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# CHEST Physician

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**Although more research is needed, the expectation is that sleep apnea treatment will reduce stroke risk, said Dr. Vahid Mohsenin.**

## Links Tighten Between Sleep Apnea and Stroke

BY SHARON WORCESTER
*Elsevier Global Medical News*

SALT LAKE CITY — Studies consistently show a link between obstructive sleep apnea and stroke, with the most recent data showing that sleep apnea is an independent risk factor for stroke and death.

The cumulative data in regard to sleep apnea and stroke suggest that patients with sleep apnea should be treated with continuous positive airway pressure (CPAP) or other measures, Dr. Vahid Mohsenin said at the annual meeting of the Associated Professional Sleep Societies.

The evidence supporting the efficacy of CPAP is overwhelming—with good compliance, efficacy is about 90%—and the expectation is that treatment will reduce the risk of stroke, although more research is needed to confirm this, said Dr. Mohsenin, professor of medicine and director of the Yale Center for Sleep Medicine, Yale University, New Haven, Conn.

In fact, a guideline from the American Heart Association/American Stroke Association Stroke Council for the primary prevention of ischemic stroke was updated earlier this year to incorporate new information about stroke prevention, including data on the role of sleep-disordered breathing in stroke. The guideline was initially published in 2001.

Although the guideline stops

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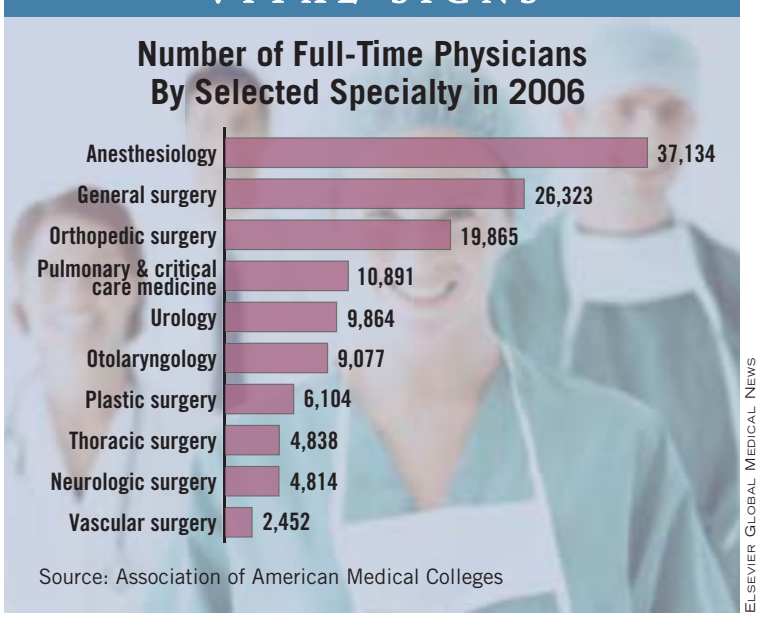
## VITAL SIGNS




Elsevier Global Medical News

## Resistant TB Strain Is Proving Deadly To HIV Patients

*52 of 53 patients killed in outbreak.*

BY FRAN LOWRY
*Elsevier Global Medical News*

TORONTO — A lethal strain of extensively drug-resistant tuberculosis (XDR-TB), which has been found to be widespread in South Africa and also is present in the United States, kills patients who are coinfected with HIV almost immediately after they are found to be infected with the disease, according to a late-breaking study presented at the 16th International AIDS Conference.

The virulent strain of tuberculosis has been a virtual death sentence, killing 52 of 53 patients during an outbreak in a rural South African hospital within 2 weeks of their diagnosis, said Dr. Neel R. Gandhi, formerly of Emory University, Atlanta, and now of Albert Einstein College of Medicine, N.Y.

All 53 XDR-TB patients were from KwaZulu Natal, an area of South Africa in which the TB/HIV coinfection rate is greater than 80%.

"These patients did not even appear to be terribly sick. They were not thought to be dying when they were hospitalized," he said.

There is an epidemic of TB and HIV coinfection in South Africa, Dr. Gandhi said. Although antiretroviral therapy has significantly reduced mortality from HIV in this part of the world, drug-resistant strains of tuberculosis are negating this benefit, with 67% of deaths now attributed to multidrug-resistant (MDR) strains of TB, he said.

Dr. Gandhi and colleagues made their grim discovery after they did sputum culture and drug susceptibility testing on patients with known or suspected TB between January 2005 and March 2006. Sputum collected from 1,540 patients revealed that 536 (35%) were positive for TB. Of these, 221 patients (41%) had MDR-TB, and 53 (24%) had XDR-TB,

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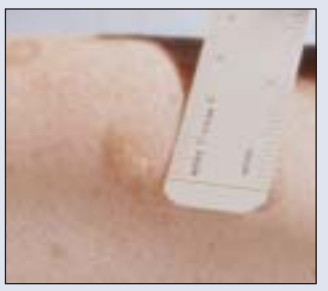

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## GAPP Shows Holes in Asthma Care

BY PATRICE WENDLING
*Elsevier Global Medical News*

MONTREAL — There is a disconnect in communications between physicians and parents of children with asthma, according to an analysis of data from a new global asthma survey.

Parents and physicians disagree on the amount of time dedicated to asthma education in the office; who initiates discussion about medication side effects; and the level of compliance with asthma medications.

The North American pediatric findings of the Global Asthma Physician and Patient (GAPP) study also confirm what most physicians already know: Asthma medication compliance is low; patients with poor compliance experience more symptoms; and side effects lead patients to switch or drop medications.

The authors conclude that patient compliance and outcomes could be enhanced through better physician-patient communications and asthma education, and the availability of new treatment options with lower side-effect profiles, Dr. Ronald Dahl of Aarhus (Denmark) University Hospital, and his associates on the GAPP Survey Working Group reported in a poster at the Seventh International Congress on Pediatric Pulmonology.

The GAPP survey is the first-ever global quantitative survey to uncover asthma attitudes and treatment practices among patients and physicians. The survey was conducted between May and August 2005 in 16 countries and included a total of 5,482 online and telephone interviews with

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# Public Health Chiefs Take Aim at Drug-Resistant TB

BY JONATHAN GARDNER
*Elsevier Global Medical News*

International public health officials last month announced actions necessary to combat deadly new strains of tuberculosis that are resistant to most drugs on the market.

Officials from the South African Medical Research Council, the World Health Organization, and the Centers for Disease Control and Prevention called for rapid surveys of the prevalence of extensive drug-resistant TB in high-risk countries, increased laboratory capacity to carry out vital culture and drug resistance testing, improved clinical capacity, infection control precautions, and research support for new drugs and diagnostic tests.

Of particular concern are countries with a high prevalence of HIV/AIDS, which public health officials warned has the potential to turn extensive drug-resistant TB into "an uncontrollable epidemic." They called for universal access to antiretroviral drugs in joint TB/HIV projects.

Extensive or extreme drug-resistant TB describes strains that are resistant to the two most potent anti-TB drugs, isoniazid and rifampin, and at least three of six classes of second-line drugs.

International public health leaders met last month in Johannesburg in an emergency session with public health authorities from 11 southern African countries to discuss how to combat extensive drug-resistant TB.

"It is an area where the global community will need to be helpful to the countries that don't have resources, but locally, there needs to be ownership of the issue," Ken Castro, director of the CDC's division of tuberculosis elimination, said in a press conference in Johannesberg to discuss extensive drug-resistant TB.

New drugs and vaccines are in the works, officials said. Dr. Castro said four agents look promising as drugs, but must still be proved through trials.

Use of vaccines, including the BCG vaccine, is a possible approach, Dr. Castro said, although he added, "we will not be able to rely on vaccines [alone] to address the problem confronting us."

Infection control in health care facilities is a priority, he said. To keep extensive drug-resistant TB from spreading to other patients, health care facilities need to promptly identify patients suffering from it, separate them from the rest of the patients, and make use of respiratory devices. ■

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# XDR-TB Threatens

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with resistance to all first- and second-line drugs—isoniazid, rifampin, ethambutol, streptomycin, ciprofloxacin, and kanamycin.

Spoligotyping—a polymerase chain reaction–based typing system—revealed that 90% of the XDR-TB patients were infected with a genetically similar strain, Dr. Gandhi said.

"We suspect that these cases of TB were transmitted in the hospital because 64% of these XDR-TB patients were hospitalized before they developed this aggressive strain of TB and 36% had no prior TB. The same outbreak also killed six healthcare workers in the hospital," he said in an interview.

The emergence of both MDR-TB and XDR-TB is significant, both in the United States and worldwide, he added. "The threat of these strains puts the gains in survival that we have achieved with antiretroviral therapy and TB DOTS [directly observed therapy, short course] in peril, and we need to be very vigilant and increase our surveillance, not only in South Africa but everywhere, especially in resource-poor settings," Dr. Gandhi said. ■

***Dr. Aymarah Robles, FCCP, comments:*** *MDR-TB is defined as resistance to INH and rifampin and requires the use of second-line TB drugs (SLD) for therapy. Extensive or extreme drug resistant TB laboratories performed from 2000 to 2004 revealed that of 17,690 tested isolates, 20% were MDR-TB and 2% were XDR-TB (MMWR Rep 2006; 55:301-5).*

*XDR-TB poses a grave public health threat, especially in populations with high rates of HIV and where there are few health care resources. Recommendations outlined in the WHO Guidelines for the Programmatic Management of Drug Resistant Tuberculosis include "strengthen basic TB care to prevent the emergence of drug resistance, ensure prompt diagnosis and treatment of drug resistant cases to cure existing cases, and prevent further transmission, increase collaboration between HIV and TB control programmes to provide necessary prevention and care to co-infected patients, increase investment in laboratory infrastructures to enable better detection and management of resistant cases."*

# Asthma Survey

**GAPP** • *from page 1*

1,017 parents of children diagnosed with asthma, 1,006 physicians who treat children with asthma, 1,726 adults over 18 years of age with asthma, and 1,733 physicians who treat adults.

The study, supported by an educational grant from Altana Pharma and conducted in cooperation with the World Allergy Organization and American College of Allergy, Asthma, and Immunology, was sufficiently powered to ensure statistical significance globally and in each country. The analysis presented here was based on 618 interviews conducted in North America among 314 parents and 304 physicians.

According to parents, physicians don't discuss specific asthma management issues such as the development of an individual management plan (66%); correct inhaler technique (69%); and keeping daily symptom/medication diaries (25%). In every case, physicians' perceptions of the incidence of these discussions were higher (90%, 97%, 53%, respectively).

Consistently, parents also perceive that less time is spent on asthma education than do physicians. While 18% of parents reported that during a typical office visit, no time is spent on asthma education, about 84% of physicians report spending at least half of their office time on education.

Overall, 27% of parents answered "false" or "not sure" when asked whether mild asthma attacks could be fatal. A disparity was seen regarding lack of parental awareness of both short- and long-term side effects of inhaled corticosteroids. In all, 29% of parents reported that their children had experienced short-term side effects while taking asthma medications and 5% reported long-term side effects.

Reported treatment compliance also differed between parents and physicians. Only 16% of parents reported that their children were compliant 51%-80% of the time, whereas physicians reported that this occurred 46% of the time.

