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CRITICAL CARE ALERT™

A monthly update of developments in critical care and intensive care medicine

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Variability of Arterial PaO_2 in Critically Ill Patients

ABSTRACT & COMMENTARY

In this study from taiwan, the spontaneous variability of arterial oxygen tension (PaO_2) was determined in 23 critically ill but "stable" medical ICU patients. The patients all had pulmonary artery catheters and were being ventilated in pressure control mode for a variety of diagnoses, including acute respiratory distress syndrome (ARDS) in nine, severe sepsis in eight, and acute pulmonary edema in three. At a time when the patients were hemodynamically stable and judged not to be changing clinically, they were switched for one hour each among three combinations of inspiration-to-expiration (I:E) ratio and positive end-expiratory pressure (PEEP). Under each condition, after airway suctioning, with the patients deeply sedated and with no changes in ventilator settings or other therapy, arterial blood was drawn every 15 minutes for blood gas analysis.

There was substantial variability in PaO_2 from measurement to measurement. Although mean PaO_2 varied under the different conditions of I:E ratio and PEEP (from a low of 97 mmHg with I:E 1:2 and PEEP 5 cm H_2O to a high of 127 mmHg on the same I:E ratio and 15 cm H_2O PEEP), there was also substantial variation from sample to sample under each set of ventilation conditions. The coefficient of variation among the samples drawn every 15 minutes under the different conditions ranged from 5.9% to 7.2%, a difference that was not statistically significant. The intrapatient range of individual PaO_2 values varied from 4-65 mmHg; this range of PaO_2 values within a single patient was more than 20 mmHg during at least one of the one-hour observation periods in 15 of the 23 patients, and more than 30 mmHg at some time in seven of them.

Mixed venous oxygenation was also studied, and also demonstrated substantial measurement-to-measurement variation. The coefficients of variation for the alveolar-arterial oxygen tension difference [$P(A\text{-}a)O_2$)] and ratio of arterial to alveolar oxygen tension (PaO_2/PAO_2) were about the same as for PaO_2 alone, while that for $P(A\text{-}a)O_2/PaO_2$ was significantly greater (mean 12.5%). Tsai and colleagues conclude that, in critically ill medical ICU patients, despite sedation, the spontaneous variability in PaO_2 over time is substantial, but that this variability is similar under different conditions of I:E ratio and PEEP.

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INSIDE

COMMENT BY DAVID J. PIERSON, MD, FACP, FCCP

This study confirms the earlier findings of Thorson et al (*Chest* 1983;84:14-18), Hess and Agarwal (*J Clin Monit Comput* 1992;8:111-115), and Sasse et al (*Chest* 1994;106:187-193), that "stable" patients who are ill enough to require invasive monitoring and other interventions in an ICU demonstrate more spontaneous variability in arterial blood gases—particularly in PaO_2—than is commonly appreciated.

The fact that PaO_2 varies on spot samples every 15 minutes by an average of about 7%—and by more than 20 mmHg in most patients at least some of the time—creates a real problem for management. In a patient with ARDS, a drop in PaO_2 from 80 to 60 mmHg in two successive arterial specimens would likely trigger a ventilator change—an increase in inspired oxygen fraction, PEEP, or I:E ratio, for example—and yet such a change may well just reflect the baseline instability of oxygenation in such a patient. This problem is compounded several-fold by continuous monitoring with pulse oximetry, with which even momentary dips in arterial saturation are detected and often lead to management changes.

Should we ignore a 20 mmHg drop in PaO_2, or the pulse oximeter's alarm that saturation has dipped below 90%? Of course not. However, it is important to know that such changes may just reflect the instability of gas exchange at a time of critical illness rather than a change in the patient's condition that mandates a change in ventilator settings or other intervention.

