or as written here:

$$\dot{V}A = \dot{Q} \times \dot{V}A/\dot{Q} \quad (8)$$

Equations 7 and 8 show that knowledge of retention implies knowledge of excretion and that knowing the distribution of blood flow, we know the distribution of ventilation. From a theoretical point of view, it means we could measure the $\dot{V}A/\dot{Q}$ distribution either from the excretions or the retentions – they are two reflections of the same function. However, in using MIGET, we measure both excretion and retention because together they provide two views of the distribution and improve its information content, much as a PA and lateral chest X-ray together are better than either alone, even though both are seeing the same lung.

Figures 3, 4 and 5 bring all of this together and show retentions, excretions, and the distributions of ventilation and blood flow for three representative lungs: a normal lung; a lung with 10% shunt; and a lung with 33% of the cardiac output perfusing very poorly ventilated alveoli, respectively. In each case, anatomic dead space (at 30% of tidal volume) is present. Such dead space serves to dilute expired inert gas concentrations, reducing excretion values for all gases by the same proportion (here, by 30%).

These figures take some getting used to, but the main point here is that different $\dot{V}A/\dot{Q}$ patterns underlie different retention/excretion patterns, such that by measuring the latter we can deduce the characteristics of the former.

What is MIGET's information content?

What MIGET obviously provides is the quantitative shape and position of the distributions of ventilation and blood

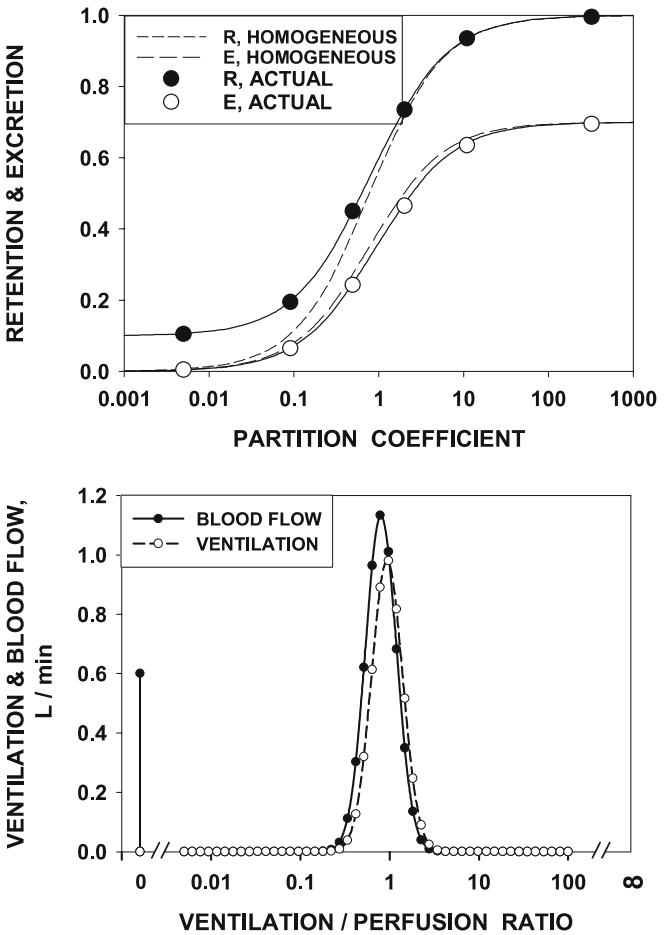

Fig. 4 Retention (and excretion)/solubility curves for a lung that contains a 10% shunt (in which $\dot{V}A/\dot{Q} = 0$) but is otherwise normal (*upper panel*) and corresponding distributions of ventilation and blood flow (*lower panel*). Shunt is shown by the *closed circle* at $\dot{V}A/\dot{Q} = 0$. Such distributions commonly reflect atelectasis, pneumonia, pulmonary edema, or pneumothorax

