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The little sticker significantly increased the odds of a child receiving appropriate therapy, said Dr. Sandra F. Braganza.

## Chart Stickers Prompt Better Pediatric Asthma Care

BY JANE SALODOF  
MACNEIL  
*Elsevier Global Medical News*

SAN FRANCISCO — A small intervention had a sizable impact on documentation of asthma severity and appropriate treatment of children at an inner-city health center, according to results of a randomized controlled trial reported in a poster at the annual meeting of the Pediatric Academic Societies.

Every other week for 6 weeks, Dr. Sandra F. Braganza and her colleagues affixed 2-by-3-inch stickers to the charts of children scheduled for health center visits who had previously been diagnosed with asthma.

The stickers listed the National Asthma Education and

Prevention Program (NAEPP) criteria for asthma severity classification. Highlighted in red were the criteria for prescribing inhaled steroids.

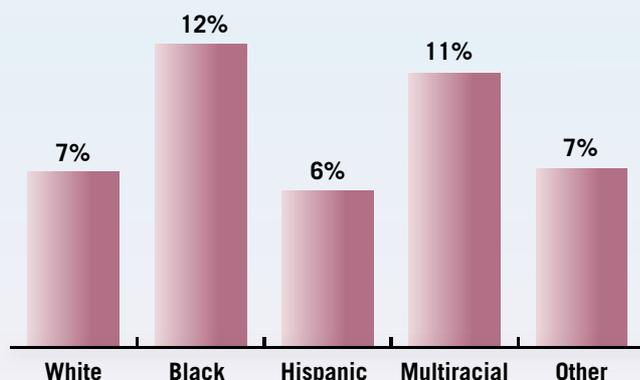
"It prompts the physicians to classify asthma severity, and by physicians classifying asthma severity we hope they are properly treating the child's asthma," Dr. Braganza of Albert Einstein College of Medicine and Montefiore Medical Center, New York, said, describing the rationale behind the stickers.

The children's appointments were not necessarily for asthma, she noted in an interview at the meeting, which was sponsored by the American Pediatric Society, Society for Pediatric Research,

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## VITAL SIGNS

### Percentage of Children Affected by Asthma, By Race and Ethnicity



Note: Based on 102,353 parental interviews, 2003-2004.  
Source: Department of Health and Human Services, National Survey of Children's Health

YENLING LIU/ELSEVIER GLOBAL MEDICAL NEWS

## Conservative Fluid Management Is Tops In Acute Lung Injury

*FACTT findings should change practice.*

BY JANE SALODOF  
MACNEIL  
*Elsevier Global Medical News*

SAN DIEGO — Acute lung injury patients in a large randomized, controlled trial fared better with a conservative fluid management strategy than with a more liberal approach that researchers described as similar to what many physicians do normally when caring for these patients.

The Fluid and Catheter Treatment Trial (FACTT) reported conservatively managed patients spent fewer days on mechanical ventilators and in intensive care units.

Despite concerns that conservative management could harm other organs, neither shock nor dialysis increased in patients who were not heavily infused with fluids. The trial's primary outcome, 60-day mortality, was similar for participants managed with conservative and liberal strategies: 25.5% and 28.4%, respectively.

"[Conservatively managed patients] achieved a benefit without harm overall. This should lead to a change in practice," Dr. Herbert P. Wiedemann, FCCP, said during a press briefing at the International Conference of the American Thoracic Society, where he reported fluid management results from the 1,000-patient study.

The National Heart, Lung, and Blood Institute's Acute Respiratory Distress Syndrome Clinical Trials Network investigators conducted the trial, which was subsequently published in the *New England Journal of Medicine* (2006;354:2564-75).

FACTT employed a complex protocol aimed at weaning patients from mechanical ventilation during the 28 days after randomization at 20 sites in North America.

Management of patients in the conservative cohort was guided by a target range of less than 4 mm Hg in central

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## Surgeon General: Secondhand Smoke Kills

BY NANCY NICKELL  
*Elsevier Global Medical News*

The science is clear: Secondhand tobacco smoke causes premature death and disease in children and adults who don't smoke—and there is no safe exposure level, U.S. Surgeon General Dr. Richard H. Carmona warned in a comprehensive new report.

In a return to a public health issue last addressed in a 1986 surgeon general's report, the nation's top physician found significant progress in the campaign to reduce Americans' exposure to secondhand smoke. But new scientific evidence in the intervening 20 years strengthens the causal links between secondhand smoke and a host of harmful cardiovascular, respiratory, and reproductive effects.

In particular, the surgeon general's report cautioned that exposure to secondhand smoke increases nonsmokers' risk of developing heart disease by 25%-30% and lung cancer by 20%-30%.

In addition, the home is surpassing work as the primary source of secondhand smoke exposure—a trend that poses special danger for children, who are at increased risk for sudden

infant death syndrome (SIDS), ear problems, asthma, and acute respiratory infections.

As a result, physicians "should routinely ask about secondhand smoke exposure, particularly in susceptible groups or when a child has an illness caused by secondhand smoke, such as pneumonia," Dr. Carmona stated in his 709-page review, "The Health

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## Appropriate Therapy Encouraged

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Ambulatory Pediatric Association, and American Academy of Pediatrics.

"It could be a well-child visit. There are so many things that are ordinarily done during a well-child visit," she said, emphasizing the busy workload of the health center's 14 pediatric residents and 9 pediatric attending physicians.

After each visit—during weeks when the stickers were used and the alternate weeks when they were not—a research assistant interviewed the children's parents about the severity of each child's asthma and each child's use of

medications. The assistant was blinded to what the physicians had written and prescribed.

Analysis of charts and parent interviews showed significant differences in asthma care between the intervention group and the control group of children who visited the clinic when stickers were not used.

The clinicians documented asthma severity for 135 (98%) of 138 children who had stickers on their charts but only 128 (73%) of 175 children in the control group who did not.

Moreover, review of 263 charts with notations for asthma severity revealed that physicians were significantly more likely to classify severity correctly when they

had information on the classification criteria in front of them.

They did so on 46% of charts with stickers but only 28% of charts for children in the control group.

The charts with the stickers affixed also were more likely to contain records of appropriate therapy, as defined by use of inhaled corticosteroids in children whose symptoms were consistent with persistent asthma.

Appropriate therapy was recorded on 64% of charts with stickers but only 50% of charts for the control group.

Dr. Braganza and her colleagues calculated that the little sticker more than doubled the odds of a child having a correct asthma severity classification (adjusted odds ratio, 2.58).

In addition, the sticker significantly increased the odds of a child receiving appropriate therapy according to NAEPP criteria (adjusted odds ratio, 1.77).

While the intervention did not perfect asthma classification and asthma medication use, the researchers suggested the reminders could be useful in "improving appropriate therapy for children with asthma."

### THERE WERE SIGNIFICANT DIFFERENCES IN ASTHMA CARE BETWEEN THE INTERVENTION GROUP AND THE CONTROL GROUP.

## Inhaled Steroids Didn't Prevent Asthma in Infants

BY MELINDA TANZOLA  
Elsevier Global Medical News

Inhaled corticosteroid therapy did not prevent the development of asthma in infants or young children, according to the results of two prospective studies.

In a study of 411 1-month-old infants with at least one episode of wheezing, inhaled budesonide had no effect on the progression to persistent wheezing in the first 3 years of life (N. Engl. J. Med. 2006;354:1998-2005).

"Such very early intervention is the distinguishing feature of this study," wrote the investigators. "However, the study is confounded because in many children, symptoms of pre-asthma are present, but asthma does not develop."

In the randomized, double-blind, controlled Prevention of Asthma in Childhood (PAC) study, Dr. Hans Bisgaard and colleagues at the Danish Pediatric Asthma Center at Copenhagen University Hospital in Gentofte randomized infants to receive a 2-week regimen of 400 mcg budesonide/day by pressurized metered-dose inhaler with a spacer, or a matching placebo.

Treatment was initiated after the third day of symptoms. By a mean age of 11 months, 294 infants had received at least one treatment.

Over the 3-year study period, episodes of wheezing, defined as 3 consecutive days with wheezing symptoms, occurred at a rate of 3.1 per child/year with budesonide vs. 2.7 with placebo, a nonsignificant difference. Persistent wheezing, which was defined as five episodes within 6 months, required study discontinuation and occurred in 24% of budesonide-treated infants and 21% of those receiving placebo.

Corticosteroid treatment was equivalent to placebo, according to the number of symptom-free days (83 vs. 82), occasions requiring open-label add-on treatment (59 vs. 37), and

days free of rescue medication (91 vs. 94). Presence of atopic dermatitis or respiratory virus did not affect responses to treatment.

In another study evaluating the ability of corticosteroids to prevent asthma, a 2-year course of fluticasone propionate failed to alter the development of asthma symptoms during a third treatment-free year in children aged 2-3 years at high risk for asthma (N. Engl. J. Med. 2006;354:1985-97).

The double-blind Prevention of Early Asthma in Kids (PEAK) trial, conducted by Dr. Teresa W. Guilbert at the Arizona Respiratory Center at the University of Arizona in Tucson and associates, randomized 285 children to receive a 2-year regimen of either inhaled fluticasone propionate at two 44-mcg doses twice daily by metered-dose inhaler with a valved spacer with mask, or matching placebo.

During the year after treatment, the adjusted proportion of episode-free days was not statistically different between the corticosteroid and placebo arms (86.8% vs. 85.9%, respectively) nor were other asthma-related measures, including use of bronchodilators, hospitalization and unscheduled physician visits, and lung-function tests.

"Our data suggest that inhaled corticosteroids have little therapeutic effect on the processes that determine the progression of the disease from its initial intermittent stages to a more chronic form," wrote the study investigators.

However, children receiving fluticasone had significantly better symptom control during the treatment period according to proportion of episode-free days (93.2% vs. 88.4%), number exacerbations requiring systemic corticosteroids (57.4 vs. 89.4/100 child-years) and other treatment and clinical measures.

The frequency of asthma-like symptoms increased during the study period in both groups.

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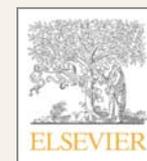
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# Consensus Reached on Long-Term Oxygen Therapy

BY DAMIAN McNAMARA  
Elsevier Global Medical News

NAPLES, FLA. — Many recommendations about long-term oxygen therapy emerged from the Sixth Oxygen Consensus Conference, according to a presentation by Dr. Dennis E. Doherty, FCCP, at the annual meeting of the National Association for Medical Direction of Respiratory Care.

About 1 million Americans receive long-term oxygen therapy (LTOT) at a cost of more than \$2 billion per year. This cost is

anticipated to increase to \$3 billion per year and account for 1% of the annual budget of the Centers for Medicare and Medicaid Services, said Dr. Doherty, chief of the pulmonary, critical care, and sleep medicine division at the University of Kentucky, Lexington.

Many new LTOT technologies are emerging, and evidence to support their use can lag a few years behind. "Some areas are weak in evidence-based medicine. Sometimes it takes common sense or consensus to make a decision," Dr. Doherty said.

The Sixth Oxygen Consensus Conference, held in Denver in August 2005, was designed to reach consensus on prescriptions, reimbursement, access, education, and research for LTOT. Participants included LTOT patients, who were "the central focus for most of the recommendations," Dr. Doherty said. "All societies and professional and lay organizations should incorporate LTOT patients into their advocacy efforts for LTOT. This is very important," he added.

The consensus conference was attended

by physicians, nurses, respiratory therapists, and other respiratory care professionals, as well as representatives from government and regulatory agencies, LTOT patient groups, device manufacturers, and providers. "I'll tell you, getting about 100 people into a room to reach consensus is not easy," Dr. Doherty said.

An official summary of what transpired at the conference was published (*Respir. Care* 2006;51:519-25).

Although attendees agreed on categories for LTOT delivery devices (stationary, portable, and wearable), they did not reach a consensus on specifications, such as the weight or configuration of such devices. "Evidence-based criteria are needed to define what is ambulatory, portable, or

## MANY LONG-TERM OXYGEN THERAPY TECHNOLOGIES ARE EMERGING, AND EVIDENCE TO SUPPORT THEIR USE CAN LAG A FEW YEARS BEHIND.

wearable. Until we have this evidence, we need the physician, patient, and HME [home medical equipment] provider to collaborate effectively," Dr. Doherty said.

Consensus was reached on these issues:

► LTOT education is needed. "To ensure quality LTOT patient care, comprehensive education is necessary," Dr. Doherty said. One recommendation at the meeting was further development of educational materials in different modalities, including print, Internet, and audiovisual-based formats.

► Training of all health professionals in disciplines caring for LTOT patients is needed.

► All patients should have access to the appropriate LTOT delivery systems and accessories to optimize care. There are many technologies, including liquid oxygen systems, oxygen concentrator systems, and lightweight, portable oxygen concentrator systems. "It is laudable to all the investigators that so many devices that are of benefit to patients have come to market," Dr. Doherty said.

► Standards for LTOT should be developed further into clinical practice guidelines.

► Reimbursement should be based on the LTOT device that is "best for the patient" as prescribed by a physician.

► LTOT should be reimbursed adequately for the specific device or class of device. "CMS and other payer organizations should be encouraged to support appropriate reimbursement so new technologies can be developed," Dr. Doherty said.

► LTOT should be incorporated into disease management or a health maintenance approach to comprehensive care of patients.

► A demonstration project should be developed to evaluate resource utilization for LTOT and to incorporate data into a recertification process when LTOT is prescribed in an acute setting. "This was somewhat controversial," Dr. Doherty said. ► Funding is needed for research to evaluate outcomes and the cost-effectiveness of LTOT.

**CHANTIX**  
(varenicline) TABLETS



Before prescribing, please consult Full Prescribing Information.

### INDICATIONS AND USAGE

CHANTIX is indicated as an aid to smoking cessation treatment.

### PRECAUTIONS

**General** Nausea was the most common adverse event associated with CHANTIX treatment. Nausea was generally described as mild or moderate and often transient, however, for some subjects, it was persistent over several months. The incidence of nausea was dose-dependent. Initial dose-titration was beneficial in reducing the occurrence of nausea. Nausea was reported by approximately 30% of patients treated with CHANTIX 1 mg BID after an initial week of dose titration. In patients taking CHANTIX 0.5 mg BID, the incidence of nausea was 16% following initial titration. Approximately 3% of subjects treated with CHANTIX 1 mg BID in studies involving 12 weeks of treatment discontinued treatment prematurely because of nausea. For patients with intolerable nausea, dose reduction should be considered. **Effect of smoking cessation:** Physiological changes resulting from smoking cessation, with or without treatment with CHANTIX, may alter the pharmacokinetics or pharmacodynamics of some drugs, for which dosage adjustment may be necessary (examples include theophylline, warfarin and insulin).

**Drug Interactions** Based on varenicline characteristics and clinical experience to date, CHANTIX has no clinically meaningful pharmacokinetic drug interactions (See Full Prescribing Information, CLINICAL PHARMACOLOGY, Drug-Drug Interactions).

**Carcinogenesis, Mutagenesis, Impairment of Fertility** Carcinogenesis. Lifetime carcinogenicity studies were performed in CD-1 mice and Sprague-Dawley rats. There was no evidence of a carcinogenic effect in mice administered varenicline by oral gavage for 2 years at doses up to 20 mg/kg/day (47 times the maximum recommended human daily exposure based on AUC). Rats were administered varenicline (1, 5, and 15 mg/kg/day) by oral gavage for 2 years. In male rats (n = 66 per sex per dose group), incidences of fibroma (tumor of the brown fat) were increased at the mid dose (1 tumor, 5 mg/kg/day, 23 times the maximum recommended human daily exposure based on AUC) and maximum dose (2 tumors, 15 mg/kg/day, 67 times the maximum recommended human daily exposure based on AUC). The clinical relevance of this finding to humans has not been established. There was no evidence of carcinogenicity in female rats.

Mutagenesis. Varenicline was not genotoxic, with or without metabolic activation, in the following assays: Ames bacterial mutation assay; mammalian CHO/HGPRT assay; and tests for cytogenetic aberrations *in vivo* in rat bone marrow and *in vitro* in human lymphocytes.

Impairment of fertility. There was no evidence of impairment of fertility in either male or female Sprague-Dawley rats administered varenicline succinate up to 15 mg/kg/day (67 and 36 times, respectively, the maximum recommended human daily exposure based on AUC at 1 mg BID). However, a decrease in fertility was noted in the offspring of pregnant rats who were administered varenicline succinate at an oral dose of 15 mg/kg/day (36 times the maximum recommended human daily exposure based on AUC at 1 mg BID). This decrease in fertility in the offspring of treated female rats was not evident at an oral dose of 3 mg/kg/day (9 times the maximum recommended human daily exposure based on AUC at 1 mg BID).

**Pregnancy** Pregnancy Category C. Varenicline succinate was not teratogenic in rats and rabbits at oral doses up to 15 and 30 mg/kg/day, respectively (36 and 50-times the maximum recommended human daily exposure based on AUC at 1 mg BID, respectively). **Nonteratogenic effects** Varenicline succinate has been shown to have an adverse effect on the fetus in animal reproduction studies. Administration of varenicline succinate to pregnant rabbits resulted in reduced fetal weights at an oral dose of 30 mg/kg/day (50 times the human AUC at 1 mg BID); this reduction was not evident following treatment with 10 mg/kg/day (23 times the maximum recommended daily human exposure based on AUC). In addition, in the offspring of pregnant rats treated with varenicline succinate there were decreases in fertility and increases in auditory startle response at an oral dose of 15 mg/kg/day (36 times the maximum recommended human daily exposure based on AUC at 1 mg BID). There are no adequate and well-controlled studies in pregnant women. CHANTIX should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Nursing mothers** Although it is not known whether this drug is excreted in human milk, animal studies have demonstrated that varenicline can be transferred to nursing pups. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from CHANTIX, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. **Labor and delivery** The potential effects of CHANTIX on labor and delivery are not known. **Pediatric Use** Safety and effectiveness of CHANTIX in pediatric patients have not been established; therefore, CHANTIX is not recommended for use in patients under 18 years of age. **Geriatric Use** A combined single and multiple-dose pharmacokinetic study demonstrated that the pharmacokinetics of 1 mg varenicline given QD or BID to 16 healthy elderly male and female smokers (aged 65-75 yrs) for 7 consecutive days was similar to that of younger subjects. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. Varenicline is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function (see DOSAGE AND ADMINISTRATION, Special Populations, Patients with Impaired Renal Function). No dosage adjustment is recommended for elderly patients (see DOSAGE AND ADMINISTRATION, Special Populations).