More of the survey's findings are available at www.gappsurvey.org. ■



**CHEST PHYSICIAN**

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# Inflammation's Role Complicates New CF Therapies

BY PATRICE WENDLING
*Elsevier Global Medical News*

MONTREAL — A variety of new therapeutic approaches are being utilized to control airway inflammation in cystic fibrosis, but the optimal form of therapy remains to be defined, Dr. Felix Ratjen said at the Seventh International Congress on Pediatric Pulmonology.

Airway inflammation is present in most cystic fibrosis (CF) patients even before the onset of chronic infection, but it is not yet known whether this is specific to CF or related to a defect of mucus airway clearance. Two therapeutic approaches have emerged—one that directly targets inflammation and a second that addresses the underlying mucociliary clearance defect.

In either case, a better understanding of the factors regulating inflammation in the CF lung is needed, because any intervention that decreases airway inflammation may be accompanied by the detrimental effect of promoting airway infection.

"The question we really need to understand in the future is how much inflammation is needed to fight infection in CF and how much downregulation we can accept in our patients," said Dr. Ratjen of the Hospital for Sick Children, Toronto.

Dr. Ratjen reviewed the following kinds of intervention:

► **Antibiotics** are being used to treat chronic infection, but also have been shown to have an impact on inflammation. In an induced sputum study, antibiotics significantly reduced neutrophil counts and interleukin (IL)-8 production in CF patients. Intravenous antibiotic therapy has been shown to significantly reduce arginase levels, which are elevated in CF patients and thought to contribute to low airway nitric oxide formation and impaired lung function (Am. J. Respir. Crit. Care Med. 2005;172:1523-8). "There's some promise, but we need more data in order to see how useful this will be," he said.

**'We really need to understand ... how much inflammation is needed to fight infection in CF.'**
**DR. RATJEN**

► **Osmotic agents** are being explored to address depletion of airway surface fluid in CF lungs that contribute to delayed mucociliary clearance. So far, only hypertonic saline has been tested. Although hypertonic saline improves lung function, it did not affect airway inflammation. The studies were relatively short in duration, and longer study is needed, he said.

► **Inhaled corticosteroids** are widely used, but so far there is no evidence that they are useful in downregulating inflammation. A recent multicenter, double-blind randomized controlled trial in the United Kingdom revealed no impact in time to first exacerbation when inhaled fluticasone was withdrawn from CF patients (Am. J. Respir. Crit. Care Med. 2006;173:1356-62). One explanation is that inhaled steroids fail to have an impact on elastase, which is thought to be an important factor in CF lung tissue destruction, Dr. Ratjen said. Systemic corticosteroids have some anti-inflammatory effects but are not viable because of their side effects.

► **Antielastase therapy** has been shown to be safe in CF patients. But in a recent phase II study, nebulized recombinant human α-1 antitrypsin (an inhibitor of neutrophil elastase) did not affect the amount of elastase in CF sputum samples after 4 weeks of treatment (Pediatr. Pulmonol. 2006;41:177-83). The finding may be related to dose, he said. Newer agents that are resistant to oxidation are being tested and show promise.

► **Leukotriene $B_4$** is important in driving neutrophils into the airways in CF. But a large phase II trial of a $LTB_4$-receptor antagonist was stopped early due to a higher rate of pulmonary exacerbations in treated patients. "This raises the question of what's the balance of inflammation we should have in CF patients," he said. "Maybe this was too effective as an anti-inflammatory agent, and if we block neutrophil influx into the lung, this may have a negative effect on patients over time."

► **Glutathione,** a pivotal antioxidant in neutrophil production, is reduced in CF patients. A phase I study (Proc. Natl. Acad. Sci. USA 2006;103:4628-33) showed deficient glutathione levels in circulating neutrophils in CF patients, and a marked decrease in sputum elastase activity and neutrophil burden after treatment with oral N-acetylcysteine, a glutathione prodrug that has been available for years in Europe. The results are promising, but additional data are needed to confirm its benefits in CF patients, Dr. Ratjen said. ■

***Dr. Steven M. Rowe, MSPH, FCCP, comments:*** *Significant interest lies in identifying an agent that controls the intense inflammatory milieu of the CF lung that is generalizable to a diverse CF population and without the side effects seen with high-dose ibuprofen or systemic corticosteroids. Identification of an agent that is efficacious without increasing the risk of infection faces future challenges and may depend on whether the patient is irreversibly colonized with* Pseudomonas *or other virulent pathogens.*

# Low-Dose Avian Flu Vaccine Shows Preliminary Promise

BY ROBERT FINN
*Elsevier Global Medical News*

A whole-virion vaccine for the H5N1 avian influenza virus produces acceptable levels of immunity even at low doses, researchers found in a preliminary study.

Developed at the Sinovac Biotech Co. in Beijing, the vaccine appears to be effective when delivered in two 10-mcg doses 28 days apart. A different whole-virion vaccine required two 90-mcg doses, and a split-virion vaccine required two 30-mcg doses.

Given current manufacturing constraints, supplies of that split-virion vaccine would be limited to about 225 million people, far lower than worldwide demand in the event of an avian flu pandemic.

A much greater number of people could be treated if the new dosage-sparing vaccine is found effective in larger clinical trials.

Dr. Jiangtao Lin, FCCP, of the Chinese-Japanese Friendship Hospital, Beijing, and colleagues reported on a placebo-controlled, double-blind, phase I trial of 120 volunteers aged 18-60 years.

The participants were given either two injections of placebo or two injections of an inactivated, whole-virion influenza A (H5N1) vaccine at four doses between 1.25 mcg and 10 mcg. Aluminum hydroxide was added as an adjuvant, a practice previously shown to reduce the dosage needed to produce immunogenicity.

While all four doses produced immune responses, the 10-mcg dose produced 78% seropositivity, significantly higher than that produced by the other doses (Lancet 2006 Sept. 7 [Epub DOI:10.1016/S0140-6736(06)69294-5]).

No serious adverse events were reported at any dose level up to 56 days after the first injection. Local and systemic reactions were all rated as mild and transient. Pain at the injection site in the deltoid muscle was more frequently reported in the vaccine groups than in the placebo group, but there were no significant differences in systemic reactions, the most common of which were fever, headache, myalgia, and nausea.

In an accompanying editorial, Dr. Iain Stephenson of the Leicester (England) Royal Infirmary noted that vaccination will be central to any response to an avian flu pandemic (Lancet 2006 Sept. 7 [Epub DOI:10.1016/S0140-6736(06)69340-9]). The 1918 influenza pandemic—also derived from an avian virus—caused up to 50 million deaths. Dr. Stephenson said that the dose-sparing approach described by Dr. Lin could be crucial for obtaining a global supply of the vaccine.

He also noted that earlier whole-virion vaccines were associated with febrile reactions, especially in children. Although larger clinical trials will certainly be necessary before widespread immunization, Dr. Stephenson suggested that a modest amount of reactogenicity might be acceptable in the face of the threat of a worldwide pandemic.

The authors of the study acknowledged that funding came from the Sinovac Biotech Co., which had a role in both study design and monitoring. They said the company had no role in data collection or in writing the report. ■

# Referral Program Cut Waiting Times for Lung Cancer Patients

CALGARY, ALTA. — A community hospital–based virtual lung clinic staffed with a clerical navigator was able to improve waiting times from chest x-ray to diagnosis for patients with suspected lung cancer from 107 days to 31 days, Dr. Robert Zeldin reported at the annual Canadian Surgery Forum.

"Fast tracking lung cancer patients does work," said Dr. Zeldin of the division of thoracic surgery at Toronto East General Hospital.

In current practice, he said, "from the time of suspicion of lung cancer to the time of treatment, the patient journey is fragmented."

**The goal was to get a patient with suspected lung cancer referred to a specialist in 3 working days.**
**DR. ZELDIN**

To shorten these patients' waiting times, Dr. Zeldin and his associates set up a "virtual lung clinic," which involved the referring primary care physicians, hospital-based specialists, and a regional cancer center. The goal was to get a patient with suspected lung cancer referred to a respirologist or thoracic surgeon within 3 working days.

The investigators hired a clerical navigator to answer what they called a "lung hotline" and to process forms they created for referring primary physicians. That way, Dr. Zeldin said, "when a patient comes in with either a suspected symptom of lung cancer or a suspicious chest x-ray, then it becomes an easy method of referral for the family doctor. They're directed on the form to schedule with the appropriate specialist."

The clerical navigator also booked CT scans and bronchoscopies as indicated. A tumor board consisting of two thoracic surgeons and three respirologists oversaw the coordination of care.

Over a 3-month period, the researchers compared waiting time intervals between chest x-ray and diagnosis from a group of 52 historical controls and a group of 61 patients who participated in the new referral program. The wait times improved dramatically, from a mean of 107 days in the control group to a mean of 31 days in the referral program patients.

Dr. Beldin said that a larger study is underway to determine the impact of the referral program on disease staging at time of diagnosis and subsequent treatment.

Cancer Center Ontario and the Ontario Ministry of Health and Long-Term Care funded the study.

**—Doug Brunk**

# New Options Taking Shape In TB Diagnostic Testing

BY BRUCE JANCIN
*Elsevier Global Medical News*

LISBON — Better diagnostic tests are seen as essential in the campaign to control the global tuberculosis epidemic—and help is on the way.

The archaic, nearly 100-year-old tuberculin skin test was until recently the sole tool available for diagnosis of latent TB infection. The skin test has several limitations, chiefly its low specificity due to cross-reactivity with the BCG vaccine and false-positives in persons infected with non-TB mycobacteria, Dr. Karin Weldingh said at the 12th International Congress on Infectious Diseases.

Major international aid organizations including the Foundation for Innovative New Diagnostics, the Stop TB Partnership, and the World Health Organization have declared development of faster, simpler, more convenient, and more accurate TB diagnostic tests to be a high priority.

Recently, two novel cell-mediated immune response–based assays have become widely commercially available as alternatives to the skin test for detection of latent TB. The in vitro assays—the QuantiFERON-TB Gold and T-SPOT.TB assay—measure interferon-γ released by sensitized T cells following stimulation by antigens specific to *Mycobacterium tuberculosis,* including culture filtrate protein-10 (CFP-10) and early secreted antigenic target-6 (ESAT-6).

Studies show these assay kits have better specificity for detection of latent TB and are at least as sensitive as the skin test for active TB; plus, they're interpreted more objectively, with results available in a day, said Dr. Weldingh of the Statens Serum Institute, Copenhagen.

The QuantiFERON-TB Gold assay was first to win approval by the Food and Drug Administration. Late in 2005, the Centers for Disease Control and Prevention recommended its use in all situations where the skin test has been used.

