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CHEST Physician

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A short-course treatment for latent infection would probably have the biggest impact of all on the epidemic, said Dr. Ann Ginsberg.

Shorter, Simpler TB Regimen Is Top Priority

BY BRUCE JANCIN
Elsevier Global Medical News

LISBON — Tuberculosis experts now generally agree that the number-one priority for improving TB therapy is to shorten and simplify the regimen for active disease, Dr. Ann Ginsberg said at the 12th International Congress on Infectious Diseases.

"This will have the greatest impact on the epidemic as compared to trying specifically to improve treatment of MDR [multidrug-resistant] TB and of TB/HIV-coinfected patients. Those are also extremely important problems, but epidemiologically speaking they don't involve the same number of patients as standard active disease," noted Dr. Ginsberg, head of clinical development at the Global Alliance for TB Drug Development, New York.

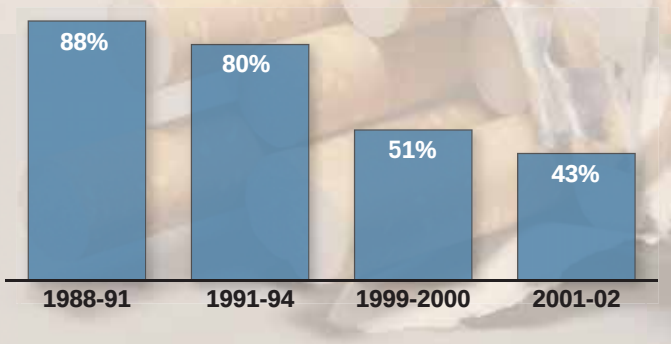
A short-course treatment for latent infection—the norm today remains 9 months of isoniazid—would probably have the biggest impact of all on the epidemic. But it's not yet feasible. Not enough is understood about the biology underlying TB latency to permit rational drug development, she said.

Treatment for active drug-responsive TB today typically involves a minimum of 6 months of therapy with complex combinations of four drugs: isoniazid, rifampicin, pyrazinamide, and ethambutol. The length and complexity of this regimen result in poor compliance, which promotes increased drug resistance.

See **TB Regimen** • *page 2*

VITAL SIGNS

Percentage of Nonsmokers Exposed to Secondhand Smoke on the Decline



Note: Based on National Health and Nutrition Examination surveys; participants were aged 4 years and older.
Source: Environ. Health Perspect. 2006;114:853-8

ELSEVIER GLOBAL MEDICAL NEWS

Use of Long-Acting β-Agonists Carries Asthma Attack Risks

But black boxes haven't changed practice.

BY MARY ELLEN SCHNEIDER
Elsevier Global Medical News

Treatment with long-acting β-agonists increases the risks of a life-threatening asthma attack, asthma-related deaths, and hospitalization due to asthma exacerbation, compared with placebo, said Dr. Shelley R. Salpeter of Santa Clara Valley Medical Center in San Jose, Calif., and her colleagues.

The risks are similar whether using salmeterol or formoterol and between children and adults, they reported (Ann. Intern. Med. 2006;144:904-12).

"Black box warnings on the labeling for these agents clearly outline the increased risk for asthma-related deaths associated with their use, but these warnings have not changed prescribing practices of physicians," the researchers said. "This information could be used to reassess whether these agents should be withdrawn from the market."

Dr. Salpeter and her associates performed a meta-analysis of the use of long-acting β-agonists (LABAs) in randomized, placebo-controlled trials published between 1966 and December 2005. The primary analysis included 19 trials with 33,826 total participants who were followed for nearly 17,000 patient-years. The mean duration of the trials was 6 months. Salmeterol and formoterol were the LABAs used in the studies.

The odds ratio for hospitalization was 2.6 for patients taking LABAs, compared with placebo, and the risk difference for hospitalization for patients taking LABAs was 0.7% over 6 months. For life-threatening asthma exacerbations, the odds ratio was 1.8 for long-acting β-agonists, with a risk difference of 0.12% over 6 months, the investigators said.

For asthma-related deaths, there was also an increase in the pooled risk difference. When all trials, both with and without

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INSIDE

Steroids: Promising for Severe Pneumonia

BY BRUCE JANCIN
Elsevier Global Medical News

LISBON — The use of corticosteroids to reduce the morbidity and mortality of severe bacterial pneumonia is supported by results from two positive randomized trials, multiple observational studies, and animal models, Dr. Antoni Torres said at the 12th International Congress on Infectious Diseases.

However, the strategy is not ready for prime-time clinical practice or incorporation into treatment guidelines because the trials that produced the highly favorable results were relatively small, said Dr. Torres of the University of Barcelona. In addition, key questions remain, such as what level of systemic inflammation warrants adjunctive corticosteroid therapy, and when, how, and for how long steroids should be given, he added.

Dr. Torres said he anticipates that answers to these questions will emerge from an ongoing randomized controlled trial he and his coworkers are conducting. The trial, which should be completed within a year, is restricted to community-acquired pneumonia (CAP) patients who are at high mortality risk and have a baseline C-reactive protein (CRP) level of at least 15 mg/mL, because there is evidence to suggest that reducing the inflammatory response in patients with a CRP below that benchmark may be dangerous.

Severe pneumonia is now recognized as an inflammatory state involving elevated pulmonary and circulating

See **Pneumonia** • *page 5*

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LABAs Linked to Adverse Effects

Asthma Attacks • *from page 1*

deaths, were included in the analysis, the absolute risk difference was 0.07% over 6 months, which was statistically significant.

Concomitant use of inhaled steroids did not guard against the adverse effects of long-acting β-agonists in the pooled studies. Concomitant inhaled steroids were used by 53.9% of participants in the long-acting β-agonist group and 53.2% of patients in the placebo group. In addition, all trials allowed the use of short-acting β-agonists as needed, Dr. Salpeter and her associates said.

Physicians should continue to follow current guidelines that call for the use of inhaled corticosteroids as first-line treatment for patients with mild to moderate persistent symptoms of asthma, Dr. Jeffrey Glassroth, FCCP, of Tufts University, Boston, said in a commentary that accompanied the study (Ann. Intern. Med. 2006:144:936-7).

Based on the results of the meta-analysis, it may make sense, for patients who do not achieve good control, to increase the dose of inhaled steroids before moving to combination therapy with LABAs, he said. And when long-acting β-agonists are added, physicians should carefully monitor patients.

Dr. Glassroth noted that the meta-analysis did not fully address the role of disease severity, cotreatments, and adherence in contributing to adverse events. ■

Dr. Susan M. Harding, FCCP, comments: Although this study carries with it the weaknesses of a meta-analysis, we need to examine the potential risks of prescribing long-acting β-agonists (LABAs) for our individual asthmatics. It's time to perform translational research on this topic on a wide-scale basis. Specific polymorphisms within the β_2-adrenergic receptor gene can impact airway responses to β-agonists. Individuals homozygous for the arg/arg genotype at the 16th amino acid position have declines in airflow and worsening asthma control while taking β-agonists. This arg/arg genotype occurs in approximately 16% of the U.S. population and is even more prevalent in certain ethnic groups, including African Americans. Until more information is available from translational research, I am heeding the FDA's black box warning label, especially in my African American patients.

IN THIS ISSUE

Ventilator Recalled Due to Design Flaw

Respironics California Inc. has recalled the PLV Continuum ventilator (PLVC I), used to control or assist breathing. A design flaw can cause lead wires in the air flow valve to break during use, stopping mechanical ventilation.

Customers should not use the ventilators to treat patients and should safely transition patients onto other comparable ventilators or contact the company to make alternative arrangements. For more information or to arrange return/replacement, contact the company by calling 760-918-7328.

—Kerri Wachter

Goal: Shrink Treatment to 2 Weeks

TB Regimen • *from page 1*

Treatment of TB patients coinfected with HIV—a large and growing population—is essentially the same, with the added complication that rifampicin interacts adversely with key antiretroviral agents.

The near-term goal of the Global Alliance and other groups is to replace the current regimen, which entails taking up to 14 pills per day for 6 months, with 2-3 months of once-weekly therapy.