### Information for Patients:

- Patients should be instructed to set a date to quit smoking and to initiate CHANTIX treatment one week before the quit date.
- Patients should be advised that CHANTIX should be taken after eating, and with a full glass of water.
- Patients should be instructed how to titrate CHANTIX, beginning at a dose of 0.5 mg/day. Prescribers should explain that one 0.5 mg tablet should be taken daily for the first three days, and that for the next four days, one 0.5 mg tablet should be taken in the morning and one 0.5 mg tablet should be taken in the evening.
- Patients should be advised that, after the first seven days, the dose should be increased to one 1 mg tablet in the morning and one 1 mg tablet in the evening.
- Patients should be encouraged to continue to attempt to quit if they have early lapses after quit day.
- Patients should be informed that nausea and insomnia are side effects of CHANTIX and are usually transient; however, patients should be advised that if they are persistently troubled by these symptoms, they should notify their prescribing physician so that a dose reduction can be considered.
- Patients should also be provided with educational materials and necessary counseling to support an attempt at quitting smoking.
- Patients should be informed that some medications may require dose adjustment after quitting smoking.
- Patients intending to become pregnant or planning to breast-feed an infant should be advised of the risks of smoking and risks and benefits of smoking cessation with CHANTIX.

### ADVERSE REACTIONS

During the premarketing development of CHANTIX, over 4500 individuals were exposed to CHANTIX, with over 450 treated for at least 24 weeks and approximately 100 for a year. Most study participants were treated for 12 weeks or less. In Phase 2 and 3 placebo-controlled studies, the treatment discontinuation rate due to adverse events in patients dosed with 1 mg BID was 12% for CHANTIX compared to 10% for placebo in studies of three months' treatment. In this group, the discontinuation rates for the most common adverse events in CHANTIX treated patients were as follows: nausea (3% vs. 0.5% for placebo), headache (0.6% vs. 0.3% for placebo), insomnia (1.2% vs. 1.1% for placebo), and abnormal dreams (0.3% vs. 0.2% for placebo). Adverse Events were categorized using the Medical Dictionary for Regulatory Activities (MedDRA, Version 7.1).

The most common adverse events associated with CHANTIX (>5% and twice the rate seen in placebo-treated patients) were nausea, sleep disturbance, constipation, flatulence, and vomiting. Smoking cessation, with or without treatment, is associated with nicotine withdrawal symptoms.

The most common adverse event associated with CHANTIX treatment is nausea. For patients treated to the maximum recommended dose of 1 mg BID following initial dose titration, the incidence of nausea was 30% compared with 10% in patients taking a comparable placebo regimen. In patients taking CHANTIX 0.5 mg BID following initial titration, the incidence was 16% compared with 11% for placebo. Nausea was generally described as mild or moderate and often transient; however, for some subjects, it was persistent throughout the treatment period.

Table 3 shows the adverse events for CHANTIX and placebo in the 12-week fixed dose studies with titration in the first week (Studies 2 (titrated arm only), 4, and 5). MedDRA High Level Group Terms (HLGT) reported in ≥ 5% of patients in the CHANTIX 1 mg BID dose group, and more commonly than in the placebo group, are listed, along with subordinate Preferred Terms (PT) reported in ≥ 1% of CHANTIX patients (and at least 0.5% more frequent than placebo). Closely related Preferred Terms such as "insomnia", "initial insomnia", "middle insomnia", "early morning awakening" were grouped, but individual patients reporting two or more grouped events are only counted once.

Table 3: Common Treatment Emergent AEs (%) in the Fixed-Dose, Placebo-Controlled Studies (≥1% in the 1 mg BID CHANTIX Group, and 1 mg BID CHANTIX at least 0.5% more than Placebo)

SYSTEM ORGAN CLASS High Level Group Term Preferred Term	CHANTIX 0.5 mg BID N=129	CHANTIX 1mg 1mg BID N=821	Placebo N=805
<b>GASTROINTESTINAL</b>			
GI Signs and Symptoms			
Nausea	16	30	10
Abdominal Pain*	5	7	5
Flatulence	9	6	3
Dyspepsia	5	5	3
Vomiting	1	5	2
GI Motility/Defecation Conditions			
Constipation	5	8	3
Gastroesophageal reflux disease	1	1	0
Salivary Gland Conditions			
Dry mouth	4	6	4

(Table 3 continued)

<b>PSYCHIATRIC DISORDERS</b>			
Sleep Disorders/Disturbances			
Insomnia**	19	18	13
Abnormal dreams	9	13	5
Sleep disorder	2	5	3
Nightmare	2	1	0
<b>NERVOUS SYSTEM</b>			
Headaches			
Headache	19	15	13
Neurological Disorders NEC			
Dysgeusia	8	5	4
Somnolence	3	3	2
Lethargy	2	1	0
<b>GENERAL DISORDERS</b>			
General Disorders NEC			
Fatigue/Malaise/Asthenia	4	7	6
<b>RESPIRATORY/THORACIC/MEDIAST</b>			
Respiratory Disorders NEC			
Rhinorrhea	0	1	0
Dyspnea	2	1	1
Upper Respiratory Tract Disorder	7	5	4
<b>SKIN/SUBCUTANEOUS TISSUE</b>			
Epidermal and Dermal Conditions			
Rash	1	3	2
Pruritis	0	1	1
<b>METABOLISM &amp; NUTRITION</b>			
Appetite/General Nutrit. Disorders			
Increased appetite	4	3	2
Decreased appetite/Anorexia	1	2	1

\* Includes Pts Abdominal (pain, pain upper, pain lower, discomfort, tenderness, distension) and Stomach discomfort

\*\* Includes Pts Insomnia/Initial insomnia/Middle insomnia/Early morning awakening

The overall pattern, and the frequency of adverse events during the longer-term trials was very similar to that described in Table 3, though several of the most common events were reported by a greater proportion of patients. Nausea, for instance, was reported in 40% of patients treated with CHANTIX 1 mg BID in a one-year study, compared to 8% of placebo-treated patients.

Following is a list of treatment-emergent adverse events reported by patients treated with CHANTIX during all clinical trials. The listing does not include those events already listed in the previous tables or elsewhere in labeling, those events for which a drug cause was remote, those events which were so general as to be uninformative, and those events reported only once which did not have a substantial probability of being acutely life-threatening. **BLOOD AND LYMPHATIC SYSTEM DISORDERS. Infrequent:** Anemia, Lymphadenopathy. **Rare:** Leukocytosis, Thrombocytopenia, Splenomegaly. **CARDIAC DISORDERS. Infrequent:** Angina pectoris, Arrhythmia, Bradycardia, Ventricular extrasystoles, Myocardial infarction, Palpitations, Tachycardia. **Rare:** Atrial fibrillation, Cardiac flutter, Coronary artery disease, Cor pulmonale, Acute coronary syndrome. **EAR AND LABYRINTH DISORDERS. Infrequent:** Tinnitus, Vertigo. **Rare:** Deafness, Meniere's disease. **ENDOCRINE DISORDERS. Infrequent:** Thyroid gland disorders. **EYE DISORDERS. Infrequent:** Conjunctivitis, Dry eye, Eye irritation, Vision blurred, Visual disturbance, Eye pain. **Rare:** Acquired night blindness, Blindsight, Cataract subcapsular, Ocular vascular disorder, Photophobia, Vitreous floaters. **GASTROINTESTINAL DISORDERS. Frequent:** Diarrhea, Gingivitis. **Infrequent:** Dysphagia, Enterocolitis, Eructation, Gastritis, Gastrointestinal hemorrhage, Mouth ulceration, Esophagitis. **Rare:** Gastric ulcer, Intestinal obstruction, Pancreatitis acute. **GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS. Frequent:** Chest pain, Influenza like illness, Edema, Thirst. **Infrequent:** Chest discomfort, Chills, Pyrexia. **HEPATOBIILIARY DISORDERS. Infrequent:** Gall bladder disorder. **IMMUNE SYSTEM DISORDERS. Infrequent:** Hypersensitivity. **Rare:** Drug hypersensitivity. **INVESTIGATIONS. Frequent:** Liver function test abnormal, Weight increased. **Infrequent:** Electrocardiogram abnormal, Muscle enzyme increased, Urine analysis abnormal. **METABOLISM AND NUTRITION DISORDERS. Infrequent:** Diabetes mellitus, Hyperlipidemia, Hypokalemia. **Rare:** Hyperkalemia, Hypoglycemia. **MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS. Frequent:** Arthralgia, Back pain, Muscle cramp, Musculoskeletal pain, Myalgia. **Infrequent:** Arthritis, Osteoporosis. **Rare:** Myositis. **NERVOUS SYSTEM DISORDERS. Frequent:** Disturbance in attention, Dizziness, Sensory disturbance. **Infrequent:** Amnesia, Migraine, Parosmia, Psychomotor hyperactivity, Restless legs syndrome, Syncope, Tremor. **Rare:** Balance disorder, Cerebrovascular accident, Convulsion, Dysarthria, Facial palsy, Mental impairment, Multiple sclerosis, Nystagmus, Psychomotor skills impaired, Transient ischemic attack, Visual field defect. **PSYCHIATRIC DISORDERS. Frequent:** Anxiety, Depression, Emotional disorder, Irritability, Insomnia. **Infrequent:** Aggression, Agitation, Disorientation, Dissociation, Libido decreased, Mood swings, Thinking abnormal. **Rare:** Bradyphrenia, Euphoric mood, Hallucination, Psychotic disorder, Suicidal ideation. **RENAL AND URINARY DISORDERS. Frequent:** Polyuria. **Infrequent:** Nephritis, Nocturia, Urine abnormality, Urinary syndrome. **Rare:** Renal failure acute, Urinary retention. **REPRODUCTIVE SYSTEM AND BREAST DISORDERS. Frequent:** Menstrual disorder. **Infrequent:** Erectile dysfunction. **Rare:** Sexual dysfunction. **RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS. Frequent:** Epistaxis, Respiratory disorders. **Infrequent:** Asthma. **Rare:** Pleurisy, Pulmonary embolism. **SKIN AND SUBCUTANEOUS TISSUE DISORDERS. Frequent:** Hyperhidrosis. **Infrequent:** Acne, Dermatitis, Dry skin, Eczema, Erythema, Psoriasis, Urticaria. **Rare:** Photosensitivity reaction. **VASCULAR DISORDERS. Frequent:** Hot flush, Hypertension. **Infrequent:** Hypotension, Peripheral ischemia, Thrombosis.

### DRUG ABUSE AND DEPENDENCE

**Controlled Substance Class** Varenicline is not a controlled substance. **Humans:** Fewer than 1 out of 1000 patients reported euphoria in clinical trials with CHANTIX. At higher doses (greater than 2 mg), CHANTIX produced more frequent reports of gastrointestinal disturbances such as nausea and vomiting. There is no evidence of dose-escalation to maintain therapeutic effects in clinical studies, which suggests that tolerance does not develop. Abrupt discontinuation of CHANTIX was associated with an increase in irritability and sleep disturbances in up to 3% of patients. This suggests that, in some patients, varenicline may produce mild physical dependence which is not associated with addiction. In a human laboratory abuse liability study, a single oral dose of 1 mg varenicline did not produce any significant positive or negative subjective responses in smokers. In non-smokers, 1 mg varenicline produced an increase in some positive subjective effects, but this was accompanied by an increase in negative adverse effects, especially nausea. A single oral dose of 3 mg varenicline uniformly produced unpleasant subjective responses in both smokers and non-smokers. **Animals:** Studies in rodents have shown that varenicline produces behavioral responses similar to those produced by nicotine. In rats trained to discriminate nicotine from saline, varenicline produced full generalization to the nicotine cue. In self-administration studies, the degree to which varenicline substitutes for nicotine is dependent upon the requirement of the task. Rats trained to self-administer nicotine under easy conditions continued to self-administer varenicline to a degree comparable to that of nicotine, however, in a more demanding task, rats self-administered varenicline to a lesser extent than nicotine. Varenicline pretreatment also reduced nicotine self-administration.

### OVERDOSAGE

In case of overdose, standard supportive measures should be instituted as required. Varenicline has been shown to be dialyzed in patients with end stage renal disease (see Full Prescribing Information, CLINICAL PHARMACOLOGY, Pharmacokinetics, Pharmacokinetics in Special Patient Populations), however, there is no experience in dialysis following overdose.

### DOSAGE AND ADMINISTRATION

**Usual Dosage for Adults** Smoking cessation therapies are more likely to succeed for patients who are motivated to stop smoking and who are provided additional advice and support. Patients should be provided with appropriate educational materials and counseling to support the quit attempt. The patient should set a date to stop smoking. CHANTIX dosing should start one week before this date. CHANTIX should be taken after eating and with a full glass of water. The recommended dose of CHANTIX is 1 mg twice daily following a 1-week titration as follows:

Days 1-3:	0.5 mg once daily
Days 4-7:	0.5 mg twice daily
Days 8-End of treatment:	1 mg twice daily

Patients who cannot tolerate adverse effects of CHANTIX may have the dose lowered temporarily or permanently. Patients should be treated with CHANTIX for 12 weeks. For patients who have successfully stopped smoking at the end of 12 weeks, an additional course of 12 weeks treatment with CHANTIX is recommended to further increase the likelihood of long-term abstinence. Patients who do not succeed in stopping smoking during 12 weeks of initial therapy, or who relapse after treatment, should be encouraged to make another attempt once factors contributing to the failed attempt have been identified and addressed.

### Special Populations

**Patients with impaired renal function** No dosage adjustment is necessary for patients with mild to moderate renal impairment. For patients with severe renal impairment, the recommended starting dose of CHANTIX is 0.5 mg once daily. Patients may then titrate as needed to a maximum dose of 0.5 mg twice a day. For patients with End-stage renal disease undergoing hemodialysis, a maximum dose of 0.5 mg once daily may be administered if tolerated well (See Full Prescribing Information, CLINICAL PHARMACOLOGY, Pharmacokinetics, Pharmacokinetics in Special Populations, Renal Impairment). **Dosing in elderly patients and patients with impaired hepatic function** No dosage adjustment is necessary for patients with hepatic impairment. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function (See PRECAUTIONS, Geriatric Use). **Use in children** Safety and effectiveness of CHANTIX in pediatric patients have not been established; therefore, CHANTIX is not recommended for use in patients under 18 years of age.

Rx only

May 2006, Version LAB-0327-2.0

# Cochrane Panel: Steroids Achieve Best Asthma Control

## Inhaled steroids beat sodium cromoglycate in a systematic review of clinical trials.

BY DOUG BRUNK

Elsevier Global Medical News

Inhaled corticosteroids are better than sodium cromoglycate in measures of lung function and asthma control in children and adults with chronic asthma, the first-ever systematic review of its kind has concluded.

"The results suggest that the superiority of ICS over SCG may be independent of asthma severity, since results were generally similar among those with milder and more severe asthma," wrote the researchers, who were led by Dr. James P. Guevara of the department of pediatrics at the University of Pennsylvania, Philadelphia.

"The results also suggest that the superiority of ICS over SCG may depend on the dosage of inhaled steroid, since results in favor of ICS were generally stronger among studies with

moderate doses than among those with low doses," said Dr. Guevara.

However, no conclusions could be made about possible differences in adverse events between ICS and SCG because adverse events in the trials chosen for analysis "were reported inconsistently, and most trials were short-term," they noted. "This may have limited our ability to identify adverse effects, particularly those such as growth retardation that require more prolonged monitoring."

The researchers reviewed 25 randomized, controlled trials that compared the effects of ICS with those of SCG in children and adults with chronic asthma. Of the 25 trials, 17 included 1,279 children and 8 included 321 adults (Cochrane Database System. Rev. 2006; DOI:10.1002/14651858.CD003558.pub2).

In the trials of children, use of

ICS was associated with a higher mean forced expiratory volume in 1 second (FEV<sub>1</sub>) (a mean weighted difference of 0.07 L) and a higher final end-point peak expiratory flow (PEF) rate (a mean weighted difference of 17.3 L/minute), compared with use of SCG.

Use of ICS also was associated with fewer exacerbations (a mean weighted difference of -1.18 per patient year), lower asthma symptom scores, and less bronchodilator use, compared with use of SCG.

In the trials of adults, use of ICS was associated with a higher mean FEV<sub>1</sub> (a mean weighted difference of 0.21 L) and a higher final end-point PEF rate (a mean weighted difference of 28.2 L/minute), compared with use of SCG.

Use of ICS also was associated with fewer exacerbations (a mean weighted difference of -3.30 per patient year) and less bronchodilator use, compared with use of SCG.

Use of ICS was associated with

lower asthma symptom scores than was SCG in the three crossover trials reviewed as part of the analysis, but not in the one parallel group trial reviewed.