It is difficult to construct a management algorithm that eliminates the need for experience and clinical judgment. In this era of increasing comfort with "permissive hypercapnia," clinicians in the ICU need to learn when to allow "permissive hypoxia" as well. A pulse oximeter alarm indicating a saturation below 90%, or a "routine" arterial blood gas result with a PaO_2 lower than on the last specimen, should trigger a close look at the patient rather than an automatic change in management. If the vital signs have not changed and the patient is clinically the same as before, there is probably time to watch and wait, at least for the next 15 minutes, and to repeat the measurements if there are no signs of deterioration at the bedside. ❖

The average coefficient of variation in arterial oxygen tension in critically ill patients who do not appear to be changing clinically is approximately:

a. 1%.
b. 2%.
c. 4%.
d. 7%.
e. 13%.

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EXECUTIVE EDITOR: Glen Harris.
ASSISTANT MANAGING EDITOR: Robin Mason.
COPY EDITORS: Michelle Moran, Neill Larmore, Holland Johnson.

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Customer Service E-Mail Address: customerservice@ahcpub.com.

Editorial E-Mail Address: michelle.moran@medec.com

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Please call **Robin Mason,** Assistant Managing Editor, at (404) 262-5517 or **Michelle Moran,** Copy Editor, at (404) 262-5589 between 8:30 a.m. and 4:30 p.m. ET, Monday-Friday.

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Effects of Tracheotomy on Work of Breathing

ABSTRACT & COMMENTARY

Synopsis: *Both work of breathing and intrinsic PEEP in patients on pressure support were significantly reduced when their endotracheal tubes were replaced by tracheostomy tubes of the same inner diameter. Studies of resistive work of breathing through the endotracheal tubes removed from the patients showed that it was measurably higher than through unused tubes of the same size, suggesting a subtle buildup of secretions on the tubes' inner walls.*

Source: Diehl J-L, et al. *Am J Respir Crit Care Med* 1999;159:383-388.

Diehl and colleagues at the university of Paris measured work of breathing (WOB) in eight patients before and after they underwent tracheotomy because of the anticipated need for prolonged mechanical ventilation. The patients had a variety of medical illnesses; all were unable to be weaned completely from ventilatory support after a mean of 31 days but all were

able to breathe spontaneously on pressure support (PS) ventilation. The inner diameter of the tracheostomy tube was matched in each instance to that of the previous endotracheal tube. Both on the day before and six hours after tracheotomy, Diehl et al measured the patients' WOB on their baseline PS settings (which ranged from 8-20 cm H_2O) and again at both 5 cm H_2O less (PS-5) and 5 cm H_2O more (PS+5) than this initial inspiratory pressure level. WOB was calculated from esophageal pressure-tidal volume loops as both WOB per liter and the power of breathing (WOB/min).

At the patients' baseline PS levels, WOB fell from 0.9 ± 0.4 to 0.4 ± 0.2 J/L after tracheotomy, a statistically significant difference. This was associated with a drop in intrinsic positive end-inspiratory pressure (auto-PEEP) from 4.0 ± 1.6 to 0.8 ± 1.0 cm H_2O ($P < 0.05$). Both the initial and post-tracheotomy values for WOB and auto-PEEP were greater while the patients breathed at PS-5, and less while they were on PS+5, but the changes (all significant) were all in the same direction as in the baseline measurements. The pressure-time index of the respiratory muscles at the patients' baseline PS levels also decreased after tracheotomy, from 181 ± 92 to 80 ± 56 cm H_2O.s/min ($P < 0.05$). Three of the patients had ineffective breathing efforts prior to tracheotomy and all had improved ventilator synchrony after the procedure.

Diehl et al also made in vitro measurements using the endotracheal tubes removed from the patients in comparison with new endotracheal tubes of the same size and with the tracheostomy tubes used in the patients. At the baseline PS levels for the patients, the mean resistive WOB was 0.46 J/L with the patients' endotracheal tubes, 0.33 J/L with the new endotracheal tubes, and 0.26 J/L with the tracheostomy tubes. Mean percentage reduction in resistive WOB with tracheostomy tubes was 21% vs. new endotracheal tubes, and 43% vs. the removed endotracheal tubes at the same PS level. The differences in WOB between the new and removed endotracheal tubes of the same manufactured inner diameter were accounted for by deposition of small but significant amounts of secretions on the walls of the latter.