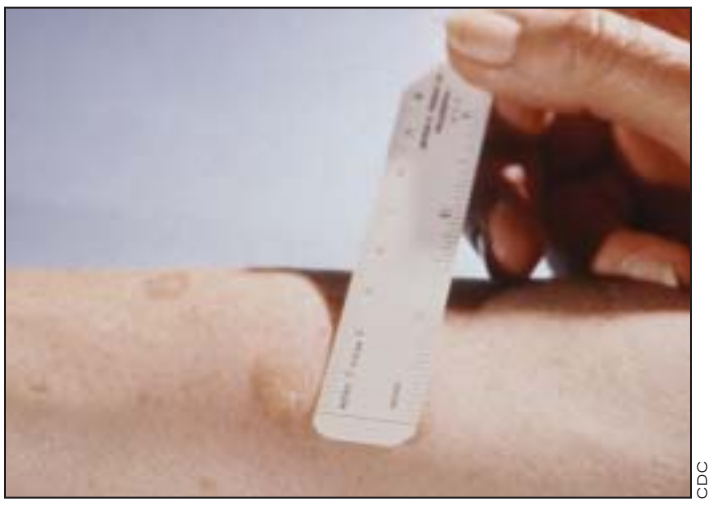
The downsides of using these assays in the developing world are that they require living cells and ready access to a lab for enzyme-linked immunosorbent assay. "This means you have to process blood samples within 12 hours," she explained at the congress sponsored by the International Society for Infectious Diseases.

Dr. Weldingh sees the assays ultimately being most useful for latent TB case finding via contact tracing and screening of high-risk groups in low-endemic, highly developed areas such as Western Europe and the United States. The tests should also prove useful in areas with an intermediate TB incidence and good infrastructure, such as parts of Brazil.

In places where TB rates are high, roads poor, and laboratories hard to come by, these tests aren't practical. The solution in such places is probably an improved skin test that utilizes *M. tuberculosis*–specific antigens rather than the traditional purified protein derivative; such tests are now under evaluation in field studies.

Another approach involves serologic antibody tests. These are much less temperature-sensitive and fragile than the interferon-γ tests, they don't require living cells or access to a laboratory, and they yield results in 15-30 minutes.

The newer ones, which utilize *M. tuberculosis*–specific antigens, perform best. They'll never serve as a stand-alone test for diagnosis of active TB, but they could have a role as rule-in screening tests that trigger definitive testing, she said. ■



CDC

**Recently, two novel cell-mediated immune response–based assays have become widely commercially available as alternatives to the tuberculin skin test for detection of latent TB.**



# FDA Approves Generic Forms of IV Ciprofloxacin

BY ELIZABETH MECHCATIE
*Elsevier Global Medical News*

Several generic versions of the intravenous formulation of the widely used fluoroquinolone ciprofloxacin have been approved by the Food and Drug Administration, as part of what the agency says is its effort to make lower-cost generic drugs more widely available.

The generic formulations are versions of the trade formulation of CIPRO IV, approved in 1991 and marketed by Bayer Corp. Ciprofloxacin injection is provided in a concentration of 10 mg/mL, and is packaged in 20-mL and 40-mL vials, and in a 120-mL pharmacy bulk package, according to a statement issued Aug. 28 by the FDA to announce the approval.

Drug Topics, an online magazine, listed Cipro IV injection as the top-selling drug in its list of the 200 highest-selling brand name drugs in the United States in 2005, according to the statement. The wholesale acquisition cost of the drugs used in hospitals totaled $115,353,072.

Ciprofloxacin injection is approved for treating infections caused by susceptible strains of designated microorganisms for certain infections in adults, including urinary tract infections, lower respiratory tract infections, nosocomial pneumonia, bone and joint infections, complicated intraabdominal infections, skin and skin structure infections, acute sinusitis, and empirical therapy in febrile patients with neutropenia. It is approved for treating complicated UTIs and pyelonephritis due to *Escherichia coli,* in patients aged 1-17 years, but not as a first choice, according to the CIPRO IV label. It is also approved to reduce the incidence of inhalational anthrax after exposure to aerosolized *Bacillus anthracis* in adult and pediatric patients.

The approval of these generic versions of ciprofloxacin injection "can bring significant savings to the millions of Americans who have certain bacterial infections that can be treated with ciprofloxacin," Gary J. Buehler, a pharmacist and director of the FDA's Office of Generic Drugs, said in the FDA statement. ■

# Elective Pneumonectomy May Lead to Low Mortality

BY DOUG BRUNK
*Elsevier Global Medical News*

CALGARY, ALTA. — Elective pneumonectomies carry a low mortality rate and result in shorter hospital stays, according to a long-term study carried out at a high-volume regional academic medical center for thoracic surgery.

However, more complicated pneumonectomies may carry an increased risk of death or clinical problems, Jennifer Rattenbury reported at the annual Canadian Surgery Forum. The finding is important because according to the medical literature pneumonectomies "are associated with a higher rate of complications and a higher mortality rate," said Ms. Rattenbury, who is a clinical research coordinator with the division of thoracic surgery at the University of British Columbia, Vancouver.

"This is compounded by the fact that in recent years the patient base [for the procedure] is broadening to patients that are older and have more comorbid diseases," as well to those who have undergone neoadjuvant therapy.

In the medical literature, she added, the mortality rates for pneumonectomy range from 0% to 25%, but generally stand at 10%. The complication rates vary between 15% and 43%.

She and her associates reviewed the records of 128 patients with a mean age of 61 years who underwent an elective pneumonectomy at Vancouver General Hospital between March 2001 and January 2006. More than half (69) were male and 67 of the procedures were left sided. A total of 85 of the procedures were simple pneumonectomies, and 43 were complex.

Of the 128 patients, 111 (87%) had either smoked or been exposed to secondhand smoke on a regular basis, and 13 (10%) had undergone neoadjuvant therapy prior to the operation.

Of these, three received chemotherapy, two had radiation, and eight had a combination of the two.

Primary lung cancer was the indication for pneumonectomy in 120 of the patients, while metastatic cancer to the lung was the indication for the remaining 8. More than half of patients (63%) had stage II or III disease.

Of the 128 patients, 77 (60%) had no complications while 51 (40%) had one or more complications.

Overall, 20% of the complications were considered to be minor, including pleural effusion, recurrent nerve paralysis or injury, and pericarditis, while the rest were considered to be major, including arrhythmia, pneumonia, respiratory failure, bronchial fistula, and pulmonary edema.

**OF THE 128 PATIENTS, 60% HAD NO COMPLICATIONS, WHILE 40% HAD ONE OR MORE. OVERALL, 20% OF THE COMPLICATIONS WERE CONSIDERED TO BE MINOR.**

Ms. Rattenbury reported that 5 of the 128 patients died, for a mortality rate of 3.9%. Four of the 5 patients who died had a complex pneumonectomy, making the mortality rate for that subset of 43 patients 9.3%.

"All five died after developing pneumonia and respiratory failure," she said. "Interestingly, none of them had received any neoadjuvant therapy."

Logistic regression analysis revealed that only two factors predicted a major complication: an increase in age or an increase in the Charleston Comorbidity Index score. The extent of the disease, the extent of the pneumonectomy, preoperative lung function, time under anesthetic, and neoadjuvant therapy were not predictive factors.

"Our overall mortality rates are on the lower end, and our complication rates are similar to those previously reported," Ms. Rattenbury said.

She hypothesized that the mortality rates are low because Vancouver General Hospital is a high-volume facility for thoracic surgery. "It's been published that there is a relationship between hospital volume and mortality rates," she said. "Our hospital experience is probably part of that." ■

***Dr. Robert J. Cerfolio, FCCP, comments:*** *Although pneumonectomy has increased risk when compared to other types of elective pulmonary resection, if it is the only operation possible that achieves a complete margin negative resection, then it remains a viable option for the patient with non–small cell lung cancer.*

# Necrotizing Pneumonia Rises in Pediatric Cases

BY PATRICE WENDLING
*Elsevier Global Medical News*

MONTREAL — Necrotizing pneumonia is a more common complication of community-acquired pediatric pneumonia than was previously appreciated, Dr. Gregory Sawicki and associates reported at the Seventh International Congress on Pediatric Pulmonology.

An analysis of 80 cases at Children's Hospital Boston identified a rise in cases from 12 during 1993-1996 to 29 in 2003-2005, and a troubling increase in new pathogens.

"Though pneumococcus was the prevailing pathogen, we observed a rising trend of different causative microbiology including MRSA [methicillin-resistant *Staphylococcus aureus*]," said Dr. Sawicki of the hospital's division of respiratory diseases.

Despite the serious morbidity, massive parenchymal damage, and prolonged hospitalization observed in the series, long-term clinical outcomes were universally excellent, he said.

The cases were retrospectively identified from a database of CT scans spanning January 1993 to February 2005, followed by a full chart review. To varying degrees, all cases had large areas of decreased parenchymal enhancement and loss of normal lung parenchymal architecture, with multiple thin-walled and fluid-filled cavities. Nosocomial and significant preexisting disease cases were excluded from analysis.

The median age of the children was 3.6 years (range 3 months to 19 years). Forty-two were male, and 14 had a history of respiratory disease. They were symptomatic for an average of 9 days before hospitalization, and the median length of stay was 12 days (range 3-84 days).

Remarkable laboratory findings were leukocytosis (mean white blood cells 18,400 cells/μL); anemia (mean hemoglobin 10.4 g/dL); and hypoalbuminemia (mean albumin 2.0 g/dL).

Positive cultures were identified in 38 (48%) cases, including *Streptococcus pneumoniae* in 18. Since 2002, an increasing number of other organisms were identified, including *Fusobacterium* species, *Pseudomonas aeruginosa*, MRSA, methicillin-susceptible *S. aureus*, and *S. nonaureus*.

Even though 68% of patients received antibiotics prior to hospitalization, recovery of a positive culture was not significantly affected by pretreatment with antibiotics, he said.

Pleural effusion was frequent and found in 69 of 80 (86%) patients. CT scans were particularly useful in helping to differentiate between fluid on a plain field x-ray and actual parenchymal disease, Dr. Sawicki said. "A lot of times when you get a large pleural effusion or large pneumonia in a patient, a plain field is not able to distinguish it as well, and one may rush to aggressive intervention when in fact it may not be warranted," he said.

**EVEN THOUGH 68% OF PATIENTS RECEIVED ANTIBIOTICS PRIOR TO HOSPITALIZATION, RECOVERY OF A POSITIVE CULTURE WAS NOT SIGNIFICANTLY AFFECTED.**

Interventions in effusion patients included chest tube in 47 patients (68%); pigtail catheter placement in 41 patients (59%); chest tube and surgery in 16 patients (23%); thoracentesis only in 6 patients (9%); thrombolysis in 17 patients (25%); open thoracotomy/pleural decortication in 3 patients (4%); and one partial lung resection. Patients with effusion had pleural drainage ranging from 1 to 52 days (median 6 days).

In the series, conservative management with chest drainage alone resulted in outcomes similar to those of surgical management, with no significant differences reported in length of hospital stay, length of fever, or length of pleural fluid drainage, Dr. Sawicki reported.

Overall complications included 10 patients (13%) who developed a bronchopleural fistula, 1 who needed extracorporeal circulation membrane oxygenation, 25 (32%) who needed ICU care, and 8 (10%) who were readmitted. All 63 patients seen post discharge at a median of 6 months had clinical resolution of symptoms within 2 months.

Audience members questioned whether necrotizing pneumonia is really increasing or whether identification has become more frequent with the use of CT scans. That question could not be definitely answered by the study, Dr. Sawicki said. However, the number of scans for a diagnosis of pneumonia has increased at his institution, he noted. ■

## Child Health Web Site Open

The National Institute of Child Health and Human Development has unveiled its redesigned Web site. The Web site is a portal to a wide array of information for patients and scientists—from child health to developmental disorders to women's health to basic and clinical research. For more information, visit the NICHD at www.nichd.nih.gov.