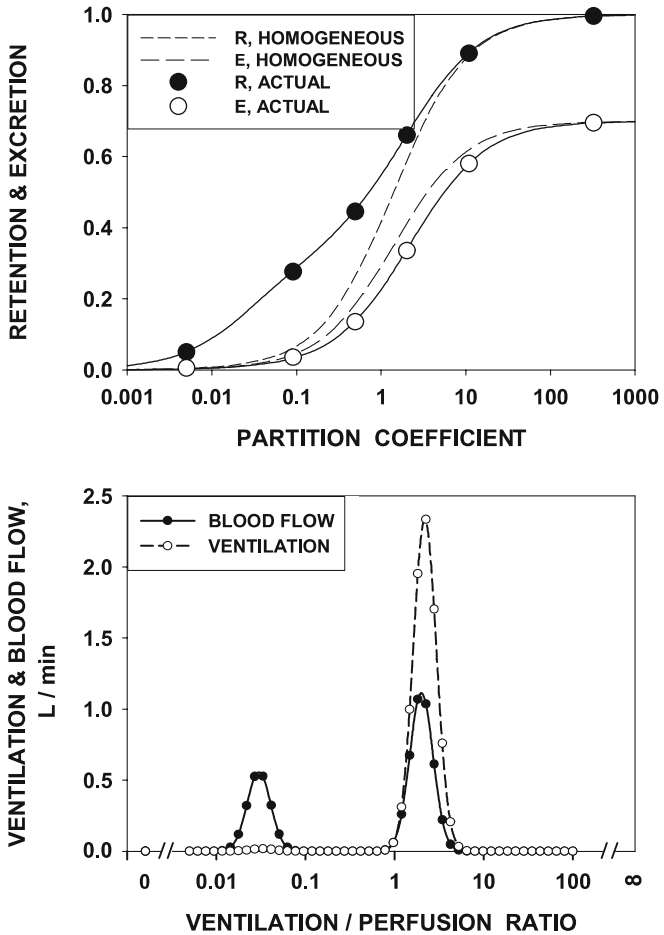

Fig. 5 *Upper panel:* Retention (and excretion)/solubility curves for a lung in which 33% of the blood flow perfuses units with a very low $\dot{V}A/\dot{Q}$ and the rest flows through units of normal $\dot{V}A/\dot{Q}$. *Lower panel:* Corresponding distributions of ventilation and blood flow. This pattern is common in chronic airway obstruction from asthma or COPD

flow with respect to $\dot{V}A/\dot{Q}$ ratio, as shown in Figs. 3–5. This pictorial representation can be reduced to a number of parameters that summarize the modality, position, dispersion, and (a)symmetry of the two curves. These parameters complement the visual image and are useful in allowing statistical comparison of distributions under different conditions. Importantly, as Figs. 4 and 5 show, a special strength of MIGET is that it distinguishes regions of low $\dot{V}A/\dot{Q}$ ratio from unventilated regions (shunt). Symmetrically, it also separates areas of high $\dot{V}A/\dot{Q}$ ratio from unperfused regions (which thus have infinitely high $\dot{V}A/\dot{Q}$ ratio).

MIGET allows additional insights into gas exchange, however. First, the presence of diffusion limitation for O_2 can be identified. Second, the role of so-called extrapulmonary factors on arterial PO_2 and PCO_2 can be quantified.

Diffusion limitation of O_2 exchange

All gases cross the pulmonary blood–gas barrier by diffusion. If the end-capillary partial pressure of any exchanging gas is not equal to its alveolar value in any homogeneous lung region, diffusion limitation is said to be present. For O_2, this may cause hypoxemia additional to that caused by any $\dot{V}A/\dot{Q}$ inequality that is present. The key point here is that inert gases reach equilibration (between capillary blood and alveolar gas) about 10 times faster than does O_2. Even when O_2 is diffusion-limited, inert gases are not. As a result, MIGET's inert gases faithfully indicate only $\dot{V}A/\dot{Q}$ inequality even when O_2 is diffusion-limited. Under such circumstances, the actual arterial PO_2 will be lower than that which MIGET would predict from $\dot{V}A/\dot{Q}$ inequality alone. Such a difference, due to diffusion limitation of O_2, is exploited within the MIGET software by computing the O_2 diffusing capacity that would have to exist to explain the additional hypoxemia [19].