COMMENT BY DAVID J. PIERSON, MD

This study provides physiologic documentation of the benefit of tracheotomy with respect to WOB, and also shows that the latter can be affected measurably by insidious obstruction of endotracheal tubes during their clinical use. Tracheotomy thus reduces WOB in three ways. The effective radius of a tube exerts an effect on resistance to airflow that is inversely proportional to its fourth power, so that small changes in this effective radius can have a great effect on resistance and WOB. Because resistance is also directly proportional to the length of a tube, the shorter tracheostomy tube has less total resistance even if its diameter is unchanged. And, because auto-PEEP is reduced by tracheotomy, the WOB related to overcoming this pressure in initiating breaths from the ventilator (or breathing spontaneously during a T-piece trial) is also reduced accordingly.

Tracheotomy clearly tends to facilitate weaning in difficult-to-wean patients. I have always thought that this was mainly because of its effects on the clinician's thinking rather than on the patient's physiology. Because for many of us it tends to be hard to think of discontinuation of positive-pressure ventilation (that is, weaning) and removal of the endotracheal tube (extubation) as separate clinical steps, uncertainty about whether a patient can breathe without assistance tends to prolong the duration of mechanical ventilation, since, if the answer is "no," the patient may have to be reintubated. In contrast, with a tracheostomy it is a simple matter to wean off the positive-pressure breaths and then to put them back again if the patient does not tolerate spontaneous breathing.

That there are physiologic as well as psychologic reasons for easier weaning with a tracheostomy is nicely shown by the findings of Diehl et al in this study. The differences in WOB and auto-PEEP before and after tracheotomy are not great in magnitude, but they may be sufficient to make a difference clinically in the frail, hard-to-wean patient.

The decrease in effective diameter of an endotracheal tube after a period of clinical use (also shown by other investigators: Wright et al. *Am Rev Respir Dis* 1989;140:10-16; Villafane MC, et al. *Anesthesiology* 1996;85:1341-1349) is troubling. There has been a tendency in many centers to extend the period of endotracheal intubation and to avoid tracheotomy for as long as possible if there was a reasonable hope that the patient could eventually be weaned and extubated. Seldom do we think of changing the endotracheal tube in such cases, and it is often left in place, as in this study, for many weeks. However, if deposits on the tube's inner walls gradually increase resistance to flow and thus WOB for the patient, this practice may need to be reconsidered. ❖

Tracheotomy in ventilator-dependent patients produces which of the following changes?

a. Higher work of breathing, lower auto-PEEP
b. Lower work of breathing, no change in auto-PEEP
c. No change in either work of breathing or auto-PEEP
d. No change in work of breathing, higher auto-PEEP
e. None of the above

Quality of Survival After In-Hospital CPR

ABSTRACT & COMMENTARY

Synopsis: *Most patients who survive an episode of in-hospital cardiopulmonary resuscitation and are discharged from the hospital are able to live independently and to return to a satisfactory quality of life.*

Source: de Vos R, et al. *Arch Intern Med* 1999; 159:249-254.

In this study from a 1000-bed teaching hospital in the Netherlands, the outcomes of inpatients who underwent cardiopulmonary resuscitation (CPR) during a seven-year period were determined. Survivors were assessed for quality of life using measures of physical, psychological, and social functioning, including the 136-item self-reporting Sickness Impact Profile (SIP).

Of the 827 patients who underwent CPR during the study period, 385 initially survived and 162 (20%) were discharged alive from the hospital. Follow-up data were unobtainable for only 10 patients. Fifty-one patients had died, 29 within the first six months after discharge. Of the remaining 101 survivors (12% of the total group), 90 (89%, 50 men, mean age 64 years) participated in the interview and form the basis of de Vos and colleagues' results. Mean time from CPR to interview was 15 months (range, 3-72 months).