# Preterm Birth and Small Size Have Lasting Effect on Lungs

BY PATRICE WENDLING
*Elsevier Global Medical News*

MONTREAL — The first long-term follow-up of infants with bronchopulmonary dysplasia suggests that the consequences of preterm birth lessen over time, but are enduring.

"The consequences of preterm birth clearly seem to lessen over time going from the newborn period into early adult life; but being small for gestational age and preterm, the effects are much more long-lasting, both in terms of airflow obstruction and cardiovascular reprogramming," Dr. Andrew Bush said at the International Congress on Pediatric Pulmonology.

**The effects of being preterm in terms of airflow obstruction are much more long-lasting.**
**DR. BUSH**

The analysis included 60 adults, aged 20-22 years, from an original cohort of 300 babies with chronic lung disease of prematurity, and 50 new, age-matched term controls. The preterm group included 23 adults who were defined as small for gestational age (less than 1,500 g) and 37 defined as appropriate for gestational age (1,500-2,000 g). Evaluations included spirometry, exhaled nitric oxide testing, skin-prick tests, and exercise tests.

Forced expiratory volume in 1 second ($FEV_1$) *z* scores were not significantly different among the three groups. But when those scores were plotted by birth weight, birth weight was found to be a significant determinant of $FEV_1$ outcomes for preterm small-for-gestational-age (SGA) babies even after 20 years of environmental influences and self-abuse, said Dr. Bush, professor, National Heart and Lung Institute, Royal Brompton Hospital, London.

Birth weight also was a determinant of $FEV_{25-75}$ scores in this group. No association between birth weight and lung function was found in preterm appropriate-for-size survivors or controls, he said.

Using respiratory mass spectrometry, the investigators, led by Indra Narang, also of Royal Brompton Hospital, measured cardiac output and carbon monoxide transfer ($DL_{CO}$). During exercise in healthy subjects, there can be a fivefold rise in cardiac output as a result of increases in both heart rate and stroke volume. $DL_{CO}$ can increase by up to 50% because of recruitment and distention of the pulmonary capillaries, notaby in the upper airways.

Cardiac output and $DL_{CO}$ were reduced at rest, but normalized on exercise in preterm SGA survivors. These findings were not present in the other groups.

"Is it possible that being SGA in utero you're programmed to protect your brain and kidneys at times of starvation, at times of low oxygen supply, and that this effect is persisting into adult life; so that at rest you have persistent low blood flow as an adaptive mechanism that's been programmed into you before birth?" he suggested. "I emphasize this is tentative and hypothesis generating."

Dr. Bush acknowledged that the follow-up numbers are small, but called the findings intriguing.

Questions for the future include how to monitor this aging preterm population, whether their lung function will deteriorate faster as they age, and how to address new bronchopulmonary consequences that will arise as neonatologists become more skilled at salvaging even more immature babies. ■

## Asthma, Smoking Raise Infant Bronchiolitis Risk

SAN FRANCISCO — Maternal smoking, maternal asthma, or both are independent risk factors for the development of bronchiolitis in infants, according to findings of a large retrospective study.

After controlling for maternal race, region of residence, infant sex, infant birth weight, and whether the child has one or more living siblings, children of women who had a history of asthma and who smoked during pregnancy were 47% more likely to develop bronchiolitis during their first year of life than children whose mothers had neither risk factor, Dr. Kecia Carroll reported at the annual meeting of the Pediatric Academic Societies.

Children of mothers who had asthma alone had a 39% increased risk of bronchiolitis, and children of mothers who smoked but did not have asthma had a 14% increased risk. All of these adjusted hazard ratios were statistically significant.

Dr. Carroll and her colleagues from Vanderbilt University, Nashville, Tenn., combined records from the state of Tennessee's Medicaid program with public records data from 1995 through 2003, and isolated 101,459 mother-infant dyads that met certain criteria: All mothers were enrolled in Medicaid continuously beginning at least a year before the birth through a year after the birth, and the infants were all healthy, full-term, singleton babies without chronic lung or heart disease.

Overall, about 20% of the infants developed bronchiolitis during their first year of life. Before adjusting for the potential confounders mentioned above, about one-third of infants with both maternal asthma and maternal smoking had at least one clinic, emergency department, or hospital visit for bronchiolitis, compared with 24% of infants with maternal asthma, 24% of infants with maternal smoking, and 18% of infants with neither risk factor.

Maternal smoking, asthma, or both also increased the risk for severe bronchiolitis, defined as disease requiring 3 or more days of hospitalization. The risk increased a statistically significant 19% for maternal smoking, 52% for maternal asthma, and 39% for both smoking and asthma. The meeting was sponsored by the American Pediatric Society, Society for Pediatric Research, Ambulatory Pediatric Association, and American Academy of Pediatrics.

**—Robert Finn**

AMERICAN COLLEGE OF CHEST PHYSICIANS

# NEWS FROM THE COLLEGE

BY W. MICHAEL ALBERTS, FCCP

## PRESIDENT'S REPORT
# My Final Column

I have just returned from the ACCP Pulmonary Board Review Course in Orlando. As it is just "down the street" from Tampa, I drove over, gave three lectures, and dropped by the office on my way home to "put out a few fires" and commit my editorial thoughts to paper, before taking off tomorrow for the European Respiratory Society meeting in Munich. The triple ACCP board review courses (sleep medicine, critical care medicine, and pulmonary, all held at the Dolphin Resort at Disney World, one after another) were outstanding and extremely well attended. The College does many great things, and the board review courses rank near the top.

This President's Report is bittersweet, as it will be my final column as a sitting President. The year has literally flown by.

As advised by one of my predecessors, the year will be challenging and exhausting but the most professionally rewarding of your career. As the end of my term approaches, I find that I could not agree with him more.

During my presidential report at the Board of Regents meeting in July, I estimated that when averaged over the year, I would spend 3 hours per day on College business, whether that be brainstorming with Al Lever on the phone, preparing for the Executive Committee conference calls, answering e-mails, or any of a myriad of other tasks.

Yet, the work did not seem onerous, as 99% of the presidential duties were rewarding and satisfying and advanced the College's vision and mission.

While I have the floor and your attention, let me thank some very special people.

First and foremost, I would like to thank my wife Debra, my daughter Katie, and my son Michael. I sincerely appreciate their support and patience during the year. At times, Debra was busier than I with College business in her role as Chair of the Ambassadors Group. I am extremely proud of her accomplishments in this position.

I would also like to thank the University of South Florida College of Medicine and the Moffitt Cancer Center for permitting me to serve in this presidential role. I would like to thank Al Lever and the entire ACCP and CHEST Foundation staff. After working so closely with this group for the past year, I feel qualified to reiterate that we have the best in the business working with us.

Thanks is also due any number of other individuals, including the Executive Committee, the Board of Regents, the Governors, the NetWork Chairs, the Committee Chairs, and on and on. The College is blessed with many talented and committed individuals who share in the ACCP mission and vision.

Let me close by thanking you, the membership of the ACCP, for affording me the privilege of serving as your President. It is an honor that I will forever cherish.

I leave the presidency in good hands and the College in great shape, both financially and organizationally. There are challenges looming but nothing that ACCP CEO and Executive Vice President Al Lever, President-Elect Mark Rosen, President-Designate Al Thomas, and the entire ACCP family can't handle. ■

# CHEST Foundation Presents Tobacco Education Panel

The CHEST Foundation presented its tobacco educational work at the 13th World Conference on Tobacco OR Health, July 12-15, 2006, in Washington, DC. This meeting is held every 4 years with heavy participation from WHO, CDC, and a number of international organizations. The 90-minute symposium/panel on "Tobacco Education in Women: International Tools," in which The CHEST Foundation participated, was moderated by Dr. Terry Fontham.

Dr. Deborah Shure, Master FCCP and Past President of ACCP, started the panel and spoke about the evolution and the history of The CHEST Foundation and its focus on tobacco prevention that is particularly geared to women and girls. Dr. Kay Guntupalli, FCCP, past Trustee of The CHEST Foundation, followed and spoke about the development of age and culturally specific tools for children globally and for the Indian subcontinent. She shared details on the development, evaluation, and impact of tools that she has developed for The CHEST Foundation. Dr. Judith Mackay, past honoree of The CHEST Foundation and the ACCP, presented the adaptation of the USA kit for the Asian countries that she developed for The CHEST Foundation.

A lively, interactive discussion followed. CHEST Foundation CDs of many of its tobacco education tools were distributed to the attendees. Dr. Robert McCaffree, Master FCCP and Past President of ACCP and current President of The CHEST Foundation, and Dr. Mary Anne McCaffree, active participants in the development and implementation of these programs, also added input during the discussion. ■

***Dr. Kay Guntupalli, FCCP:*** *"This was a great opportunity to showcase the tools developed by The CHEST Foundation. The response and interest from the packed audience was very gratifying. It emphasizes the need for continued work in this area."*

***Dr. Deborah Shure, Master FCCP:*** *"This was a lively, international session with great interest expressed in the use of CHEST Foundation speakers kits and educational material on tobacco control. Many participants shared their experiences and ideas for further adaptations. The impact of The CHEST Foundation's involvement in this area is truly significant and appreciated."*

***Dr. D. Robert McCaffree, Master FCCP:*** *"This World Congress reinvigorated our total antipathy toward the tobacco industry, which is engineering the greatest pandemic the world has seen—a pandemic that is killing 5 million people annually now and will soon be killing 20 million people worldwide. It is always inspiring to be with people strongly committed to fighting tobacco and sharing ideas of ways to protect our youth and our communities."*

NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS

# ACCP in the News

BY JENNIFER STAWARZ
*Senior Manager, ACCP Public Relations*

Studies published in the journal *CHEST* have kept the American College of Chest Physicians in the spotlight throughout the summer. In early May, a study illustrating the gender differences associated with lung cancer gained coverage in the *Washington Post*, *Los Angeles Times*, *The Tennessean*, and *The Vancouver Sun*. The study was also featured in nearly 50 television broadcasts in such markets as Los Angeles, Detroit, Philadelphia, Baltimore, and on MSNBC Live.

In late May, the Health Resources and Services Administration (HRSA) submitted a report to the US Department of Health and Human Services regarding the critical care workforce shortage. In response, the ACCP and other specialty medical societies distributed a joint press release outlining the findings of the HRSA report and potential solutions for the shortage of critical care workers. As a result, the Associated Press published a story regarding the critical care workforce shortage, which, subsequently, ran on numerous consumer and medical Web sites and television stations around the country.

In June and July, ACCP evidence-based guidelines for antithrombotic therapy (September 2004) were mentioned in the *Canadian Pharmacists Journal* and *Washington Pharmacy* magazine. The ACCP guidelines for atrial fibrillation (August 2005) also appeared in *The Medical Post*, *Emergency Medicine*, and *Drug Topics*. Additional *CHEST* studies were featured in the *Baltimore Sun*, *Hartford Courant*, *Dayton Daily News*, *Hospital Pharmacy*, *Vitality*, *Women's Health Magazine*, and CNN and CBS news online.

Access ACCP press releases at www.chestnet.org/about/news.php. ■

# Lung Cancer Alliance Is Committed to Patient Education

The Lung Cancer Alliance (LCA) is the only national nonprofit organization providing patient support and advocacy exclusive to those living with or at risk for lung cancer. Headquartered in Washington, DC, LCA is committed to making lung cancer a national public health priority.