The longer-term goal is to shrink treatment to 2 weeks or less, much as other respiratory infections are treated. That must likely await better understanding of the mechanisms involved in TB persistence, Dr. Ginsberg explained at the congress, which was sponsored by the International Society for Infectious Diseases.

The last new class of TB drugs was introduced in the 1960s. Drug development then stagnated for more than 3 decades. That began to change a few years ago. Today the TB drug development pipeline is richer than at any point in the last half-century.

New compounds being developed target the TB bacillus. Most are still in preclinical development. However, at least a half-dozen are in clinical trials, including gatifloxacin, now in phase III trials, and moxifloxacin, slated to begin phase III studies within several months. Both fluoroquinolones have pharmacokinetics amenable to weekly dosing, as does rifapentine, a long-acting rifamycin developed in the 1990s.

Animal studies suggest a shorter, simpler 2- to 3-month regimen of weekly therapy is probably achievable with drugs now in development, perhaps used in combination with some current drugs. However, all of the current first-line drugs have suboptimal profiles, and none may wind up in a new optimized regimen, according to Dr. Ginsberg.

Developing a truly novel TB drug regimen in a timely fashion will require new guidelines from the Food and Drug Administration and other regulatory agencies. The conventional development process evaluates one new drug at a time, substituting it in studies for one of the agents in the current regimen. With the conventional process, a regimen with multiple new drugs could take 30 years to gain approval. "Given the urgency of the global TB epidemic, this is not acceptable," she said.

The Global Alliance has supported an alternative pathway to clinical development, one in which whole new regimens would be tested against the standard combination. In this way, a more efficacious optimized regimen could be established in a 6-year clinical development period if all goes smoothly, Dr. Ginsberg said. ■

Dr. Aymarah M. Robles, FCCP, comments: Rapid diagnostic tests for TB are crucial if a dent is going to be made in the current TB pandemic now circling the globe. Effective simpler shorter course therapy is a crucial component in winning the global TB war. Here are the basics of rifamycins: Rifampin (RIF) is a keystone of effective antituberculous therapy. A once-weekly regimen, rifapentine (RPT), may be used in continuation therapy in HIV-negative patients without cavitary disease. Sputum must be drug susceptible and smear negative at completion of initial 2-month therapy phase. Rifabutin as a substitute for RIF is reserved for patients on medications that interact adversely with RIF. Warnings regarding gatifloxacin-induced (Tequin) hypo/hyperglycemia in special groups (older age, abnormal kidney function, and concomitant glycemic altering medications), as well as contraindications for diabetic patients, were instituted in the spring of 2006. Subsequently in May, Bristol Myers Squibb announced the removal of gatifloxacin from the market and the return of drug rights to Kyorin Pharmaceutical Company in Japan. This makes a list of new antituberculous medications even shorter.

CHEST PHYSICIAN

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Spacers Win by a Nose for Acute Asthma in Children

BY SHARON WORCESTER
Elsevier Global Medical News

Spacers appear to have several advantages over nebulizers for the delivery of β_2-agonists in children with acute asthma, according to a Cochrane review of the literature.

However, the findings should be viewed with caution, according to Dr. Paul Williams, chair of the section on allergy and immunology, American Academy of Pediatrics.

The updated review includes four new trials conducted in emergency department and community settings and findings from six trials of inpatients with acute asthma. Data on 2,279 children and 642 adults enrolled in a total of 31 trials show that length of stay in the emergency department was significantly shorter in children (but not in adults) who used a spacer, compared with those who used a nebulizer (mean difference of –0.47 hours).

Pulse rate also was lower in children who used a spacer (mean difference, 7.6% of baseline), Dr. Christopher J. Cates of St. George's University of London and colleagues reported (Cochrane Database Syst. Rev. 2006;[2]:CD000052).

There did not appear to be any difference in admission rates in children treated with spacers vs. nebulizers (relative risk 0.65).The findings show that spacers are less expensive in the community setting and do not require a power source, the investigators noted. However, Dr. Cates and his associates also pointed out some limitations of the studies.

"Overall, this review supports the equivalence of wet nebuliser and MDI [metered-dose inhaler] with spacer administration of β_2-agonists in the treatment of acute asthma, when treatments are repeated and titrated to the response of the patient. This review also suggests that paediatric patients given β_2-agonists by spacer and MDI may have shorter stays in the ED, less hypoxia, and lower pulse rates, compared to patients receiving the same β_2-agonist via wet nebulisation," they wrote.

But, they added, the findings are limited by a relative lack of studies in the community setting, by the exclusion of patients with life-threatening asthma exacerbations from the studies, by the fact that few authors reported specifically on numbers of patients who were excluded from each study, and by a lack of reporting of intention to treat analyses. Further, the analysis of data regarding lung function tests lacks standardized reporting in many of the studies, and standard evaluations related to the changes that were measured were sometimes not reported.

Emergency department stays were shorter in children who used a spacer.

"There are several cautions that should be expressed when presenting the results," said Dr. Williams, who also is with the University of Washington, Seattle. For example, only two of the studies were conducted in a community emergency department; thus, the results may not be applicable to such settings, he said. Also, the doses of albuterol given via spacer were different among the studies. For the nebulizer, the doses are fairly well defined and accepted, but for the MDI and spacer, the doses varied from 2 puffs every 20 minutes, to 1 puff every 12 seconds, up to 12 puffs per hour.

As recommended by the authors, more studies are needed using frequent dosing titrated to patient response, Dr. Williams agreed. But of most concern, he said, is that the studies included in the review used specially trained nurses to administer the medications. "In a community setting, many, if not most, nurses and perhaps even MDs are not familiar with different spacers and techniques for using spacers," he said.

He added that he would like to see studies that look at a standardized regimen of dosing using the spacer and MDI, as well as dissemination of information on using spacers for children through a source such as the American Academy of Pediatrics online PediaLink Module (www.pedialink.org/index.cfm). ■

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Consider Step-Down Therapy for Mild, Persistent Asthma

A daily fluticasone and salmeterol combination was as effective as low-dose fluticasone twice a day.

BY JANE SALODOF MACNEIL
Elsevier Global Medical News

SAN DIEGO — Once-a-day step-down therapy can be an option for patients with mild, persistent asthma that has been stabilized by an inhaled corticosteroid, according to preliminary results from a 500-patient clinical trial presented at the international conference of the American Thoracic Society.

Dr. Stephen P. Peters, FCCP, reported that one puff a day of a fluticasone (100 mcg) and salmeterol (50 mcg) combination was as effective as 100 mcg of low-dose fluticasone twice per day. Only 20% of patients on either therapy failed treatment during the 15-week study.

A third group of patients did not fare as well on a pill containing 5 mg or 10 mg of montelukast each day. About 30% failed. Investigators calculated the relative risk of treatment failure as 60% higher than with fluticasone alone or fluticasone/salmeterol.

Even so, the patients on montelukast fared well enough that all three regimens are viable, advised Dr. Peters, director of research in pulmonary and critical care medicine at Wake Forest University, Winston-Salem, N.C.

"While twice-a-day inhaled corticosteroid remains the treatment of choice for persistent asthma, alternatives could be considered on a case-by-case basis," he said, citing the fluticasone/salmeterol combination.

"Don't forget," he added, "there are still a lot of folks … that also did well even on montelukast … and you might be able to consider that alternative as well."

Twice-a-day inhaled corticosteroids work, but adherence is only about 30%.
DR. PETERS

Known as the Leukotriene Modifier or Corticosteroid or Corticosteroid-Salmeterol Trial, the study was sponsored by the American Lung Association's Asthma Clinical Research Centers. An unrestricted grant from GlaxoSmithKline provided financial support.

In the trial, 168 patients were randomized to fluticasone, 162 patients to fluticasone/salmeterol, and 165 patients to montelukast after a phase-in period during which mild asthma was stabilized on an inhaled corticosteroid.

Dr. Peters said all patients took a pill and used inhalers without knowing which one of their treatments contained an active ingredient and which two were placebo.