On average, the survivors rated their own quality of life as 7 on a scale of 10. Most of them (74%) were independent in daily life; 12 survivors (13%) had restrictions in daily life but were able to look after themselves, and 12 (13%) were either partially or totally dependent. Seventeen percent were cognitively impaired and 16% had symptoms of depression. Multivariate analysis showed that quality of life and cognitive function were determined by two factors—the reason for admission and age—readily available prior to CPR. Patients older than age 70 and those who were not independent prior to admission were more likely to die during follow-up. However, factors during and shortly after CPR, such as prolonged cardiac arrest and initial coma, were not significant determinants of either quality of life or cognitive functioning among survivors. Quality of life among the CPR survivors in this study was not as good as that of a reference group of elderly persons, but was better than that of a reference group of patients with strokes.

COMMENT BY DAVID J. PIERSON, MD

The results of this study are encouraging. They demonstrate that, although in-hospital CPR is frequently unsuccessful, patients who survive to hospital discharge tend to have a relatively good subsequent quality of life. Only five patients among the 827 in the total cohort were discharged from the hospital in a vegetative state, and four of these died within three months. Both the likelihood of survival and subsequent quality of life are influenced by the patient's age and underlying state of health. Thus, these findings, as well as those from similar studies, may enable clinicians and patients to make better decisions in the future about the advisability of CPR should cardiac arrest occur in the hospital. For patients who are successfully resuscitated, the outlook may be better than we have come to expect. ❖

Patients who survive CPR in the hospital and are subsequently discharged are more likely to die during follow-up if they:

a. are older than age 70.
b. are female.
c. were initially comatose following CPR.
d. required prolonged CPR.
e. All of the above

Special Feature

Invasive Pulmonary *Aspergillus* in the ICU

By Stephen W. Crawford, MD

Many intensivists have infrequently diagnosed and treated patients with invasive pulmonary aspergillosis in the past. This has been a disease of immunosuppressed hosts and organ transplant units. However, there is an increasing incidence of neutropenic and immunosuppressed hosts in the intensive care unit (ICU). This is due to the rise in the use of solid organ and hematopoietic stem cell transplantation, as well as the use of more intensive chemotherapies to treat malignancies. In addition, numerous infections, drugs, and systemic diseases are associated with neutropenia, a major risk factor for invasive pulmonary aspergillosis. (*See Table 1.*)

Table 1

Some Causes of Neutropenia

Drug myelosuppression
Chemotherapy
Ganciclovir

Trimethoprim-sulfamethoxazole
Viral infection
Late stages of AIDS
Herpes group virus infection
Congenital deficiency
Inherited cyclic neutropenia
Functional defects
Corticosteroids
Chediak-Higashi syndrome
Myeloperoxidase deficiency
Chronic granulomatous diseases

Issues for the ICU

Invasive pulmonary aspergillosis increasingly is becoming a critical care issue since the ICU now cares for increased numbers of immunosuppressed and neutropenic patients. Invasive pulmonary aspergillosis is often a complication in immunosuppressed patients who have another critical illness. Often, invasive pulmonary aspergillosis is not the primary reason for ICU admission, and often may not be the cause of death. More troublesome to the intensivist, invasive pulmonary aspergillosis is often an unsuspected diagnosis in patients not thought to be at high risk (such as those with severe COPD or AIDS).

Numerous infections are emerging as problems, especially in patients with neutropenia. These infections include an increasing incidence of infection with Gram-positive cocci, such as *Streptococcus viridans*, vancomycin-resistant enterococci, and coagulase-negative staphylococci. Potentially more disturbing is an increasing problem with invasive fungi. Reports of *Candida* infections have increased 20-fold since the 1980s. *Aspergillus* infections show a 14-fold increase. In addition, there is an increasing recognition of "unusual" fungal species, such as *Trichosporon*, *Fusarium*, and *Mucor*.