Through a hotline (800-298-2436) and a Phone Buddy Program, one-on-one support to people affected by lung cancer is delivered. The Hotline receives 450 to 500 calls per month from all over the United States. The Phone Buddy program is a peer-to-peer support network made up of 150 survivors and caregivers who have volunteered to share their experiences and be empathetic listeners. LCA makes approximately 40 matches per month between volunteers and those in need. Phone Buddies do not give medical advice. Volunteers receive ongoing training and support. This is the only peer-to-peer national resource specific to lung cancer.

LCA provides not only one-on-one support but is building a community of people to support each other and a movement to make lung cancer a national public health priority. This is doen through programs, publications, and communications. LCA hosts a blog www.lungcanceralliance blog.org and an online support community. The LCA Survivors Community is a safe, trusted environment in which those at risk, those living with the disease, and those who love them can share and support one another.

An additional resource for patients is the LCA Clinical Trials Matching Service. The Service ensures that patients diagnosed with lung cancer know all of their treatment options, including clinical trials.

Physicians' offices can receive sets of brochures about LCA services for patients and family members, so they have a place to turn for support and education. The quarterly Spirit & Breath newsletter shares information on congressional and executive branch news relevant to lung cancer, as does the LCA Web site at www.lungcanceralliance.org. ■

AMERICAN COLLEGE OF CHEST PHYSICIANS

# NEWS FROM THE COLLEGE

## ACCP Worldwide

**11th Congress of the Asian Pacific Society of Respirology**
**November 19-22, 2006**
**Kyoto, Japan**
The main theme of the APSR 2006 is "New Horizons of Respirology—Harmonization Beyond Diversity."

The President of the 11th Congress, Dr. Yoshinosuke Fukuchi, FCCP, remarks that some of the meeting highlights include a satellite symposium in Tokyo on respiratory physiology; a special seminar on the creation of scientific papers (with a faculty of the Editors in Chief of APSR, ACCP, ATS, and ERS); a symposium on GOLD revision 2006 (featuring six Executive Members), and many more symposia/seminars embracing major respiratory diseases common to that part of the world.

Leaders from the ACCP will be participating in several special sessions.

More information is available at www.apsr2006.org/index.php.

**World Asthma Meeting (WAM) 2007**
**June 22-25, 2007**
**Istanbul, Turkey**
The theme of WAM 2007 is "Bridging Various Aspects of Asthma." Professor Elif Dagli, Chair of the WAM Committee, notes, "The WAM Committee wished to discuss regional perspectives of asthma in a city on two different continents, historically and geographically connecting Northern Africa, Middle East, Central Asia, and East Europe. Please come and let yourself be spoiled with the famous Turkish hospitality." The scientific program will include postgraduate courses, keynote lectures, plenary sessions, symposia, and hot topic sessions on obesity and asthma; severity vs control; new insights in immunopathogenesis; and safety of LABAs. The ACCP serves on the WAM 2007 Committee, and ACCP members will be participating in the program.

More information is available at www.wam2007.org/.



## EDUCATION INSIGHTS
# The Transformation of Medical Education

BY ED DELLERT, RN, MBA
*Vice President, ACCP Educational Resources*

Most models of medical education are based upon the content of the curriculum, the organization of the teaching, assessment of the learner, and the evaluation of the educational program. Over the last several years, there have been concerns raised about the educational impact as to how teachers are helping learners obtain the information they really want them to know.

Much is at stake, including the effectiveness of the education program to the careers of the individual students. This spills over into what students will take with them and practice throughout their practice careers through continuing medical education efforts.

**A NEW CME SYSTEM NEEDS TO FOCUS ON THE VALUE OF AN EDUCATIONAL ACTIVITY THAT IS MEASURED BY IMPROVED PERFORMANCE AND NOT BY TIME.**

How serious is this to the future of medical education and continuing medical education providers? If one were to ask me, I would respond that change in medical education is inevitable. This opinion is based upon three sources of information: (1) American Medical Association (AMA) Initiative to Transform Medical Education; (2) prior publications to change the CME credit system; and (3) the September 2006 release of new Accreditation Council for Continuing Medical Education (ACCME) criteria.

A recent report from the AMA highlights the work of a committee called the "Initiative to Transform Medical Education" (ITME) that indicates its goal as follows:

"Our AMA should assume a leadership role in creating the forums, strategies, and structures appropriate for reforming the American Medical Education system across the continuum of education and professional training to enable physicians to meet the needs of patients and the public through the health-care delivery system in the twenty-first century."

The ITME is scheduled to make recommendations to the AMA by the end of the 2006 calendar year on how best to change the continuum of medical education, factors that will facilitate or inhibit the implementation of such a change, and assuring that appropriate groups and organizations are supportive of these proposed recommendations. As for continuing medical education (CME) credit, the current time-based system has assumed that awarding such credit would lead toward a change in physician behavior and improved patient care. Physician participation in CME activities and its correlation to this desired change has been a subject of debate, with results that are sporadic, at best. This was highlighted by an article by Nancy Davis and Charles Willis (2004, *The Journal of Continuing Education in the Health Professions*). It indicated that a new CME system needs to focus on the value of an educational activity that is measured by improved physician performance and not by time.

To CME providers and educators, this means change to the structure of future educational programs.

On September 5, 2006, the ACCME published updated criteria for CME providers to implement in stages between November 2008 and November 2012. The focus of the ACCME updated elements is on enhancements to CME programs through their mission statement and assessing how they achieve their mission, concentrating on the impact of their educational activities upon physician performance-in-practice or patient outcomes.

Change in medical education and how physicians participate in these educational activities is altering. These models described in this article only highlight that change appears to be on the horizon and that change will include demonstrating how knowledge, competence, or performance was improved based upon participation in high-quality educational designs and programs.

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NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS

## CRITICAL CARE COMMENTARY

# Pain Management: The Need for a Systematic Approach

Pain is defined as an unpleasant sensory or emotional experience associated with actual or potential tissue damage that typically leads to evasive action. When asked, the majority of critically ill patients report that they experienced pain during their ICU hospitalization (Desbiens et al. *Crit Care Med* 1996; 24:1953; Walder et al. *Intensive Care Med* 2002; 28:S109), and the pain is often sufficiently intense to require strong analgesic medications. While pain associated with recent surgery, trauma, or invasive procedures is expected, the discomfort associated with immobility and common components of routine care is often underappreciated (Puntillo et al. *Crit Care Med* 2004; 32:421). Further, these activities are typically performed repeatedly during an average day in the ICU. Accordingly, the identification, documentation, evaluation, and management of pain must be done consistently and in a systematic manner.

This picture of pain in ICU patients is made more complex by the presence of underlying medical illnesses that may go unrecognized, particularly after an unscheduled ICU admission. Additionally, the interplay between pain, anxiety, and sleep deprivation is worth noting. These factors act synergistically to increase pain perception. The frequent use of sedative medications in the ICU, particularly for patients supported by mechanical ventilation, may obscure detection of pain by reducing the ability for the patient to report pain. Accordingly, the literature suggests that structured approaches to managing sedation and analgesia in the ICU often emphasize addressing pain first, before administering sedative medications (Jacobi et al. *Crit Care Med* 2002; 30:119; Sessler et al. *Semin Respir Crit Care Med* 2001; 22:211; Brook et al. *Crit Care Med* 1999; 27:2609).

The most important consequences of pain are the mental anguish and raw distress that accompany the sensation of pain. Additional important consequences include the physiologic stress response, accompanied by increased sympathetic outflow and high levels of circulating stress hormones. It is likely that many events that are perceived as "agitation," in fact, represent the distress and elevated stress response from uncontrolled pain. Ongoing, unmanaged pain may limit movement, including splinting of limbs and inhibiting coughing and deep breathing, and possibly lead to atelectasis and pneumonia. Finally, there are interactions between nocioception and analgesic medications and alterations in immunity and inflammation, potentially having implications for impairing immune function and wound healing (Ritter et al. *Eur J Pain* 2005; 9:109).

In recent years, great attention has been paid to detecting and documenting pain that is experienced by any patient. Typically, detection relies upon self-reporting by a coherent, conversant patient. This is often in the form of identifying a level of pain using a 10-point numeric scale and may incorporate cartoons of faces varying from happy to frowning. ICU patients present unique challenges for this form of assessment, because many have impaired level of consciousness and/or reduced ability to communicate. The scheduled interruption of sedative medications, often performed on a daily basis (Kress et al. *N Engl J Med* 2000; 342:1472), presents an opportunity for care providers to inquire about pain during this period of relative alertness.

When a practitioner is unable to solicit a description of the pain or its rating, then the presence or absence of pain is often inferred by care providers based upon observed behaviors and changes in vital signs. In a study of nearly 6,000 ICU patients, Puntillo and colleagues noted certain facial, body movement, and verbal behaviors to be associated with pain induced by various procedures (Puntillo et al. *Crit Care Med* 2004; 32:421). Grimacing, a rigid body position, wincing, and eye closure were among the most often observed behaviors. Activation of the sympathetic nervous system is common during pain and often results in tachycardia, tachypnea, hypertension, and papillary dilatation. However, changes in these parameters have not proven to be reliable reflections of presence or absence of pain, because many other conditions stimulate sympathetic discharge and the stress response. In addition, many medications can blunt the sympathetic response, whereas, others will further stimulate the sympathetic nervous system.

Self-reporting of pain is often difficult to achieve among ICU patients, so clinicians and investigators have sought to develop valid instruments to detect and, perhaps, quantify pain. In the 12-point Behavioral Pain Scale (BPS) (Payen et al. *Crit Care Med* 2001; 29:2258), facial expression and upper limb posture are two of the three domains (compliance with ventilation is the third) that are used to determine the presence and severity of pain in patients who are nonverbal. As a form of validation, the authors observed an increase in BPS with noxious procedures, compared with nonnoxious procedures. The scale was most reliable during light sedation, however, and was not particularly robust for detecting pain when deep sedation was present.

Blenkharn and colleagues (Blenkharn et al. *Intensive Crit Care Nursing* 2002; 18:332) developed the Observational Pain Scoring Tool that incorporates hypertension, tachycardia, sweating, papillary dilatation, facial grimacing, and distressed movements into a rating of zero to three points that is utilized in a management protocol. An attractive feature of the proposed management strategy is that self-reporting of pain by the alert patient is utilized first to guide treatment. The downside to implementing this as a unit-wide tool is that these authors did not prospectively validate this management algorithm. Chanques and colleagues (Chanques et al. *Crit Care Med* 2006; 34:1691) tested the impact of a systematic management strategy for pain and agitation and demonstrated impressive results. They utilized a numerical rating scale and the BPS for pain evaluation and the Richmond Agitation-Sedation Scale for agitation. The protocol lists specific actions to be taken by the clinician in response to detecting pain or agitation and includes a search for underlying conditions that might be corrected and the selection of an appropriate analgesic agent based upon World Health Organization classification. This matches specific medications with pain severity. In a two-phase, prospective, controlled study, this strategy led to more therapeutic changes—both escalation and de-escalation of therapy—and was associated with a significant reduction in the incidence of pain and agitation. The intervention was associated with shorter duration of mechanical ventilation and fewer nosocomial infections. The ICU length of stay and survival remained unchanged.