The population was evenly divided between men and women and had an average age of 31 years. About 18% of patients were children. More than a third of patients were African American or Hispanic. As a group, they were longtime asthma patients with an average of 16 years since diagnosis. Dr. Peters characterized the participants as "the group we are used to seeing."

The trial's primary outcome was time to treatment failure, which the investigators defined in seven ways, including physician judgment. Patients who had treatment failures could have more than one reason for a treatment failure.

There were 50 treatment failures with montelukast, 34 with fluticasone, and 33 with fluticasone/salmeterol.

The most common reason was a 20% or greater drop in forced expiratory volume in one second (FEV_1), which 48% of patients with treatment failures experienced: 26 patients on montelukast, 16 on the combination, and 14 on single-agent fluticasone.

Three components of asthma exacerbation accounted for a total of 48% of treatment failures: systemic steroids, inhaled corticosteroid use (not counting exercise medication), and urgent care.

The proportion of patients with asthma exacerbation was similar: 13% with montelukast, 11% with fluticasone/salmeterol, and 10% with fluticasone alone. The only significant difference was in inhaler use when montelukast was compared to fluticasone/salmeterol (23% vs. 17%).

In other measures, Dr. Peters said montelukast was "slightly inferior" for nocturnal awakenings, prebronchodilator FEV_1, and responses on the Asthma Control Questionnaire. Fluticasone/salmeterol was "slightly superior" for morning peak expiratory flow.

He reported no difference in the Asthma Symptom Utility Index, Adult Asthma Quality of Life, serious adverse events, or percentage of symptom-free days (79% vs. 86%).

For all three groups, he emphasized, most days were symptom free and rescue inhaler use was infrequent.

In an interview at the meeting, Dr. Peters focused on adherence as the underlying issue. Twice-a-day inhaled corticosteroids work, he said, but adherence is only about 30%.

"The fact is, if you are taking it one-third of the time, it's not as good as two-thirds of the time," he said, estimating montelukast adherence at 70%. ■

Dr. Susan M. Harding, FCCP, comments: The American Lung Association–sponsored Asthma Clinical Research Centers continue to examine important clinical questions in asthma care. Although twice-a-day inhaled corticosteroids are considered treatment of choice in mild persistent asthma, adherence rates are low. Caution is suggested in prescribing long-acting β-agonists for mild persistent asthma.

Combined Scans Define Tx for Non–Small Cell Lung Cancer

BY DOUG BRUNK
Elsevier Global Medical News

SAN DIEGO — Combining ^{18}fluorodeoxyglucose PET scans with CT images may supply the best information for maximizing treatment planning in patients with non–small cell lung carcinoma, a multicenter French study showed.

The approach results in "a better definition of nodal disease and tumor extent, especially in cases of atelectasis," Dr. Francesco Giammarile said at the annual meeting of the Society of Nuclear Medicine. "In our study, the approach to radiotherapy was modified in about 40% of patients."

Dr. Giammarile, of the Centre Léon Bérard, Lyon, France, and his associates evaluated 120 men and 28 women with non–small cell lung cancer. The mean age of patients was 61 years, and 77% had stage IIIA or higher disease.

To define the gross clinical and target volumes, they first used CT data only, followed by coregistered FDG-PET/CT data. They designed treatment plans with the CT data, but they left open the possibility for treatment modifications based on what the combined FDG-PET/CT data showed.

Dr. Giammarile said that by combining FDG-PET with CT, additional diagnostic information was provided for 61% of the patients and unexpected tumor localization was shown in 42%. Of these, 8% were at extrathoracic metastatic sites.

In 26% of cases, there was no pathologic uptake at known disease sites. "Four patients were thus shifted from radical to palliative radiotherapy for metastatic disease or very large tumor size," the researchers wrote in their abstract. The switch resulted in an estimated per-patient savings of 490 euros in additional treatment costs, or about 616 U.S. dollars.

COMBINED FDG-PET/CT DATA PROVIDED ADDITIONAL DIAGNOSTIC INFORMATION AND SHOWED UNEXPECTED TUMOR LOCALIZATION.

Dr. Giammarile and his associates added that the effect of FDG-PET on target volume definition "led to a change in the planned dose in 39% of cases, mainly due to inclusion or exclusion of nodal disease, and to better definition of tumor extent, especially in cases of atelectasis, thus reducing normal tissue toxicity."

The study was supported by a grant from the French Ministry of Health. ■

Steroids Need More Study

Pneumonia • *from page 1*

inflammatory cytokine levels. Steroids can modulate this inflammatory response, and the hypothesis under examination is that doing so will improve clinical outcomes.

Pneumonia is the community-acquired infection that most frequently leads to patients being admitted to the ICU. Up to 20% of patients with CAP are hospitalized, and one-quarter of those end up in the ICU.

Research interest in systemic inflammation in pneumonia has been driven by the fact that the mortality rate for severe CAP in the ICU setting has remained relatively steady at 20%-50% over the last 50 years, despite the availability of effective antimicrobial agents and excellent supportive measures, Dr. Torres said at the congress.

A prospective observational study by Dr. Torres and his coworkers involving 1,424 CAP patients hospitalized at 15 medical centers was among the work that fanned interest in the use of steroids in severe pneumonia and eventually led to randomized trials.

In that study, 15% of the patients experienced empirical treatment failure, which was associated with an adjusted 11-fold increase in hospital mortality.

The independent risk factors for treatment failure included multilobar CAP, radiologic cavitation, pleural effusion, liver disease, leukopenia, and pneumonia risk class (Thorax 2004;59:960-5).

However, it was the factors identified as protective against treatment failure, such as the influenza vaccination, initial treatment with a fluoroquinolone, and especially chronic obstructive pulmonary disease (COPD), that caught the researchers' attention.

Dr. Torres and his coworkers hypothesized that COPD's protective effect might involve the use of steroids in affected patients.

The first randomized trial was a multicenter, double-blind, Italian study involving 46 patients with severe CAP on placebo or 200 mg of hydrocortisone as an IV bolus, followed by 7 days of therapy at 10 mg/hour.

The prolonged low-dose hydrocortisone group had significant reductions in mortality, duration of mechanical ventilation, chest x-ray scores, and length of hospital stay. Their CRP levels also dropped significantly (Am. J. Respir. Crit. Care Med. 2005;171:242-8).

The second randomized trial, conducted by other investigators, showed that an initial bolus of methylprednisolone followed by a 9-day taper in patients on ceftriaxone and levofloxacin resulted in a significantly shorter time to resolution of pneumonia symptoms and sepsis, Dr. Torres said.

Those study results have not yet been published. ■

AMERICAN COLLEGE OF CHEST PHYSICIANS

NEWS FROM THE COLLEGE

PRESIDENT'S REPORT

Successful Finance and ATS Leadership Meetings

The deadline for the Presidential column is the first day of the preceding month. Somehow, despite the monthly promise to myself to *start earlier next month*, June 30 (today) has crept up on me. I have a fairly good excuse in that June was a very busy and productive month for the ACCP.

BY DR. W. MICHAEL ALBERTS, FCCP

For example, this past weekend, I was in Northbrook to attend the Finance Committee meeting and a presidential retreat with the leadership of the American Thoracic Society (ATS). Both meetings were held at the ACCP headquarters. I mention the location as segue to invite all ACCP members to visit the building at 3300 Dundee Road at some point in their career. It's an impressive edifice.

In regards to our finances, it is a challenging time to be in the medical society business, but, as usual, the ACCP is at the leading edge of innovation. The old saying "no money, no mission" applies to most organizations, including ours.

The ACCP has a very noble vision, and expert management of those funds is crucial to success. At this point, let me thank ACCP Treasurer Dr. Jeff Vender, FCCP, and The CHEST Foundation Treasurer Dr. John Alexander, FCCP, for their hard work and attention to detail. Both work closely with Stratton Davies, Vice President of Finance, and all take their responsibilities very seriously. The proposed budget for 2007 will be presented for approval at the summer Board of Regents meeting.

For the third year in a row, the leadership of the ACCP and the ATS met for a day and a half to discuss items of mutual interest.