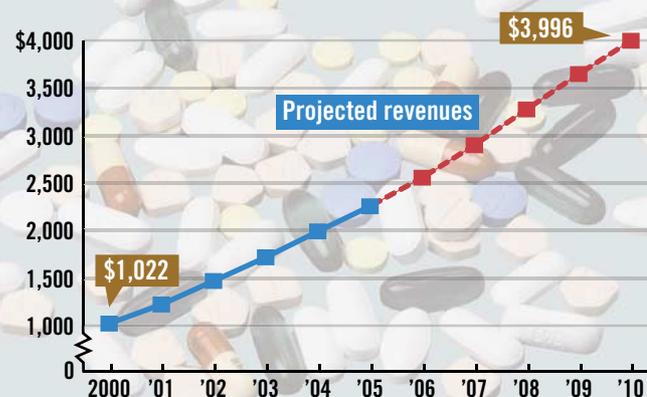
Dr. Guevara and his associates acknowledged that a key limitation of the review "was the underreporting of health care

utilization and adverse effects among eligible studies.

"With only two trials reporting health care use in pediatrics and no trials in adults, there are insufficient data to clarify whether ICS reduces health care utilization compared to SCG," said Dr. Guevara.

## DATA WATCH

### World Prescription Generic Market Is Expected To Climb for Allergy and Respiratory Drugs (revenues in millions)



Note: Based on U.S. manufacturers' revenues in 2005 dollars. Source: Kalorama Information

## Trial Compares Fluid Strategies

Conservative • from page 1

venous pressure (CVP) or less than 8 mm Hg in pulmonary artery occlusion pressure (PAOP). The targets for patients in the liberal group were a CVP of 10-14 mm Hg or a PAOP of 14-18 mm Hg.

As a result, patients in the liberal group gained an average of 7 L of fluids during their first 7 days in the trial, according to Dr. Wiedemann, chairman of pulmonary, allergy, and critical care medicine at the Cleveland Clinic. Patients in the conservative arm had no significant difference in fluids from when they entered the study. Average cumulative fluid balance during the first 7 days was 6,992 ± 502 mL for the liberal arm vs. -136 ± 491 mL for the conservative arm.

To determine how the two strategies compared to what physicians normally do, the investigators reviewed data from large trials the network had conducted during the previous decade. "In these trials, the average patient gained exactly 7 L over the course of 7 days," Dr. Wiedemann said.

The investigators do not claim that the liberal approach is the standard of care, he said, but rather that the "net fluid balance is very similar to what physicians are doing."

A description of baseline characteristics showed that the 503 patients in the conservative arm had higher average creatinine levels than did the 497 patients in the liberal arm. Otherwise, the two cohorts were balanced. The most common primary lung injury was pneumonia in nearly half

the population, followed by sepsis and aspiration.

Patients in the conservative cohort spent significantly more days outside the intensive care unit during the first 7 days after randomization (0.9 days vs. 0.6 days) and the first 28 days after randomization (13.4 days vs. 11.2 days), compared with those in the liberal group. They also experienced significantly more ventilator-free days during this period (14.6 days vs. 12.1 days).

Going into the trial, the investigators were concerned that the conservative strategy would lead to more adverse events such as kidney and cardiovascular failure. "We were glad to report we did not see that," Dr. Wiedemann said.

Indeed, he reported a trend favoring conservative management with respect to kidney failure. Only 10% of conservative management patients required dialysis within 60 days of entering the study, compared with 14% of the liberal management patients.

"I don't find it surprising," Dr. Wiedemann said. "I find it a bit gratifying that we were able to achieve the potential benefit of conservative therapy without inducing potential harm. We were able to thread the needle."

In an editorial accompanying the journal article, Dr. Emanuel P. Rivers, FCCP, held that the protocol was not really identical to standard practice, in that the trial excluded patients receiving

hemodialysis as well as those with overt renal insufficiency or heart failure. As a result, he said, the approximate age of 50 years was younger than the typical population with acute lung injury (N. Engl. J. Med. 2006;354:2598-600).

Dr. Rivers, of Henry Ford Hospital and Wayne State University, Detroit, called conservative fluid strategies "therapeutically sound," but said the timing of these interventions is important.

He noted that the protocol was initiated 43 hours on average after the patients were admitted to the intensive care unit, and 24 hours after acute lung injury was established. Consequently, he said, most patients had already been optimized hemodynamically.

"Fluid may be a friend when appropriately titrated during the resuscitation, or ebb, phase of acute lung injury. However, excess fluid becomes an enemy when it is no longer physiologically needed," Dr. Rivers wrote. He added, "In contrast to what is true in politics, in fluid management of acute lung injury, it is OK to be both liberal and conservative."

### Dr. Curtis N. Sessler, FCCP, comments:

The findings of this important research—that a conservative fluid management strategy is associated with shorter time on the ventilator without sacrificing renal function—will likely change the management of acute lung injury and ARDS in ICUs around the world.

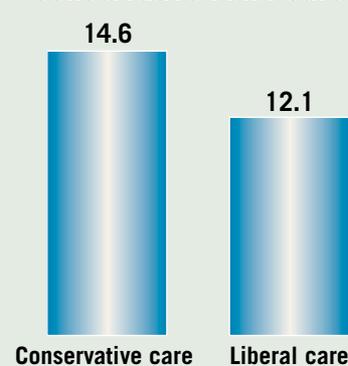
Although practitioners generally try to avoid unnecessary fluid administration, in many circumstances oliguria and/or hypotension occur, and clinicians must contemplate whether to administer additional fluids. Previous research suggests that many clinicians follow a relatively "liberal" fluid policy. Unfortunately, our tools to assess "fluid responsiveness" are imprecise.

In the second major management issue addressed by the ARDSNet investigators in this study, guidance by CVP led to similar outcomes, compared with use of pulmonary artery occlusion pressure (N. Engl. J. Med. 2006;354:2213-24). However, both of these measurements have been criticized as having only marginal accuracy in predicting changes in cardiac output following fluid administration.

Nevertheless, in the management strategies of both the current study and the early goal-directed therapy for septic shock study by Rivers et al. (N. Engl. J. Med. 2001;345:1368-77), measurement of central venous pressure plays a pivotal role in guiding fluid administration (or diuresis). Major considerations in the conservative fluid management strategy tested include CVP, mean arterial pressure, urinary output, and "circulation." The next challenge will be translating and implementing the key components of this conservative strategy into bedside management.

**CONSERVATIVE FLUID STRATEGIES ARE 'THERAPEUTICALLY SOUND,' BUT THE TIMING OF THESE INTERVENTIONS IS IMPORTANT.**

### Patients Have More Ventilator-Free Days With Conservative Fluid Care



Note: Based on a study of 1,000 patients with acute lung injuries at 28 days. Source: Dr. Wiedemann

# Adjuvant Chemo Is Questioned in Early-Stage NSCLC

BY JANE SALODOF MACNEIL  
Elsevier Global Medical News

ATLANTA — Updated results from a clinical trial that helped establish adjuvant chemotherapy with paclitaxel and carboplatin as the standard of care for stage IB non-small cell lung cancer no longer show a significant improvement in overall survival.

At a median follow-up of 57 months, 5-year overall survival was 59% for adjuvant chemotherapy patients and 57% for those randomized to observation in the Cancer and Leukemia Group B (CALGB) trial known as CALGB 9633. The 2% difference was not statistically significant. Patients given adjuvant chemotherapy did benefit from significantly improved 2- and 3-year survival in the new analysis. They also had a significantly longer failure-free survival duration, with a hazard ratio of 0.74.

Dr. Gary M. Strauss reported the new data on behalf of CALGB at the annual meeting of the American Society of Clinical Oncology (ASCO). Despite some positive effects, CALGB 9633 “can be interpreted as a negative study and, perhaps I should say, should be interpreted as a negative study,” he said.

In a shift from his presentation 2 years ago at the same meeting, Dr. Strauss of Brown University, Providence, R.I., said that “the results of CALGB 9633 do not mandate adjuvant chemotherapy as the standard of care in all stage IB patients.”

He added that the investigators believe the results do, however, support continued

consideration of adjuvant paclitaxel and carboplatin for stage IB patients, in particular, those with tumors 4 cm or more in diameter.

CALGB 9633 had been the only trial among three influential adjuvant therapy studies to report a survival advantage in NSCLC patients with stage IB tumors.

At the ASCO meeting 2 years ago, Dr. Strauss reported an 8% improvement in survival with adjuvant chemotherapy (hazard ratio 0.62). A data safety monitoring board closed the trial early because its primary outcome had been reached.

The early stopping was justified but “potentially problematic,” Dr. Strauss said. It did not negate the earlier results, but left the study without sufficient statistical power to detect “smaller differences that are nonetheless clinically significant.”

Investigators had already revamped CALGB 9633 from an initial goal of 500 patients to a target of 384 patients because of slow accrual. The curtailed trial enrolled 344 patients between Sept. 15, 1996, and Nov. 26, 2003. All were included in the intent-to-treat analysis presented this year.

After complete resection of their tumors, 171 patients were randomized to observation and 173 patients to four cycles

during each of which they received 200 mg/m<sup>2</sup> of paclitaxel and carboplatin AUC 6 for 3 weeks.

Chemotherapy was reported to be well tolerated. About a third of patients had grade 3 or 4 neutropenia, but there were no therapy-related deaths.

As of April 19, 2006, the latest data cut-off, median overall survival was 95 months for patients who had received adjuvant

chemotherapy and 78 months with observation. Although the hazard ratio was 0.80, the difference between the groups was not statistically significant.

Overall survival was significantly better for the adju-

vant chemotherapy arm at 2 years (90% vs. 84% for the control arm) and at 3 years (79% vs. 71%), but not thereafter.

Failure-free survival favored adjuvant chemotherapy, with a median of 89 months vs. 52 months in the observation arm. The difference was significant at 3 years, when 66% of the adjuvant arm but only 57% of the observation arm had no recurrence.

In an unplanned subset analysis reported by Dr. Strauss, the investigators did find a significant survival benefit for patients whose tumors were 4 cm or larger in diameter (hazard ratio 0.66), but not for those with smaller tumors.

As only 137 of 155 deaths required for final analysis have so far been observed, Dr. Strauss emphasized that the new report is still only a preliminary analysis.

In conclusion, he said the significant advantages in 3-year and in disease-free survival suggest that the regimen is effective and may delay recurrence, even if it does not enhance the likelihood of a cure. ■

**Dr. Gerard A. Silvestri, FCCP, comments:** While the findings of this study are clearly disappointing, the results confirm other studies that showed no benefit for patients with stage IB disease.

What remains so perplexing is that benefit is seen in stage II and stage IIIA patients. With the expected outcome of stage IA and B disease relatively high with surgery alone, one can postulate that there would be little extra benefit to adding chemotherapy for this stage of disease. One is left wondering if a benefit would be seen if greater numbers of patients were enrolled in this study.

It should be noted that patients with early-stage breast cancer are offered chemotherapy after surgery with reported benefits in as little as 4%.

Chemotherapy should still be strongly considered for stage II and IIIA resected patients, as this group has an additional survival benefit of approximately 10% if they are offered chemotherapy following surgery.

**OVERALL SURVIVAL WAS SIGNIFICANTLY BETTER WITH ADJUVANT CHEMOTHERAPY AT 2 YEARS AND 3 YEARS, BUT NOT THEREAFTER.**

## No Smoke Is ‘Safe’ Smoke

Secondhand Smoke • from page 1

Consequences of Involuntary Exposure to Tobacco Smoke: A Report of the Surgeon General.”

The president of the American College of Chest Physicians, Dr. W. Michael Alberts, FCCP, praised the “strong and direct language” of the surgeon general and predicted “snowballing” pressure against smoking. The report gives chest physicians more clout with their patients who smoke, and gives workers who are still exposed to smoke in the workplace extra clout to seek a ban, said Dr. Alberts, chief medical officer at the H. Lee Moffitt Cancer Center and Research Institute in Tampa, Fla.

### Clearing the Air

The new report acknowledges that the levels of secondhand smoke have cleared significantly since the last look at the topic 20 years ago. Thanks to the spread of smoke-free environments at work sites and other public places, levels of cotinine, a biologic marker for secondhand smoke exposure, have fallen in nonsmokers by 70% since the late 1980s. The proportion of nonsmokers with detectable cotinine levels has been halved from 88% in 1988-1991 to 43% in 2001-2002.

Nonetheless, nearly half of all nonsmoking Americans are still regularly exposed to secondhand smoke, and children’s median cotinine levels were more than twice those of adult nonsmokers.

The California Environmental Protection Agency highlighted secondhand smoke’s human toll in a 2005 study cited by the U.S. surgeon general. Exposure resulted in an estimated 3,400 deaths annually from lung cancer, 46,000 deaths from cardiac-related illnesses, and 430 deaths from sudden infant death syndrome.

### The Cardiorespiratory Costs

Two decades of new data further cement the causal links connecting secondhand smoke to cardiovascular and respiratory disease.

Sufficient evidence now exists to infer a causal relationship between secondhand smoke exposure and lung cancer in lifetime nonsmokers—a conclusion that extended to all secondhand smoke exposure, regardless of location. The evidence is also sufficient to back a causal link between secondhand smoke and increased risk of coronary heart disease.

The science tying secondhand smoke to other conditions is

suggestive but less certain. For example, the surgeon general’s report deemed the evidence of increased risk of stroke or atherosclerosis as “suggestive but not sufficient.” The data supporting a causal link between exposure and breast cancer are likewise suggestive but not sufficient.

Among people with asthma, the evidence is suggestive but not sufficient to infer a causal relationship between secondhand smoke exposure and acute respiratory symptoms such as cough, wheeze, chest tightness, and difficulty breathing. The evidence was also suggestive but not sufficient to draw a causal link between exposure and an acute decline in lung function and short-term secondhand smoke in people with asthma.

The data supporting a causal link between secondhand smoke and risk for chronic obstructive pulmonary disease were deemed suggestive but not sufficient, while the report said the evidence was “inadequate” to infer the presence or absence of a causal relationship between exposure and morbidity in patients with COPD.

### Pediatric Impact

Because of young children’s high levels of exposure, secondhand smoke should be considered a significant pediatric issue,

according to the report. The pediatric findings are especially stark for mothers.

In its 2005 report, Cal/EPA estimated that, nationwide, secondhand smoke exposure annually resulted in between 24,300 and 71,900 low-birth-weight or preterm deliveries, about 202,300 episodes of childhood asthma (new cases and exacerbations), between 150,000 and 300,000 cases of lower respiratory tract illness in children, and about 789,700 cases of middle ear infections.

According to the report, the evidence is sufficient to infer a causal relationship between secondhand smoke exposure from parental smoking and SIDS, as well as lower respiratory tract illnesses in infants and children. Sufficient evidence also exists to infer a causal relationship between parental smoking and middle ear disease in children, including acute and recurring otitis media and chronic middle ear effusion.

For childhood asthma, a causal relationship was found between exposure from parental smoking and the onset of wheeze illnesses in early childhood. However, the evidence was only suggestive of a causal relationship between secondhand smoke exposure from parental smoking and the onset of childhood asthma.

The latest data on lung growth

and pulmonary function showed a causal relationship between maternal smoking during pregnancy and persistent adverse effects on lung function during childhood.

### Seeking Solutions

To prevent these risks, the surgeon general said, the smoke must be stopped—everywhere.

Creating separately ventilated rooms isn’t an answer to preventing exposure, nor are typical air cleaning strategies sufficient. “The only way to protect nonsmokers from the dangerous chemicals in secondhand smoke is to eliminate smoking indoors,” according to the report.

Arguments that such no-smoking policies would cripple the hospitality industry carry no weight in the surgeon general’s report. Assessing the evidence demonstrates that “smoke-free policies and regulations do not have an adverse economic impact on the hospitality industry,” the report stated.

The report “absolutely” gives physicians more clout with smokers, said Dr. Shirish Gadgeel, an oncologist at the Barbara Ann Karmanos Cancer Institute at Wayne State University in Detroit. Now, he said, physicians can point to the report and say that smokers risk the health of their “near and dear ones” by smoking. ■

# Dark Fungi Emerging as Cause of Often Lethal Infections

*Melanin in the cell wall provides coloration of these pathogens and seems to protect against free radicals.*

BY NANCY WALSH  
Elsevier Global Medical News

LAS VEGAS — Dematiaceous, or darkly pigmented, fungi are emerging as an important cause of disease, and certain types of infections with these pathogens are associated with high rates of mortality, even among the immunocompetent, Dr. Sanjay G. Revankar said at a meeting on fungal infections sponsored by Imedex.

This is a heterogeneous group of fungi that includes more than 60 genera and 100 species found worldwide in soil and air. Melanin, present in the cell wall, provides the coloration of these pathogens and appears to be a virulence factor, providing protection from free radicals, hydrolytic enzymes, and ultraviolet damage.

One of the clinical syndromes associated with various species of dematiaceous fungi increasingly being seen is phaeohyphomycosis. Most of the species implicated are opportunists, but some may be true pathogens, said Dr. Revankar of the University of Texas Southwestern Medical Center, Dallas.

The diagnosis of phaeohyphomycosis requires expert interpretation of colony and microscopic morphology. The histologic findings that are typically observed with this species include irregularly swollen hyphae and yeastlike forms. In contrast to many other fungi, there are no adequate serologic or antigen tests for the species that cause phaeohyphomycosis, he said.

The range of clinical syndromes in

phaeohyphomycosis includes the following:

► **Superficial infections.** These typically manifest as subcutaneous nodules appearing after minor trauma to the skin and inoculation with species of *Exophiala*, *Alternaria*, or *Phialophora*. Successful treatment often requires only excision, although an azole is sometimes also given.