Analgesic medications are widely prescribed in the ICU setting to treat or manage pain. Opioids were administered on 36% of days in a large cohort of mechanically ventilated ICU patients (Arroliga et al. *Chest* 2005; 128:496). Although these drugs are used in a targeted fashion to treat pain, particularly by intermittent administration, they are also widely used in sedation management, often by continuous infusion, within the context of "analgosedation."

In support of this practice, a combination of a benzodiazepine and opiate infusion has been suggested to be more reliable and easier to titrate than benzodiazepine infusion alone (Richman et al. *Crit Care Med* 2006; 34:1395), even for patients without a recognized need for pain relief.

Because of the complexity of pain management in ICUs, there is a need for more widespread adoption of a systematic approach to evaluating and managing pain in ICUs.

Some of the work discussed provides a starting point, with regard specifically to utilization of tools for detecting and documenting pain. Additionally, a framework for development of management strategies is an area for more research.

There are important aspects of pain management for which clear gaps exist, including a research basis for management, dissemination of information, and an incorporation of this knowledge into daily clinical care. Pain recognition in the nonverbal patient, individualized analgesic drug selection and dosing, management of GI hypomotility related to opioid analgesics, and nonpharmacologic strategies for easing discomfort or preventing pain are examples of common issues that the critical care community must address.

There are certain aspects of pain management that present unique challenges. For example, neuropathic pain is underappreciated as a cause of pain, and nontraditional management options, such as anticonvulsants, antiarrhythmics, local anesthetics, and antidepressants may be more effective than opioids; and antiinflammatories, yet, are often not considered. The role of central neuroaxis drug administration also must be examined. Last, symptom relief, particularly the elimination of pain in end-of-life situations, is a crucial issue and must be addressed by the critical care team.

With support from the ACCP Critical Care Institute and the American Association of Critical-Care Nurses, an expert panel has been convened to address these many issues, with the goal of eliminating "unmanaged" pain in the ICU. ■

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Pulmonary Perspectives

# Talc Pleurodesis: All Talc Is Not Created Equal

*A lingering concern about the use of talc is the occurrence of ARDS after talc pleurodesis.*

Pleurodesis is indicated for the treatment of malignant pleural effusion, spontaneous pneumothorax, and selected cases of benign pleural effusion. Although a number of agents have been used for pleurodesis, talc is the most effective. In addition to achieving pleurodesis, talc also induces apoptosis in malignant mesothelial cells but not in normal pleural mesothelial cells, even at a dose less than one hundredth of that used in pleurodesis (Najmunnisa et al. *Am J Respir Crit Care Med* 2000; 161:595).

## Variable Physical Properties of Talc

Talc is a pulverized form of a naturally occurring hydrated magnesium silicate with variable amounts of aluminum, iron, or manganese. In nature, talc is not found in a chemically pure state. It may be contaminated by other minerals, including asbestos, although medical grade talc is asbestos-free.

There is marked variation in the diameter of talc particles. In one study of preparations from various countries, the median diameter varied from 7.8 μm to 31.3 μm, while 10th percentile diameters were as low as 2.4 μm, and 90th percentile diameters were as high as 60.6 μm (Ferrer et al. *Chest* 2001; 119:1901). Preparations from the United States had the smallest particle size.

## Mechanisms of Pleurodesis

Talc pleurodesis causes injury to the pleural mesothelium, followed by inflammation and fibrosis. The injury is mediated by pleural mesothelial cell production of interleukin-8, monocyte chemotactic protein-1, intercellular adhesion molecule-1, and basic fibroblast growth factor (Najmunnisa et al. *Am J Respir Crit Care Med* 1998; 158:971). Intrapleural instillation of talc is rapidly followed by influx of neutrophils and subsequent accumulation of macrophages. A decrease in pleural fibrinolytic activity also occurs.

## Talc and ARDS

A lingering concern about the use of talc is the occurrence of ARDS after talc pleurodesis. The reported incidence of post-talc ARDS in large, observational studies varies from 0 to 9% (Kennedy et al. *Chest* 1994; 106:342; Campos and Werebe. *Lancet* 1997; 349:251; Rehse et al. *Am J Surg* 1999; 177:437). A causal relationship between extrapleural dissemination of talc and the occurrence of ARDS has been suggested by the finding of talc particles in the BAL fluid of patients with post-talc ARDS (Campos and Werebe. *Lancet* 1997; 349:251). Disseminated talc has also been found at necropsy in one patient with post-talc ARDS (Campos and Werebe. *Lancet* 1997; 349:251), lending additional support to the role of extrapleural dissemination in the pathogenesis of post-talc ARDS. The influences of talc size and dose have been investigated as factors in dissemination.

**A BASIC CONCLUSION IS THAT THE RISK OF SEVERE SYSTEMIC INFLAMMATION AND ARDS WILL BE DECREASED BY THE USE OF TALC PREPARATIONS WITHOUT SMALL PARTICLES.**

## Talc Size

ARDS is more common in the United States, where talc particle sizes are smaller, suggesting an association between particle size and the risk of ARDS. Further support for this association is found in a study of the use of facial talc, with a relatively larger particle size, vs medical grade talc, with a relatively smaller particle size. No cases of ARDS occurred with the use of sterilized facial talc for pleurodesis (Khoja et al. *J Bronchol* 2004; 11:226).

A rabbit model of talc slurry pleurodesis using smaller or larger talc particles provided further evidence of the importance of talc particle diameter in dissemination. Smaller and larger talc particle slurries achieved equivalent pleurodesis, but smaller talc particle slurries caused more deposition of talc particles in the ipsilateral lung and other organs. Talc reached the lung parenchyma by disrupting the integrity of the mesothelium and the elastic layer. Aggregates of talc particles accumulated mainly in the periphery of the lung parenchyma, but some talc particles followed the bronchovascular spaces to reach small blood and lymphatic vessels (Ferrer et al. *Chest* 2002; 122:1018).

Definitive evidence of the clinical importance of talc particle size comes from a prospective, randomized trial of talc slurry pleurodesis using samples of differing particle size in 48 patients. The slurries with smaller talc particles caused greater increases in alveolar-arterial oxygen gradient, greater decreases in arterial oxygen tension, and greater increases in plasma C-reactive protein level. Pleurodesis was similarly successful in both groups among survivors at 3 months (Maskell et al. *Am J Respir Crit Care Med* 2004; 170:377).

## Talc Dose

Most cases of post-talc pleurodesis ARDS have occurred with high doses of talc. In one report, three cases of ARDS were found after talc pleurodesis for malignant effusions using 10 g of talc (Rinaldo et al. *J Thorac Cardiovasc Surg* 1983; 85:523). In another series of 78 patients undergoing pleurodesis for recurrent effusion or pneumothorax, 7 patients (9%) developed ARDS. All of the patients who developed ARDS had received a talc dose of 5 g (Rehse et al. *Am J Surg* 1999; 177:437). These observations suggest that extrapleural dissemination of talc is a dose-dependent phenomenon.

The dose-dependent hypothesis was tested in a rabbit model of talc slurry pleurodesis (Montes et al. *Am J Respir Crit Care Med* 2003; 168:348). Rabbits in the high-dose group were more likely to have talc deposition in the ipsilateral and contralateral lung, mediastinum, pericardium, and liver, compared with rabbits in the low-dose group.

## Methods of Sterilization and Delivery

Talc may be sterilized effectively by dry heat, gamma irradiation, or ethylene oxide gas, although dry heat is the least expensive method (Kennedy et al. *Chest* 1995; 107:1032).

Intrapleural instillation of talc slurry via a chest tube and thoracoscopic talc poudrage are similarly effective in achieving pleurodesis (Kennedy and Sahn. *Chest* 1994; 106:1215; Dresler et al. *Chest* 2005; 127:909). In a slurry, the talc particles tend to aggregate. After instillation in the pleural space, aggregates of talc particles may quickly gravitate to, and accumulate in, the dependent part of the pleural space.

Thoracoscopic talc poudrage may be done in an operating department or endoscopy suite. In either case, thoracoscopic talc poudrage is a more expensive procedure than intrapleural instillation of talc slurry via a chest tube. Pleurodesis with thoracoscopic talc poudrage may result in a shorter duration (4.4 days) of chest tube drainage, compared with talc slurry (Aelony et al. *Ann Int Med* 1991; 115: 778; Kennedy et al. *Chest* 1994; 106:342). The increased procedure costs of thoracoscopic talc poudrage may, thus, be offset by decreased hospital costs, if the shorter duration of chest tube drainage allows earlier discharge from the hospital (Aelony. *Chest* 1995; 108:289).

Talc may also be delivered thoracoscopically, from pressurized canisters containing a dose of talc suspended in pressurized dichlorodifluoromethane (CFC-12). The talc is deposited on the lung as the pressurized gas is released from the canister.

However, as CFC-12 is released from the canister, it expands adiabatically and cools to nonphysiological temperatures. Furthermore, the high-velocity talc suspension jet may harm the visceral pleura by a mechanical action.

## Conclusion

The ideal agent for pleurodesis should be safe, effective, widely available, easy to administer, and inexpensive. Talc is the most effective agent in current use, and it is widely available and inexpensive.

We now have clear evidence that presence of small talc particles increases the risk of extrapleural talc deposition, systemic inflammation, and hypoxemia, while the absence of small particles does not hamper the ability of talc to achieve effective pleurodesis.

A basic conclusion is that the risk of severe systemic inflammation, severe hypoxemia, and ARDS after talc pleurodesis will be decreased by the use of talc preparations without small particles (diameter < 15 μm) and by the use of lower doses (2 g).

Further study is needed to show which physical properties, other than size, might be relevant to the safety and effectiveness of talc pleurodesis. ■

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## Editor's Insight

Despite years of clinical experience, the best method of chemical pleurodesis remains a complex issue.

This *Perspective* highlights talc pleurodesis and provides important information about the roles of particle size and dose in avoiding post-talc ARDS. Successful pleurodesis agents induce a systemic, as well as a local, inflammatory state (Ukale et al. *Lung Cancer* 2004; 43:323).

Worldwide, agents, such as quinacrine, silver nitrate, and oral tetracycline (filtered and sterilized for parenteral use), may still have roles in pleurodesis, depending on local costs and accessibility. In the United States, consideration will need to be given to particle size in order to avoid ARDS.

We still have much to learn about a very old technique.

*—Editor*

NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS

# NetWorks: Disaster Response, Home Care

### Disaster Response

Disaster Response NetWork Steering Committee member, COL John M. Cho, MC, USA, FCCP (Commander, Evans Army Community Hospital, USA MEDDAC, Fort Carson, CO, and Director, Denver Federal Coordinating Center, National Disaster Medical Service, Fort Carson, CO), led a multiorganizational group in MOUTAIN MOVE 2006 to enhance disaster preparedness in the state of Colorado. The details are outlined on the Disaster Response NetWork Web page at www.chestnet.org/ networks/ disaster_response/index.php.


The Disaster Response NetWork strives to provide ACCP members with tools to facilitate preparedness in their hospitals and community.

### Home Care

The Home Care NetWork continues its commitment in each of the three mission goals that include: (1) providing NetWork members access to medical, organizational, educational, and financial information regarding home care, (2) enhancing ACCP members' knowledge about the clinical aspects of care in the home, and (3) serving the ACCP as a resource for the "state of the art" in home care.