The ACCP presidential triumvirate (Dr. Paul Kvale, FCCP; Dr. Mark Rosen, FCCP; and I), plus the President-Designate (Dr. Alvin Thomas, Jr., FCCP), met with ATS President Dr. John Heffner, FCCP, and members of their leadership succession (Drs. Peter Wagner, David Ingbar, Jo Rae Wright, Randy Curtis). This group, along with the respective executives Al Lever and Carl Booberg, discussed a wide range of topics, including critical care medicine, sleep-disordered breathing, workforce issues, conflict of interest, relations with other international societies, among many other items. While our respective societies have unique interests (*eg*, the basic science component of the ATS and the multispecialty focus of the ACCP), we have many common interests that can be advanced more effectively when we work together. By all counts, the retreat was a major success. ■

CHEST Makes a Giant Impact Factor Leap

CHEST has reached its highest impact factor ever, rising from seventh to third place out of 33 respiratory journals. With an impact factor of 4.008 for 2005, up from 3.11 the previous year, *CHEST* broke the 4.0 barrier for the first time in its history.

Editor in Chief, Dr. Richard S. Irwin, FCCP, comments: "We are delighted that our impact factor has risen and that we are number 2 in number of articles cited. This assures us and our contributing authors that we are on the right track to reach our short-term goal of an impact factor of 5 without sacrificing the clinical nature that has made *CHEST* patient-focused and clinically relevant and resulted in it having the largest circulation of all the respiratory journals." ■

Impact Factor Rankings Released June 2006 for Top Five Journals

Rank	Abbreviated Journal Title	Total Cites	Impact Factor
1	Am J Respir Crit Care	36,400	8.689
2	Thorax	12,422	6.150
3	CHEST	30,567	4.008
4	Am J Respir Cell Mol	8,720	3.988
5	Eur Respir J	14,120	3.947

This Month in *CHEST*: Editor's Picks

BY DR. RICHARD S. IRWIN, FCCP
Editor in Chief, CHEST

- ▶ Nurse-Conducted Smoking Cessation in Patients With COPD Using Nicotine Sublingual Tablets and Behavioral Support. Dr. Philip Tønnesen, et al
- ▶ Interpreting the Histopathology of Chronic Cough: A Prospective, Controlled, Comparative Study. Dr. Richard S. Irwin, FCCP, et al
- ▶ Bench Model To Simulate Upper Airway Obstruction for Analyzing Automatic CPAP Devices. Dr. Jordi Rigau, et al
- ▶ Bench Evaluation of Flow Limitation Detection by Automated CPAP Devices. Dr. Frédéric Lofaso, et al
- ▶ Can GOLD Stage 0 Provide Prognostic Information on Long-term Mortality in Men? Dr. Knut Stavem, et al
- ▶ Systemic Inflammation in Patients With COPD and Pulmonary Hypertension. Dr. Pavol Joppa, et al

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AMERICAN COLLEGE OF CHEST PHYSICIANS

NEWS FROM THE COLLEGE

NetWorks: Finding Your Home Within the College

BY TRACY GOODE
Vice President, Member Activities

What is a network? If you do a Google search for "networks," what will you find? Your search will hit upon hundreds of Web sites about systems of computers, terminals, and databases connected by communication lines. If you select any one of these Web sites, you might get lost in the technological jargon. Needless to say, you might feel uncomfortable or out of place.

Now, modify your search: NetWorks ACCP. You will soon be linked to www.chestnet.org/networks, where you can access information from any one of ACCP's 26 NetWorks, and, if you are a member, you can immediately join as many NetWorks as you wish. You will become a welcome participant in a special interest group of other members who share similar expertise and concerns relative to clinical practice and community health issues. You will find your "home" within the ACCP.

The concept of NetWorks as organizational groups representing the special interests of ACCP members became a reality at the CHEST annual meeting in 2000. The vision of then ACCP President Allen Goldberg, MD, Master FCCP, and the diligent efforts of other ACCP leaders has resulted in the transition from 14 Sections in 2000 to 26 NetWorks in 2006. NetWorks were designed to provide ACCP members the opportunity to take an active role in the work of the ACCP.

As NetWorks have grown, many of their 33,000 members have become vital participants and leaders in ACCP activities. NetWorks provide the structures for information development, exchange, and dissemination. They provide pathways to raise issues and an avenue for action on local, national, and global levels.

NetWorks are the building blocks and serve as content experts for a broad spectrum of ACCP activities. Over the past 2 years, they have been working closely with the Continuing Education Committee to design the ACCP's core curriculum. These topic domains now provide the basis for content of the annual meeting. Currently, the NetWorks are in the process of determining and refining the subtopic areas that will fall under each of those topic domains, helping to better identify gaps and redundancies in ACCP educational programs and products.

The NetWorks provide input to the annual CHEST meeting and plan more than half of the educational sessions. Each NetWork is responsible for developing its NetWork Highlights. The CHEST Scientific Program Committee includes the Council of NetWorks Chair and the Chair of each NetWork, who ensure that the interests of their NetWorks are adequately reflected in the educational content of the annual meeting. Some NetWorks have developed postgraduate courses, while others host special events, such as the Women's Health NetWork Luncheon.

The combined forces of several NetWorks comprise the governance and expertise for the ACCP Critical Care and Sleep Institutes. The Critical Care Institute steering committee includes the Chair and Vice-Chair of the Critical Care NetWork, and the Sleep Institute includes the Chair and Vice-Chair of the Sleep Medicine NetWork on its steering committee. There has also been representation and assistance from several other NetWorks whose members have provided the needed knowledge and

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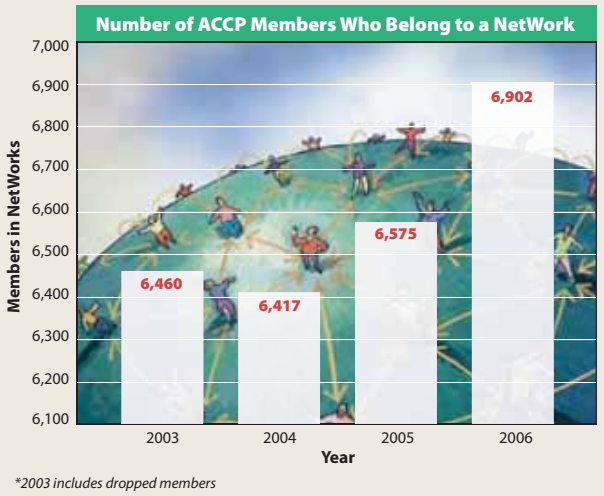
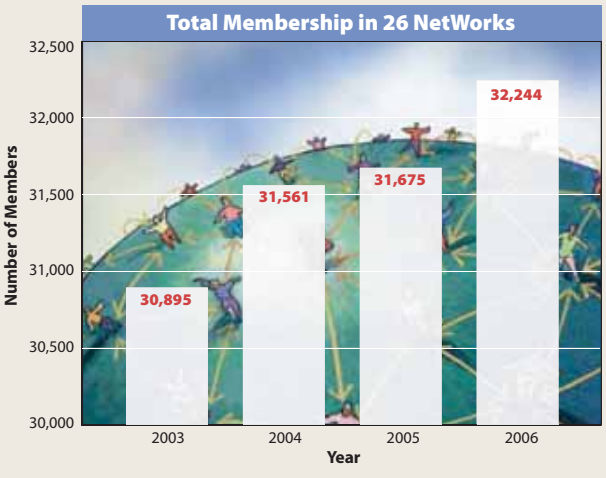
experience for specific projects.

Each year, the NetWorks assist The CHEST Foundation in the administration of some of its awards programs. Many NetWork Chairs and/or steering committee members serve on panels to review applications and select awardees. For example, the Palliative and End-of-Life Care NetWork steering committee serves as the review committee for the Roger C. Bone Memorial Lecture Award for Advances in End-of-Life Care. The Foundation also supports a Distinguished Scholar Awards Program to provide multiyear research grants to ACCP members. Leaders from the Critical Care, Airways Disorders, and Pulmonary Vascular Disease NetWorks not only helped select the scholars but also continue to play a role in monitoring the progress of the three scholars' projects.