► **Allergic disease.** Most cases of sinusitis and bronchopulmonary mycosis are caused by species of *Curvularia* or *Bipolaris*. Sinusitis is characterized by the presence of allergic mucin and elevated IgE; treatment includes surgery plus corticosteroids. Bronchopulmonary mycosis is associated with elevated IgE or eosinophilia, and treatment relies on corticosteroids. Antifungal therapy is not routinely used for these infections, Dr. Revankar said.

► **Pneumonia.** This has been seen most in immunocompromised patients, and may be characterized by hemoptysis. Among the pathogens implicated are species of *Exophiala* and *Chaetomium*.

Lipid amphotericin B is the preferred

treatment for these seriously ill patients, followed by an azole if the patient stabilizes, but mortality is high, he said.

► **CNS phaeohyphomycosis.** This infection shows a 3:1 male predominance and has been reported worldwide. "What is really unusual is that more than half of patients seem to have no risk factors—no chemotherapy, HIV, or other immunodeficiency," Dr. Revankar said.

In a series of 101 patients with CNS infection, the classic triad seen with bacterial

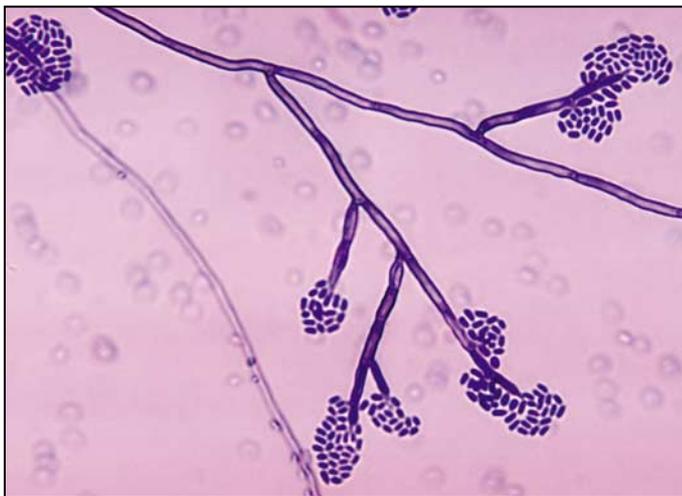
of amphotericin B, 5-fluorocytosine, and itraconazole was associated with improved survival, but only six patients in the series received this combination. Voriconazole and posaconazole have shown in vitro activity, but there is very little clinical experience with these agents for this indication, he said.

► **Disseminated phaeohyphomycosis.** "This has been seen increasingly during the past 10-15 years, probably reflecting the type of patients we are seeing, such as those who are immunocompromised from treatment for other diseases," Dr. Revankar said. Prior cardiac surgery, particularly involving bioprosthetic valve replacements, also has been identified as a risk factor.

In a series of 72 patients, fever was present in only 76%. Skin lesions were seen in 33%, sepsis in 11%, and eosinophilia in 11% (Clin. Infect. Dis. 2002;34:467-76). Blood cultures were positive, most commonly revealing *Scedosporium prolificans* in more than half of patients. Most of the cases were in Spain and Australia.

Overall mortality was 79%. In the immunocompromised it was 84%, and in the immunocompetent it was 65%.

*S. prolificans* is resistant to all available agents, and no single drug or combination of drugs was associated with improved outcome in this series. In two cases, however, the combination of an azole plus terbinafine was successful. "I wouldn't recommend this routinely, but if you have no other options it might be something to consider. Terbinafine is not considered a particularly useful systemic drug because of its pharmacokinetics, but in these cases there really is not much else left," he said. ■



Dematiaceous fungi such as *Exophiala* are among the pathogens implicated in pneumonia in immunocompromised patients.

CDC/DR. LIBERO AJELLO

brain abscess—fever, headache, and neurologic deficits—was present in fewer than 5% of patients (Clin. Infect. Dis. 2004;38:206-16). Overall mortality was 72%.

Many species have been isolated in CNS infections, but in nearly half of cases *Cladophialophora bantiana* was implicated.

There was little evidence of efficacy for any particular antifungal regimen in these patients with CNS disease. A combination

# Hyperglycemia Linked to ICU Mortality in Specific Disorders

BY JEFF EVANS  
Elsevier Global Medical News

WASHINGTON — Hyperglycemia is associated with increased mortality in ICUs, independent of the severity of illness, according to the largest and most definitive report on the subject to date.

In a review of 216,775 consecutive patients who were admitted for the first time to ICUs at Veterans Affairs medical centers, the association between hyperglycemia and increased ICU mortality was strongest in patients with cardiovascular disorders, such as myocardial infarction, unstable angina, and stroke, and in those without diagnosed diabetes, Dr. Mercedes Falciglia reported at the annual scientific sessions of the American Diabetes Association.

For cardiovascular disorders and many other diseases for which hyperglycemia was associated with increased ICU mortality, the risk of death increased in a stepwise fashion with increases

in the level of mean blood glucose from 111-145 mg/dL to more than 300 mg/dL.

Patients without diagnosed diabetes had an increased risk of death associated with hyperglycemia that ranged from 40% at the lowest level of hyperglycemia to a fourfold greater risk at the highest levels, while individuals with diagnosed diabetes did not have a significantly increased risk of death unless their blood glucose level exceeded a value of 146 mg/dL.

The study involved mostly men (97%) in 177 surgical, medical, and cardiac ICUs at 73 VA medical centers during 2002-2005. Two-thirds of the patients in the study were older than 60 years of age, and 29% had diagnosed diabetes.

Using a model that has been validated in determining the severity of illness, Dr. Falciglia and her colleagues analyzed the likelihood of mortality associated with different glycemic levels (70-110 mg/dL, 111-145 mg/dL,

146-199 mg/dL, 200-300 mg/dL, and greater than 300 mg/dL) in groups of patients in 78 diagnostic categories.

"Even among those disorders where there was a significant relationship between hypergly-

**IN MANY DISEASES, THE RISK OF DEATH IN THE ICU INCREASED IN A STEPWISE FASHION WITH INCREASES IN THE LEVEL OF MEAN BLOOD GLUCOSE.**

cemia and mortality, there was still variability in the magnitude of the mortality risk," noted Dr. Falciglia, of the division of endocrinology at the University of Cincinnati.

For hyperglycemia in the lowest and highest ranges, patients with ischemic stroke were between 3 and 15 times more likely to die than were those with a normal mean blood glucose level (70-110 mg/dL). But although

hyperglycemia was significantly associated with ICU mortality in patients with pneumonia, the likelihood of death did not change in step with the severity of hyperglycemia.

Other diseases, such as chronic obstructive pulmonary disease and liver failure, showed no significant relationship between hyperglycemia and ICU mortality.

Previous studies have reported hyperglycemia as a significant risk factor for mortality in the ICU in patients with an acute myocardial infarction, coronary artery bypass graft, or stroke, and for patients in general staying in pediatric or adult ICUs. But many of these studies have been limited by inadequate adjustment for the severity of illness, small sample sizes, and measurement of blood glucose levels only at entry to the ICU, Dr. Falciglia said.

Randomized trials of critically ill patients in surgical and medical ICUs have shown that tighter

control of blood glucose levels reduces morbidity and mortality. But a few recent trials involving patients with acute myocardial infarction have reported mixed results, which have been attributed to insufficient power and the inability to establish glycemic control in intervention groups. This led many investigators to wonder whether the benefits of tighter glycemic control are generalizable across all critically ill patients and all disease types, she said.

Findings from the current study suggest that "future randomized trials examining glycemic control in hospitalized patients may benefit from focusing on diseases where the risk of death from hyperglycemia appears to be greatest," Dr. Falciglia said.

"In diseases where we were not able to demonstrate an association between hyperglycemia and mortality, elevated blood glucose may still impact other adverse outcomes that we did not measure in this study," she added. ■

# Treatment of Obstructive Sleep Apnea Protects the Heart

*An Italian study points to a correlation between bradyarrhythmias and hypoxemia during sleep.*

BY KATE JOHNSON  
Elsevier Global Medical News

BOSTON — Obstructive sleep apnea is a risk factor for cardiac arrhythmias, and cardiologists should consider the diagnosis and treatment of this sleep disorder in terms of cardioprotective benefit, according to Dr. Maria Teresa La Rovere.

In a study she presented in a poster at the annual meeting of the Heart Rhythm Society, Dr. La Rovere found a significant correlation between oxygen desaturation in obstructive sleep apnea syndrome (OSAS) and bradyarrhythmias, but not tachyarrhythmias.

"We found strong evidence that bradyarrhythmias are related to sleep apnea syndrome—while for tachyarrhythmias, the role of oxygen desaturation is more controversial," said Dr. La Rovere in an interview.

Other factors may contribute to tachyarrhythmias, such as  $\beta_2$ -agonist treatment, which was found to be more common among patients who had tachyarrhythmias, she said.

The study included 300 subjects who were referred for sleep studies because of snoring. OSAS was diagnosed in 248 (83%) of them.

Although there was a trend toward more arrhythmias in the patients with OSAS than in those without OSAS (18% vs. 11%), the difference was not significant, reported Dr. La Rovere, a cardiologist at the Fondazione Salvatore Maugeri clinic in Pavia, Italy.

Patients who exhibited arrhythmias during sleep were older than nonarrhythmic subjects (58 vs. 52 years) and had more profound oxygen desaturation (23% vs. 15% total sleep time spent with less than 90% oxygen saturation).

While no significant relationship was found between tachyarrhythmias and hypoxemia, bradyarrhythmias were significantly correlated. Patients who had

bradyarrhythmias had significantly more hypoxemia, compared with nonarrhythmic patients, with an apnea-hypopnea index of 54 vs. 31 and an oxygen saturation nadir of 69% vs. 77%.

Dr. La Rovere said a recently published study performed in the general population and using a stricter definition of OSAS found similar evidence that people with

sleep-disordered breathing have between two and four times the odds of having complex cardiac arrhythmias, compared with those without sleep apnea (*Am. J. Respir. Crit. Care Med.* 2006;173:910-6).

Specifically, the results of the study showed that sleep-disordered breathing was associated with four times the odds of atrial fibrillation, three times the odds of nonsustained ventricular tachycardia, and almost twice the odds of complex ventricular ectopy, after adjustment for age, sex, body mass index, and prevalent coronary heart disease.

Another recently published study found that OSAS was associated with almost

double the risk of stroke or death, even after adjustment for age, sex, race, smoking status, alcohol consumption, body mass index, diabetes mellitus, hyperlipidemia, atrial fibrillation, and hypertension (*N. Engl. J. Med.* 2005;353:2034-41).

While treatment of OSAS with continuous positive airway pressure (CPAP) is well established for the relief of sleep disturbances and improvement in quality of life, Dr. La Rovere says cardiologists should also recognize its value in preventing the development of cardiac arrhythmias.

"The mechanism of breathing disorders also affects cardiac functioning. So in the long term, these subjects may also develop heart failure," she said.

"I think there is an increasing awareness," but cardiologists have not yet focused on the cardiac benefits of treating sleep apnea.

She added that while CPAP not only prevents sleep-related heart rhythm disturbances but also can correct them, it is advisable to consider a pacemaker for patients whose CPAP compliance is questionable. "I know the CPAP will correct my patient's arrhythmia, but I do not know if my patient will use the CPAP," she said.

**A RECENT STUDY SHOWED OSAS WAS ASSOCIATED WITH ALMOST DOUBLE THE RISK OF STROKE OR DEATH, EVEN AFTER ADJUSTMENT FOR A HOST OF FACTORS.**

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## OSAS Underestimated in Pediatric Down Syndrome

BY KATE JOHNSON  
Elsevier Global Medical News

Young children with Down syndrome should be routinely evaluated for sleep abnormalities, regardless of whether their parents perceive any problems, according to Dr. Sally R. Shott of the Cincinnati Center for Developmental Disabilities, and her colleagues.

Their 5-year longitudinal study of 56 children with Down syndrome (DS) revealed that while 80% had abnormalities revealed on polysomnography (PSG), only 23% of parents correctly predicted the problem (*Arch. Otolaryngol. Head Neck Surg.* 2006;132:432-6). All children entered the study at age 2 years or younger.

"In general, parents of children with DS significantly underestimate the severity of their child's sleep disturbances," the investigators said. Because of the high incidence of obstructive sleep apnea syndrome in young children with Down syndrome, and the poor correlation between parental impressions of sleep problems and PSG results, the investigators recommended baseline PSG in all children with Down syndrome at age 3-4 years.

The study involved overnight PSG that was performed in all children at a mean age of 42 months. If parental history or examination results suggested possible upper airway obstruction before the scheduled PSG, the test was performed earlier. Twenty-two of the 56 children underwent multiple PSGs.

The PSG generated data regarding sleep duration, percentage of time spent in var-

ious stages of sleep, sleep arousals, apnea index (number of obstructive sleep apnea episodes per hour of sleep), hypopnea index (number of hypopneas per hour of sleep), apnea/hypopnea index or obstructive index (OI), desaturation index (number of oxygen desaturation episodes per hour of sleep), time spent during sleep with oxygen desaturation less than 90%, peak and average end-tidal carbon dioxide, and time during sleep with end-tidal carbon dioxide greater than 45 mm Hg and greater than 50 mm Hg.

Of the 56 children, 57% had abnormal results as defined by abnormal OI, hypercarbia, and/or hypoxemia—evidence of obstructive sleep apnea syndrome (OSAS). However, when an elevated arousal index was included, abnormalities were seen in 80%.

"The significance of an elevated arousal index alone, with the other measured components of the PSG being normal, has not yet been fully established," noted the authors. However "the increased arousal rate in children with DS may affect their daytime function and could exacerbate learning or behavior disorders." These problems may then be "assumed to be caused by the limited intellectual abilities commonly assigned to children with DS."

Before the sleep study, 35 of the 56 parent couples completed questionnaires about their children's sleep. Eleven of the 35 parents reported that their children had sleep problems, but only 36% of these parents were correct. Of the 24 parents who reported no sleep problems in their children, 54% were incorrect.

# Bocavirus Reported for First Time in U.S. Children

*The virus was found in 5.2% of respiratory patients younger than 2 years in New Haven, Conn.*

BY JANE SALODOF MACNEIL  
Elsevier Global Medical News

SAN FRANCISCO — A new parvovirus linked to respiratory tract infections in young children is circulating in the New Haven area of Connecticut, an infectious disease laboratory at Yale University has reported.

Dr. Deniz Kesebir said the laboratory found the pathogen, human bocavirus (HBoV), in respiratory specimens from 22 (5.2%) of 426 children under the age of 2 years who presented with respiratory symptoms at hospitals and clinics associated with the university.

"To our knowledge, this is the first description of human bocavirus in the United States," Dr. Kesebir, of Yale University, New Haven, said at the annual meeting of the Pediatric Academic Societies.

Canine and bovine forms of the virus are known to infect animals of all ages, but cause illness primarily in infants of those species, according to Dr. Kesebir. She said young infected cattle can have massive diarrhea.

Investigators working at Karolinska University Hospital, Huddinge, Sweden, published the first report of a bocavirus infecting a human in September of last year (Proc. Natl. Acad. Sci. USA 2005; 102:12891-6). They identified the virus in

17 (3.1%) of 540 children less than 3 years old who were hospitalized for respiratory disease.

A month later, an Australian group reported finding the new pathogen in 18 (5.6%) of 324 children in the same age group who had respiratory tract infections (J. Clin. Virol. 2006;35:99-102).

Japanese investigators published a third report this March (J. Clin. Microbiol. 2006;44: 1132-4). They found HBoV in 18 (5.7%) of 318 nasal swabs from children under the age of 3 years who were treated for respiratory tract infections.

Dr. Kesebir said the Yale infectious diseases laboratory headed by Dr. Jeffrey S. Kahn did a retrospective search for HBoV in children less than 2 years of age who presented with respiratory symptoms but screened negative on a direct immunofluorescence assay (DFA) for adenovirus, respiratory syncytial virus, and various influenza viruses.

All the positive samples were taken from children who presented with symptoms from October through April. Specimens collected from May through September were negative for HBoV.

The group also screened specimens from a matched control group of 96 children in an ongoing epidemiologic study of respiratory viruses in children. None of the asymptomatic children were positive for HBoV.

Rare polymorphisms in the positive samples established that the New Haven virus is identical to two HBoV genotypes identified in Sweden.

Asked in an interview how the same virus got from Sweden to Yale, or vice versa, Dr. Kesebir said the question was on a long list of questions the investigators are trying to answer about the new pathogen. "That's interesting. I don't know. It's exactly the same," she said.

Dr. Kesebir reported on 20 of the 22 positive cases at the meeting, which is sponsored by the American Pediatric Society, Society for Pediatric Research, Ambulatory Pediatric Association, and American Academy of Pediatrics. Her presentation excluded data on one child whose chart was unavailable for review and another who was coinfecting with an adenovirus.

She said 15 (75%) of the remaining 20 infected children were hospitalized for up to 18 days. Nine children were hospitalized for 1-3 days and three for 4-18 days. Another three developed nosocomial infections. The other five children were seen in

an emergency department or clinic. Seventeen children (85%) had a comorbidity, which she defined as asthma, eczema, bronchopulmonary dysplasia, or seizures.

For signs and symptoms, she reported that 19 children presented with rhinorrhea, 15 with fever, and 14 with cough. Ten children presented with wheezing, and six had oxygen saturation levels below 87%.

Abnormal chest x-rays were seen in 13 (72.2%) out of 18 children for whom chest x-rays were available. Dr. Kesebir cited peribronchial cuffing, infiltrates, and hyperinflation.

Of particular interest were eight children who presented with gastrointestinal symptoms. Dr. Kesebir and her colleagues concluded that HBoV is associated with upper and lower respiratory tract disease in children, and speculated that it also may be the cause of gastrointestinal symptoms.