Role of extrapulmonary factors in O_2 exchange

Arterial hypoxemia is classically considered due to one or more of four phenomena: $\dot{V}A/\dot{Q}$ inequality, shunt, diffusion limitation, and hypoventilation [1]. What is less well appreciated is that so-called extrapulmonary factors play a modulating role, affecting the level of hypoxemia produced by the above four factors. For example, if cardiac output suddenly falls in a patient with $\dot{V}A/\dot{Q}$ inequality, so too will arterial PO_2 because of the concomitant reduction in pulmonary arterial PO_2. MIGET software allows the user to separate out the quantitative effects of such changes in extrapulmonary variables. The extrapulmonary variables that can play a role are: FIO_2, metabolic rate ($\dot{V}O_2$), total alveolar ventilation, cardiac output, Hb concentration and P_{50}, acid/base status, and body temperature [20]. Each forms a specific input to the MIGET software such that desired changes in each can be read in and the consequences for arterial PO_2 assessed.

What are MIGET's limitations?

MIGET can only approximate the true distribution of $\dot{V}A/\dot{Q}$ ratios in the lung. We estimate that the human lung consists of about 100,000 individual gas exchange units (in essence, the acini) [21]. Thus, it is theoretically possible that 100,000 different $\dot{V}A/\dot{Q}$ ratios could exist, and using just six gases it would be impossible to identify them individually – it would take 100,000 gases! This is more of a theoretical than a practical concern, however, because just as with any distributed biological variable, by the time you have 100,000 units the ensuing distribution is highly likely to be smooth and therefore basically definable by a small number of measurements. The other major limitation is that caused by random experimental error. We use a smoothing algorithm [5] to control error effects. In other words, we enforce a measure of smoothing just sufficient to stabilize results when measurements are repeated (i.e., when sequential distributions would vary only due to random error). What this does is limit the resolution of MIGET—it is not possible to accurately recover a distribution that is very narrow. In numbers, any distribution whose actual dispersion is < 0.3 cannot be identified as such and will likely be depicted as having a dispersion at that limit. (This unit of dispersion is called "LOG SD" and is a dimensionless number that is the second moment (on a log scale) of the distribution about its mean). Normal subjects usually show log SD values of 0.4–0.6; moderate disease is reflected by log SD in the range of 1.0; and severe disease such as acute lung injury and ARDS would show values of 1.5–2.5. Again, this limitation is more theoretical than practical as normal subjects rarely show log SD values at the lower limit of 0.3. Finally, it needs to be mentioned that while the distributions recovered by MIGET describe the total functional abnormality of the lung, there is no regional anatomical information available, just as is the case with the classical indices of gas exchange – venous admixture, physiological dead space and the alveolar–arterial PO_2 difference.

Implementation of the MIGET

Implementing MIGET is relatively straightforward:

1. The six gases (Fig. 2) are dissolved in a sterile bag of saline or dextrose by bubbling gas (SF6, ethane, cyclopropane) or injecting liquid (enflurane, ether, acetone) into that bag in a sterile manner.
2. This sterile solution is infused into any peripheral vein at a rate in ml/min equal to about 1/4 of the minute

ventilation expressed in l/min. Thus, at rest the rate is about 2–3 ml/min. This rate of infusion produces concentrations of each gas in the ppm range or lower. At rest, the infusion should run about 20 min before samples are collected to allow development of steady-state inert gas exchange. During exercise, a steady state is reached far more quickly, and by the time O_2 uptake itself is stable, so too is inert gas exchange.