When to Suspect *Aspergillus* in the ICU

Incidence and severity of fungal infection depends on the depth of neutropenia (e.g., < 500 cells/mL), as well as its duration. Increasingly, it is apparent that profound phagocyte dysfunction contributes as well. The role of phagocyte function is illustrated by the reports of nosocomial *Aspergillus* fungal infections in the ICU. Several centers have reported hospital-acquired invasive pulmonary aspergillosis among patients exposed to high levels of fungal spores from ventilation system sources while receiving high-dose corticosteroids, even when these drugs have been administered only for a short period. Clearly, steroid-induced neutrophil dysfunction can predispose one to invasive pulmonary aspergillosis when the exposure is sufficient.[1,2]

We can draw much about the risks for invasive pulmonary aspergillosis in the ICU from the experiences in neutropenic patient populations. The complications of severe, short-duration neutropenia in patients with peripheral stem cell transplantation demonstrate the protective effect of a short duration of neutropenia on invasive fungal infections. Neutropenia was nearly universal among these patients in a recent report, but lasted for less than five days. Neutropenic fever was noted in 94% and the patients defervesced in a median time of four days. Bacteremia was noted in 39% with Gram-positive cocci the predominant organism. Unlike previous reports from bone marrow transplant recipients with prolonged neutropenia, pulmonary infiltrates were detected in only 5% and no fungal infections were noted. There were no infection-related deaths.[3]

Pneumonia in a patient with neutropenic fever is an ominous finding. Infection is documented as the cause of neutropenic fever in less than one-third of cases. Lung and skin are the most commonly identified sites when a source of infection is localized. Involvement of these sites tends to occur days later in the fever course and portends a worse prognosis. Notably, more than half of documented lower respiratory infections are due to fungi.[4] Not surprisingly, the initial antibiotic choices do not significantly affect the resolution of pneumonia in patients with neutropenic fever after chemotherapy. The reported response rates are 61-73%. Most empiric broad-spectrum antibiotic regimens are equally effective. Only 27% of these patients with pneumonia respond without the addition of antifungal agents.[5] These facts strongly suggest that more than half of the cases of neutropenic fever with pneumonia have fungal infection.

Barton and Schuster recently examined the cause of fever after resolution of neutropenia due to chemotherapy. They observed that 20% of patients developed fever after the blood leukocyte count had returned to normal. The ascribable etiologies were "unknown" or "noninfectious" in 62%. Bacteria accounted for 17% and fungal for 21%. Among the fungal infections, one-third were *Candida* species and two-thirds were *Aspergillus* species.[6]

Table 2 summarizes the key points in considering infection in neutropenic patients.

Table 2

Key Points About Infection in Neutropenia

Duration of severe neutropenia is critical to severe infection risk
If the fever is prolonged—think fungus

If the fever is recurrent—think fungus

If there is pneumonia after fever—think fungus

Fungal infection can occur even after resolution of neutropenia

Improved Diagnosis of Invasive Pulmonary Aspergillosis

The diagnosis of invasive pulmonary aspergillosis requires the identification of fungus by stain or culture in a patient with appropriate clinical risk factors and radiographic findings. The clinical settings include recent significant neutropenia and/or high-dose steroid use. Confirmation of tissue invasion is neither feasible nor required in most cases. Fever, although common among neutropenic patients, is not present in all patients with invasive pulmonary aspergillosis. The typical radiographic presentation is one or more focal infiltrates, usually densely consolidated because of lung infarction. Cavitation is a relatively late finding, and often is associated with recovery of the neutrophil count and resolution of the infection. CT scanning appears to be the most sensitive procedure to detect clinically significant invasive pulmonary aspergillosis.[7]

The diagnostic approach to invasive pulmonary aspergillosis often involves procedures to acquire respiratory samples for stain and culture. Stain provides a more rapid diagnosis than culture. It is unclear whether fungal culture or direct staining of samples (most often with methenamine silver) is more sensitive. The sensitivity likely depends on the source of the sample, the amount of material subjected to stain, and the number of stained slides examined.

The diagnostic yield of procedures to detect invasive pulmonary aspergillus varies. (*See Table 3.*) Bronchoscopy detects about half of cases with infection. Washings or bronchoalveolar lavage is more sensitive than biopsy because of the larger area of lung sampled. My personal experience suggests that open lung biopsy may miss the fungus in as many as 20% of lesions due to infection. I doubt that even autopsy reveals all the infections. It is disquieting to think that currently there may not be a gold standard for detection of invasive pulmonary aspergillosis. The absolute confirmation of invasive pulmonary aspergillosis may not be crucial. Among marrow transplant recipients there is no difference in outcome between those with "proven," as opposed to "suspected," invasive pulmonary aspergillosis.[8] A strong clinical suspicion should to lead to treatment.