Among the future studies planned are screening of children up to age 5 for HBoV, DFA screening of positive specimens for coinfection with other viruses, and a search for the cause of gastrointestinal symptoms.

In the interview, Dr. Kesebir said the researchers do not know whether the virus jumped species or just had not been detected in humans before.

"It is in adults as well, but most of the findings of symptoms are in children," she said. "Probably the adults are carriers, and are less symptomatic or immune," she added. ■



**The researchers do not know whether the virus jumped species or just had not been detected in humans before.**

DR. KESEBIR

## Prednisolone Eased Rhinovirus-Linked Recurrent Wheezing

BY HEIDI SPLETE  
Elsevier Global Medical News

Children with rhinovirus who received oral prednisolone suffered significantly less recurrent wheezing compared with children with respiratory syncytial virus who also received the steroid or children who received placebo.

Dr. Tuomas Jartti of the department of pediatrics at Turku (Finland) University Hospital, and associates analyzed 78 children aged 3-35 months who completed hospitalization for rhinovirus (40 children) or respiratory syncytial virus (RSV) infections (38 children). The children were randomized to receive an initial oral dose of 2 mg/kg prednisolone, followed by 2 mg/kg/day in three divided doses for 3 days (46 patients), or placebo (32 patients).

The children with rhinovirus were significantly more likely to be older, atopic, and recurrent wheezers, and they had significantly higher blood eosinophil levels and exhaled nitric oxide levels than did the children with RSV (Pediatr. Infect. Dis. J. 2006;25:482-8). Children in the RSV group were significantly more likely to have acute otitis media and to have been treated with antibiotics than were those in the rhinovirus group.

The results of the study showed that children with rhinovirus or RSV who received oral prednisolone did not leave the hospital more quickly than children in

the placebo group (22 hours vs. 30 hours).

By reducing recurrent wheezing, prednisolone use significantly decreased the need for outpatient visits in children with rhinovirus infections—but not in children with RSV infections—compared with

children who received placebo.

The findings support results from previous studies in which corticosteroids offered no significant benefit to patients with RSV infections.

"We speculate that an early asthma-like

inflammation could explain the beneficial effect of prednisolone in the rhinovirus group," the investigators said.

Prednisolone was well tolerated; no clinically significant adverse events were reported. ■



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**THE power of 10**

# Pulmonary Perspectives

## New Drivers of ICU Policy and Organizational Change

*Physician and nurse supply, regulatory agencies, and the public's expectation of quality care will drive changes.*

Recently, the ICU has experienced fundamentally new drivers of policy and organizational change that have and will continue to result in new directions of care for all critically ill patients, even those not yet admitted to the ICU. These drivers include the effects of new evidence-based medicine, supply and organization of critical care personnel, organization of the ICU, and pressing internal and external influences.

### Pre-ICU Care

Evidence-based medicine has always driven care of the ICU patient, but several papers now describe data that require a fundamental change in our thinking about the approach to the initial care of the critically ill patient.

In years past, intensivists primarily focused on the ICU patient in the ICU, especially continuing management, sometimes over a long period of time. Recent data suggest the importance of very early diagnosis and early intensive therapy in acutely ill patients, especially those with sepsis. Early and goal-directed therapy, initiated within 6 h in the emergency department, as compared to standard therapy, reduced the mortality of severe sepsis and septic shock (Rivers et al. *New Engl J Med* 2001; 345:1368). The approach involved adjustments of cardiac preload, afterload, and contractility to balance oxygen delivery with oxygen demand.

This concept of immediate and aggressive care has been extended to the acutely ill hospitalized patient, not yet in the ICU. Teams of skilled professionals are formed with the goal of rapidly responding to a pre-identified hospitalized patient at risk in order to provide early onset of therapy.

Like early therapy for sepsis, implementation of a rapid response team is also associated with improved outcomes in the hospitalized patient (Bellomo et al. *Crit Care Med* 2004; 32:916). The team of hospital personnel, usually including an ICU nurse, respiratory therapist, and/or physician, responds to set patient distress triggers and treats patients immediately. Common patient triggers include hypotension, tachypnea, desaturation, oliguria, or sometimes, simply, the nurse's assessment that the patient "just doesn't

look right." This approach to acute and immediate care of the hospitalized patient is one of six initiatives in the Institute of Healthcare Improvement's "Saving 100,000 Lives" Campaign ([www.ihl.org](http://www.ihl.org)). At the University of Kansas, the institution of a rapid response team has been accepted and utilized. Initial data suggest a decrease in codes outside the ICU.

Both of these initiatives represent a fundamentally different approach to the initial diagnosis and care of a critically ill patient. Trauma surgeons have always described the importance of the "golden hour" of immediate care in trauma patients. Early, goal-directed therapy of sepsis and the rapid response team approach to a hospitalized patient in distress represents an understanding of the importance of reversing pathophysiologic mechanisms early in the course of the illness, rather than treating aggressively when the disease is fully developed. Important improvements in outcome are present with such an approach, especially in sepsis.

### The Team Approach

One of the important concepts of the rapid response team is that it is a team of skilled professionals bringing different competencies to care for the patient.

In the last 10 to 15 years, the concept of intensive care medicine becoming a "team sport" has developed. In contrast to the physician being captain of the ship, now the physician is seen as part of the team that cares for the ICU patient. This team includes doctors, nurses, respiratory therapists, physical therapists, nutritionists, social workers, and other skilled professionals. Discussions and decisions are made using a team approach.

An excellent example of this approach is the multidisciplinary team rounds concept, where short, patient-directed rounds are made with the team at the beginning of the day. Ward rounds follow. Multidisciplinary team rounds have the advantage of brevity, information supplied from all members of the team, and focused decision-making. The recent University Health System Consortium ICU benchmarking study indicated that ICU units, with an intensivist-directed team and multidisciplinary team rounds, are better performers of evidence-based guidelines (Keroack et al. *Am J Med Qual* 2006; 21:91).

### Workforce Issues

A very important driver of current and future ICU care is the increased demand for intensivists, a demand not met by supply.

Almost 6 years ago, the American College of Chest Physicians, the American Thoracic Society, and the Society of Critical Care Medicine collaborated in a workforce project that indicated an inadequate

supply of intensivists (Agnus et al. *JAMA* 2000; 284:2762). The data have proven accurate in describing the demand but underestimated the rate at which the demand has increased. Popular opinion 10 years ago was that there was a physician surplus, especially in specialty medicine. Now, it is clear that a physician shortage exists, especially for ICU physicians.

Recently, specific recommendations have been developed by the same three societies to meet the crisis. They include the adoption of standards to ensure uniformity and quality, leverage of information technology, development of incentives to attract health-care professionals into critical care, and research to define the optimal role for ICU professionals in delivery of critical care (Ewart et al. *Chest* 2004; 125:1518).

(For information on a recently released government report on this topic entitled, "US Department of Health and Human Services Report to Congress: The Critical Care Workforce: A Study of the Supply and Demand for Critical Care Physicians," please access [www.chestnet.org/practice/gr/hrsa.php](http://www.chestnet.org/practice/gr/hrsa.php).)

### Quality of Care

In addition to this demand, internal and external factors are affecting ICU policy and organization.

The national Leapfrog Group is promoting several criteria that they believe improve the quality of care delivered. A consortium of businesses directs their employees to choose hospitals that meet the Leapfrog ICU standards. These ICU standards include the presence of an intensivist during daytime hours, who provides care exclusively in the ICU, as well as returns pages and returns to the bedside within 5 minutes. Currently, only 10% of hospitals in the United States meet this standard.

Another important external influence is the mandated Joint Commission on Accreditation of Healthcare Organizations ORYX performance measures.

Measures are available for multiple disease states, such as community-acquired pneumonia, acute myocardial infarction, and congestive heart failure. ORYX measures for the ICU are being developed.

Draft measures include stress ulcer prophylaxis, deep venous thrombosis prophylaxis, appropriate sedation, use of intensivists, length of stay measures, and risk-adjusted mortality. Current measures are compiled by each hospital and publicly reported on the Internet. It is anticipated that ICU core measures would also be publicly reported.

Quality of care is an expectation, not only from patients, but also from hospitals and independent agencies.

The objectives of the Institute of Healthcare Improvement's "Save 100,000 Lives" Campaign is to save lives through the introduction of six, proven, health-care interventions over 18 months (ended June 14, 2006) and to enroll a minimum of 1,600 hospitals to accomplish the goal.

In addition to deployment of rapid response teams, initiatives impacting the ICU are prevention of central line infections, prevention of surgical site infections, and prevention of ventilator-associated pneumonia.

### Increasing Demands for Care

Societal issues are also impacting the ICU. As the baby boomers age, there will be increasing numbers of geriatric patients in the ICU. The doubling of patients over the age of 65 years by 2030 will require a marked expansion of ICU resources, unless other strategies, such as rationing, are pursued. Additionally, the potential of a worldwide pandemic, such as the avian flu, would require the same increases in ICU resources, but they would be needed now, not 20 years from now.

### Conclusion

Many forces, influences, and new data are changing our approach to the care of the ICU patient. External forces, such as physician and nurse supply, regulatory agencies, and the public's expectation of quality care, will clearly continue to drive ICU policy and organizational structure. ■

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## Editor's Insight

Many changes in patient care in the past 15 years have seemed less-than-helpful to many physicians. There has been a sense of barriers created by intervening levels of organizational control.

The changes described by Dr. Pingleton in this *Perspective* are actually welcome ones that should fit with our training and our community's approach to patient care. It is encourag-

ing to see the team approach, utilizing the skills of many health-care professionals, recognized as an effective tool. The concepts of early and targeted therapy, based on solid outcomes studies, will also be welcome by many physicians. It is time to exercise intensive care *prevention*, as well as intensive care. We can all look forward to more advances in this area.

—Editor

NEWS FROM THE COLLEGE



PRESIDENT'S REPORT

The Importance of Health-care Teams

In a departure from my usual habit of “penning” the monthly President’s Report in an airport, I am, at the moment, back in my office at the H. Lee Moffitt Cancer Center and Research Institute. I have just emerged from the mountain of e-mails that awaited my return from California, where I attended the American Association of Critical-Care Nurses (AACN) National Teaching Institute and Critical Care Exposition and the American Thoracic Society (ATS) meeting. Al Lever and I spent a considerable amount of time going back and forth on Interstate 5 in an attempt to be in two places at one time.

Despite the hectic nature of the trip, it was an unqualified success.

If you ever have a chance to attend the AACN meeting, by all means, attend (more importantly, advise your

ICU nurses to attend). I was very impressed, not only by the quality of the program, but the vast array of subject matter and presentations.

I was most impressed, however, by the enthusiasm of the attendees. The feeling was almost palpable. The ACCP values its strategic alliance with the AACN.

Much as we do at CHEST each year, the AACN presents a Presidential Symposium, at which the presidents of the ACCP, the AACN, and the Society of Critical Care Medicine (SCCM) join to deliver short talks on a theme, followed by a panel discussion. (The ATS was unable to participate

this year due to the proximity of their meeting). This year’s AACN topic, as chosen by President Debbie Brinker, was “Team Competence.” My talk ad-

ressed the efficient and effective team. I thought I would relay a few facts from my talk:

A number of factors have worked against the use of teams in health care, but new team-oriented organizational structures and work patterns are evolving. The easy part has been changing the organizational chart and writing the “P&Ps.” The more

difficult part has been modifying interpersonal and interprofessional relationships, along with the modified work patterns.



BY DR. W. MICHAEL ALBERTS, FCCP

For teams to be effective, the “teamwork” concept must be embraced by all components of the organization.

Clinicians, especially physicians, have been slow to adapt to the concept. Traditional training does not include the study of teams or teamwork. Moreover, the education of physicians promotes and values independence and personal responsibility for individual decisions, rather than team (or collective) decision-making.

This view works against the development of effective multidisciplinary teams in the clinical setting.

There is no doubt that health care in 2006 is a team sport. The development of effective and efficient health-care teams is crucial to the delivery of quality, patient-focused care as we go forward.

Inside ACCP: Health Affairs Division Continues to Grow

BY LYNNE MARCUS

ACCP Vice President of Health Affairs

AND

MARLA BRICHTA

ACCP Assistant Vice President, Health Affairs

The ACCP Health Affairs Division grew from a seed that was planted in 1954 when the Tobacco Industry Research Committee was advised to send representatives to the ACCP annual meeting.

Their mission was to report back on the results of research conducted on the health effects of tobacco and to counter the results with a public relations campaign promoting “Big Tobacco’s” agenda.

The information presented at the 1954 ACCP annual meeting and throughout the years in the CHEST journal propelled the ACCP toward understanding the importance of initiating a public dialogue that included educating lawmakers about the importance of changing how tobacco use was perceived at a national level.

This began the ACCP’s role in tobacco issue advocacy. Over succeeding years, additional issues became important to the ACCP.

In 1991, with the advent of the Resource Based Relative Value System (RBRVS), our attention was drawn to the need for practice management issues. Medicine was becoming a business, as well as a profession, and, as a medical specialty society, it was evident that we too needed to get into the business of practice management support for our members.

In 2003, the Division of Health Affairs was created as the umbrella for the Government Relations Committee, the Practice Management Committee, and two vitally important NetWorks, Practice Administration and Private Practice.

Many advocacy initiatives were undertaken

before the formulation of the Government Relations Committee in 1990, initially chaired by Dr. Douglas Gracey, FCCP.

The Practice Management Committee, initially chaired by Dr. Walter O’Donohue, FCCP, was created in 1993 in response to the RBRVS and the creation of the Current Procedural Terminology and Relative Value Update Committees of the American Medical Association.



Al Lever, ACCP Executive VP and CEO, welcomes US Rep. Mark Kirk (R-IL) to ACCP headquarters.



Sen. Dick Durbin (D-IL) talks with Dr. Jim Parish, FCCP, Dr. Udaya Prakash, FCCP, and Ms. Lynne Marcus.

Health Affairs: Past, Present, and Future

**1968:** Deliberated with the US Public Health Service on tobacco control

**1979:** Initiated the non-smoking pledge at the ACCP annual meeting Convocation

**1983:** Worked to pass the Smoking Prevention Health and Education Act of 1983

**1990:** Worked with (now Senator) Richard Durbin advocating for smoking bans on domestic flights; formed the Government Relations Committee

**1991:** Submitted amicus brief in Cipollone v Liggett Group Supreme Court case

**1993:** Formed the Practice Management Committee

**1994:** Held the 1st ACCP Capitol Hill Caucus; submitted amicus brief in Mississippi v The American Tobacco Company et al

**1996:** Published 1st edition of *Appropriate Coding for Critical Care Services and Pulmonary Medicine*

**2004:** Successfully elected a representative to serve

a 2-year term on the Relative Value Update Committee of the American Medical Association

**2006:** Successfully advocated for the writing and publication of the Health Resources and Services Administration report on the pulmonary and critical care workforce crisis; launched a Webinar series on practice management topics

**2007:** Will publish an expanded 11th edition of *Appropriate Coding for Critical Care Services and Pulmonary Medicine*.

**2008:** To successfully advocate for appropriate reimbursement for physician services under Medicare

**2010:** To work with Congress to write and pass legislation addressing the demand for increasing the critical care workforce

**2020:** To successfully advocate for federally mandated education addressing the hazards of tobacco—to result in further elimination of chest diseases related to tobacco use

## Ambassador Organizes 3K Race for Kids' Lung Health

**A**mbassadors Group member, Monir Almassi, organized a very successful 3K Walk/Run for Kids' Lung Health at Wisconsin Hills Middle School on May 3, 2006.

About 200 students, parents, and staff participated in this event, which

is in its second year. A lesson on how smoking affects your lungs and how to keep your lungs healthy was presented, which was followed by the walk/run.

Each participant received a Love Your Lungs™ wristband and a Puffree

keychain. Mrs. Almassi also distributed a booklet about teens and smoking that she secured from her area Police Department.

The art teachers encouraged the children to create posters with an anti-smoking message, and these posters lined the school's hallways during the week of the walk/run.

The CHEST Foundation salutes Monir Almassi and thanks her for all her efforts in organizing this very successful event!

### Join the Ambassadors Group

The Ambassadors Group is looking for volunteer members to help support the mission of The CHEST Foundation and the ACCP!

Ambassadors Group members seek out new opportunities to educate the

general public about the dangers of smoking, to communicate the values and mission of The CHEST Foundation; and to network with other exceptional ACCP members and their

families. Recent Ambassadors Group activities have included providing lung health education in schools, universities, and sororities; funding an annual Humanitarian Recognition Award; increasing

health awareness through the "Love Your Lungs™" wristband project; and publishing the *Stories at the End of Life* booklet set.

Join us and be amazed at what a difference you can make!

Tom Syverson, CPA, MBA  
 Chair

Communications/Marketing Subcommittee



ACCP

About 200 students, parents, and staff participated in the 3K Walk/Run for Kids' Lung Health at Wisconsin Hills Middle School, held May 3, 2006.

**Update** your medical knowledge.

**Improve** your practice management skills.

**Maximize** the care you provide your patients.

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**SALT LAKE CITY**

## NEWS FROM THE COLLEGE



## SLEEP STRATEGIES

## Sleep Medicine: The Times They Are a Changin'

In the last edition of Sleep Strategies, Dr. Peter Gay quoted a Neil Young song about tin men in his article about recent changes in CMS coding and reimbursement for central sleep apnea and complex sleep-disordered breathing. Not to be outdone in the music department, in this month's Sleep Strategies, I offer my own quotation from another mid-western singer-songwriter, Bob Dylan. Just as Dylan sang about the tumultuous '60s and how "the times they are a changin'," the field of sleep medicine is experiencing tumultuous times, as well. These are times of tremendous growth (practitioners and laboratories), changes in physician credentialing (new board certification opportunities), and changing technology (increasingly sophisticated diagnostic and treatment options). Another trend that is beginning to have an impact on sleep medicine is the quality of care movement.