**2003 includes dropped members*

In addition to all of the ways that NetWorks integrate with the programs and activities described above, most of them pursue individual projects. These range from educational products for physicians in the form of consensus or policy statements, pocket guides, and brochures; to patient education guides; to speakers kits; to standalone courses. One current project is a collaborative effort of the Pediatric Chest Medicine and Home Care NetWorks to write and publish a consensus statement on respiratory support and perioperative care of patients with Duchenne muscular dystrophy who require anesthesia or sedation. In another project, the Pulmonary Vascular Disease NetWork seeks to determine the degree of training offered in the field, as well as the perceived level of training that fellows receive in this field. These two project examples illustrate how NetWorks provide a venue for ACCP members to address issues important to them in their every day practice of medicine.



It is apparent that NetWorks contribute to almost every aspect of ACCP business. They have grown from fledgling groups to well-functioning, integrated structures. They work individually, collaborate with each other, and interact with other committees. In some cases, they have served as resources and reached out to external organizations. These joint efforts will utilize the best pool of knowledge and talent, eliminate redundancy, and conserve time and human resources.

The vision of NetWorks is for every member of the ACCP to be involved and actively participate in at least one NetWork. This may be "pie in the sky" (as visions are supposed to be), but those who do decide to have a piece of this pie will derive more value from their ACCP membership. ■

AMERICAN COLLEGE OF CHEST PHYSICIANS

NEWS FROM THE COLLEGE

EDUCATION INSIGHTS

Practice Guideline Development: Variety of Processes

BY CARLA T. HERRERIAS, MPH
Health and Science Policy

There has been a huge momentum in the development of scientifically sound, evidence-based clinical practice guidelines in the past decade. Because formal, structured, quality improvement and performance programs are becoming the mandate in clinical practice, physicians are relying more and more on evidence-based policy to assist in decision-making in order to provide the best care for patients. Patients are also becoming more evidence-savvy and can look to a multitude of resources for information on health care. To determine how evidence-based policy contributes to changes in physician practice, it is important to track the most influential ways of improving quality of care and, at the same time, maintain health-care costs.[1]

In 2004, the ACCP Department of Health and Science Policy developed a survey to determine the range of activities related to development and use of practice guidelines among general and subspecialty societies. The survey contained five domains of guideline processes on (1) development, (2) grading of evidence, (3) dissemination and implementation strategies, (4) review of guidelines, and (5) resource allocation for guideline programs. Forty-nine medical specialty societies in the United States and Canada were included in this survey. A total of 34 responses were received and included in the results.

The survey confirmed that the process for developing clinical practice guidelines is highly varied, as is the degree of evidence used in providing evidence-based guidelines. Although 79% of organizations indicated that they have a formal process in place to develop guidelines, approximately 19% of these processes rely on consensus-based methods for their recommendations. Half of the organizations surveyed had in place a formal review and approval process for guidelines that included peer review and approval through an oversight body, such as a board. Most organizations stated that they have a dissemination and implementation strategy in place to distribute practice guidelines; however, most of these do not go further than publication in the official journal of the organization. Only 18 organizations indicated that they submit their guidelines to the National Guidelines Clearinghouse, and very few organizations stated that they incorporated guidelines into continued medical education or other structured programs. Very few organizations had any kind of implementation process in place. Organizations that have a process use tool kits and other physician resources to encourage the use of the guidelines in decision-making practices. A few organizations indicated that they have begun incorporating guidelines into electronic medical records systems.

Grading of evidence proved to be widely varied among organizations. The ACCP has adopted a very succinct, user-friendly method of grading recommendations based on the balance of benefit and harms and the quality of studies used to back the recommendations. A systematic review,[2] conducted in 2000, identified over 120 grading systems in use. Our survey concluded that most grading systems are adapted from existing criteria; however, no two systems were identical. The Grading of Recommendation Assessment, Development, and Evaluation (GRADE) Working Group, a collaboration interested in addressing issues related to grading systems, has put forth a sensible and reliable system that may help narrow the variety of grading systems currently in place.[3] The ACCP has based its system on the concepts of the GRADE Working Group.

The results of this survey point toward a substantial interest by medical specialty societies in developing clinically sound, evidence-based, practice guidelines and show the variety of processes in place used to achieve these goals. The Department of Health and Science Policy continues to refine its process and adapt to changes in the environment of evidence-based medicine. We are in the process of developing a second survey to further gather information on implementation of practice guidelines, especially related

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Salt Lake City: Save Some Time for …

Fun! It's around every turn, and, when planning your Salt Lake City itinerary, you'll never have to wonder "what to do next." With a menu of choices that goes on and on, Salt Lake's many attractions are sure to exhaust you before you can exhaust your options.

Boasting the state capitol, a planetarium featuring an IMAX theater, and several museums, it's easy to take in that Salt Lake culture. Research your own history by visiting the Family History Library—the world's largest repository of genealogical records. Here, records from around the world, experienced specialists, and foreign language assistance are all available on site, to make tracing your ancestry as easy as possible—even for international visitors.

Delight in animal antics at Utah's Hogel Zoo, peruse visual art exhibitions at the Salt Lake Art Center, or set sail around the Great Salt Lake on a sunset dinner cruise. After that, treat yourself to a concert by the world-famous Mormon Tabernacle Choir or swing by Olympic Park, home of the 2002 winter games. And Salt Lake City is home to the first department store in the United States, so don't forget to squeeze in some window-shopping.

Whatever you choose to do, take advantage of downtown Salt Lake City's free public busses or TRAX light-rail service. And Salt Lake International Airport services 700 flights daily, which means booking flights are easy at any hour. So, make room for fun. Taking the time to play all day provides the perfect excuse to arrive early to CHEST 2006 or to stay late.

For a complete list of all there is to do, visit www.visitsaltlake.com.

To learn more about CHEST 2006, visit www.chestnet.org/CHEST.

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to performance measurement and pay-for-performance, as this becomes increasingly important to physicians. Data from this survey should help ACCP tailor its guidelines to best meet physician needs.

In January 2006, two articles were published in *CHEST* that addressed issues of grading of evidence and resource allocation.[4,5] These articles have become the basis for ACCP guidelines use in development of recommendations.

The ACCP accepts applications for development of evidence-based clinical practice guidelines. We encourage NetWorks and other groups and individuals to submit topics to the Health and Science Policy Committee for consideration for guideline development.

The application is available online at www.chestnet.org/education/guidelines/proposal/index.php.

For further information on this survey or ACCP guideline development, contact a member of the Health and Science Policy team at (847) 498-8388 or cherrerias@chestnet.org. ■

References

1. Heffner JE. Altering physician behavior to improve clinical performance. Top Health Inf Manage 2001; 22:1-9
2. Users' guide to the medical literature: a manual for evidence-based clinical practice. Guyatt G, Rennie D, eds. Chicago, IL: American Medical Association, 2002
3. Atkins D, Best D, Briss PA, et al. Grading quality of evidence and strength of recommendations. BMJ 2004; 328:1490
4. Guyatt, G, Gutterman D, Baumann M, et al. Grading strength of recommendations and quality of evidence in clinical practice guidelines: a report from the American College of Chest Physicians task force. Chest 2006;129:174-181
5. Guyatt G, Baumann M, Pauker S, et al. Addressing resource allocation in recommendations from clinical practice guidelines: suggestions from the ACCP task force. Chest 2006; 129:182-187

Reserve Your Spot for the Annual CHEST Foundation Dinner

Join your colleagues and friends for this exciting celebration of The CHEST Foundation's 10th anniversary and the 2006 Humanitarian Recognition Award and Project Development Grant ceremonies.

This year's Making a Difference Awards Dinner will again be hosted by musician and TV personality, Paul Shaffer, of The Late Show with David Letterman. The dinner will be held on Saturday, October 21, 2006, 7:00 PM–10:30 PM, at the scenic Wells Fargo Building, 23rd Floor, in downtown Salt Lake City, Utah. Bus service to and from The Grand America Hotel will be provided that evening.

