Pulmonary Disease Reviews

Volume 3

Edited by

Roger C. Bone, M.D.

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Preface

The purpose of *Pulmonary Disease Reviews* is to provide access to the latest advances that impact on clinicians and academicians concerned with pulmonary disease and critical care medicine. Expanded sections on basic mechanisms of lung injury, exercise physiology, sleep, respiratory control, and critical care medicine are displayed in this volume to illustrate recent trends. The individual chapter authors are without exception experts in the fields they review. Each is active in clinical or basic investigation of his or her subject. Their chore is to highlight the best, most provocative, or most quoted literature pertaining to their subject in the preceding year. They abstract the article, making certain that the original data are presented in enough depth to allow the reader to decide independently on the conclusions reached by the article author or chapter author. The chapter author then speculates on the clinical relevance and new research ideas raised by the reviewed papers. Hopefully, each chapter will serve as a "journal club" with an expert in the area being discussed conducting the session.

Pulmonary disease is a challenging and exciting, but demanding, subspecialty that requires the complete internist to provide optimal medical care. Hopefully, this volume will make the difficult task of staying current a little easier.

Roger C. Bone, M.D.

Contents

1
Abnormalities of Oxygen Transfer

David R. Dantzker

GAS EXCHANGE

The task of reviewing the recent literature in an area as encompassing as gas exchange allows great latitude in the selection of papers. As in past years, I have tried to select publications which deal with oxygen and carbon dioxide transfer both in the lungs and at the level of the tissues. In addition, I have tried to use as a criterion for selection the applicability of the data to clinical problems.

THE LUNG

The inaccessability of the pulmonary vascular bed to direct monitoring and the lack of good indirect means of evaluating pulmonary artery pressure makes disorders of these vessels difficult to diagnose and compounds the problem of developing proper approaches to therapy. The search for non-invasive markers of pulmonary vascular disease continues, but thus far, all have proven too insensitive to be of any value clinically. This paper evaluates the measurement of dead space as a marker of pulmonary vascular disease.

LACK OF SENSITIVITY OF MEASUREMENTS OF V_D/V_T AT REST AND DURING EXERCISE IN DETECTION OF HEMODYNAMICALLY SIGNIFICANT PULMONARY VASCULAR ABNORMALITIES IN COLLAGEN VASCULAR DISEASE

Z. Mohsenifar, D.P. Tashkin, S.E. Levy, R.D. Bjerke, P.J. Clements, and D. Furst (Department of Medicine, UCLA School of Medicine, University of California at Los Angeles, Los Angeles, California)

Am Rev Resp Dis 123:508, 1981

Wasted ventilation fraction (V_D/V_T) normally declines substantially during exercise in persons without lung disease. Failure of V_D/V_T to decrease during exercise has been reported to be one of the earliest abnormalities in patients with dyspnea caused by pulmonary

vaso-occlusive disease, suggesting that measurements of V_D/V_T at rest and during exercise are useful in the diagnosis of pulmonary vascular disorders. The authors studied pulmonary hemodynamic and V_D/V_T responses to exercise in 11 patients in the supine position with suspected pulmonary vascular involvement caused by progressive systemic sclerosis, systemic lupus erythemotosus, or recurrent pulmonary emboli, 10 of whom had dyspnea at rest and/or exertion. In contrast to previous reports of no change or an increase in V_D/V_T during exercise in patients with pulmonary vascular disease, they found V_D/V_T to decrease significantly during exercise in eight of nine patients in whom mean pulmonary artery pressures were abnormally elevated at rest and/or

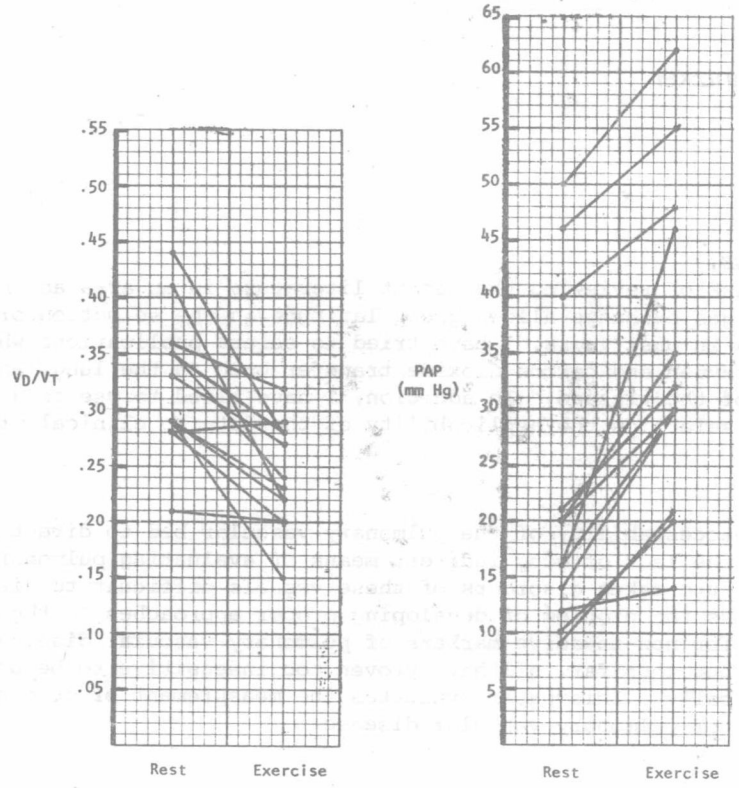

Figure 1. Shows wasted ventilation fraction measurements (V_D/V_T) and pulmonary artery pressure measurements (PAP) in 11 patients at rest and during exercise.