Table 3

Diagnostic Yield to Detect Invasive Pulmonary *Aspergillus*

Fine needle aspirate	50-67%
Bronchoscopy	~50%
(wash > BAL > transbronchial biopsy)	
Lung biopsy	< 80%
Autopsy	< 100%??

A positive fungal culture or stain from the lower respiratory tract without overt evidence of invasive disease poses a dilemma. Several studies suggest that the incidence of invasive pulmonary aspergillosis among patients with neutropenia or high-dose steroid use is high (60-80%) after identification of Aspergillus in the airway. In general, it is advisable to assume that detection of *Aspergillus* in a high-risk patient represents true infection.[9,10]

The most promising technique to detect *Aspergillus* infection is the polymerase chain reaction (PCR). Einsele and colleagues reported the results of a multicenter study of fungal PCR using primers to a wide range of fungi, including *Candida* and *Aspergillus* species.[11] The assay detected as little as 1 cfu/mL in blood. Einsele et al examined 601 blood samples from 35 controls and 86 patients. All the controls tested negative and all known infected patients tested positive. The PCR assay results preceded radiographic changes suggestive of invasive pulmonary aspergillosis by an average of four days in most cases (12 of 17). The assay became negative in patients who responded to antifungal therapy.[11] Routine clinical application of such a technology will revolutionize the care of these patients. Much of the uncertainty of diagnosis and the empiricism of treatment will evaporate. I am excited for these assays to be perfected and anticipate they will be applied to the detection of fungal products in respiratory secretions as well as in blood.

Treatment

Amphotericin B deoxycholate remains the standard treatment for invasive pulmonary aspergillosis. Unfortunately, the success rates remain poor. Many, if not most, of the patients with invasive pulmonary aspergillosis die of the underlying disease that placed them at risk for invasive pulmonary aspergillosis in the first place rather than of the fungal infection. In addition, recovery of an adequate and functional neutrophil count is the common feature among patients who recover from invasive pulmonary aspergillosis. This may explain why patients who are less intensely suppressed, such as renal or heart transplant recipients, seem to fare better than patients with leukemia and chemotherapy.[12,13]

Use of Amphotericin B is limited by toxicity, especially renal insufficiency. Recent interest in lipid-complexed Amphotericin B is based on the rationale that these highly lipophilic preparations have decreased toxicity to human cells due to a high affinity to fungal ergosterols. There are three commercially available preparations, and all are less toxic than conventional Amphotericin B. Amphocil (Amphotericin B Colloidal Dispersion or "ABCD") is a "ribbonlike" drug-phospholipid complex. Albecet (Amphotericin B Lipid Complex or "ABLC") is a "disk-like" complex of Amphotericin B and cholesteryl sulfate. AmBisome (Liposomal Amphotericin B) is the only true liposomal preparation and is composed of Amphotericin B and two phospholipids. While each has less toxicity than Amphotericin B, AmBisome displays the least and ABCD the most.[14,15]

The decreased toxicity profiles have led to the expectation that increased doses of the lipid-complexed Amphotericin B preparations could be administered. Unfortunately, the pharmacokinetics of these agents are difficult to follow. They are preferentially taken up by the reticuloendothelial system so that blood levels are of limited use. Exact dosing guidelines are uncertain. At this time, there are few data to suggest an improved response among patients receiving these agents.

Fluconazole is effective in *Candida* and Cryptococcal infections after organ transplantation. It has no activity against *Aspergillus*. Itraconazole, however, is an azole with activity against *Aspergillus*. It is only available in oral form in the United States. An intravenous preparation is under study. Unpredictable absorption limits its use in the acute care setting. Itraconazole may be a reasonable alternative in ambulatory settings with chronic forms of *Aspergillus* infection, but I believe it has little role in the treatment of invasive pulmonary aspergillosis in the ICU presently.