The NetWork is in the midst of generating a Web-based Home Ventilator Management Resource Center that will serve both the ACCP and the greater medical community as an up-to-date reference on home ventilation. Equipment requirement lists and general guidelines for proper application will be featured.

Members of the steering committee have been involved in advocating for providers and patients regarding reimbursement for home care devices and services. We have worked closely with the Government Affairs Committee, as well as other allied organizations, in addressing these recent changes in Medicare policy.

More information on the Home Care NetWork is available at www.chestnet.org/networks/ home_care/index.php.

# Practice Management News: The National Provider Identifier

As Medicare transitions to National Provider Identifier (NPI) compliance, remember that there is no charge to get an NPI. Providers can apply online for their NPI, free of charge, by visiting https://nppes.cms.hhs.gov or by calling (800) 465-3203 to request a paper application.

The CMS NPI page, which is located at www.cms.hhs.gov/NationalProvIdentStand/, is the only source for official and authoritative education on the NPI initiative; all products located on this site are free.

CMS continues to urge providers to include legacy identifiers on their NPI applications, not only for Medicare but for all payers. If reporting a Medicaid number, include the associated state name. If providers have already applied for their NPI, CMS asks them to go back into the NPPES and update their information with their legacy identifiers.

This information is critical for payers in the development of crosswalks to aid in the transition to the NPI. Getting an NPI is free—not having one can be costly.

AMERICAN COLLEGE OF CHEST PHYSICIANS

NEWS FROM THE COLLEGE

# Long-Acting Beta-Agonists: True Concern or False Alarm?

BY DR. ALAN FEIN, FCCP; DR. JILL OHAR, FCCP; AND DR. FRANK LEONE, FCCP

Recently a "black box" warning was issued by the FDA for salmeterol and the combination salmeterol/fluticasone (Advair). This warning has been extensively covered in the lay press and has resulted in apprehension and uncertainty about the appropriate role of these agents and about the safety of long-acting beta-agonists (LABA), in general.

This labeling change was based on the results of the SMART study (salmeterol multicenter asthma research trial), a 28-week observational safety study conducted to evaluate the impact of salmeterol on respiratory deaths. Diagnosis of asthma was based on the clinical judgment of the study physician, with exclusion of those with previous use of a long-acting $\beta_2$-agonist. Subjects were randomly assigned to receive either 42 µg of salmeterol twice daily or placebo, in addition to their usual asthma therapy. When enrollment began in 1996, subjects were recruited by media advertisements and did not necessarily have uniform medical care. Subsequently, participants were recruited by physician investigators, thereby facilitating closer follow-up. The study was terminated in 2003 with 26,355 subjects enrolled when an interim analysis revealed a significantly increased frequency of deaths among subjects receiving salmeterol. There were 13 deaths in the salmeterol group and 3 in the placebo group; 7 of the 13 were African-American, although they represented only 20% of the study population. African-Americans had lower inhaled steroid use (38% vs 49%) and greater utilization of hospital and critical care services. This study remains controversial and the subject of extensive review and opinion. Although concern about increased mortality related to LABA has periodically surfaced over the past 20 years, no specific cause and effect mechanism has been identified to link salmeterol to these asthma deaths.

Another recent development has been the long-awaited preliminary report of the TORCH (TOwards a Revolution in COPD Health) study. TORCH compares the effect of salmeterol/fluticasone 50/500 µg, fluticasone 500 µg, or salmeterol 50 µg vs placebo, when given for 3 years. All-cause mortality was chosen as the primary end point, while COPD morbidity, exacerbations, need for long-term oxygen, and safety were also secondarily examined. Over 6,100 subjects were enrolled. Results reported so far include a 2.6% absolute (17.5% relative) reduction in mortality (p=0.052), a 25% reduction in moderate to severe exacerbations (p=0.001), an improved quality of life by St. George Respiratory Questionnaire, and a 92 mL improvement in $FEV_1$ (p=0.001) in the group receiving the LABA/ICS combination compared with placebo. There were no excess deaths experienced in the salmeterol group, with cardiorespiratory deaths most common (62%), followed by malignancy (21%). Full results await publication; no information regarding the likelihood of type II error is currently available.

The overall safety of these medications in the TORCH study may provide some additional comfort to physicians and patients when using these medications. The reduction in all-cause mortality with combination salmeterol/fluticasone among patients with COPD is also encouraging. We anxiously await the full reporting of these results in order to estimate their clinical impact on the approach to patients with COPD. ■

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### Disclosures

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**Frank Leone, MD, FCCP**
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National Cancer Institute; The PA consortium on tobacco disparities (PACTD).
Pennsylvania Department of Health: Philadelphia Residents Empowered to Stop Smoking (The PRESS project).
Philadelphia Department of Public Health.
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## Asthma Practice Improvement

The American Board of Internal Medicine has developed the Asthma Practice Improvement Module for use by physicians recertifying in internal medicine and its subspecialties. This self-evaluation tool will focus on physicians' actual practice patterns on the chronic illness, asthma. The module uses CD-ROM technology to provide a template for chart review of key patient care outcomes and processes, along with a review of key components of the practice system (information management, patient self-care support, access to the practice, patient safety measures, teamwork, and the practice's improvement process). The module also includes an anonymous telephone survey for patients that addresses functional status, self-care knowledge and behaviors, and satisfaction with care. ABIM aggregates these data to provide an interactive practice work-up report that enables the physician to develop an individualized practice improvement plan based on important and feasible goals for his/her own practice.

Information on the module can be found at www.abim.org. The ACCP offers supplemental educational resources to assist physicians using this module. These can be found at: www.chestnet.org/education/online/abim/chart/index.php and www.chestnet.org/education/online/abim/practice/index.php. ■

NEWS FROM THE COLLEGE

AMERICAN COLLEGE OF CHEST PHYSICIANS

## INSIDE ACCP

# Marketing: Walking Elephants, Laughing Mayors

There is an often-used anecdote that illustrates the principles of marketing and aptly describes the role of the ACCP Marketing Division: If the circus is coming to town and you paint a sign saying "Circus Coming to the Fairground Saturday," that's *advertising*. If you put the sign on the back of an elephant and walk it into town, that's *promotion*. If the elephant walks through the mayor's flower bed, that's *publicity*. If you get the mayor to laugh about it, that's *public relations*. And, if you planned the whole thing, that's *marketing*.

Prior to the creation of the ACCP Marketing Division, departments within the ACCP were responsible for their own marketing. As the ACCP evolved and grew to meet the needs of its members, the demand for marketing services increased, and it became clear a formal marketing division was needed. Since its inception in the early 1990s, the ACCP Marketing Division has been planning and executing marketing plans that include advertising, promotion, publicity, and public relations for ACCP products and services.

An ACCP Marketing Committee was established to create a forum for exchange of information and ideas. Comprising ACCP members and staff, the committee first met during CHEST 1999 and set forth priorities and goals. Meeting regularly since that time, it provides valuable input to help identify member needs and increase the ACCP profile. Today, the Marketing Division develops strategic marketing campaigns for the annual CHEST meeting, education courses and products, ACCP membership, *CHEST*, The CHEST Foundation, and more.

The science published in *CHEST* and presented at annual CHEST meetings was increasingly newsworthy and was generating opportunities to raise public awareness about the ACCP. Now, monthly press releases from *CHEST* are sent to a variety of media outlets, and special outreach efforts are consistently made for CHEST meetings. The success of the public relations efforts is evident from the recent press coverage for the *Diagnosis and Management of Cough: ACCP Evidence-Based Clinical Practice Guidelines*, published in *CHEST*, and the ever-increasing number of placements in worldwide print publications, broadcast media, and on the Internet.

The strength of the current ACCP marketing activities can be attributed to an integrated approach. Current examples of an integrated approach include the campaigns for CHEST 2006 and The CHEST Foundation's 10th anniversary celebration. Ads, direct mail, and e-mails are advertising and promoting, while publicity and public relations are enhancing and maximizing the impact. The primary goal of these integrated campaigns, and others, is to deliver a message that builds awareness and participation and generates revenue.

As the ACCP moves forward, the Marketing Division will continue crafting strategies to best promote the ACCP's resources and meet the ACCP goals. Stay tuned for walking elephants and laughing mayors. ■

*By Rich Waters*
*Vice President, ACCP Marketing*
*and Kathy Jewett*
*Senior Marketing Coordinator*

AMERICAN COLLEGE OF CHEST PHYSICIANS

# NEWS FROM THE COLLEGE

## ACCP Joins NHLBI in New COPD Awareness Campaign

Among the nation's leading killers, COPD is the only disease with a mortality rate that continues to climb.

But, the vast majority of those at greatest risk for the disease are largely unaware of COPD and, in many cases, don't even realize that their condition has a name.

The National Heart, Lung, and Blood Institute (NHLBI) of the US Department of Health and Human Services recently initiated a national awareness and education campaign to increase recognition and understanding of COPD and its risk factors, and to underscore the benefits of detection and treatment in slowing the disease and improving quality of life. The ACCP has joined NHLBI as a partner in this effort.

This first phase of the NHLBI campaign, *COPD: Learn More Breathe Better*, will encourage health-care providers, particularly those in the primary care setting, to consider a COPD diagnosis in patients with shortness of breath, excess sputum production, and other symptoms, and to be mindful that proactive treatment may slow the disease progress and improve their patients' quality of life.

The campaign's second phase—introducing COPD to men and women at risk—will begin in early 2007.

"COPD has always been a top priority for the ACCP. We are excited to join NHLBI in helping to promote better understanding of this disorder among our members, to our colleagues in the primary care arena, and among our patients," said ACCP President, Dr. W. Michael Alberts, FCCP.

ACCP members can access campaign materials, including a pocket reference card; an informational poster for doctor's offices, clinics, and hospitals; fact sheets for diagnosed patients and those at-risk for COPD; and a speaker's guide with slide presentations for promoting awareness of COPD to potential patients, as well as among provider peers and colleagues, by visiting the campaign's Web site at www.LearnAboutCOPD.org. ■

## This Month in *CHEST*: Editor's Picks


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

▶ **Emergency Department Hypotension Predicts Sudden Unexpected In-Hospital Mortality: A Prospective Cohort Study.** *Dr. Alan E. Jones, et al*

▶ **The Current Treatment of Pulmonary Arterial Hypertension: Time To Redefine Success.** *Dr. Stuart Rich, FCCP*

▶ **Association Between Lung Cancer Incidence and Family History of Lung Cancer: Data From a Large-Scale Population-Based Cohort Study–The JPHC Study.** *Dr. Jun-Ichi Nitadori, et al*

▶ **Prospective Analysis of Cystic Fibrosis Transmembrane Regulator Mutations in Adults With Bronchiectasis or Pulmonary Nontuberculous Mycobacterial Infection.** *Dr. Tomasz M. Ziedalski, et al*

▶ **Predictors of Mortality for Methicillin-Resistant *Staphylococcus aureus* Healthcare-Associated Pneumonia: Specific Evaluation of Vancomycin Pharmacokinetic Indices.** *Dr. Meghan N. Jeffres, et al*

www.chestjournal.org

# Palliative Care Gains ABMS Subspecialty Recognition

BY MARY ELLEN SCHNEIDER
*Elsevier Global Medical News*

The field of palliative care took a major step forward in September when members of the American Board of Medical Specialties voted to approve hospice and palliative medicine as a recognized subspecialty.

