Ventilation-Perfusion Relationships and Gas Exchange

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Introduction

The most common cause of hypoxemia at sea level is mismatched ventilation and perfusion. Common clinical problems such as pneumonia, pulmonary embolism, obstructive lung disease and many other diseases produce regional hypoventilation as compared to perfusion, resulting in incompletely oxygenated blood leaving the pulmonary capillary in hypoventilated regions and returning to the left heart.

The relationship of ventilation to perfusion or Va/Qc refers to the turnover of air in the alveoli (VA) compared to the flow of blood through pulmonary capillaries (Qc). A VA/Qc of one would consist of one L of air ventilating the alveoli and one L of blood flowing through the pulmonary capillary bed during the same period of time.

The measurement of overall VA/Qc in the human subject requires measurement of alveolar ventilation by the collection of expired air and measurement of arterial pCO2 as well as measurement of cardiac output. This relationship is usually around 0.8. When total alveolar ventilation is inadequate for the needs of the patient, then hypoventilation causes hypoxemia and hypercapnia. In the clinical states mentioned, the authors are interested in regional mismatch of ventilation and perfusion usually referred to as V/Q mismatch. Regional V/Q mismatch or regional hypoventilation compared to perfusion produces hypoxemia and low or normal pCO2; in some instances it may also produce hypercapnia.

Until the development of radioactive gas techniques for measurement of regional ventilation and perfusion by Knipping in 1953,3, V/Q ratios for the entire lung could be obtained but no methods were available to estimate these relationships regionally. Since that time, extensive research has been carried out by many investigators who have used these techniques both for clinical description and for better understanding of basic physiology of the lung. West and others5 have described a V/Q mismatch in the normal upright subject where V/Q is higher at the apex than at the base. The net effect of this mismatch is not sufficient to alter arterial pO2 significantly, however. These studies do, however, point out the variation in regional perfusion dependent on body position and change in ventilation required to maintain adequate matching of ventilation to perfusion. Such matching avoids overventilation of portions of the lung that are poorly perfused. Recent evidence has been obtained showing that measurements of ventilation and perfusion at resting lung volumes using clearance of perfused 133Xenon during normal breathing shows V/Q to be more evenly matched than was observed previously.2 The practical clinical application of these methods
in the diseased lung, however, brings up some problems that are not of great importance in the normal lung.

In order to correct for volume variation as well as variation in absorption of radioactive gas contained in a spirometer, this index is a ratio of what is actually deposited in a given region, by perfusion or inhalation, to what should have been deposited if all the radioactivity had been distributed equally in all alveoli. The index as defined by Ball et al. is

\[
\text{Ventilation Index} = \frac{V_r}{V_t} = \frac{E_r}{E_t}
\]

**Figure 1.** This shows a 40 X 40 matrix using a digital scale of 0-99 with the highest numbers representing the highest counting rates. The matrix illustrates the distribution of perfusion after an intravenous injection of $^{133}$Xenon during a breathhold at Functional Residual Capacity.
Perfusion Index =
\[
\frac{\text{Perfusion Regional Activity}}{\text{Perfusion Total Lung Activity}} \quad \frac{\text{Steady State Regional Activity}}{\text{Steady State Total Lung Activity}}
\]
\[
= \frac{Q_R/Q_T}{E_R/E_T}
\]

This is not a difficult achievement in the normal lung where all alveoli are presumably evenly ventilated. In the diseased lung, however, equilibrium may be difficult if not impossible to obtain and matching ventilation and perfusion indices impossible to calculate.

The use of radioactive techniques of measuring perfusion and ventilation promises to offer important contributions to the measurement of regional lung function in the normal. In the abnormal subject, measurement of perfusion and clearance by injection of $^{133}$Xenon in saline and its clearance from the alveoli by normal breathing (ventilation) offers an approach to the quantitation of regional lung function in the diseased lung.

**Methods**

Perfusion of the lung can be measured with intravenously injected macroaggregated human serum albumin labeled either with $^{131}$Iodine or $^{99m}$Technetium or with $^{133}$Xenon injected intravenously in solution. In the first instance, the intensity of radioactivity is related to the tagged albumin that has been strained out in the pulmonary capillary bed. In the second, Xenon, a highly insoluble gas, is 95 percent cleared in its passage through air containing alveoli. The advantages of labeled albumin are that it identifies sites that are perfused but contain no alveolar air and thus can identify perfusion of totally non-air containing alveoli, such as in pneumonia. The radioactivity remains in the pulmonary capillaries for a number of hours, permitting study of the patient in several different projections such as lateral, oblique, etc. This advantage also represents a potential disadvantage in that the study cannot be repeated in different positions and at different breathholds. The advantage of the Xenon is that it behaves as a gas and can be used to measure not only perfusion but clearance (or ventilation) from the alveolus. When labeled albumin is used, ventilation must be measured by the inhalation of tagged gas
from a spirometer. It is impossible, however, to be sure that gas inhaled from a spirometer and measured outside the chest by a radioactive detector is in conducting airways or alveoli. For this reason, the measurement of clearance would seem to offer a more reliable index of ventilation in the abnormal lung.

Radioactivity can be measured either with multiple probes or with a gamma camera which permits visualization of most of the chest simultaneously. The use of the multi-detector method requires the calculation of indices of ventilation and perfusion by the method of Ball\textsuperscript{1} and samples larger regions, from the point of view of resolution, than the gamma camera. When the camera is used, values for ventilation and perfusion can be normalized and regional ratios easily derived.