Quality of care is something that all of us strive for in our clinical work, no matter what our practice circumstances are. All would agree that delivering quality care is something of a central tenet of our profession. After all, who among us would want to be associated with anything less than the highest "quality of care"? Quality of care, while certainly not new, is currently receiving a great surge of attention from physicians, insurers, health policy makers, and regulatory agencies. Part and parcel of quality of care is our attempt to improve the care we give our patients. Implicit in quality of care discussions is that we are never satisfied with quality care; we want to improve it, to make the quality better. Hence, the recent interest in quality improvement initiatives, both within the ACCP and outside, is understandable. The quality of care revolution has not gone unnoticed by the ACCP sleep medicine community. The Sleep Institute and Sleep Medicine NetWork have discussed this in various ways over the past year.

Other groups in the field are doing likewise. A few months ago, the American Sleep Apnea Association (ASAA), a sleep apnea patient advocacy group, wrote an open letter to the sleep disorders community about the state of care

given to patients with obstructive sleep apnea (OSA). A copy of the letter was sent to the ACCP Sleep Institute. The letter discussed the ASAA's views about the current state quality of care for patients with OSA, the fact that many patients remain undiagnosed (and, therefore, untreated), and that access to care for sleep apnea is uneven across the United States.

In its open letter, the ASAA makes the following three points concerning access to quality care for "every American with sleep apnea":

- (1) "All sleep apnea patients should be guaranteed access to diagnosis and treatment, even when financial limitations exist in the local health-care system. In particular, all patients should have access to some type of reliable diagnostic study for sleep apnea, and this should be available within a 100-mile radius of their home and within thirty days of referral."
- (2) "Patients should expect to have the same attention given their therapy and follow-up as was given to their diagnosis. When positive pressure therapy is prescribed, all resources available to the prescribing physician should be employed to assure satisfactory outcomes with this therapy. Other therapeutic modalities need to be reviewed when treatment with first-line therapy fails. The burden of documentation of successful outcomes in this setting is no different than in any other aspect of medicine and resides with the prescribing physician. Collaboration between sleep specialists and other health-care professionals will help the prescribing physician provide efficient care. Patients should expect periodic follow-up and unfettered access to an appropriate specialist should problems arise."
- (3) "Patients have the right to quality care independent of where they receive it. This is especially the case when the outcome of at-home or portable testing does not confirm the clinical pretest suspicion of sleep apnea. Patients who undergo unattended sleep testing must also have access to currently accepted diagnostic

tests until there are management pathways shown to have the appropriate predictive positive (for diagnostic) or negative (for screening) value when compared to currently accepted norms."

With their open letter to the "sleep community," what is the ASAA telling us? First, patients deserve the best care that can be given to them. The ACCP Sleep Institute agrees with this wholeheartedly. Our response to this challenge is embodied in two ACCP initiatives that should foster better quality of care for patients with sleep disorders. These initiatives take-on two well-recognized problems among patients with sleep apnea.

The first problem we are tackling is the largest one in the field of sleep medicine: lack of awareness of sleep disorders. Many physicians lack an

awareness of the importance of these disorders or perhaps choose to ignore them. This is not only true of sleep apnea but is also well-documented for restless legs syndrome and for the need for adequate sleep, in general. If front-line physicians do not recognize sleep apnea or other sleep disorders in their patient, then that patient is likely to go undiagnosed and untreated. My firm belief is that front-line physicians (including nonphysician providers) sincerely want to identify disease when their patients have it; they just have limited experience with sleep disorder recognition. Many reasons exist for this, but the main ones are time pressures and the fact that sleep medicine is not a significant part of their training. To remedy this, the ACCP Sleep Institute is developing a series of half-day seminars for front-line physicians (and physicians extenders) in 20 cities around the country. The seminars will be CME-certified and geared to the practical needs of busy practitioners. At the end of each seminar, sleep tool kits will be distributed, designed to improve sleep disorder recognition by these practitioners and their teams. The regional sleep meetings will kick-off in the fall of 2006.

Educating our primary care colleagues is essential to better recognition of disease. But knowing how to give sleep apnea patients the best care possible in order to optimize clinical results is equally important. The ASAA addresses this in point 2 of its letter: as much attention needs to be given to the long-term management of the patient as is given to making the appropriate diagnosis in the sleep laboratory.

The Sleep Institute fully agrees. That's why the other large project we are planning is a consensus conference on the "continuing care" of the patient with sleep apnea. Continuing care is an important but poorly understood aspect of care that I have often termed a "black box." Looking inside "the box," we see a web of relationships that sleep apnea patients have with home care companies, their primary care physician, their insurance company, and, perhaps, a sleep medicine specialist. One can rightly ask, "Who is in charge?" and "How do we know that the patient is successful with therapy?" The answer to these questions is that we don't know. Often, the patient is left unsupported because the parties involved assume someone else is taking care of the patient. In reality, no one is taking care of that patient. The Continuing Care Consensus Conference aims to open up the black box and try to make sense of what we find inside. Ultimately, we plan to develop recommendations about rationalizing the continuing care of the patient with sleep apnea. All the main constituencies will be represented at the conference, including sleep apnea patients themselves. The conference is planned for early September.

Times are changing, as Bob Dylan reminds us. The quality of care revolution is upon us, as are many other important structural changes in the sleep medicine landscape. The ACCP plans to be at the heart of improving the quality of care for patients with sleep apnea and other sleep disorders. Our patients deserve no less. ■

Charles W. Atwood, MD, FCCP  
Section Editor, Sleep Strategies  
Chair, ACCP Sleep Institute

## Sleep Institute

American College  
of Chest Physicians

## Practice Management Update: OIG Reports to Congress

The Office of Inspector General (OIG) posted its Semi-annual Report to Congress for October-March of FY 2006 and an accompanying press release ([www.oig.hhs.gov/publications/docs/press/2006/Semiannualspringrelease2006.pdf](http://www.oig.hhs.gov/publications/docs/press/2006/Semiannualspringrelease2006.pdf)). The Department of Health and Human Services (HHS) OIG in the report

announced expected recoveries of \$1.02 billion for the first half of fiscal year (FY) 2006 from efforts to reduce fraud, waste, and abuse in HHS programs.

OIG's \$1.02 billion in expected recoveries encompasses \$288 million in audit-related recoveries and \$732.4 million in investigative-related recoveries. Additional savings from imple-

mented recommendations are calculated annually and will be reported in the fall.

"These recoveries reflect our dedicated efforts to reduce fraud, waste, and abuse in HHS programs," said Inspector General Daniel R. Levinson. "It is through a combination of vigilant oversight, outreach to the

health care community, and partnership with government agencies at all levels that we are able to accomplish this mission."

Protecting the integrity of HHS programs is at the core of OIG's mission. OIG continues to be a strong force within HHS to improve the efficiency and effectiveness of the De-

partment and to sanction those who defraud its programs. The Semiannual Report describes OIG investigations and evaluation and audit reports finalized during the reporting period.

To read about OIG activities go to: <http://oig.hhs.gov/publications/semiannual.html>. ■

## ACCP WORLDWIDE

# International Meetings Successful in Italy and Spain

Dr. Francesco de Blasio, FCCP, and Mr. Antonio Schiavulli submitted the following report:

The ACCP Italian Chapter National Meeting was held May 4-6, 2006, at Science City Congress Center, Naples, Italy. Co-Chairmen of the meeting were Dr. Francesco de Blasio, FCCP; Dr. Mario Del Donno, FCCP; and Dr. Mario Polverino, FCCP. Presidents of the meeting were Dr. Dario Olivieri, FCCP, and Dr. Giuseppe U. Di Maria, FCCP.

The scientific program included three postgraduate courses (pulmonary rehabilitation, pulmonary diagnostic, and cardiopulmonary exercise testing), one ACCP forum on COPD, nine plenary sessions focusing on different cardiopulmonary topics, one clinical and radiological grand round, one interactive case session, and two original communications oral presentation sessions.

The meeting registered the highest total attendance ever, with more than 750

registered participants (120 faculty included). ACCP President Dr. W. Michael Alberts, FCCP; CHEST Editor in Chief Dr. Richard S. Irwin, FCCP; and ACCP CEO Mr. Alvin Lever, FCCP(Hon) were among invited faculty and actively participated in the opening ceremony with the awards recognition to young researchers and acknowledgments for those international officers whose terms are ending this year. Dr. Giuseppe U. Di Maria, FCCP, International Regent for the ACCP Italian Chapter, announced that Dr. Francesco de Blasio, FCCP, was unanimously nominated by the Italian Chapter Board of Officers as the new International Regent.

Dr. Jorge Sinclair Avila, FCCP, submitted the following report:

### Successful Meeting in Spain

The "First International Campus of Respiratory Care" took place in Madrid, Spain, from May 3-5, 2006, with the endorsement

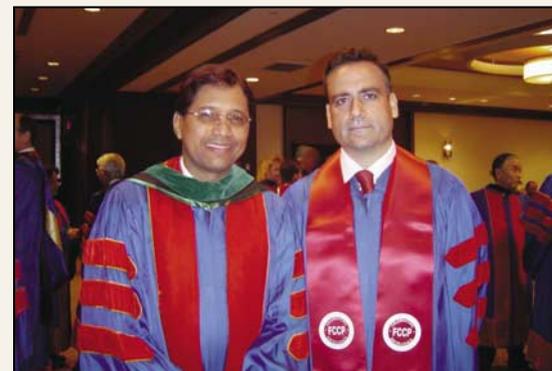
of the ACCP. Forty-two distinguished professors from nine countries comprised the faculty, and the scientific committee had representatives from SECUR (Spanish Society of Respiratory Care), the ACCP, the American Association of Respiratory Care, The International Council of Respiratory Care, and the International Alliance of Respiratory Care and Applied Technologies. Antonio Esquinas, MD, FCCP, President of SECUR, and Jorge Sinclair Avila, MD, FCCP, Chair of the ACCP Council of International Regents and Governors, were Director and Co-Director of the congress.

More than 150 attendees represented clinicians, intensivists, pulmonologists, respiratory therapists, nurses, and critical care residents. There were three master lectures and 20 seminars, covering such topics as organization, equipment, and techniques of respiratory care; respiratory care in conventional mechanical ventilation; ventilator technology; respiratory care in cardiopulmonary resuscitation; and preventing infection in the ICU.

Dr. Avila discussed the roles of the



At the ACCP booth in Naples, L-R: Mr. Alvin Lever, FCCP (Hon); Dr. Francesco de Blasio, FCCP; Dr. Richard Irwin, FCCP; Mr. Antonio Schiavulli (Midia); Ms. Debora Finotti (Midia); Dr. Giuseppe Di Maria, FCCP; Dr. Mario Polverino, FCCP; Dr. W. Michael Alberts, FCCP; and Dr. Mario Del Donno, FCCP.



L-R: Jorge Sinclair Avila, MD, FCCP, and Antonio Esquinas, MD, FCCP, directed the ICRC in Spain.

ACCP and The CHEST Foundation and invited attendees from several countries to become members of the College. The meeting was regarded as a great educational event by everyone involved.

## Collaborating To Advance Care.

### Detection and Management of Depression and Anxiety in COPD: A Multidisciplinary Scientific Workshop



September 15 – 16, 2006  
American College of Chest Physicians  
Northbrook, IL  
Chair: Janet Maurer, MD, MBA, FCCP  
Co-Chair: Nicola A. Hanania, MBBS, FCCP

Join a multidisciplinary team of investigators and clinicians to discuss the interplay of depression and anxiety in patients with COPD. This cooperative review of best practice standards and examination of patient care issues will promote understanding that will empower:

Investigators to identify research needs and direct future studies.

Clinicians to better diagnose and treat patients with COPD.

#### Attendees will:

- ⊙ Review the prevalence of depression and anxiety in patients with COPD.
- ⊙ Assess the accuracy of currently validated screening tools.
- ⊙ Evaluate the efficacy of current therapies by integrating results from high-grade published studies.
- ⊙ Identify the future research needed to improve diagnosis and management strategies.
- ⊙ Disseminate the findings and recommendations of attendees to key audiences.

Register now for discounted fees.

Online registration available at [www.chestnet.org](http://www.chestnet.org).

Supported by NIH grant R13MH073228.  
Additional support from the Alpha One Foundation.

## Collaborative Care to Manage Depression and COPD

BY SOO BORSON, MD  
Workshop Planning Committee  
and Faculty Member

Depression is a common complication of COPD and is often associated with significant anxiety. Managing depression and anxiety effectively in primary and specialty medical settings is considerably more complicated than prescribing an antidepressant medication.

Over the last 10 years, extensive evidence has been developed that collaborative care—that is, collaboration between a mental health provider or team and the patient's principal physician—achieves much better outcomes for mood disorders than management by the physician alone.

Collaborative care is a structured approach to managing patients who are not responding adequately to antidepressant interventions offered by

the primary physician. A specially trained depression care manager, who works in the patient's primary health-care site, collaborates with the primary care provider to improve the depression outcomes. Collaborative care models facilitate access to specialized mental health interventions without requiring that patients leave their usual medical care setting.

Evidence supporting the value of collaborative care for patients with serious medical illness will be presented during the "Detection and Management of Depression and Anxiety in COPD" multidisciplinary scientific workshop to be held on September 15 and 16, 2006, at the ACCP headquarters in Northbrook, IL. The workshop is funded by the National Institute of Mental Health.

Visit [www.chestnet.org/education/courses/dmdaCOPD06/index.php](http://www.chestnet.org/education/courses/dmdaCOPD06/index.php), or call ACCP Customer Relations at (800) 343-2227.

# NEWS FROM THE COLLEGE



## EDUCATION INSIGHTS

# Board Certification: What Does It Mean to You?

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

**B**oard certification and maintenance of certification are of great importance to physicians—more so today than in any other period in history.

As of 2005, board certification issues time-limited certificates that necessitate subsequent recertification. Most board certifications are at intervals of 10 years or less, with application fees for renewal ranging from \$1,000 to \$2,000 or more. However, time-limited certification is not a new concept in all areas of medicine. The American Board of Family Medicine has issued time-limited certificates since 1970, and the American Board of Surgery has had a program in place since 1976. The future theme is that board certification for life is a thing of the past. In addition, maintenance of certification is now a growing program that entails shifting from testing that is conducted every 6 to 10 years to a more continuous process of assessing physician competence. Maintenance of Certification includes the evaluation of four components: (1) professional standing; (2) continued learning; (3) cognitive expertise; and (4) performance in practice.

As of January 2006, the American Board of Internal Medicine (ABIM) implemented the completion of a self-evaluation module for practice performance, a peer-and-patient-feedback module, and participation in approved quality improvement programs developed by a medical group, a health plan, an insurer, or a medical society.

Board certification changes represent

a response to the quality improvement concerns of the public and those of the Institute of Medicine. This was further highlighted in the February 2005 issue of the *Annals of Internal Medicine* by Dr. Choudhry and colleagues. He and his colleagues found, through a systematic review of the literature, an inverse relationship between the number of years that a physician has been in practice and the quality of care that the physician provides (Choudhry NK, Fletcher RH, Soumerai SB. Systematic review: the relationship between clinical experience and quality of health care. *Ann Intern Med* 2005; 142:260-273).

Interestingly, patients are also increasingly more convinced that there is a connection between physician quality and board certification. The ABIM commissioned a poll to assess the importance of certification to the public, and the results were outlined by the Gallup Organization in 2004. Key findings indicated the relative importance of physician's quality indicators, as expressed by patients:

1. 73% = Re-evaluation of physician qualification is necessary every so often.
2. 68% = Physicians should periodically pass a written test of medical knowledge or have a high success rate for the diseases/conditions they treat most often.
3. 66% = Physicians should have a low number of malpractice claims.
4. 64% = Physicians should have evaluations by an independent board of doctors.
5. 58% = Physicians should have high ratings from their patients.
6. 52% = Physicians should practice technical skills in a simulated situation.
7. 49% = Physicians should obtain high

ratings from the physicians with whom they work.

8. 47% = Physicians should earn a credential or award for high quality patient care.

9. 43% = Physicians should obtain high ratings from the nurses with whom they work.

The era of certification and maintenance of certification is not without critics. There are many who have indicated that these new requirements place unnecessary administrative and financial burdens on physicians. There are others who have indicated that the processes in place will not establish the expected goals, which is improved medical practice and patient care. The ACCP is working with ABIM on how best to structure their system and educate physicians about these new requirements. Identifying collaborative efforts with ABIM to assist in this

transition is by far the best strategy.

More can be learned about this during ACCP's August 2006 Pulmonary, Critical Care, or Sleep Medicine Board Review courses in Orlando, FL. Visit [www.chestnet.org/education/calendar.php](http://www.chestnet.org/education/calendar.php).

Information about ABIM's board certification and Maintenance of Certification program and requirements can be found at [www.abim.org/resources/publications/D04-03212006.pdf](http://www.abim.org/resources/publications/D04-03212006.pdf).