As part of the 10th anniversary celebration, there will be a special reception honoring all previous ACCP pro bono service award winners going back to the inception of the program in 1998. Current 2006 award and grant winners, including the special Hurricanes Katrina and Rita Relief Fund project winners and the special Ambassadors Group Humanitarian Recognition Award winner, will be joined at this reception by past Governors Community Service Award winners and Humanitarian Recognition Award and Project Development Grant winners for an opportunity to share the current status of their projects and continued successes with one another and dinner attendees.

Seating is limited, so reserve your place early! Price per ticket is $150, and registration is available at www.chestfoundation.org. As a show of appreciation, CHEST Foundation annual donors at the $500 and $1,000 levels will be provided with one or two tickets, respectively. Please contact Teri Ruiz at truiz@chestnet.org, if you would like more information. ■

AMERICAN COLLEGE OF CHEST PHYSICIANS

NEWS FROM THE COLLEGE

CRITICAL CARE COMMENTARY

Medical Simulation: Solution to Critical Care Education?

For years, residency programs have relied heavily on clinical experience to teach physicians critical care during their training. Many of us learned procedural skills by the time-honored tradition of "see one, do one, teach one." Long hours of patient care in the ICU supplemented by attending rounds and didactic lectures provided residents with the core knowledge and skills to effectively manage critically ill patients.

New clinical evidence, work hour restrictions, reimbursement requirements, and an increasing focus on patient safety have brought this traditional educational model into question. Fatigue under the traditional work schedule can cause residents to fall asleep during ICU rounds and to make medical errors (Lockley et al. *N Engl J Med* 2004; 351:1829), prompting the recently mandated reduction in work hours. Yet, work hour limitations result in less opportunity for experiential learning. Survey data from senior medicine residents, for example, identify significant knowledge deficits in the core critical care skill of mechanical ventilation (Cox et al. *Am J Respir Crit Care Med* 2003; 167:32). These issues are not confined to physicians in training. Continuous professional development, maintenance of clinical skills, and requirements for outcomes-based assessments of clinical competence remain significant issues.

Simulators were introduced into education to make advanced training more standardized, safe, and less expensive. The first medical simulator was Resusci-Anne (Laerdal Medical; Norway), developed in the 1960s to teach cardiopulmonary resuscitation (Grenvik et al. *Crit Care Med* 2004; 32:S56). After a long period of slow growth, recent demand for standardized clinical assessments in medical training and credentialing, and an increasing number of available medical simulation devices have sparked a more broad-based interest in medical simulation.

Acquisition of skills, knowledge, and behavior in the context in which it will subsequently be used has been shown to enhance learning and recall (Norman et al. *Acad Med* 1992; 67:557-565). Since the early 1990s, there has been a trend in medical education to emphasize active learning techniques and develop clinical judgment and problem-solving skills by employing problem-based learning over traditional, passive, lecture-based formats (Distlehorst et al. *Acad Med* 2005; 80:294). Simulation and problem-based learning share the same training format, but simulation includes a realistic environment and integrates tasks and skills required in patient management (Murray et al. *Crit Care Med* 2006; 34:252).

Gaining practical experience and procedural skills in the ICU setting can be challenging due to the high risk, high stakes nature of the practice of critical care medicine. This makes medical simulation a particularly attractive option.

As the focus and subject matter of a simulated encounter is controlled, simulation experiences can provide exposure to uncommon but medically important emergencies, such as anaphylaxis and malignant hyperthermia. This has stimulated significant interest in simulation in the field of disaster medicine, providing reality-based training in such areas as chemical and biological casualty management. Available simulation tools include the standardized patient, computer-based scenarios, task trainers designed to develop specific procedural skills, and high fidelity human patient simulators.

Although there is no clearly prescribed method to develop a simulation scenario, most facilitators start by developing a needs assessment for the target audience and identifying two to three learning objectives to accomplish. The script, simulator programming, necessary medical equipment, and actor roles are developed to create a realistic setting. Learners are provided with a brief introduction to start the clinical encounter; then, they manage the subsequent clinical situation based upon verbal and visual cues from the simulator, actors, and available tools. Learner actions are assessed against a checklist of critical actions that are considered to be essential to successfully complete the task. The facilitator reviews these critical actions as part of a debriefing session with the learners to reinforce the goals and objectives of the session.

Critical care decision-making is performed in a highly dynamic environment and requires an integrated team approach to simultaneously and rapidly perform diagnostic procedures, therapeutic interventions, and monitor their consequences, while minimizing the effects of distracting factors (Lighthall et al. *Crit Care Med* 2003; 31:2427). Simulation scenarios have been shown to help develop familiarity with the work environment and improve team communication, delegation, and organization to maximize task completion and performance in the critical care setting (DeVita et al. *Crit Care Med* 2004; 32:S61).

Critics of medical simulation largely focus on the substantial resources required for training and on the lack of objective validation of teaching methods and outcome measurements of clinical proficiency. Creating and maintaining a realistic simulation environment for training can require significant resources, manpower, and time. While there are a number of centers of excellence across the United States that have made the investment to create state-of-the-art simulation centers, some experts question whether this technology can be successfully generalized to smaller academic centers and community hospitals.

Most published studies on simulation education in critical care are descriptive narratives of individual institution or group experiences, using qualitative assessments of knowledge and clinical confidence as the primary outcome measures. Simulation has been employed to evaluate the analytic and psychomotor skills of medical students before and after completion of a critical care elective (Rogers et al. *Crit Care Med* 2000; 28:550) to provide hands-on experience during courses designed to develop code management and resuscitation skills among residents (Lighthall et al. *Crit Care Med* 2003; 31:2437), and to strengthen organization and communication between members of crisis management teams (DeVita et al. *Crit Care Med* 2004; 32:S61).

A recent, prospective, randomized study found simulation-based training to be superior to problem-based learning. In this comparison, fourth year medical students were randomized to receive simulation-based training or problem-based learning for identical lengths of time during a 1-week acute care course. Both groups demonstrated similar baseline skills during an initial simulation-based assessment and received the same didactic lectures and contact time for practical training. The simulation-based training group scored significantly higher on their final assessment at the completion of the course (0.71 vs 0.52 out of a possible score of 1.0, $p < 0.0001$) using a standardized checklist of tasks emphasized during training (Steadman et al. *Crit Care Med* 2006; 34:151).

Airway management has been a focus of many simulation courses, with perhaps the best clinical outcome data in this field thus far. Mayo and colleagues demonstrated that immediate training of essential airway management tasks after a simulated encounter with a patient in respiratory failure predicted greater retention of these skills at 1 month (Mayo et al. *Crit Care Med* 2004; 32:2422). In a subsequent study, his group demonstrated that the training intervention could be successfully performed by an experienced attending or trained senior house staff member with no degradation in learner performance (Rosenthal et al. *Chest* 2006; 129:1453). Intern compliance and application of these airway management steps in real clinical situations over the next 10 months was very high (99 to 100%).

Although these clinical data represent important steps toward proving that simulation-based learning is an effective educational tool in critical care, issues remain: cost, paucity of outcomes research, and need for standardization. The high cost of the technology will accelerate the demand for more outcomes data before widespread acceptance and adoption of medical simulation occurs. For now, medical simulation remains an exciting new tool for critical care education, with applications that can only expand as the technology improves and methodology becomes more refined. ■

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Look for the "Simulation Center" in the exhibit hall at CHEST 2006.

Depression Management in COPD: A Patient's Perspective

COPD happens to a patient and a family. Psychosocial issues can be obfuscated by pressing medical procedures and priorities. However, many questions and concerns of the patient and the family, if not discerned and addressed promptly during the diagnostic and treatment phase, can turn into depression, anxiety, or other forms of emotional burden, complicating subsequent COPD treatment and rehabilitation.

Specific suggestions, from a patient's perspective, for the assessment of depression and depressive equivalents, interventions for the emotional aspects of the disease, and empowerment of the patient and the family to improve the quality of life will be presented at **Detection and Management of Depression and Anxiety in COPD: A Multidisciplinary Scientific Workshop**, September 15 and 16, 2006, at the ACCP headquarters in Northbrook, IL. The workshop is funded by the National Institute of Mental Health and supported by the Alpha-1 Foundation.