3. When desired, samples are then collected: about 7–8 ml each of systemic and pulmonary arterial blood (heparinized) and 20 ml of mixed expired gas, all in gas-tight, glass syringes. Samples for conventional blood gases (PO_2, PCO_2, pH, O_2 saturation, [Hb]) are taken simultaneously. We almost always take duplicate samples for both conventional and inert gases to both estimate and reduce error variance. Note that should pulmonary arterial blood not be available, it is just as good to calculate the mixed venous inert gas levels. However, this requires an estimate or measurement of cardiac output so that the Fick principle can be used with measured arterial and expired inert gas values.
4. The inert gas concentrations are measured by gas chromatography. Details can be found elsewhere [3, 22]. In brief, SF6 is measured by ECD (electron capture detector) while the other five gases are measured by FID (flame ionization detector). Stainless-steel (1/8th in., 6–12 ft long) columns packed with Poropak-T 80/100 mesh are used to separate the gases, which are eluted in a total of 4–5 min isothermally at about 150°C at a carrier flow rate (FID: helium; ECD: N_2) of around 30 ml/min. A constant-volume (1–2 ml) gas sample valve is used to introduce samples into the column. Mixed expired gas from the subject is directly injected into the chromatograph, but inert gases in blood samples must first be extracted by equilibrating the blood sample with N_2 gas in a closed syringe [3], and then introducing that gas to the chromatograph. Through principles of mass conservation, the original blood concentrations (prior to N_2 equilibration) can then be calculated if the partition coefficients of the gases and the volumes of blood and gas in the syringe are measured. It is recommended that the partition coefficients of all six gases be measured in each subject. This is done by (a) equilibrating a sample of the inert gases between blood and N_2 in a closed syringe, (b) measuring their levels in that N_2, (c) repeating the equilibration process with a fresh sample of N_2, and (d) measuring the new, equilibrated, inert gas levels in the N_2. The ratio of the inert gas concentrations from the two successive equilibrations reflects, and is thus used to calculate, the partition coefficient [3]. While these measurements by chromatography are not difficult, they are undeniably painstaking and must be done with great care and accuracy.
5. The inert gas concentrations and partition coefficients together with ancillary data (arterial/mixed venous blood gases, ventilation, cardiac output, inspired gas, acid/base status, and temperature conditions) are then read into the MIGET software. This software consists of two programs that are run in sequence. The first program simply takes all of the input data, computes the retention and excretion values for the sample, and creates an input data file for the second program, which reads those data and performs the least-squares analysis to come up with the $\dot{V}A/\dot{Q}$ distributions and their associated summary parameters mentioned above. It also computes the arterial PO_2 and PCO_2 expected to result from the $\dot{V}A/\dot{Q}$ inequality estimated from the inert gases, and, if requested, will compute the O_2 diffusing capacity when measured arterial PO_2 is less than that estimated from $\dot{V}A/\dot{Q}$ inequality. The two programs could easily be merged into one, but great value is seen in looking at the data produced by the first program for obvious problems before submitting them to the second program.

Conclusions: what does the future hold for MIGET?

MIGET was initially developed in the early 1970s. It remains in use in a small number of centers around the world, but the flurry of research in its first 20 years has subsided as many of the key questions it was able to shed light on have been answered. It has never evolved from a research tool to a clinical test for two reasons: First, because of its operational complexity. However, some attempts are currently under way to simplify the method and make it usable by the non-expert. Second, it provides more information than we can currently use clinically in patient management and therefore is difficult to justify.

That said, there is one key domain in which MIGET has not yet been rigorously evaluated as a clinical monitoring tool: the intensive care unit. In this setting, patients have often rapidly evolving lung disease, and extrapulmonary factors such as ventilation, FIO_2, cardiac output, hemoglobin concentration, acid/base status, and body temperature can all change quickly. We all have experiences with, or know of, patients with pre-existing heart and lung disease undergoing unrelated surgery and having a difficult recovery. Post-operative atelectasis and/or lung infection causing a shunt and low $\dot{V}A/\dot{Q}$ regions; use of PEEP causing high $\dot{V}A/\dot{Q}$ regions; post-operative bleeding reducing hemoglobin concentration; worsening cardiac function reducing cardiac output; fever; and the need to elevate and frequently change FIO_2 are all common problems in this situation, and MIGET has the capability of separating and quantifying the effects on arterial PO_2 of every one of these phenomena. Separating what is evolving lung disease from the effects of changes in extrapulmonary variables could have great clinical value, yet this is difficult to do using simpler, conventional tools. It would be useful to design and implement a clinical

trial of MIGET as an evaluative tool guiding therapy in the ICU to answer the question of whether the large amount of information MIGET provides would lead to more rational therapy and thereby improve morbidity or mortality. While this would require substantial effort, it would help to answer the question of whether such detailed physiological information was of clinical value in critically ill patients who have multiple abnormalities with complex interactions that together determine arterial oxygenation.

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