I hope this article has highlighted some of the important points that you, as a physician, should be aware of and the value your patients might be placing upon having board certification. ■

For supplemental information, please contact: American Board of Internal Medicine, 510 Walnut Street, Suite 1700, Philadelphia, PA 19106-3699; [www.abim.org](http://www.abim.org)

### Pulmonary and Critical Care Subspecialty Examination: 2001-2005 First-Time Taker Pass Rates

Year	Number of First-Time Test Takers	Percent Passed, %
2001	392 (Pulm)	88 (Pulm)
	346 (CC)	79 (CC)
2002	427 (Pulm)	83 (Pulm)
	393 (CC)	86 (CC)
2003	406 (Pulm)	93 (Pulm)
	407 (CC)	89 (CC)
2004	410 (Pulm)	94 (Pulm)
	464 (CC)	87 (CC)
2005	442 (Pulm)	92 (Pulm)
	423 (CC)	90 (CC)

Source: ACCP

## Salt Lake City: Let's Eat!

**F**ood, drink, and fun are readily available any day of the week in Salt Lake City. It's true! Restaurants, bars, clubs, and even breweries offer an array of options to suit any liking. During your stay, prepare to take a taste of Salt Lake, where the dining scene has arrived and is ever-expanding.

Start the night off right by indulging in whatever you crave. Even the most sophisticated of palates are sure to be impressed by the culinary offerings of Salt Lake

City. Regional favorites can be sampled at any of the casual family restaurants around town.

For a more intimate experience, try fresh pastas and seafood at one of the many fine-dining eateries. Or, indulge in the exotic and explore delightful ethnic options, ranging from Afghan to Vietnamese cuisine. And, Salt Lake's restaurants do

serve alcohol with the purchase of food.

Did you know that the Salt Lake City area is the fourth fastest growing restaurant market in the nation? With over 600 restaurants and eating establishments, Salt Lake City offers a vast

selection, sure to fit any taste or budget. Thanks to the TRAX light-rail service, you can treat yourself to one of greater Salt Lake County's 1,400 restaurants, nestled in the outlying areas.

So, whether you are looking for gourmet or buffet, family style or high profile, you're

guaranteed to find your appetite's delight. Salt Lake City's food with a view is the perfect excuse to arrive early or stay late at CHEST 2006, October 21-26.

For more information about Salt Lake City, visit [www.visitsaltlake.com](http://www.visitsaltlake.com). Questions about CHEST 2006? Visit [www.chestnet.org/CHEST](http://www.chestnet.org/CHEST). ■



## Product Highlight: ACCP-SEEK

**T**he Assessment in Critical Care and Pulmonology Self-Education and Evaluation of Knowledge (ACCP-SEEK) is a self-study opportunity in printed format for pulmonary and critical care physicians and fellows-in-training.

It is designed to stimulate and challenge clinical thought processes regarding recall, interpretation, and problem-solving skills.

The case-based questions contain histories, laboratory results, and images and provide education concerning current diagnostic and treatment strategies.

Each volume contains 75% new questions, answers, and rationales,

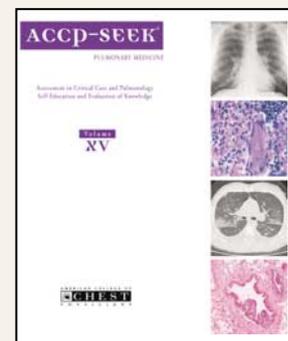
in addition to selections from the previous volumes that are considered by the expert editors to be the best-written items.

The rationales provide thorough explanations and reasoning for the correct and incorrect answers. Each ACCP-SEEK volume has a total of 200 questions.

ACCP-SEEK is used most commonly as an invaluable study tool for physicians interested in certifying and recertifying in pulmonary and critical care specialties.

Watch for the August 2006 release of the newest ACCP-SEEK Volume XVI—Critical Care Medicine.

ACCP-SEEK can be purchased online at [www.chestnet.org](http://www.chestnet.org) or by calling (800) 343-2227. ■



# NetWorks: Partnering Inside and Outside the ACCP

## Palliative and End-of-Life Care

The Palliative and End-of-Life Care (PEOLC) NetWork strives to fulfill its mission and objectives through a number of collaborative educational activities. The ACCP and the European Respiratory Society (ERS) are cosponsoring a symposium, "Improving End-of-Life Care" at the Annual Congress of ERS at Munich, Germany. Representatives from the PEOLC Steering Committee include symposium co-chair Dr. Gerald Baum, FCCP, and speakers Dr. Randall Curtis, FCCP, and Dr. Basil Varkey, FCCP.

A small, but growing number of ACCP members practice palliative medicine as their primary area or are devoting a major portion of their time to clinical, educational, and research aspects of palliative care. Several members have been awarded the Roger C. Bone Advances in End-of-Life Care Award. Those interested in a mentor in this area can contact the PEOLC NetWork at [networks@chestnet.org](mailto:networks@chestnet.org). The PEOLC Steering Committee invites you to visit its

Web page at [www.chestnet.org/networks/pelc/index.php](http://www.chestnet.org/networks/pelc/index.php).

## Pediatric Chest Medicine

The Pediatric Chest Medicine NetWork currently has 436 members and encourages all ACCP members with pediatric interests to join. For more information about the NetWork, please contact Lee Ann Fulton, Staff Liaison, at [networks@chestnet.org](mailto:networks@chestnet.org).

We look forward to an excellent pediatric program at CHEST 2006. Pediatric highlights will include pulmonary complications of gastroesophageal reflux disease and sickle cell disease. The Pediatric Chest Medicine NetWork Open Meeting, to be held on Wednesday, October 25, from 8:15 AM - 9:45 AM, will feature a talk by Dr. Greg J. Redding, FCCP, Chief, Pulmonary Division at Seattle Children's Hospital, on the current state of the pediatric pulmonary workforce and fellowship training. The 8th Pediatric Fellows Conference will take place on Sunday, October 22.

## Practice Administration

*The Practice Administration NetWork encourages you to bring your practice administrators and managers to CHEST 2006.*

In 1997, five pulmonary practice administrators attended the annual CHEST meeting in New Orleans hoping that the ACCP would become the organization to provide resources and educational opportunities specific to the business of running a chest medicine practice. Recognizing this growing need, the ACCP committed to providing resources on national policy development, regulatory compliance, and reimbursement issues affecting management of specialty practices.

Today, there are 88 practice administrators who are allied health members of the ACCP. Their involvement and hard work has brought new expertise to our multiprofessional society.

At CHEST 2006, the practice management and administration curriculum includes two half-day postgraduate courses—"Physician Reimbursement Essentials: Basic Office and Hospital Documentation, Coding, and Compliance for Pulmonary, Critical Care, and Pediatric Pulmonary Patients," and New Procedural Coding and Novel Practice Management Issues."

## Private Practice

A major focus of the ACCP leadership is to enhance the value of membership. In recent years, the College has become an important resource in the area of practice management and serves to enhance the value of individual practices for physicians and their patients.

The ACCP Practice Management Department was created in 2004 with the goal to *provide education, advocacy, and resources to members for efficient practice management for optimal patient care*. Both the Private Practice and Practice Administration NetWorks help the Practice Management Department and the Practice Management Committee achieve these goals.

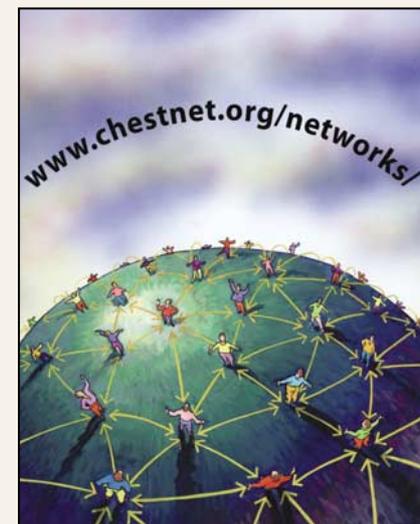
While the NetWork is specifically designed to represent and promote the interests of clinicians working in the private practice setting, the NetWork leadership recognizes many areas of shared interest among physicians in academic settings.

The NetWork also works closely with the Practice Management Committee and the Government Affairs Committee to address issues of coding and reimbursement, evaluation, and management guidelines, as well as workforce and manpower issues. It is the goal of the Private Practice NetWork to involve the ACCP private practice community

in leadership and in advocacy at the local and national level.

## Pulmonary Function, Physiology, and Rehabilitation

The Pulmonary Function, Physiology, and Rehabilitation (PPFR) NetWork is contributing to a number of ACCP projects and activities.



Several of the members of the PPFR NetWork Steering Committee are serving on the Health and Science Policy Committee panel to update the "Pulmonary Rehabilitation: Joint ACCP/American Association of Cardiovascular and Pulmonary Rehabilitation Evidence-Based Guideline." The previous review was published in 1997.

An updated guideline should add significantly to the current knowledge base in the field of pulmonary rehabilitation.

Progress is ongoing with the education training survey. The survey was developed to determine deficiencies and needs in physiology training programs. An update will be provided at CHEST 2006.

Members of the NetWork represented the ACCP on a joint committee made up of representatives from the multiple societies and organizations that recently met to discuss sending a proposal to the American Medical Association Current Procedural Terminology Editorial Panel for pulmonary rehabilitation services.

The committee came to agreement regarding the next step to improve the billing, coding, and reimbursement for pulmonary rehabilitation services under Medicare. The consensus of the group is being forwarded to each of the respective organizations for approval.

Web pages for the 26 ACCP NetWorks can be viewed at [www.chestnet.org/networks/descriptions.php](http://www.chestnet.org/networks/descriptions.php). To keep members informed of current activities, the minutes of the steering committee conference calls are posted on the individual NetWork Web pages.

# CLASSIFIEDS

## PROFESSIONAL OPPORTUNITIES

### Kentucky

#### Pulmonary Physician

Join a well-established and very reputable group of pulmonary physicians  
Louisville, KY - Louisville Pulmonary Associates, PSC

**Join a pulmonary practice** with 2 ABIM BE/BC pulmonary physicians that was established in 1983. We have office locations in Louisville and Southern Indiana both adjacent to major hospitals in the area. We provide service to patients at hospitals in Louisville and Southern Indiana. Applicant must be ABIM/BE/BC in internal medicine and pulmonary disease.

**We offer:** Guaranteed salary plus bonus, partnership track, full benefits package, shared call schedule.

**Community Info:** The Louisville area offers year round golf, country clubs, biking, tennis, running, extreme sports, fine dining, arts, entertainment, family recreation, boating, camping, excellent schools. We are home to the University of Louisville Cardinals, River Bats Baseball, Louisville Fire Arena Football and Historic Churchill Downs.

**Contact:** Send your CV to: Stacy Ralston, 4402 Churchman Avenue, Suite 305, Louisville, KY 40215 Fax: 502 368-9616 Email: [sralston3@hotmail.com](mailto:sralston3@hotmail.com)

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Go Up in Smoke.

Smoking Kills.  
Don't Smoke.



The wristbands are a project of the Ambassadors Group, supporting the philanthropic programs of The CHEST Foundation.

To get your own wristband, or to learn more, visit The CHEST Foundation website at [www.chestfoundation.org](http://www.chestfoundation.org)

# NEWS FROM THE COLLEGE



## 'Late Show' Musician to Host CHEST Foundation Dinner

The CHEST Foundation's Making a Difference Awards Dinner will be a celebration worth remembering. Join your colleagues and friends for this exciting celebration of The CHEST Foundation's 10th anniversary and the 2006 Humanitarian Recognition Award and Project Development Grant ceremonies.



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

There will be a special reception honoring all previous ACCP pro bono service award winners going back to the inception of the

program in 1998. Current 2006 award and grant winners, including the special Hurricanes Katrina and Rita Relief Fund project winners and the special Ambassadors Group

Humanitarian Recognition Award winner, will be joined at this reception by past Governors Community Service Award winners and Humanitarian Recognition Award

and Project Development Grant winners for an opportunity to share the current status of their projects and continued successes with one another and dinner attendees.

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

## This Month in CHEST: Editor's Picks

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



- ▶ **A Randomized Controlled Trial of Follow-Up of Patients Discharged From the Hospital Following Acute Asthma: Best Performed by Specialist Nurse or Doctor?** Dr. James A. Nathan, et al
- ▶ **Improvement in Bronchodilation Following Deep Inspiration After a Course of High-Dose Oral Prednisone in Asthma.** Dr. Annelies M. Slats, et al
- ▶ **Quantitative Analysis of Fibroblastic Foci in Usual Interstitial Pneumonia.** Dr. Noriyuki Enomoto, et al
- ▶ **Delayed Administration of Antibiotics and Atypical Presentation in Community-Acquired Pneumonia.** Dr. Grant W. Waterer, FCCP, et al
- ▶ **Antibiotic Timing and Diagnostic Uncertainty in Medicare Patients With Pneumonia: Is It Reasonable To Expect All Patients To Receive Antibiotics Within 4 Hours?** Dr. Mark L. Metersky, FCCP, et al
- ▶ **The Controller-to-Total Asthma Medication Ratio Is Associated With Patient-Centered, as Well as Utilization, Outcomes.** Dr. Michael Schatz, et al

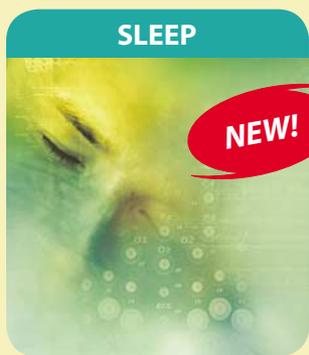
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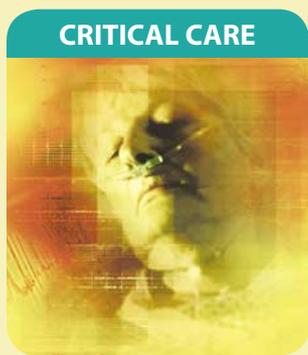
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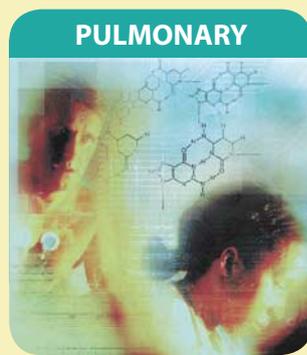
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# Use These Resources to Maximize Reimbursement

BY DAMIAN McNAMARA  
Elsevier Global Medical News

NAPLES, FLA. — A myriad of online and other resources are available for keeping current with reimbursement, coding, documentation, and compliance, according to a presentation at the annual meeting of the National Association for Medical Direction of Respiratory Care.

“Although this takes constant vigilance and more work, you will have higher reimbursement, lower costs, fewer appeals, fewer denials, and improvements in account receivables” if you stay up to date, said Sam Birnbaum, a certified medical practice executive and a practice management consultant in Hilton Head, S.C.

Information overload and limited time can cause some physicians to react solely to practice concerns rather than to fundamental management, Mr. Birnbaum said.

“You can lose money—that is really bad. You may be asked to return some payments from CMS,” he said. The Centers for Medicare and Medicaid Services (CMS) gets money returned in some cases after filing a claim against a medical practice under the False Claims Act.

“The worst thing of all that can happen

is incarceration,” Mr. Birnbaum said. “I do know of one case, a dermatologist in Sarasota [Fla.], who, shall we say, is going away for a while.”

For respiratory care specialists, Mr. Birnbaum recommended the “Appropriate Coding for Critical Care Services and Pulmonary Medicine 2006,” published by the American College of Chest Physicians (ACCP). “I urge you to keep a copy of this book on your desk,” he said. Mr. Birnbaum has no financial relationship with any book or product he recommended at the meeting.

A more comprehensive source of coding information is Code Manager, published by the American Medical Association in print and CD-ROM formats.

“It’s my favorite,” Mr. Birnbaum said. “It’s pretty easy to use.” One CD-ROM contains all the CPT codes, the ICD-9M codes, the Healthcare Common Procedure Coding System codes from Medicare, Relative Value Units, and local fee calculations according to geographic location.

“It tells you what Medicare should be reimbursing you for a particular code in your area.” Subscription includes quarterly electronic updates, he added.

Solutions in Practice Management is “another great new product,” Mr. Birnbaum said. The ACCP produces this series of CD-ROMs, which is available to its members on its Web site. The product “encompasses just about everything we have talked about this morning.

“The Internet is a wonderful resource of information for Medicare, training courses, meetings, etc.,” Mr. Birnbaum said. CMS national

coverage policy and local coverage policy are explained at [www.cms.hhs.gov/mcd](http://www.cms.hhs.gov/mcd). “This site offers a graph where you can put in your carrier’s name and the CPT code you are looking for,” Mr. Birnbaum said. “It will tell you all the things you need to do to satisfy the requirements for that CPT code, as well as the requirements of the carrier.”

Another recommended Web site is [www.cms.hhs.gov/nationalcorrectcoding](http://www.cms.hhs.gov/nationalcorrectcoding), which explains CMS’s National Correct Coding Initiatives.

Medlearn Matters articles on the CMS Web site are written specifically for office staff, Mr. Birnbaum said. The information, written in an understandable way with a lot of graphics, is available at

[www.cms.hhs.gov/MLNMattersArticles](http://www.cms.hhs.gov/MLNMattersArticles).

“I also recommend that you subscribe to local contractor bulletins and newsletters. They will advise you of any changes by e-mail,” Mr. Birnbaum said. “This is a great way to stay up to date. You also can search monthly or quarterly archives of these newsletters.”

Documentation guidelines and contractor audit sheets are also available online and include unique variations for each contractor, Mr. Birnbaum said. A good example is a contractor that offers comprehensive information for the state of Pennsylvania at [www.hgsa.com](http://www.hgsa.com). These sites feature a list of comprehensive error rate testing (CERT) contractors.

A meeting attendee asked Mr. Birnbaum if he recommended requesting a CERT consult from a contractor. “It sounds like a good idea, but I agree it could be hazardous,” he responded. “It’s easy to download the audit sheets and do self-audits. Just use a checkoff sheet, and you grade it yourself.” If you have more than one physician in your practice, have each one do the self-audit, he added.

