
To the Editor:

In presuming to comment on the recent article by K. B. Lake et al (Chest 1983; 83:138-39), I chose to consider the particular circumstances of asthmatic patients stricken with pneumonia and respiratory failure, and the pronounced effects of corticosteroids on T-cell function. Dr. Gilmore and collaborators, and Drs. Peters and Atkinson remind us that there are many other epidemiologic and immunologic aspects of Aspergillus infections, for which I thank them. As to the likelihood of invasive aspergillosis affecting patients with the acquired immunodeficiency syndrome, Dr. Peters may well be right—time will tell.

Denise J. Strieder, M.D., Associate Professor of Pediatrics Massachusetts General Hospital, Boston

Nitroglycerin Therapy of Asthma

To the Editor:

A 12-year-old steroid-dependent asthmatic boy with iatrogenic Cushing's disease, was receiving theophylline sufficient to produce therapeutic blood levels. He was also taking metaproterenol orally, as well as inhaled albuterol, beclomethasone and ipratropium bromide, an investigational anticholinergic derivative. His doses of prednisone ranged between 50 and 100 mg per day. Sodium cromolyn had been ineffective when given prophylactically in a relatively asymptomatic period. Short-term inhaled albuterol did not improve results of pulmonary function tests. It was decided to try the nonspecific smooth muscle dilator, nitroglycerin, continuing all other medications at their previous dosages.

Prior to administration of 0.15 mg of nitroglycerin sublingually, the FEV,
1 was 1.54 (54% of predicted) and the patient was in moderate respiratory distress. Five minutes later the FEV, was 2.11 (74% of predicted) and the patient was symptomatically improved. He is now using a 10 cm² transdermal patch containing 25 mg of nitroglycerin daily with minimum side effects (very mild intermittent dizziness), and has tapered his steroid dosage to nothing. There has been no orthostatic hypotension. Follow-up has been three months.

It would appear that nitroglycerin dilates bronchial smooth muscle by a mechanism unrelated to that usually affected by current bronchodilating medications. The patient's spirometric results were not altered by inhaled albuterol, indicating maximal adrenergic effect and probable nonresponsiveness to parenteral epinephrine. Although there is little information on its use in pediatric patients, the literature gives conflicting reports about the efficacy of nitroglycerin in acute asthma. I was unable to discover any reports of long-term therapy. It seems that nitroglycerin may have therapeutic benefit when given on a long-term basis, as well as short-term, although tachyphylaxis to its antiangi all effects is known to occur in adult patients.

The mode of action of nitroglycerin on bronchial smooth muscle can only be speculated upon. It is known to relax tracheal smooth muscle when given intravenously. Nebulized isosorbide dinitrate, a related drug, was found to be effective in seven patients aged 14-49 with extrinsic and reproducible exercise-induced asthma. This compound has been found to produce vasodilation in the endothelium of coronary artery smooth muscle by the reproduction of nitric oxide which stimulates guanylate cyclase, producing cyclic GMP.

Nitroglycerin has also been shown to stimulate production of prostacyclin in human endothelial cells, thereby stimulating adeny cyclase. It has been suggested that this enhancement may be caused by inhibition of thromboxane A2 synthesis, thereby preferentially shunting precursor into the prostacyclin synthetase pathway.

Caution should be used when prescribing nitroglycerin for the hypovolemic patient, since it may produce hypotension, an effect which may even occur in the normovolemic patient.

Nitroglycerin treatment of pediatric asthma is worthy of further trials and may be indicated in selected patients.

Jay A. Goldstein, M.D. Anaheim Hills, California

Reprint requests: Dr. Goldstein, 500 South Anaheim Hills Road, Anaheim, California 92807

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Noninvasive Measurement of Mixed Venous Pco₂

To the Editor:

We would like to comment on the report on mixed venous Pco₂ in the article "Non-invasive monitoring of arterial blood gases: a report of the ACCP Section on Respiratory Pathophysiology" (Chest 1983; 83:666-70). We have been using the equilibration rebreathing technique for measurement of mixed venous Pco₂ (FPCO₂) in patients for many years and have published several articles designed to help the physician understand and use this technique. We feel, however, that Drs. Burki and Albert's description of the two rebreathing techniques for measurement of FPCO₂ may confuse the reader, and also contains some inaccuracies.

Two methods of estimating the FPCO₂ by rebreathing are in common clinical use. The Campbell and Howell technique is a two-stage procedure, in which the patient breathes for 1½ minutes from a bag containing pure oxygen, breathes air for 2 min, then rebreathes from the bag for 20 sec. The FPCO₂ is the Pco₂ in the bag at the end of the second period of rebreathing. The choice and latitude of these times and volumes are explained in a later paper. This two-stage method has the advantage of not requiring a rapidly responding analyzer, but it does require constant practice. We find it quite satisfactory when performed by trained technicians and use it in the general wards and clinic.
For speed, ease and reliability we have adopted the Collier\textsuperscript{4} technique using a mobile unit designed for the purpose.\textsuperscript{3} The technique requires only a 30-sec period of rebreathing, which is more easily tolerated by patients than the 1/4 min first-stage of the two-stage technique. The rebreathing bag is filled to about 1/4 times the patient’s tidal volume with a suitable mixture of oxygen and carbon dioxide (not pure oxygen, as stated by Drs. Burki and Albert) adjusted to give a bag Pco\textsubscript{2} about 10 mm Hg above the expected PVCO\textsubscript{2}, but neither the volume nor the initial Pco\textsubscript{2} need be exact, and the procedure is repeated if an equilibrium plateau is not obtained. The technique is applicable to patients breathing spontaneously whether intubated or not, and also to patients on artificial ventilation.