The findings suggest that normal responses of V_D/V_T to exercise do not exclude hemodynamically significant pulmonary vaso-occlusive disease.

COMMENTS

The authors demonstrate that the Bohr dead space (or V_D/V_T) cannot be counted on as an early indicator of pulmonary vascular abnormalities despite suggestions by prior investigators (Nadel

et al. Am J Med *44:16, 1968;* James et al. Br Med J *1:1089, 1965). Other studies also have failed to corroborate the sensitivity of this test. Reidel, for example* (Bull Europ Physiopath Resp *16:209, 1981) found that only 9% of his patients with proven vascular obstruction subsequent to pulmonary emboli failed to have a fall in* V_D/V_T *with exercise.*

The lack of sensitivity of the V_D/V_T *as a predictor of pulmonary vascular disease is not surprising when the underlying physiology is considered. The dead space, as determined from measurements of arterial and mixed expired* pCO_2 *represents contributions from two distinct lung compartments. The first consists of regions of the lung which are ventilated but not perfused. This includes the conducting airways or anatomical dead space, and alveoli whose blood flow has been occluded. The second compartment represents lung units whose alveolar* pCO_2 *is lower than the overall arterial* pCO_2*, i.e., units with a high* $\dot{V}_A/\dot{Q}$ *ratios. It has previously been demonstrated that patients with chronic obliterative pulmonary vascular disease may have normal* $\dot{V}_A/\dot{Q}$ *distributions despite widespread vascular occlusion* (Dantzker and Bower. J Clin Invest *64:1050-1055, 1979). Thus, a normal* V_D/V_T *at rest cannot rule out pulmonary vascular disease.*

Changes in the dead space with exercise are likely to result from the summation of a number of mechanisms. The absolute volume of the anatomic dead space will increase as tidal volume increases, but the ratio of the volume of the anatomic dead space to the tidal volume will fall. The ventilation of unperfused alveoli may increase with larger breaths as the ability of hypocapnic bronchoconstriction fails in its ability to minimize $\dot{V}_A/\dot{Q}$ *inequality. The contribution of high* $\dot{V}_A/\dot{Q}$ *units to the dead space may decrease or increase as exercise leads to either an improvement or further worsening of the degree of* $\dot{V}_A/\dot{Q}$ *inequality. In addition, because of the alinear relationship between arterial* pCO_2 *and the* $\dot{V}_A/\dot{Q}$ *ratio, an excessive increase in minute ventilation with no increase in* $\dot{V}_A/\dot{Q}$ *inequality can also increase the measured* V_D/V_T*. The ultimate effect of exercise on* V_D/V_T*, therefore, will depend on how the increased minute ventilation is partitioned among these various lung compartments.*

A voluminous amount of literature has been accumulated which demonstrates the lung's ability to maintain an optimal matching of blood flow and ventilation in the face of regional lung disorders. The response of the pulmonary vasculature to hypoxia has been well characterized and is thought to play a major conservative role. However, experimental studies have demonstrated that this reflex is easily interfered with by factors such as elevated left atrial pressure, anesthetic agents, and drugs with vasoactive potential. In addition, recent clinical studies have failed to demonstrate a significant role for hypoxic vasoconstriction in the optimization of ventilation-perfusion matching seen in asthma and pulmonary hypertension. The following article provides further evidence that hypoxic vasoconstriction may not always be depended on to maximize gas exchange.

PATHOPHYSIOLOGY OF GAS EXCHANGE AND PULMONARY PERFUSION IN PNEUMOCOCCAL LOBAR PNEUMONIA IN DOGS.

R.B. Light, S.N. Mink, and L.D.H. Wood (Sections of Respiratory and Infectious Diseases, Department of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada)