The application to recognize the subspecialty had broad support and was cosponsored by 10 medical specialty boards. As a result, physicians in a number of specialties—including internal medicine, family medicine, pediatrics, psychiatry, neurology, surgery, emergency medicine, and obstetrics and gynecology—will be able to seek certification.

The first certification examination is expected to be administered in 2008, according to Dr. F. Daniel Duffy, senior adviser to the president of the American Board of Internal Medicine.

The milestone is just the latest in a series of developments in the size and status of the field of palliative care. Between 2000 and 2004, the number of hospital-owned palliative care programs in the United States increased by nearly 75%, jumping from 632 in 2000 to 1,102 in 2004. As of 2004, 63% of large hospitals—those with at least 200 general adult beds—reported that they had some type of palliative care program in operation, according to the Center to Advance Palliative Care.

This summer, palliative medicine received a nod from the Accreditation Council for Graduate Medical Education (ACGME) when the organization voted to approve an accreditation process for hospice and palliative medicine fellowship training programs. ACGME is expected to begin accepting applications in summer 2007.

"We're well beyond the tipping point," said Dr. Diane Meier, director of the Center to Advance Palliative Care and director of the Hertzberg Palliative Care Institute at Mount Sinai School of Medicine in New York.

At her institution, palliative care has become so well accepted that asking for a palliative care consult is as routine as calling for an infectious disease consult. Now the focus has shifted from selling the concept of palliative medicine to ensuring that programs around the country have consistently high standards, Dr. Meier said.

Work is already underway in this area. The National Consensus Project for Quality Palliative Care, which is sponsored by three national palliative medicine organizations, has released quality guidelines.

In an effort to ensure that new programs have high-quality processes in place, the Center to Advance Palliative Care launched the Palliative Care Leadership Centers—six centers of excellence in palliative care around the country that train teams of health care providers. The program includes intensive, 2-day training sessions in which teams are sent to one of the six centers and leaders at the centers act as mentors for a year after training.

When the site visits started in 2004, Dr. Meier and others at the Center to Advance Palliative Care estimated that about 30% of the teams trained would successfully establish a program, she said, but it's been closer to 70% to date. ■

# CLASSIFIEDS

## PROFESSIONAL OPPORTUNITIES

# Stroke, OSA Association Significant

**Sleep Apnea** • *from page 1*

short of making specific treatment recommendations, and instead states that treatment should be individualized, it does address patient evaluation.

It is reasonable that patients and their bed partners be questioned about symptoms of sleep-disordered breathing and that appropriate patients be referred to a sleep specialist for further evaluation, the guideline states.

This is particularly important if the patient has drug-resistant hypertension or certain risk factors for stroke, such as abdominal obesity and hypertension (Stroke 2006;37:1583-633).

In making its recommendation, the American Heart Association/American Stroke Association Stroke Council cited data from several studies, including a case-control study of 181 patients, which showed an association between excessive daytime sleepiness (likely caused by obstructive sleep apnea) and stroke (odds ratio 3.07).

The council also cited a 10-year observational study of more than 1,600 men, which showed that those patients who had severe obstructive sleep apnea-hypopnea had an increased risk of fatal and nonfatal cardiovascular events including stroke, compared with healthy individuals (odds ratio 2.87 and 3.17, respectively).

The guideline noted that there are a number of biologically plausible mechanisms for a link between sleep apnea and stroke; Dr. Mohsenin agreed.

Several studies suggest that the mechanism by which sleep-disordered breathing increases stroke risk is by "leading to or worsening hypertension and heart disease and possibly by causing reductions in cerebral blood flow, altered cerebral autoregulation, impaired endothelial function, accelerated atherogenesis, hypercoagulability, inflammation, and paradoxical embolism in patients with patent foramen ovale," the guideline states.

**RANDOMIZED CONTROLLED TRIALS ARE NEEDED TO FIRMLY ESTABLISH A CAUSAL LINK BETWEEN SLEEP APNEA AND STROKE.**

But the real question, Dr. Mohsenin said, is whether there is an independent association between sleep apnea and stroke.

A recent study on which he was an author shows that there is indeed such an association.

In the observational cohort study of 697 patients with obstructive sleep apnea and 325 controls (mean apnea-hypopnea index of 35 vs. 2 in the patients and controls, respectively), obstructive sleep apnea was found to have a statistically significant association with stroke or death (hazard ratio of 1.91) after adjustment for numerous factors, including age, sex, race, smoking status, alcohol consumption, body mass index, diabetes, hyperlipidemia, atrial fibrillation, and hypertension.

A trend analysis also showed a significant dose-response relationship between sleep apnea severity at baseline and development of a composite end point of stroke or death from any cause (N. Engl. J. Med.2005;353:2034-41).

While randomized controlled trials are needed to firmly establish a causal link between sleep apnea and stroke—to "put the last nail in the coffin and say, 'OK, sleep apnea is indeed a cause of stroke in a high-risk patient population,' " as Dr. Mohsenin put it, the findings increasingly suggest this is the case.

Also, sleep apnea occurs as commonly in transient ischemic attack as it does in stroke, further underscoring the need for sleep apnea treatment in affected patients, he noted.

In addition, a number of studies have shown that sleep apnea is associated with worse functional outcomes in stroke patients, he said.

Patients with stroke who have sleep apnea have been shown to have more delirium, depression, impaired functional capacity, longer rehabilitation time, and longer hospitalization, Dr. Mohsenin explained.

"Sleep apnea does affect the outcome of stroke," he said, and he noted that in some studies the impact lasted up to 12 months.

Patients who have had a stroke should be evaluated for sleep-disordered breathing, Dr. Mohsenin advised.

In addition, patients using long-term CPAP should be reevaluated for residual symptoms of the disorder to ensure adequate treatment and compliance, he added. ■



# CPAP May Benefit Women at Risk for Preeclampsia

BY SHARON WORCESTER
*Elsevier Global Medical News*

SALT LAKE CITY — The use of continuous positive airway pressure may help prevent preeclampsia in pregnant women at risk for the condition, the results of a small study suggest.

In 9 of 12 women with risk factors for preeclampsia who used continuous positive airway pressure (CPAP) and medical therapy beginning before 9 weeks' gestation, blood pressure remained stable and pregnancy was normal, Dr. Christian Guilleminault reported in a poster at the annual meeting of the Associated Professional Sleep Societies.

**IN 9 OF 12 WOMEN WITH RISK FACTORS FOR PREECLAMPSIA WHO USED CPAP, BLOOD PRESSURE REMAINED STABLE AND PREGNANCY WAS NORMAL.**

Sleep-disordered breathing has been suggested by several studies as a possible contributor to preeclampsia.

In one study, snoring was linked with preeclampsia, with the disorder occurring in 10% of snorers compared with 4% of nonsnorers. In another study, snoring was shown to be a significant predictor of hypertension and fetal growth retardation, even after controlling for maternal weight, age, and smoking status.

Based on such findings, some researchers have recommended polysomnography and/or CPAP use in pregnant women with risk factors—including snoring—for preeclampsia.

In the current study, all 12 participants had risk factors for preeclampsia: All were snorers; seven had hypertension; two had prior preeclampsia; and three were obese, with a body mass index greater than 30 $kg/m^2$.

The women, who had a mean age of 29 years, underwent polysomnography at a mean of 7.5 weeks' gestation, and all had flow limitations at the nasal cannula without apnea or hypopnea.

Nasal CPAP was used in all participants at an initial pressure of 5-6 cm $H_2O$, and in eight women the pressure was increased to 6-9 cm $H_2O$ at between 5 and 6 months' gestation. Of the seven women with hypertension at baseline, diastolic blood pressure below 90 mm Hg was maintained without a change in medication.

All seven of the women delivered healthy, full-term infants, as did one of the women with a history of preeclampsia, reported Dr. Guilleminault, of the department of psychiatry at Stanford (Calif.) University.

One of the obese women miscarried at near 14 weeks' gestation, and another delivered at 34 weeks but did not develop preeclampsia.

The third obese patient and the second woman with prior preeclampsia developed clinical features of preeclampsia, and both underwent cesarean section at 7.5 months' gestation.

Treatment with nasal CPAP with initiation prior to 9 weeks' gestation was associated in this study with stable blood pressure and normal pregnancy in most women with risk factors for preeclampsia, Dr. Guilleminault concluded. ■

# New Risk Factors Found for Postoperative VTE

BY MITCHEL L. ZOLER
*Elsevier Global Medical News*

PHILADELPHIA — Pneumonia was one of five new risk factors for postoperative venous thromboembolism identified in an analysis of more than 75,000 patients.

Other new risk factors for venous thromboembolism (VTE) were the need for a blood transfusion because of bleeding, renal insufficiency, urinary tract infection, and a low serum albumin level, Dr. Chethan Gangireddy said at the Vascular Annual Meeting.

"These newly described risk factors can aid in further stratifying a patient's risk for postoperative VTE," said Dr. Gangireddy, a surgeon at the University of Michigan in Ann Arbor.

**Independent Risk Factors For VTE After Surgery**

| | Hazard Ratio |
|---|---|
| Pneumonia | 2.7 |
| Cardiac arrest | 2.5 |
| Myocardial infarction | 2.4 |
| Blood transfusion because of bleeding | 2.3 |
| Renal insufficiency | 1.9 |
| Urinary tract infection | 1.8 |
| Hemodialysis for renal failure | 0.23 (protective) |
| Diabetes | 0.75 (protective) |
| High level of serum albumin | 0.84 (protective) |

Note: Based on data from 75,711 patients.
Source: Dr. Gangireddy

The analysis included data that were collected by the National Surgical Quality Improvement Program of the Department of Veterans Affairs system during 1996-2001.

The database included all of the more than 118,000 patients who had surgery at any of 114 hospitals for one of the nine most common operations performed at these hospitals.

From this group, complete pre-, peri-, and postoperative data were available for 75,711 patients.

The overall incidence of VTE was 0.7%, but the incidence varied significantly based on the type of surgery.

Carotid endarterectomy carried the lowest risk for VTE, at 0.14%. Total hip arthroplasty posed the greatest risk for VTE, with a 1.3% rate.

The analysis also showed no significant change in the annual rate of VTE through the 6 years studied.

In a multivariate analysis that evaluated the independent risk added by many different clinical and demographic factors, pneumonia was the strongest risk factor, boosting the risk of venous thromboembolism 2.7-fold.

Several other risk factors each boosted the risk for VTE by about twofold (see table), and three factors were found to reduce the VTE risk.

In an analysis of the two most common manifestations of VTE, the list of significant risk factors for causing deep vein thrombosis was found to be different from the list linked with pulmonary embolism.

The top risks for deep vein thrombosis were need for a transfusion due to bleeding (a 3.3-fold increased risk), pneumonia (a 2.5-fold increased risk), and urinary tract infection (a 1.7-fold increased risk).

For pulmonary embolism, the top risk factor was demonstrated to be cardiac arrest (7.6-fold increased risk), followed by pneumonia (3.9-fold increased risk) and need for a transfusion (2.4-fold increased risk).

Another finding of the study was that patients with venous thromboembolism had a 2.4-fold increased risk of death compared with all other patients, Dr. Gangireddy said. ■