Although each physician in a group is evaluated individually by CMS, Mr. Birnbaum said, “by reviewing each other’s billing ... you get a much more appropriate billing pattern in the practice.”

Additional resources include specialty training sessions and publications, the ACCP, the Medical Group Management Association ([www.mgma.org](http://www.mgma.org)), the American Medical Association, state and local medical societies, and carrier Web sites. ■

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## Medicare Payments to Hospitals Are Now Posted

BY MARY ELLEN SCHNEIDER  
Elsevier Global Medical News

Patients and physicians can now find out how much Medicare pays hospitals for certain common elective procedures and other admissions, and by fall, similar information on outpatient and physician services will be accessible.

The hospital information, which is posted on Medicare’s Web site, includes aggregated payment information by county for fiscal year 2005.

Officials at the Centers for Medicare and Medicaid Services have also released information on the volume of these procedures at each hospital.

“People need to know how much their health care costs,” Health and Human Services Secretary Mike Leavitt said during a press briefing. “They need to know the quality of the care they receive, and they need to have a reason to care.”

Mr. Leavitt said this information is the first step to greater transparency of health care cost and quality information. This summer, CMS officials plan to post Medicare payment information for common elective procedures performed at ambulatory surgery centers. And in the fall, the agency plans to post Medicare payment information for common hospital

outpatient and physician services.

Ultimately, consumers will be able to use this type of information to make better decisions about their care, Mr. Leavitt said.

The information released last month includes the range of Medicare payments and the volume of services for 30 conditions with the highest utilization rates among all Diagnosis Related Groups, including implanting cardiac defibrillators, hip and knee replacements, and gallbladder operations.

Data also are available on conditions that were not in the top 30 DRGs but which are of interest to the Medicare community. ■

Hospital payment information is posted at [www.cms.hhs.gov/HealthCareConInit](http://www.cms.hhs.gov/HealthCareConInit).

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# Patient Registries: A Cheaper Alternative to EHRs?

BY MARY ELLEN SCHNEIDER  
Elsevier Global Medical News

PHILADELPHIA — A costly electronic health record system is not necessary to engage in quality improvement and participate in the growing number of pay-for-performance programs, Dr. Rodney Hornbake said at the annual meeting of the American College of Physicians.

Patient registry software is a lower-cost alternative that allows physicians to track their care of patients with chronic diseases.

"It's really an excellent starting place for quality improvement in the ambulatory setting," said Dr. Hornbake, an internist in private practice in Essex, Conn.

Patient registries are one of the best tools for physicians participating in pay-for-performance programs, Dr. Hornbake said. Many electronic health records (EHRs) may not have population-based functionality, and therefore cannot generate simple reports on the physician's performance on certain measures. Most EHR vendors can build interfaces with patient registry software, but that's generally an added cost, he said.

There are a number of patient registry programs available; a comprehensive program can be purchased for less than \$1,000 per provider, Dr. Hornbake said. Some are available for free.

For example, Dr. Hornbake tested the Comorbid Disease Management Database (COMMAND) software in his practice. This registry system is available for free from the Mississippi Quality Improvement Organization. And technology-savvy physicians can use programs like Microsoft Access to design their own registries, he said.

Dr. Hornbake tried out COMMAND in his practice to help keep up with the pay-for-performance programs in his local market. One insurer—Anthem Health Plans Inc. of Connecticut—has a program that offers incentives for process and outcomes measures, as well as for the use of health-related information technology, including electronic prescribing, EHRs, and patient registries. The insurer also offers incentives to physicians for generic prescribing, he said.

Dr. Hornbake said that he exported demographic information from his billing system into COMMAND and manually entered the clinical information from patient charts himself. After using the billing system to identify all of the patients who had conditions included in his registry, he had his staff put red stickers on those patient charts.

This flagged the patients for special attention from the staff, he said. For example, patients whose charts had stickers received follow-up calls if they missed an appointment. To keep the registry up to date, every 2 months the staff pulls the charts of all registry patients and Dr. Hornbake updates the system manually. He spends about 1.5 hours entering data on 125 patients, he said.

Dr. Hornbake said that he prefers to enter the information in periodic batches because it helps him to identify any chronic disease patients who have slipped through the cracks.

Even factoring in his time, Dr. Hornbake said that he saw an immediate return on investment with the patient registry system.

Unlike implementation of an EHR system, he added, patient registry software tends to fit in easily with the normal workflow of the office.

Physicians can also manage their patient care using a paper-based patient registry, he said, but once they begin to track 20 or more measures, a paper system quickly becomes unworkable.

So far, Dr. Hornbake said that he has resisted purchasing an EHR system because he still can't make a financial case for the investment.

He advised physicians to buy or upgrade an EHR system based on its ability to support pay for performance and manage a population of specific patients. Many of the other selling points for an EHR system—that it will eliminate transcription, cut down on needed staff positions, and improve coding—don't hold true for all physicians, he said.

**Dr. Michael Baumann, FCCP, comments:** Experience at the University of Mississippi Medical Center using COMMAND as a patient registry tool for patients with congestive heart failure and for patients with coronary artery disease has been quite positive. The system is user friendly and robust.

This system and other registry systems can enhance patient care and assist in tackling the issues surrounding pay for performance.



The following is a brief summary. Please consult complete prescribing information.

**CONTRAINDICATIONS:** MAXIPIME is contraindicated in patients who have shown immediate hypersensitivity reactions to cefepime or the cephalosporin class of antibiotics, penicillins or other beta-lactam antibiotics. **WARNINGS:** BEFORE THERAPY WITH MAXIPIME (CEFEPIME HYDROCHLORIDE) FOR INJECTION IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS IMMEDIATE HYPERSENSITIVITY REACTIONS TO CEFEPIME, CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. IF THIS PRODUCT IS TO BE GIVEN TO PENICILLIN-SENSITIVE PATIENTS, CAUTION SHOULD BE EXERCISED BECAUSE CROSS-HYPERSENSITIVITY AMONG BETA-LACTAM ANTIBIOTICS HAS BEEN CLEARLY DOCUMENTED AND MAY OCCUR IN UP TO 10% OF PATIENTS WITH A HISTORY OF PENICILLIN ALLERGY. IF AN ALLERGIC REACTION TO MAXIPIME OCCURS, DISCONTINUE THE DRUG. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE TREATMENT WITH EPINEPHRINE AND OTHER EMERGENCY MEASURES INCLUDING OXYGEN, CORTICOSTEROIDS, INTRAVENOUS FLUIDS, INTRAVENOUS ANTIHISTAMINES, PRESSOR AMINES, AND AIRWAY MANAGEMENT, AS CLINICALLY INDICATED.

In patients with impaired renal function (creatinine clearance  $\leq 60$  mL/min), the dose of MAXIPIME should be adjusted to compensate for the slower rate of renal elimination. Because high and prolonged serum antibiotic concentrations can occur from usual dosages in patients with renal insufficiency or other conditions that may compromise renal function, the maintenance dosage should be reduced when cefepime is administered to such patients. Continued dosage should be determined by degree of renal impairment, severity of infection, and susceptibility of the causative organisms. (See specific recommendations for dosing adjustment in **DOSAGE AND ADMINISTRATION** section of the complete prescribing information.) During postmarketing surveillance, encephalopathy (disturbance of consciousness including confusion, hallucinations, stupor, and coma), myoclonus, and seizures (see **ADVERSE REACTIONS: Postmarketing Experience**). Most cases occurred in patients with renal impairment who received doses of cefepime that exceeded the recommended dosage schedules. However, some cases of encephalopathy occurred in patients receiving a dosage adjustment for their renal function. In general, symptoms of neurotoxicity resolved after discontinuation of cefepime and/or after hemodialysis.

**Pseudomembranous colitis has been reported with nearly all antibacterial agents, including MAXIPIME, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.** Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of "antibiotic-associated colitis". After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate-to-severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against *Clostridium difficile* colitis.

**PRECAUTIONS: General:** Prescribing MAXIPIME in the absence of proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria. As with other antimicrobials, prolonged use of MAXIPIME may result in overgrowth of nonsusceptible microorganisms. Repeated evaluation of the patient's condition is essential. Should superinfection occur during therapy, appropriate measures should be taken. Many cephalosporins, including cefepime, have been associated with a fall in prothrombin activity. Those at risk include patients with renal or hepatic impairment, or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy. Prothrombin time should be monitored in patients at risk, and exogenous vitamin K administered as indicated. Positive direct Coombs' tests have been reported during treatment with MAXIPIME. In hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs' testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognized that a positive Coombs' test may be due to the drug. MAXIPIME should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis. Arginine has been shown to alter glucose metabolism and elevate serum potassium transiently when administered at 33 times the amount provided by the maximum recommended human dose of MAXIPIME. The effect of lower doses is not presently known.

**Information for Patients:** Patients should be counseled that antibacterial drugs including MAXIPIME should only be used to treat bacterial infections. They do not treat viral infections (eg, the common cold). When MAXIPIME is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by MAXIPIME or other antibacterial drugs in the future.

**Drug Interactions:** Renal function should be monitored carefully if high doses of aminoglycosides are to be administered with MAXIPIME because of the increased potential of nephrotoxicity and ototoxicity of aminoglycoside antibiotics. Nephrotoxicity has been reported following concomitant administration of other cephalosporins with potent diuretics such as furosemide. **Drug/Laboratory Test Interactions:** The administration of cefepime may result in a false-positive reaction for glucose in the urine when using Clinistix® tablets. It is recommended that glucose tests based on enzymatic glucose oxidase reactions (such as Clinistix®) be used.

**Carcinogenesis, Mutagenesis, and Impairment of Fertility:** No long-term animal carcinogenicity studies have been conducted with cefepime. A battery of *in vivo* and *in vitro* genetic toxicity tests, including the Ames Salmonella reverse mutation assay, CHO/HGPRT mammalian cell forward gene mutation assay, chromosomal aberration and sister chromatid exchange assays in human lymphocytes, CHO fibroblast clastogenesis assay, and cytogenetic and micronucleus assays in mice were conducted. The overall conclusion of these tests indicated no definitive evidence of genotoxic potential. No untoward effects on fertility or reproduction have been observed in rats, mice, and rabbits when cefepime is administered subcutaneously at 1 to 4 times the recommended maximum human dose calculated on a mg/m<sup>2</sup> basis. **Usage in Pregnancy—Teratogenic effects—Pregnancy Category B:** Cefepime was not teratogenic or embryocidal when administered during the period of organogenesis to rats at doses up to 1000 mg/kg/day (4 times the recommended maximum human dose calculated on a mg/m<sup>2</sup> basis) or to mice at doses up to 1200 mg/kg (2 times the recommended maximum human dose calculated on a mg/m<sup>2</sup> basis) or to rabbits at a dose level of 100 mg/kg (approximately equal to the recommended maximum human dose calculated on a mg/m<sup>2</sup> basis). There are, however, no adequate and well-controlled studies of cefepime use in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed. **Nursing Mothers:** Cefepime is excreted in human breast milk in very low concentrations (0.5 µg/mL). Caution should be exercised when cefepime is administered to a nursing woman. **Labor and Delivery:** Cefepime has not been studied for use during labor and delivery. Treatment should only be given if clearly indicated. **Pediatric Use:** The safety and effectiveness of cefepime in the treatment of uncomplicated and complicated urinary tract infections (including pyelonephritis), uncomplicated skin and skin structure infections, pneumonia, and as empiric therapy for febrile neutropenic patients have been established in the age groups 2 months up to 16 years. Use of

MAXIPIME (cefepime hydrochloride) in these age groups is supported by evidence from adequate and well-controlled studies of cefepime in adults with additional pharmacokinetic and safety data from pediatric trials (see **CLINICAL PHARMACOLOGY** section of the complete prescribing information.) Safety and effectiveness in pediatric patients below the age of 2 months have not been established. There are insufficient clinical data to support the use of MAXIPIME in pediatric patients under 2 months of age or for the treatment of serious infections in the pediatric population where the suspected or proven pathogen is *Haemophilus influenzae* type b. IN THOSE PATIENTS IN WHOM MENINGEAL SEEDING FROM A DISTANT INFECTION SITE OR IN WHOM MENINGITIS IS SUSPECTED OR DOCUMENTED, AN ALTERNATE AGENT WITH DEMONSTRATED CLINICAL EFFICACY IN THIS SETTING SHOULD BE USED. **Geriatric Use:** Of the more than 6400 adults treated with MAXIPIME in clinical studies, 35% were 65 years or older while 16% were 75 years or older. When geriatric patients received the usual recommended adult dose, clinical efficacy and safety were comparable to clinical efficacy and safety in nongeriatric adult patients. Serious adverse events have occurred in geriatric patients with renal insufficiency given unadjusted doses of cefepime, including life-threatening or fatal occurrences of the following: encephalopathy, myoclonus, and seizures. (See **WARNINGS** and **ADVERSE REACTIONS** sections of the complete prescribing information.) This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and renal function should be monitored. (See **CLINICAL PHARMACOLOGY: Special Populations, WARNINGS, and DOSAGE AND ADMINISTRATION** sections of the complete prescribing information.)

**ADVERSE REACTIONS: Clinical Trials:** In clinical trials using multiple doses of cefepime, 4137 patients were treated with the recommended dosages of cefepime (500 mg to 2 g IV q12h). There were no deaths or permanent disabilities thought related to drug toxicity. Sixty-four (1.5%) patients discontinued medication due to adverse events thought by the investigators to be possibly, probably, or almost certainly related to drug toxicity. Thirty-three (51%) of these 64 patients who discontinued therapy did so because of rash. The percentage of cefepime-treated patients who discontinued study drug because of drug-related adverse events was very similar at daily doses of 500 mg, 1 g, and 2 g q12h (0.8%, 1.1%, and 2.0%, respectively). However, the incidence of discontinuation due to rash increased with the higher recommended doses. The following adverse events were thought to be probably related to cefepime during evaluation of the drug in clinical trials conducted in North America (n=3125 cefepime-treated patients).

**TABLE 1**  
Adverse Clinical Reactions Cefepime Multiple-Dose Dosing Regimens Clinical Trials—North America

INCIDENCE EQUAL TO OR GREATER THAN 1%	Local reactions (3.0%), including phlebitis (1.3%), pain and/or inflammation (0.6%)*; rash (1.1%)
INCIDENCE LESS THAN 1% BUT GREATER THAN 0.1%	Colitis (including pseudomembranous colitis), diarrhea, fever, headache, nausea, oral moniliasis, pruritus, urticaria, vaginitis, vomiting

\*local reactions, irrespective of relationship to cefepime in those patients who received intravenous infusion (n = 3048).

At the higher dose of 2 g q8h, the incidence of probably-related adverse events was higher among the 795 patients who received this dose of cefepime. They consisted of rash (4%), diarrhea (3%), nausea (2%), vomiting (1%), pruritus (1%), fever (1%), and headache (1%). The following adverse laboratory changes, irrespective of relationship to therapy with cefepime, were seen during clinical trials conducted in North America.

**TABLE 2**  
Adverse Laboratory Changes Cefepime Multiple-Dose Dosing Regimens Clinical Trials—North America

INCIDENCE EQUAL TO OR GREATER THAN 1%	Positive Coombs' test (without hemolysis) (16.2%); decreased phosphorus (2.8%); increased ALT/SGPT (2.8%), AST/SGOT (2.4%), eosinophils (1.7%); abnormal PTT (1.6%), PT (1.4%)
INCIDENCE LESS THAN 1% BUT GREATER THAN 0.1%	Increased alkaline phosphatase, BUN, calcium, creatinine, phosphorus, potassium, total bilirubin; decreased calcium*, hematocrit, neutrophils, platelets, WBC

\*Hypocalcemia was more common among elderly patients. Clinical consequences from changes in either calcium or phosphorus were not reported.

A similar safety profile was seen in clinical trials of pediatric patients (See **PRECAUTIONS: Pediatric Use**).

**Postmarketing Experience:** In addition to the events reported during North American clinical trials with cefepime, the following adverse experiences have been reported during worldwide postmarketing experience. Because of the uncontrolled nature of spontaneous reports, a causal relationship to MAXIPIME treatment has not been determined.

As with other drugs in this class, encephalopathy (disturbance of consciousness including confusion, hallucinations, stupor, and coma), myoclonus, and seizures have been reported. Although most cases occurred in patients with renal impairment who received doses of cefepime that exceeded the recommended dosage schedules, some cases of encephalopathy occurred in patients receiving a dosage adjustment for their renal function. (See also **WARNINGS**.) If seizures associated with drug therapy occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated. Precautions should be taken to adjust daily dosage in patients with renal insufficiency or other conditions that may compromise renal function to reduce antibiotic concentrations that can lead or contribute to these and other serious adverse events, including renal failure.

As with other cephalosporins, anaphylaxis including anaphylactic shock, transient leukopenia, neutropenia, agranulocytosis and thrombocytopenia have been reported. **Cephalosporin-class adverse reactions:** In addition to the adverse reactions listed above that have been observed in patients treated with cefepime, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics: Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis, renal dysfunction, toxic nephropathy, aplastic anemia, hemolytic anemia, hemorrhage, hepatic dysfunction including cholestasis, and pancytopenia.

**OVERDOSAGE:** Patients who receive an overdose should be carefully observed and given supportive treatment. In the presence of renal insufficiency, hemodialysis, not peritoneal dialysis, is recommended to aid in the removal of cefepime from the body. Accidental overdosing has occurred when large doses were given to patients with impaired renal function. Symptoms of overdose include encephalopathy (disturbance of consciousness including confusion, hallucinations, stupor, and coma), myoclonus, seizures, and neuromuscular excitability. (See **PRECAUTIONS, ADVERSE REACTIONS, and DOSAGE AND ADMINISTRATION** sections of the complete prescribing information.)

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