Respirat Environ Exercise Physiol 50:524, 1981

The authors utilized a model of lobar pneumonia achieved by placing an inoculum of Streptococcus pneumoniae type III into a left lower lobe bronchus of six dogs (group P), and in six other dogs (group C) a sterile inoculum was used. Measurements of shunt ($\dot{Q}s/\dot{Q}t$) and venous admixture ($\dot{Q}va/\dot{Q}t$) were made immediately before (day 1) and 48 hours after (day 3) inoculation. All dogs in group P had extensive lobar pneumonia confirmed radiologically and at autopsy, whereas group C had only small sterile lesions at the site of inoculation. In group P, mean $\dot{Q}s/\dot{Q}t$ and $\dot{Q}va/\dot{Q}t$ increased significantly to 0.15 and 0.21 respectively. Mean lobar $\dot{Q}s/\dot{Q}t$, calculated using blood samples from lobar veins at thoracotomy on day 3, was markedly increased in the pneumonia lobe (0.69) compared with the contralateral lower lobe (0.08), and alveolar ventilation of that lobe approached zero. Perfusion of the infected lobe determined by radioactive microspheres showed a variable and statistically nonsignificant decrease between control and infected states that was not affected by oxygen breathing. In group C there was no change between days 1 and 3 in gas exchange or in distribution of pulmonary perfusion. They concluded that hypoxemia in pneumonia was due to both increased shunt and venous admixture in the infected regions, and that local hypoxic vasoconstriction was in most instances ineffective in directing blood flow away from the consolidated lobe.

COMMENTS

This well-done study points out that lobar pneumonia can cause significant hypoxemia due to the persistence of blood flow through relatively or completely unventilated alveoli. The authors suggest that some factor related to bacterial growth may interfere with hypoxic vasoconstriction. They found a rough inverse relationship between active bacterial growth and the ability of the animal to decrease blood flow to the inflamed lobe (Figure 2).

This finding may in part explain the common clinical observation that the hypoxemia of pneumonia is greatest early in the disease even though parenchymal infiltration persists or may even worsen after the initiation of antibiotics.

*While hypoxic vasoconstriction may not always be of help in correcting abnormal gas exchange, Ramolina and his colleagues pointed out that we can utilize another well-known characteristic of the pulmonary circulation to improve the hypoxemia associated with localized lung disease (*Remolina C, Kahn A, Santiago T, and Edelman N. Positional hypoxemia in unilateral lung disease. N Engl J Med *304:523-525, 1981). In a short paper, they presented data which quantitated and re-emphasized a phenomenon we are all aware of: namely, that positioning a patient with unilateral lung disease in the lateral position with diseased lung up can lead to marked improvement in arterial oxygenation. For example,*

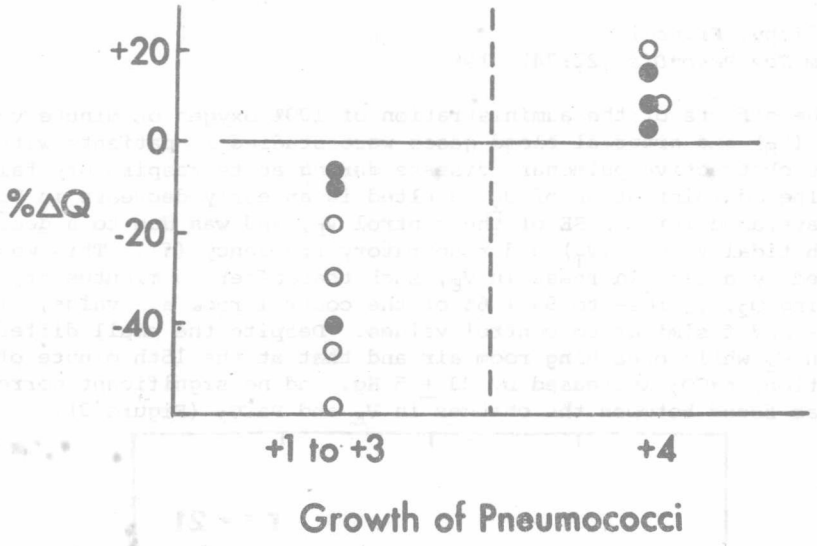

Figure 2. Effect of bacterial number of perfusion change in pneumonia. Ordinate: percentage change in LLL perfusion between days 1 and 3 (%ΔQ) in dogs with LLL pneumonia; abscissa: semiquantitative culture of cut surfaces of LLL on day 3. See text for explanation of culture grading and calculation of %ΔQ. Closed circles designate the present series, open circles an additional series (14). ($P < 0.01$, $\%\Delta Q_{LLL} + 4$ vs. $\%\Delta Q$ +1 to +3).

in one reported patient with right lower lobe consolidation, the arterial pO_2 went from 55 to 121 as the diseased lung went from the dependent to the superior position. While this observation may have some utility in therapy, it may be more important to recognize that in order to properly interpret arterial blood gases in these patients, the position the patient is in may be as important to note in the record as the inspired oxygen concentration.

It is well recognized that the administration of oxygen to patients with chronic obstructive lung disease may lead to an elevation of the arterial pCO_2. This is most pronounced in those patients who already demonstrated hypercapnia while breathing room air. The explanation usually given is that the removal of the hypoxic drive leaves these patients with little or no chemical impetus to ventilation. This next paper by Aubier and his associates, however, questions this simple explanation when applied to patients with acute exacerbations of chronic lung disease.

EFFECTS OF THE ADMINISTRATION OF O_2 ON VENTILATION AND BLOOD GASES IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE DURING ACUTE RESPIRATORY FAILURE

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