Enlarged Pulmonary Arteriovenous Vessels in COPD*

Another Possible Mechanism of Hypoxemia

Warren C. Miller, M.D., F.C.C.P.; John G. Heard, M.D.; and Kenneth M. Unger, M.D., F.C.C.P.

Among 27 patients with moderate-to-severe chronic obstructive lung disease, 22 had anatomic intrapulmonary shunting greater than that seen in normal subjects. The shunted blood passed through enlarged pulmonary vessels, as demonstrated with particles 10-90 microns in diameter. The shunt magnitude was correlated with the decrement in lung diffusing capacity. It did not correlate well with pulmonary mechanical abnormalities such as air flows and volumes or resting blood gas data. Nevertheless, shunting through enlarged pulmonary vessels may play a role in the hypoxemia seen in COPD patients, especially at exercise.

Pulmonary arteriovenous vascular channels larger than typical pulmonary capillaries have been shown to exist in patients with hepatic cirrhosis. These enlarged vessels have been demonstrated by quantitative radionuclide techniques. It has been difficult or impossible to otherwise demonstrate them during life or in post-mortem studies. These apparently dilated vessels are believed to function as shunts and thereby contribute to the heretofore enigmatic hypoxemia of cirrhosis.

The finding of such a mechanism of hypoxemia in cirrhosis patients raises the question of whether such shunts develop in other disease states. The hypoxemia of cirrhosis is often characterized by exercise-aggravation. Exercise-aggravation of hypoxemia is also typical of patients with chronic obstructive pulmonary disease (COPD). We studied patients with COPD for the presence of such dilated gas-exchanging vessels.

**Material and Methods**

Macroaggregated albumin particles tagged with 3mCi (calibrated on a Capintec model CRC-5 Dosimeter) of technetium 99m (Mallinckrodt) were injected intravenously in the supine position. The radioactivity distributed to brain, kidneys and lungs was measured with a scintillation camera (General Electric 400AT with star computer). Acquisition of counts was begun dorsally 10 minutes after injection with sequential 2-minute intervals each for lungs, kidneys and brain so that counting was completed 16 minutes after injection. The particles were 10-90 microns in diameter and would therefore lodge in normal pulmonary capillaries of about 8 microns. Any particles traversing the lungs to the systemic circulation would necessarily have to have passed through vessels larger than the 10-90 micron particle size. The amount of radioactivity in the distribution of the systemic circulation is calculated assuming that at rest 32 percent of the cardiac output goes to brain and kidneys. The fractional amount of blood shunted is therefore the radioactivity in the systemic circulation divided by the sum of that radioactivity and that remaining in the lungs. In hyperinflated COPD patients, special care is required in masking the kidneys and lower lung field in order to obtain accurate counts. If the COPD patients were on chronic oxygen or bronchodilator therapy, this was continued during injection and scanning.

Twenty-seven patients with COPD and FEV1 less than 50 percent of predicted were selected for study during the final phases of a period of hospitalization when they were clinically stable. They were free of other major medical problems. Informed consent was obtained. Other than perfusion lung scanning, no additional testing was required, and hence, the data from pulmonary function tests, blood gas determinations, and the like was limited to that requested by the attending physicians for clinical indications. Pulmonary function tests were performed on a Gould 5004 pulmonary function testing apparatus using the single breath carbon monoxide technique for the measurement of lung diffusion capacity. Arterial blood gases were drawn at different times and different positions and measured on conventional electrode (Instrumentation Laboratories).

The first ten patients studied were scanned at the same setting with the same batch of radionuclide as ten control subjects. The control subjects were hospital in-patients undergoing lung scanning for such indications as hemoptysis, chest pain of unknown etiology, etc. Their ventilation and perfusion scans and chest x-ray film findings appeared normal, but only five had pulmonary testing to exclude lung disease and four were smokers. (The lung scan itself may be a fairly sensitive measure of airway disease.) They were therefore control subjects, but not necessarily completely normal. The control subjects were studied to provide a basis for comparison and to ensure against a batch of radionuclide which might have a significant amount of untagged technetium. After the first ten paired studies, label activity was tested using a chromatograph (Atomic Products Corp) which demonstrated less than 1 percent untagged isotope.

Statistical analysis used Students' t-test for unpaired variables and Pearson correlation. Results are reported as mean ± 1 standard deviation.

**Results**

The age of chronic obstructive pulmonary disease patients (63 ± 9 years) was not significantly different from control subjects (58 ± 8 years). The shunt in the patients (11 ± 9 percent) was significantly (p < .05) higher than in control subjects (7 ± 3 percent) (Fig 1). Among the chronic obstructive pulmonary disease patients, the magnitude of the shunt was not well

---

*From Humana Pulmonary Center and Department of Radiology, Clear Lake Hospital, Webster, Texas.