Newer instrumentation permits the recording of digital information from multiple sites on a memory device at time intervals so that dynamic studies of clearance can be done. Such data can be processed by computer and clearance curves calculated for multiple sites.\textsuperscript{4} In our studies, the slope of clearance of the first 60 percent of the amount cleared is calculated by the method of least squares. Knowing the perfusion of a site and the rate of clearance or ventilation of that site, it is possible to estimate gas exchange or, by multiplying

\textbf{Figure 3.} The left hand models illustrate perfusion, clearance and gas exchange at Functional Residual Capacity; the right hand models the same patient studied at Total Lung Capacity. Note the change in perfusion of the left lung between two different breathholds. Clearance is essentially non-existent from the left lung when at TLC and gas exchange is therefore absent in the left lung. This patient had a carcinoma of the left hilum.

\textbf{Figure 4.} A patient with biopsy proven basilar interstitial fibrosis. Note the difference in perfusion of the bases between upright and supine, presumably due to the interstitial disease.
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perfusion × clearance = regional gas exchange. Sites with good perfusion and slow clearance are less capable of gas exchange than sites of good perfusion and rapid clearance. From a single injection study done at resting lung volumes followed by quiet breathing, one can calculate regional perfusion, regional clearance (ventilation), and regional gas exchange. In our studies, a matrix $40 \times 40$ (figure 1) has been used providing 1,600 sites where these values can be recorded. Because it is difficult to look at a mass of numbers, a computer drawn three dimensional model (figure 2) has been used where the Z axis represents the amount of regional perfusion, slope of the washout curve or amount of regional gas exchange.

Discussion

When radioactive techniques are used to measure regional function it may be of value to measure perfusion and ventilation at resting lung volumes and at total lung capacity as well as supine and erect. The effect of lung volume at the time of injection is illustrated in figure 3 where the left lung was essentially nonperfused at resting lung volumes and showed no clearance and no gas exchange. At maximum inspiration (Total Lung Capacity), the left lung became perfused but did not clear the radioactivity during quiet breathing. Gas exchange in that lung continued to be negligible.

The effect of body position is illustrated in another patient who had biopsy proven interstitial fibrosis. In the upright position perfusion of the bases was fairly normal (figure 4) whereas perfusion decreased to almost nothing at the base when the patient was supine.

The difference between ventilation measured by inhalation and ventilation measured by clearance is illustrated in figure 5. This patient had cystic fibrosis, and it is readily apparent that regions that appear to be well ventilated when Xenon was inhaled from a spirometer failed to show normal clearance in the post injection study. This suggests that there may have been
small airways obstruction that was not readily identified.

Another subject with acute asthma was seen to perfuse the upper lungs better than would be expected in the upright position (figure 6). Ventilation and clearance of the poorly perfused areas were seen to be markedly reduced. This is an illustration of reflex homeostasis in which perfusion and ventilation tend to match one another in the pathological state. A repeat study during an interval when the patient was relatively asymptomatic showed a more normal distribution of both ventilation and perfusion.

Another patient is illustrated in figure 7 with biopsy proven sarcoid. The chest X-ray (figure 8) shows large nodular infiltrates in both lung fields, and the Xenon scan shows regions of decreased perfusion, ventilation, and gas exchange similar to the infiltrates seen in the X-ray. Pulmonary function studies during the early management of this patient showed restrictive disease and severe gas exchange problems manifested by high A-a gradients. Following treatment, the X-ray and function studies returned to normal, but regions of decreased gas exchange could still be identified on the scan.

Summary

The use of radioisotope techniques to measure regional perfusion and ventilation represents a significant step forward in the identification of regional alteration of func-
tion. The use of macroaggregated albumin has the advantages of identifying the capillary bed even though it flows through non-aerated alveoli and offers the advantage of scanning in a number of different positions after one injection.

Xenon, when injected and used to measure perfusion and clearance, has the advantage that it behaves as a gas and measures radioactivity in perfused air containing alveoli. When the gas is cleared from alveoli, there is no question that the radioactivity in the lung may be in conducting airways rather than alveoli. Ventilation measured in this manner is, therefore, alveolar ventilation. Although it does not offer the advantage of multipositional scans after a single injection, it does make possible various positions and breathholds at the time of injection.

The calculation of indices of perfusion and ventilation requires the evaluation of lung size after breathing to equilibrium. In the diseased lung, it may be impossible to achieve equilibrium because of the radiation exposure required to ventilate slow spaces in the lung, or it may be that some areas of the lung are totally unidentifiable owing to total airway obstruction or complete filling of the alveoli with fluid or exudate. V/Q ratios, therefore, seem to have many practical disadvantages so far as routine clinical application is concerned since, even with the camera, ventilation is not assuredly in the alveoli.

The primary use of regional studies of ventilation-perfusion and gas exchange in clinical medicine is to evaluate regional disturbance of gas exchange for one of three purposes: (1) early detection of disease, (2) preoperative evaluation to avoid resection of important gas exchanging portions of the lung, and (3) better understanding of disturbed regional physiology in the study and evaluation of a disease process and/or its treatment. It is felt that the techniques described, using $^{133}$Xenon to measure regional perfusion, clearance (ventilation) and gas exchange offer the most direct and practical approach to the problem. The complicated techniques involved do present a problem for even the medium sized institution. However, the ready availability of much of the equipment in isotope laboratories of many hospitals and the increased access to computers, either in the hospital or on a long distance time sharing plan, promises to make these approaches more
feasible both technically and economically in the near future.

References


Figure 8. X-ray of subject in figure 7 showing nodular sarcoid confirmed by biopsy and subsequent course.