must exercise caution in advising patients and the public how to protect against O₃. People whose O₃ sensitivity is clinically apparent by symptoms or lung function loss are commonly advised to minimize exposure by avoiding outdoor exercise during pollution episodes. The same advice now seems appropriate for clinically “insensitive” individuals, given that they may experience asymptomatic lung function decrements, as well as lung inflammation and permeability effects that could be more harmful in the long term than temporary symptoms and lung dysfunction. Although some people may appear relatively resistant to these effects during the worst ambient O₃ pollution episodes, there is currently no practical way to identify those people, except to perform a controlled O₃ exposure. Thus, current laboratory science argues that no group can be assumed to have “low risk” from O₃ exposure and that protective efforts should target everyone.

Henry Gong, Jr., MD, FCCP, and William S. Linn, MA, Downey, California

References

Associating Poor Outcome With the Presence of Cytomegalovirus in Bronchoalveolar Lavage From HIV Patients With Pneumocystis carinii Pneumonia

We believe there may be an unrecognized factor in explaining the increasing mortality rate of patients infected with HIV who develop acute respiratory failure (ARF) with severe Pneumocystis carinii pneumonia (PCP) as reported by Hawley et al, and the higher 3- and 6-month mortality in HIV patients found to have cytomegalovirus (CMV) in their bronchoalveolar lavage (BAL) as reported by Hayner et al (see page 735 in this issue of Chest). The presumption that most clinicians have is that the immune status of the type of patients reviewed by Hawley et al is simply too impaired, or we are dealing with a “resistance” strain of PCP when these patients died of progressive ARF despite aggressive interventions, including prompt administration of corticosteroids (CS). An alternative explanation is that co-interventions such as CS or concurrent opportunistic infections such as CMV could be currently responsible for this undesirable outcome.

At most centers, CSs are widely used and generally applied early on in the clinical course of a severe episode of PCP. As shown in the recent report by Hawley et al, despite wide acceptance and early administration of CS as co-intervention, patients with PCP still went on to ARF and a higher percentage of these critically ill patients died compared with the pre-CS era (89 vs 50%). We have been observing similar outcomes at our institution. The question that remains unanswered is whether CSs are further impairing the immune system such that other latent opportunistic infections such as CMV can silently flare up and actually be responsible for some of the ARF and respiratory deaths? We would like to share our experience and suggest that further investigations be carried out in this area.

CMV has long been associated with severe pulmonary complications in transplantation recipients. Although CMV is frequently detected in the lungs of HIV-infected patients, as demonstrated by Hayner et al and others, the pathogenetic significance of CMV in the lungs remains unclear and no specific therapeutic intervention is usually recommended for HIV patients.

Experience with CMV in transplant recipients would suggest that CMV in the lungs of an immunocompromised subject can setup an immunopatho-
logic pneumonitis, which is often fatal. The main reason why the presence of CMV in the HIV-infected patients is not associated with similar severe immunologic pneumonitis is thought to be secondary to the severe and irreversible T-cell impairment of the hosts. A recent preliminary report by Vestbo et al., however, suggests that CMV may be more than a bystander in some HIV patients with PCP.

Vestbo et al. reported that in the 3 months after the detection of CMV in the BAL of HIV patients with PCP, a significantly higher percentage of patients who were positive for CMV and received CS as concurrent therapy for their PCP died compared with the other patients with PCP who were either positive or negative for CMV but did not receive CS. These preliminary but very provocative results by Vestbo et al. led us to conduct a retrospective study to examine the prevalence and significance of CMV in HIV-infected patients at our center.

Between May 1990 and April 1993, 276 bronchoscopies were performed on HIV-infected patients at the Wellesley Hospital, a tertiary HIV referral center in Toronto, Canada. Because of the research interests of one of us, BALs were routinely processed for CMV irrespective of patients’ status. One hundred two bronchoscopies were done on hospitalized HIV patients and 174 were performed on outpatients. PCP was detected by the direct fluorescent antibody (DFA) stain. CMV was detected by the conventional 16-hour shell-vial culture using DFA for early antigen.

The overall rate of detection of CMV in BAL was 163/276 (59%), which was comparable with the published rates in the literature. However, CMV was more frequently detected in the BAL of patients with PCP 84/121 (69%) than subjects negative for PCP 79/155 (51%) (p<0.005).

In PCP positive patients, CMV was found to the same extent in both hospitalized (45/65, 69%) and ambulatory (39/56, 69%) patients. In PCP negative patients, CMV was more commonly detected in the in-patient (23/37, 62%) population compared with the outpatients (56/118, 47%). Whether this suggests that sicker patients, i.e., hospitalized subjects, are more likely to be associated with CMV in the lungs or these results are merely a reflection of selection bias is unclear.

In our retrospective study, it was only possible to establish the mortality rate and cause of death in the hospitalized patients. The results show that out of the 102 in-patients, 65 were treated for PCP, 10 died giving an overall mortality rate of 15% in those patients hospitalized for the management of PCP. The most cogent finding is that all ten patients who died from PCP were positive for CMV in BAL. In distinct contrast, none of the 20 patients hospitalized for the treatment of PCP, but who were negative for CMV in their BAL, died from PCP. Also, all 10 patients who died from PCP received CS as concurrent therapy.