Visit www.chestnet.org/education/ to register. ■

Dr. Vijai P. Sharma
Clinical Psychologist
and Emphysema Patient

Pulmonary Perspectives

The Pulmonary Artery Catheter Controversy

It was assumed that optimizing tissue oxygen delivery based on PAC-derived data would improve outcomes.

The Controversy

Right heart catheterization had been used for diagnostic and research purposes for 4 decades before the introduction of the balloon-tipped, flow-directed, pulmonary artery catheter (PAC) made its use practical as a bedside tool (Swan et al. *N Engl J Med* 1970; 283:447). The immediate popularity of the PAC as a means of obtaining hemodynamic data previously limited to the catheterization laboratory was followed by its widespread use and, as some thought, overuse (Robin. *Ann Intern Med* 1985; 103:445). Over the years, there have been observational studies finding increased mortality associated with use of the device (Connors et al. *JAMA* 1996; 276:889) and calls for a moratorium on its use until appropriate studies could be performed (Dalen and Bone. *JAMA* 1996; 276:916).

DESPITE ITS YEARS OF USE, UNTIL THE 1990S, NO RANDOMIZED CONTROLLED TRIALS HAD BEEN REPORTED OF THE UTILITY OR SAFETY OF THE PULMONARY ARTERY CATHETER.

Controversy over the safety and utility of the PAC was fueled, in part, by the medical community's belief that more hemodynamic data would lead to better care of critically ill patients. Since the PAC came into use at about the same time as more sophisticated ventilators, bedside measurement and manipulation of both hemodynamic and airway parameters became possible and popular. It was assumed that optimizing tissue oxygen delivery based on PAC-derived data would improve outcomes. In fact, some degree of outrage often accompanied the suggestions that use of the PAC might be harmful, let alone not helpful.

The Importance of Randomized Controlled Trials

As with most controversies, a lack of adequate information sustains them. Despite its years of use, until the 1990s, no randomized controlled trials (RCTs) had been reported of the utility or safety of PAC. Observational studies, even with cohort designs to minimize differences between groups, cannot avoid selection bias. In addition, treatments and timing of treatments based on catheter-derived information were variable and uncontrolled. Observational studies may reflect common practice, but they do not provide unbiased evidence of safety or efficacy. Cohort designs can attempt to equalize the groups observed, but they cannot account for factors of which we are ignorant. Randomization is the only effective tool we have to equalize treatment groups.

Elimination of bias is important. We have seen many examples of procedures or drugs that have been assumed to be safe and efficacious because of widespread use that have been proven to be otherwise in RCTs. Hormone replacement therapy was thought to prevent atherosclerosis in postmenopausal women based on observational studies, until a large RCT, the WAVE trial, found it did not (Waters et al. *JAMA* 2002; 288:2432). Arthroscopic treatment of osteoarthritis of the knee was thought to be effective until the Veterans Affairs RCT found it was not more effective than a sham surgical control (Moseley et al. *N Engl J Med* 2002; 347:81). Numerous other beliefs have been found lacking when subjected to the rigor of RCTs, and our practice has been altered for the better.

The FACTT

The 1996 publication of a large, prospective, cohort study of PAC use in critically ill patients, which found increased morbidity and mortality with PAC use (Connors et al. *JAMA* 1996; 276:889), stimulated significant efforts in the pulmonary and critical care communities to tackle the issue. A joint National Heart, Lung, and Blood Institute and Food and Drug Administration workshop called for educational programs to address the oft-sited lack of expertise in obtaining and interpreting data from the PAC and for RCTs of PAC use in specific conditions (Bernard et al. *JAMA* 2000; 283:2568). The Fluid and Catheter Treatment Trial (FACTT) developed and sponsored by the National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network was an outgrowth of this workshop. The PAC arm of this study was recently published (Wheeler et al. *N Engl J Med* 2006; 354:2213) and demonstrates the role of RCTs in resolving controversies.

The FACTT enrolled 1,000 patients in a prospective RCT that compared PAC-monitored treatment to central venous catheter (CVC) monitored treatment of ARDS using either a liberal or a conservative fluid management strategy in a factorial design. Two important aspects of the study were the extensive training of the investigators in PAC use prior to patient enrollment and the use of treatment algorithms based on either PAC-derived or CVC-derived data. The training averted the long-standing complaint that PAC data would have been useful in prior studies if it had been obtained and interpreted correctly. The treatment algorithms and uniform timing of the initiation of treatment avoided the problems of variation in therapies based on catheter-derived data. The study found an increase in catheter-related complications in the PAC group, but no difference in the primary endpoint of 60-day mortality. Thus, unlike the findings of prior observational studies (Connors et al. *JAMA* 1996; 276:889), PAC use in this controlled setting was not associated with increased mortality. It did not, however, result in improved outcomes. Patients were as effectively managed with CVCs as PACs.

The results, of course, apply to the patient population studied, those with ARDS within the first 48 hours of presentation. It excluded patients with severe COPD, dialysis dependence, and significant pulmonary arterial hypertension. PAC use might be appropriate in the management of ARDS in some patients in these excluded groups (Shure. *N Engl J Med* 2006; 354:2273). In fact, information derived from right heart catheterization has diagnostic and prognostic value in pulmonary arterial hypertension and is useful in determining appropriate medication (Shure. *N Engl J Med* 2006; 354:2273).

The FACTT study provides strong evidence that the *routine* use of a PAC is not necessary in the management of ARDS. It does not exclude *any* use of the PAC. The results are similar to those reported in other recent RCTs of PAC use in the management of congestive heart failure (Binanay et al. *JAMA* 2005; 294:1625) and high risk surgical patients (Sandham et al. *N Engl J Med* 2003;348:5) in which PAC management did not improve outcomes.

Is the Controversy Over?

The controversy should be over for the disease states reported above, but established beliefs do not easily fade in the face of evidence. One month after the publication of the FACTT results, a retrospective analysis was reported of over 50,000 trauma patients of whom 3.6% were managed with PACs (Friese et al. *Crit Care Med* 2006; 34:1597). PAC use was associated with more severe injury and higher mortality, but a survival benefit was observed in severely injured patients in shock and in older patients. The authors concluded that their study was the first to show a benefit of PAC in trauma patients. But did it? The results could easily reflect earlier initiation of treatment in shock, which is known to be of benefit (Rivers et al. *N Engl J Med* 2001; 345:1368). Without appropriate controls, there are too many variables to take into account in explaining the results. We are left, again, without interpretable information, only an observation of outcomes in practice.

Conclusion

We now have solid information based on well-designed RCTs in specific conditions to be able to say, that for these disease states, routine use of the PAC does not improve outcomes. Because use of the PAC has known risks, we need to be circumspect about use of the device in these settings, including ARDS. We cannot generalize the results of these studies to other conditions that were not studied.

We need to remember that the PAC is not a treatment; it is a device used for diagnosis and to guide treatment. For use of the device to be effective, the therapy it is directing must be effective and dependent on the device-derived data (Shure. *N Engl J Med* 2006; 354:2273). If therapies become available for the conditions already studied, and those therapies appear dependent on such data, new studies would be needed. While RCTs provide the best evidence, they can be expensive and difficult to perform. However, we need to look for the best possible evidence as a basis for our treatments (Pocock and Elbourne. *N Engl J Med* 2000; 342:1907). We cannot afford to continue down the path of larger and larger observational studies without meaningful controls. ■

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Pulmonary Perspectives

Deputy Editor's Insight

The practice of medicine has long involved both art and science. Art reflects the use of clinical judgment, the integration of experience and knowledge, to treat the individual patient. Even the best studies cannot cover every variable. As this Perspective notes, there is now excellent information leading away from the widespread use of the PAC in a number of conditions, but this does not preclude its sensible use in individual cases where it may be helpful. Because there are unlikely to be RCTs covering all situations, clinicians need to use their best judgment, using available RCTs as guides. It is also important to remember basic principles of safety: use the PAC for the shortest time necessary to avoid complications, such as thrombosis and infection.