Invasive pulmonary aspergillosis often is a localized infection associated with substantial amounts of pulmonary infarction. Antifungal drugs are often ineffective. Therefore, I believe that surgical resection of infected tissue should be considered in patients with infection limited to the thorax who will likely remain neutropenic or on steroids. In addition, I consider resection in patients who appear to be at high risk of hemorrhage due to erosion into thoracic vascular structures. Successful resection of invasive pulmonary aspergillosis has been reported. However, it has been difficult to demonstrate a survival advantage because of competing causes of death in the patient populations affected.

There are alternative, and as yet unproven, strategies for treatment of invasive pulmonary aspergillosis. These include the use of granulocyte transfusions for neutropenic patients. Anecdotal reports exist, but there are no positive prospective studies. Similarly, the administration of hematopoietic growth factors to augment neutrophil number and function seems reasonable. Prophylactically administered growth factors in patients receiving treatment for lung cancer have had a favorable impact on infections in some studies. I believe there is sound rationale for their use in the neutropenic patient with invasive pulmonary aspergillosis.

The essential points in devising therapeutic strategies for invasive pulmonary aspergillosis are tempered by the recognition that it is associated with high mortality due to both the difficulty in treating the infection and the morbidity of the underlying conditions associated with the risks for infection.[16] Persistent myelosuppresion is usually fatal and restoration of adequate functioning phagocytes is critical to recovery. More sensitive diagnostic studies are needed to detect and follow the infection. At this time, intravenous Amphotericin B remains the standard of care. Lipid-complexed Amphotericin should be reserved for those who fail or are intolerant. These agents are reasonable first-line approaches in the presence of pre-existing renal dysfunction. Lastly, I believe surgical resection should be considered in cases of limited thoracic infection.

Table 4 summarizes these therapeutic strategies.

Table 4

Therapeutic Strategies for Invasive Pulmonary Aspergillosis

Invasive pulmonary aspergillosis associated with high mortality
Persistent myelosuppresion is usually fatal
More sensitive diagnostic studies needed
Amphotericin B remains the standard of care
Lipid-complexed drug should be reserved for those who fail or are intolerant
Early surgical resection should be considered

Summary

Patients with invasive pulmonary aspergillosis are increasing in numbers in the ICU and we will need to become more familiar with this disease. It is a frustrating disease because many of the patients are profoundly immunosuppressed. The high mortality rate is in part related to the underlying disease, not necessarily the infection. I believe that vigilance is required because the presentation may be subtle and the infection unsuspected in some patients (such as those with COPD). More sensitive diagnostic modalities are on the horizon. In addition, I expect that more effective and less toxic therapeutic options will help us to help these patients. ❖

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The diagnosis of invasive pulmonary aspergillosis in the ICU requires:

a. tissue confirmation of fungal invasion.
b. abnormal radiograph in a high-risk setting.
c. demonstration of fungal hyphae at bronchoscopy.
d. positive fungal serology.

In Memoriam

By David J. Pierson, MD, Editor

Associate editor doreen anardi died feb. 21 at Harborview Medical Center in Seattle, of overwhelming sepsis and ARDS complicating group A streptococcal pneumonia. Ms. Anardi, 46, had been a research nurse at Harborview for 14 years, participating in studies of the clinical epidemiology and mechanisms of sepsis and ARDS. Her creativity, hard work, patient advocacy, and relentless good cheer were highly valued by her colleagues in the Division of Pulmonary and Critical Care Medicine and the Department of Surgery.

Ms. Anardi joined the editorial board of *Critical Care Alert* in 1994, and her commentaries were invariably pertinent, insightful, and well written. Her last special feature, "Surviving ARDS: The Chances are Getting Better," appeared last September (*Crit Care Alert* 1998;6:45-48). It summarized the substantial progress that has been made during the 1990s in understanding the mechanisms and complications of ARDS, as well as in survival and other outcomes among patients who develop the syndrome. It is sad and ironic that she should fall victim herself to the very conditions she had spent a major portion of her professional career studying. The publisher, American Health Consultants, joins me in extending our appreciation and profound sympathy to her family. ❖

In Future Issues:

Secretion Buildup in Closed System Catheters

How Much Transfusion do Critically Ill Patients Need?