One can only speculate on the explanation of these results. Our limited data, however, is in full agreement with Vestbo et al., suggesting that the combination of severe PCP with the use of CS and the presence of CMV is of grave prognostic consequence. We are most interested in the CMV status of the patients who died from ARF secondary to PCP in Hawley’s study, and whether the small number of patients with PCP who were also positive for CMV in their BALs were also treated with CS in Hayner’s study.

Our data also seem to indicate that as HIV patients become sicker and thus require hospitalization, there is a higher prevalence of CMV in BAL. Possibly, CMV is a marker of the severity of AIDS-related immunosuppression. Alternatively, CMV may be a significant pathogen in HIV-infected patients contributing to their pneumonia. Until prospective and definitive evidence is available, we believe it is prudent to investigate the possibility of CMV in HIV patients who are being treated for severe PCP with concurrent CS and who are not responding to anti-PCP drugs.

Meaghan Hyland;
Melinda Chan;
Robert H. Hyland, MD, FCCP; and
Charles K. Chan, MD, FCCP

From the Department of Medicine, the Wellesley Hospital, University of Toronto, Ontario, Canada.
Reprint requests: Dr. Chan, 100 Wellesley Street East, #242, Toronto, Ontario, Canada M4Y 1J3

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Heliox for Asthma

A Trial Balloon

Combining helium and oxygen gas (heliox) results in a gas with a viscosity similar to air but with a density substantially lower. Because low density gas has the potential to decrease resistance to gas flow, heliox has been advocated for treating obstructive lesions of the larynx, trachea, and airways since 1935.1

Gas flow in airways may be laminar, turbulent, or a combination of the two. Turbulence is predicted by a high Reynolds' number—a unitless quantity proportional to the product of gas velocity, airway diameter, and gas density divided by viscosity. Reynolds' number (Re) is defined as: Re = ρdV/μ, where ρ is the gas density, d is the diameter of the airway, V is the mean linear velocity of the gas, and μ is gas viscosity.

The presence of turbulence has two implications for the pressure gradient along the airway that is needed to achieve a given gas flow.2 First, the needed pressure gradient is directly proportional to gas density. Second, the pressure gradient is proportional to the square of gas flow. The driving pressure (∆P) needed to achieve a given gas flow rate is:

\[ ∆P = k_1 \text{ (laminar flow) } + k_2 \text{ (turbulent flow)} \]

where k₁ is determined by the factors of the Hagen-Poiseuille equation and k₂ determined, in part, by gas density. These features of turbulent flow contrast with laminar flow where the pressure gradient is not dependent on gas density and is proportional simply to flow. Therefore, heliox lowers resistance to gas flow and increases ventilation for two reasons. The low density of heliox decreases the pressure gradient needed to achieve a given level of turbulent flow (by decreasing K₂) and heliox decreases the Reynolds' number, converting turbulent flow into laminar flow.

Considering these factors, it is understandable that the medical application of heliox (usually helium comprises 60 to 80% of the gas administered) is well established as a temporizing measure for the management of obstructing lesions of the large airways and trachea where turbulent gas flow dominates. Heliox is used to relieve airway obstruction due to viral and postinfection croup3 and tumors of the larynx and trachea.1,4 It also has been used to facilitate and increase safety of bronchoscopy through narrow endotracheal tubes.5

However, despite the lapse of 60 years since its use was first proposed, the role of heliox in treating the diffuse airway narrowing of acute asthma is unestablished. Most studies, including one in this issue of Chest by Kass and Castriotta (see page 757), suggest that heliox has moderate and variable effects on airway resistance in asthmatics.1,6,7 This supports the fact that the sites of lumen narrowing in acute asthma often involve small airways with laminar, nondensity-dependent flow. Nonetheless, improvement for some asthmatics does suggest that heliox might be useful in carefully selected circumstances. Heliox might be useful for maintaining adequate mechanical ventilation in those rare patients with acute asthma whose condition deteriorates despite appropriate conventional therapy.8 Also, heliox delivered by face mask might sometimes obviate the need for mechanical ventilation.7

However, much is unknown about using heliox in acute asthma. First, without controlled trials, the possibility that the apparently beneficial effects of heliox are due to concomitant conventional treatment for asthma cannot be entirely excluded. Second, because studies have been small and brief, complications of heliox may not have been detected. Asthma causes uneven ventilation of the lungs and airtrapping. For the same reasons that expiratory flow may be increased with heliox, theoretically, inspiratory flow to some alveoli might be excessive during administration of heliox, especially when heliox is delivered by a mechanical ventilator. This could lead to dynamic hyperinflation of these alveoli, and, therefore, increase the risk of barotrauma. Third, no study has defined the clinical circumstances for which heliox improves patient outcome beyond that already achievable with conventional therapy.

Therefore, heliox is one of several therapies for asthma whose niche in management has long remained undefined and anecdotal. Until controlled trials are conducted, heliox shares company with general anesthetics, bronchoalveolar lavage, magnesium sulfate, extracorporeal life support, and hypothermia as unconventional treatment reserved only for those rare patients who have clearly failed conventional therapy for asthma. These unconven-