Reprint requests: Dr. Miller, PO Box 37696, Webster, Texas 77598

704

Enlarged Pulmonary Arteriovenous Vessels in COPD (Miller, Heard, Unger)
There were a number of patients with large congenital shunts, although this is a well-recognized phenomenon. The presence of cyanosis and the degree of desaturation in these patients were not as great as those demonstrated in similar patients with congenitally large foramen ovale. The patients with the congenital foramen ovale in this study may have had a right to left shunt proportionally greater than that demonstrated in our control subjects. These patients were also usually studied in the absence of shunting from other causes, such as lung disease, whereas the control subjects were studied from the standpoint of strictly cardiac shunting.

There was a significant (p<.02) correlation between magnitude of shunt and the loss of diffusion capacity (Fig 2).

DISCUSSION

These data demonstrate that COPD patients have enlarged pulmonary vessels carrying proportionally larger blood flows than control hospital in-patients or reported normal subjects. Our control subjects demonstrated slightly higher values than the less than 7 percent reported for normal control subjects in another series.8 This may relate to the time from injection of isotope to beginning of count acquisition, since the measured magnitude of shunt increases with increasing time.9 The time of counting was not reported in the earlier series, but if it was less than the 10-minute interval we used, it might account for the observations. Our patients and control subjects were studied in a rigorously identical fashion.

Quantitative radionuclide techniques have been used to demonstrate shunting in hepatic cirrhosis,4 congenital heart disease,10 and patent foramen ovale with shunting due to pulmonary hypertension.12 This phenomenon of patent foramen ovale with shunting due to pulmonary hypertension may occur in COPD patients,13 but that seems an unlikely cause of shunting in most of our patients since many did not have clinical signs of pulmonary hypertension. Also, only about 20 percent of adults have a congenitally patent foramen ovale, whereas the shunting phenomenon occurred in 22 of 27 [81 percent] of our patients.

The degree of such shunting did not seem well correlated with conventional measures of mechanical lung damage, such as airflow obstruction or hyperinflation, but did correlate with the loss of diffusing capacity. The diffusing capacity is thought by many to be the premier test of the status of the pulmonary vasculature.

Since the great concern with shunting through large pulmonary vessels is its possible contribution to the genesis of hypoxia in COPD patients, it was disappointing that the magnitude of shunt did not correlate with either Po2 or alveolar-arterial oxygen gradient; however, this lack of correlation need not deny such a relationship. Lack of correlation could be due to technical factors such as blood gases drawn at different times and in different positions compared to injection of isotope. Alternatively, the contribution to hypoxia may only be manifest with increased blood flow and shortened pulmonary vascular transient time, such as

![Figure 1. Pulmonary shunting in COPD patients and control subjects.](http://publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21439/)

![Figure 2. Relationship between lung diffusion capacity (DL) and intrapulmonary shunting in COPD patients.](http://publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21439/)
at exercise. One can envision a series of dilated low resistance conduits which nonetheless participate in gas exchange. At rest, flow may be sufficiently slow for radial diffusion of oxygen in these large vessels to come to equilibrium. Resting hypoxia in COPD may be due to conventionally understood ventilation-perfusion imbalance. Exercise aggravation of hypoxia may be the consequence of increased flow so that the transient time is too short for oxygen equilibrium to be achieved across the relatively long distance from the periphery to the center of these large pulmonary vessels.

Finally, it is not clear how these shunt vessels evolve. Because they were first demonstrated in hepatic disease, it has been assumed that these were preexisting vessels which became widely patent because of some humoral influence as a consequence of the liver disease. It is even possible that in COPD patients, hepatic congestion from cor pulmonale may be involved. If the shunts are derived from humoral changes, the question arises if they are amenable to pharmacologic manipulation. In this regard, it is interesting to note that some of the newer vasoactive drugs have been reported to improve "ventilation-perfusion" relationships in COPD patients. Alternatively, these shunts may be an entirely passive phenomenon. They may simply be highly compliant vessels which are easily distensible when pressured by vasoconstriction or destruction of the surrounding vasculature. The finding of a higher percentage of such shunts in our patients with presumably less vasculature (because of lower diffusing capacity) lends some credence to the passive theory.

Regardless of etiology, relatively large pulmonary shunt vessels can be demonstrated in many COPD patients and probably play a role in part in the pathogenesis of hypoxemia in this disease.

ACKNOWLEDGMENTS: Ms. Maggie Griffin prepared the manuscript, Ms. Velinda Stevens performed the statistical analysis, and Ms. Sherry Small and Margie Powell performed the technical studies.

REFERENCES