—Deputy Editor

Don't Blame Infection-Related Mortality on Obesity

Some studies have demonstrated that there may be a protective effect of being obese in the ICU.

BY DOUG BRUNK
Elsevier Global Medical News

SAN DIEGO — No clear link exists between obesity and a heightened risk of mortality in infected patients in the surgical/trauma intensive care unit, according to results from a single-center study presented by Dr. Robert L. Smith at the annual meeting of the Surgical Infection Society.

Dr. Smith and his associates prospectively studied data on 807 infected patients from the surgical/trauma intensive care unit at the University of Virginia, Charlottesville, between November 1996 and December 2003. The researchers defined infections using Centers for Disease Control and Prevention criteria, said Dr. Smith of the university's surgical infectious disease laboratory.

The average Acute Physiology and Chronic Health Evaluation (APACHE II) score of the patients was 18. Nearly 55% of them received transfusions, and 52% were mechanically ventilated at the time of infection. They also had significant comorbid conditions, including hypertension (29%), cardiac disease (19%), and diabetes (17%). The average age of the patients was 57 years, and 63% were male.

Weight classes were determined using the National Health and Nutrition Examination Survey classification. The researchers categorized 4% of the patients as underweight, with a body mass index (BMI) of less than 18.5 kg/m^2; 32% as normal, with a BMI between 18.5 and 24.9; 30% as overweight, with a BMI between 25.0 and 29.9; 24% as obese, with a BMI of 30 to 39.9; and 10% as morbidly obese (BMI greater than 40).

The primary study outcome was in-hospital mortality. Of the 807 patients, 133 died during the hospital stay.

There was no association between in-hospital mortality and any of the BMI classifications. The researchers found that in-hospital mortality was closely associated with increasing age, increasing average APACHE II score, a history of diabetes, cardiac disease, hypertension, a history of cerebrovascular disease, renal insufficiency, a need for hemodialysis, a history of pulmonary disease, a requirement for mechanical ventilation while in the unit, a history of known malignancy, and a history of liver disease.

Logistic regression analysis found these characteristics independently associated with in-hospital mortality: liver disease (odds ratio 4.96), malignancy (OR 2.53), diabetes (OR 2.30), mechanical ventilation (OR 1.91), APACHE II score (OR 1.17 per integer), and age (OR 1.03 per integer).

The lack of an association between in-hospital mortality of infected patients and obesity surprised the researchers. It may be that nutritional reserve was afforded to obese patients, he said. But that is a theory he does not favor, "as there was no improved survival in this patient population as there was in other studies that have looked at obese patients in the ICU."

The lack of an effect of obesity on the mortality of patients with infections might have been a result of the staff's skill, Dr. Smith said. "Our experienced ICU staff is used to dealing with a variety of patients from various BMI categories. We have a robust bariatric patient [practice].

"Additionally, it could be that there were no differences among BMI categories because of presurgical screening, [or] maybe [the study] was underpowered to find a difference," he added.

"Obesity is estimated to be 9%-16% in those admitted to the ICU," he said. The general hypothesis is that there are worsened critical care outcomes in the obese patient population and that there are increases in morbidity rates, hospital stays, ICU stays, and numbers of health care–associated infections, he added.

"Certainly there are studies that have demonstrated [that obesity raises mortality in the ICU] in varying sample sizes. However, there are also studies that have demonstrated that there may a protective effect of being obese in the ICU," Dr. Smith said.

He added that some new basic science evidence has theorized that there may be immunologic protection for those who are moderately obese. ■

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Sleep Apnea's Effects on the Brain Worsen With Age

ARTICLES BY
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SALT LAKE CITY — The combination of obstructive sleep apnea and increased age may have an overwhelming effect on the brain's compensatory mechanisms, and early diagnosis and treatment of OSA in older patients may be important for preserving brain function, reported Liat Ayalon, Ph.D.

In a study Dr. Ayalon presented at the annual meeting of the Associated Professional Sleep Societies, 12 untreated OSA patients and 12 healthy good sleepers were studied with polysomnography and functional MRI. The interaction between group and age in regard to effects on brain function during a verbal learning task was analyzed.

Imaging studies showed that patients' brains were able to recruit additional resources to maintain intact performance and compensate for either age or OSA. Increased brain activation was noted in both older patients and those with OSA, compared with controls, specifically in the left inferior parietal lobe, thalamus, caudate, middle temporal gyrus, and fusiform; in the right anterior cingulate; and in the bilateral precuneus and cerebellum.

When patients had both increased age and OSA, however, decreased brain activation was noted, compared with younger patients, specifically in the right superior temporal gyrus and anterior cingulate, and in the bilateral parahippocampal gyri, caudate, precuneus, cerebellum, and fusiform gyrus, said Dr. Ayalon of the University of California, San Diego.

Patients ranged in age from 25 to 59 years. The groups were similar in age, gender, and body mass index. The average apnea-hypopnea index score—a measure of sleep apnea severity—was 35.1 in the OSA patient group and 1.9 in the control group.

The findings suggest that OSA in older patients is associated with decreased functioning, as evidenced by deficiencies in word recall in this study. Studies to address effects in even older patients (as this was a relatively young study population) and the effects of OSA treatment on brain function are planned, Dr. Ayalon said. ■

Sleep Study Demonstrates Lack Of Compliance With CPAP

SALT LAKE CITY — Continuous positive airway pressure adherence rates are suboptimal, findings from a study of sleep clinic patients suggest.

Of 528 adults diagnosed with obstructive sleep apnea and followed for a mean of 5 months, 63% had relatively poor adherence (use of less than 4 hours per night), 21% had adequate adherence (use of 4-6 hours per night), and only 16% had optimal adherence (use of more than 6 hours per night). Mean adherence was 3.1 hours per night, Carl Stepnowsky Jr., Ph.D., reported at the annual meeting of the Associated Professional Sleep Societies.

Adherence was specifically defined as use at the prescribed pressure, and was measured by an internal clock. Baseline disease severity correlated with higher levels of adherence.

Patients had a mean age of 59 years, and most had moderate to severe obstructive sleep apnea, with a mean apnea-hypopnea index of 38.8 events per night. Mean change scores (0.68 pounds in weight, –1.6 mm Hg in diastolic blood pressure, and –2.6 mm Hg in systolic blood pressure) were not statistically different from zero, noted Dr. Stepnowsky of the VA San Diego Healthcare System.

Suboptimal use of continuous positive airway pressure therapy results in ineffective treatment and can increase the risk of morbidity and mortality, he said.

A closer look at adherence rates showed that patterns of adherence were established as early as the first night of therapy; thus, preexisting factors might explain these patterns. Further studies are needed to replicate these findings, he said. ■

Self-Management Course Steers Patients Toward CPAP Adherence

SALT LAKE CITY — Patient education via a novel self-management training program may improve adherence in continuous positive airway pressure treatment, Carl Stepnowsky Jr., Ph.D., reported in a poster at the annual meeting of the Associated Professional Sleep Societies.

A total of 17 patients diagnosed with obstructive sleep apnea (OSA) and prescribed continuous positive airway pressure (CPAP) attended 4 weekly 2-hour self-management classes designed to provide education about OSA and solutions for common CPAP problems.

The Sleep Apnea Self-Management Program provided patients with information on OSA symptoms and consequences, problem-solving approaches for difficulties with treatment, emotional and cognitive symptom management, strategies to increase physical activity, communication skills improvement, and physician-patient partnership development.

Over the 30-day study period, CPAP adherence averaged 5.8 hours/night—close to the optimal level of at least 6 hours/night. The results compare favorably with previous studies showing that most patients have poor adherence (less than 4 hours use/night), according to Dr. Stepnowsky of the Veterans Affairs San Diego Healthcare System.

In addition, mean scores on the visual analog scale for sleepiness and the Center for Epidemiological Studies Depression scale were reduced from 7.2 to 5.5 and 11.4 to 6.9, respectively. Outcome expectations scores increased significantly, with a mean score increase from 2.7 to 4.5. ■