The statement that an elevated PaCO\textsubscript{2} invalidates the use of the formula PVCO\textsubscript{2} = 0.8 PaCO\textsubscript{2} is also incorrect. This relationship, determined empirically\textsuperscript{5} and theoretically,\textsuperscript{6,7} takes into account the nonlinear characteristic of the CO\textsubscript{2} dissociation curve and automatically corrects for the level of PaCO\textsubscript{2}. The relationship is altered by reductions in cardiac output, and decreased arterial oxygen saturation, anemia and polycythemia all have minor effects. The alteration in the relationship of PVCO\textsubscript{2} to PaCO\textsubscript{2} by these factors is predictable\textsuperscript{8} and can be used to determine reductions in cardiac output without central catheterization. Further, increases in respiratory quotient do not invalidate measurements of cardiac output using the PVCO\textsubscript{2}:PaCO\textsubscript{2} relationship, but may affect subsequent estimates of mixed venous oxygen saturation from the cardiac output.\textsuperscript{9}

In our Intensive Care Unit, arterial oxygenation and alveolar ventilation are routinely monitored by ear oximetry and PVCO\textsubscript{2} measurements, reducing the need for arterial blood gas analysis by at least 50%, and the number of arterial lines by about 75%. If a reduction in cardiac output is suspected, both PVCO\textsubscript{2} and PaCO\textsubscript{2} are measured, and the reduction in cardiac output quantified using either a graphic approach\textsuperscript{9} or a programmable pocket calculator.\textsuperscript{10} The PVCO\textsubscript{2}:PaCO\textsubscript{2} relationship may be altered by extreme disturbances in the acid base balance, or change in body temperature. These factors have been taken into account in a more complex program which may also be used in exercise testing.\textsuperscript{11}

Finally, we would emphasize that severe lung disease does not prevent the attainment of good rebreathing CO\textsubscript{2} records and accurate values of PVCO\textsubscript{2}. Our experience has led us to conclude, as Drs. Burki and Albert do, that the measurement of PVCO\textsubscript{2} by rebreathing has the advantages of noninvasiveness, speed and simplicity.

A. C. P. Powles, M.D., F.C.C.P., Associate Professor of Medicine and Director, Intensive Care Unit; N. L. Jones, M.D., Professor of Medicine and Director, Ambrose Cardiorespiratory Unit; and E. J. M. Campbell, M.D., Professor of Medicine, McMaster University Medicine Centre, Hamilton, Ontario, Canada

Reprint requests: Dr. Powles, Department of Medicine 3U3, McMaster University, Hamilton, Ontario, Canada L8N 3Z5

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To the Editor:

Dr. Powles and colleagues have made some important points regarding our article and we would like to clarify some of these points.

We have not described “two rebreathing techniques for measurement of PVCO\textsubscript{2},” we have described in detail only the Campbell and Howell technique and have not described the Collier technique in our article.

Powles et al. raise an important point concerning our statement regarding the accuracy of the relationship PVCO\textsubscript{2} = 0.8 PaCO\textsubscript{2} at high levels of PaCO\textsubscript{2}. It is important to note that McEvoy et al (Br Med J 1974; 4:687-690) derived this formula as the best approximation in a group of 19 patients, of whom 9 patients had an SaO\textsubscript{2} <90%, 3 patients had right heart failure, and 4 patients had respiratory exchange ratios >1.0. As McEvoy et al. noted, and as indicated in our article, the PaCO\textsubscript{2}, the cardiac output, SaO\textsubscript{2}, and respiratory exchange ratio, affect the relationship of PVCO\textsubscript{2} to PaCO\textsubscript{2}. Thus, the relationship PVCO\textsubscript{2} = 0.8 PaCO\textsubscript{2} is an approximation, although it is sufficiently accurate for most clinical purposes. In clinical practice, an increase in PaCO\textsubscript{2} is almost invariably associated with a decrease in SaO\textsubscript{2} and frequently with right heart failure. It was our attempt to caution the reader to take these factors into account in relating the PVCO\textsubscript{2} to the PaCO\textsubscript{2} in these clinical circumstances.

Our paper did not discuss the measurement of cardiac output by the use of these noninvasive techniques. Hence, the comments regarding the respiratory quotient and cardiac output, although interesting, are not apropos.

Nevertheless, we are in agreement with the letter from these authors in that the noninvasive measurement of PVCO\textsubscript{2}, due to its speed and simplicity, is of major clinical value—provided that the observer is aware of the factors affecting the relationship between PVCO\textsubscript{2} and PaCO\textsubscript{2}.

N. K. Burki, M.D., Ph.D., F.C.C.P., Professor and Chief, Pulmonary Division, University of Kentucky, Lexington; and Richard K. Albert, M.D., F.C.C.P., Division of Pulmonary and Critical Care Medicine, University of Washington, Seattle

Body Positional Effect on Gas Exchange In Unilateral Pleural Effusion

To the Editor:

We read with interest the article by Sonnenblick et al (Chest 1983; 83:784-85) where blood gases were analyzed in patients with unilateral pleural effusions. It was found that when the affected side was dependent, there was worsening gas exchange, as reflected in a lower PaO\textsubscript{2} when compared to gas exchange when the affected side was in the upright decubitus position. We believe, however, that the value of the study was compromised, as the authors did not rule out an accompanying “occult” contralateral effusion by more sensitive techniques than routine roentgenogram. Five of their eight patients had diseases that may have been associated with a contralateral effusion if M-mode ultrasonic examination was performed.\textsuperscript{1} Even if only bilateral decubitus chest roentgenograms were obtained, the three patients reported with cardiac failure may have been found to have bilateral effusions.\textsuperscript{2} It is therefore quite possible that the

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