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VIVIAN E. LEE/ELSEVIER GLOBAL MEDICAL NEWS

Baltimore City Health Commissioner Dr. Joshua Sharfstein testified against use of over-the-counter cough and cold products in children.

FDA Plans Guidance on OTC Cold Meds for Kids

BY ELIZABETH MECHCATIE
Elsevier Global Medical News

SILVER SPRING, MD. — The Food and Drug Administration is expected to issue interim recommendations to the public about the use of over-the-counter cough and cold products in children, in response to the advisory panel recommendation that these products not be used in children under age 6.

On Oct. 19, at the end of a 2-day meeting on the safety and efficacy of OTC cough and cold products in children, the FDA's Nonprescription Drugs and Pediatric advisory committees agreed that there was no evidence from the available scientific studies that these products were effective in children under age 12, and they expressed concerns about extrapolating evidence about efficacy and safety obtained in adults to children, and from older children to younger children.

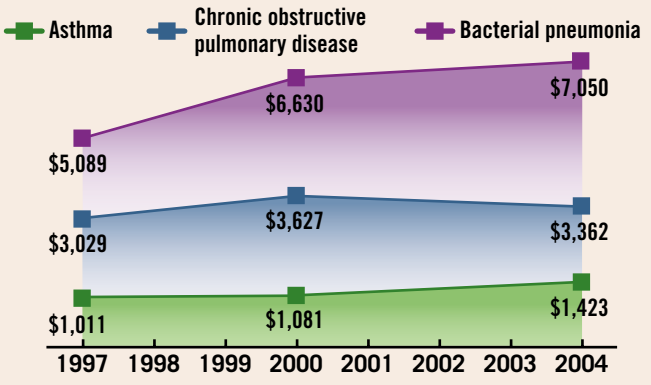
The panels voted 13-9 that these products should not be used in children aged 2-5. But they voted 15-7 against recommending that they not be used in children aged 6-11.

The committees voted 21-1 that these products should not be used for children under age 2. OTC cough and cold products are not approved by the FDA for this age group, and their labels include the statement advising consumers to ask their doctor before using these products in this age

See **Cold Meds** • *page 22*

VITAL SIGNS

Costs of Preventable Hospitalizations For Respiratory Conditions
(in millions of dollars)



Note: Amounts adjusted for inflation to 2004 dollars using the overall Consumer Price Index.
Source: Healthcare Cost and Utilization Project

ELSEVIER GLOBAL MEDICAL NEWS

Study: Invasive MRSA Is a 'Major' Health Problem

Incidence at 31.8 per 100,000 people.

BY KATE JOHNSON
Elsevier Global Medical News

The prevalence of methicillin-resistant *Staphylococcus aureus* infections in the United States may be higher than previously thought and represents a major public health problem, according to a nationwide estimate of the burden of the disease, reported R. Monina Klevens, D.D.S., of the Centers for Disease Control and Prevention, and colleagues.

The authors estimated the standardized incidence of invasive MRSA in the year 2005 to be 31.8 per 100,000 persons, with the highest rates in people aged 65 years and older (127.7 per 100,000), in blacks (66.5 per 100,000), and in males (37.5 per 100,000). The majority of disease was related to health care but occurred outside the health care setting, they noted (JAMA 2007;298:1763-71).

The study used population-based, active case-finding to come up with national estimates of invasive MRSA incidence and mortality rates. As part of the Active Bacterial Core surveillance system, a component of the Emerging Infections Programs Network of the CDC, nine sites conducted surveillance for invasive MRSA. The total population under surveillance was estimated to be 16.5 million, or approximately 5.6% of the U.S. population. Results were then used to estimate the nationwide incidence.

Medical records were used to document health care risk factors for MRSA, and cases were classified as either health care–associated or community-associated.

A standardized incidence of 31.8 per 100,000 was estimated from a total of 8,987 observed cases of invasive MRSA. The study found that 14% of infections were community associated and 85% were health care associated, with 58% of the latter being community onset and 27% being hospital onset.

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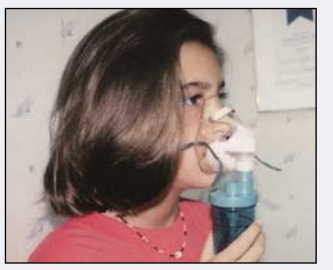
INSIDE



Gene Predicted Lung Cancer Outcomes

BY ERIK GOLDMAN
Elsevier Global Medical News

BARCELONA — Overexpression of BRCA1, one of the genes associated with aggressive breast cancer, also predicts cisplatin resistance, faster recurrence, and reduced survival in people with non–small cell lung cancers, Dr. Rafael Rosell reported at the 14th European Cancer Conference.

Dr. Rosell and colleagues at the Catalan Institute of Oncology have been studying gene expression signatures that predict the behavior and treatment responsiveness of lung tumors. They've identified nine genes, all involved in the process of DNA repair, that may have potential predictive value. By far the biggest red flag is BRCA1.

The investigators assessed expression of these nine genes in tumor tissue obtained from 126 people with stage IA-IIIA squamous cell carcinoma or adenocarcinoma. Overall, 42% of patients had stage IB tumors, and 26% had stage II lesions. BRCA1 was the only gene of the nine to show independent prognostic value as far as clinical outcomes.

Patients in the uppermost quartile of BRCA1 expression showed much greater resistance to cisplatin-based treatment regimens, and were twice as likely to die within 3 years, compared with those in the lowest quartile. Median time to recurrence was 22 months among the high BRCA1 expressors, and median survival was 29 months. Among those in the lowest quartile, the majority was still alive and disease free after 3 years.

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Antibiotics' Impact Mixed in Respiratory Infections

BY JONATHAN GARDNER
Elsevier Global Medical News

Prescribing antibiotics for respiratory tract infections rarely averts complications, although they may be effective in preventing pneumonia among older patients with chest infections, according to an analysis of British patient records.

The analysis of more than 3 million records from 162 British practices over 10 years found that the risk of mastoiditis after otitis media, peritonsillar abscess after sore throat, and pneumonia after upper respiratory infection was too low to justify antibiotics (BMJ 2007 Oct. 19 [Epub doi:10.1136/bmj.39345.405243.BE]).

The researchers from University College London and the British Health Protection Agency calculated that more than 4,000 otitis media, sore throat, or respiratory tract infections would need to be treated to avert a single complication.

However, they found a greater effect on treating chest infections. Among patients aged 65 years and older, the researchers found that treating 39 cases of chest infection with antibiotics would prevent one case of pneumonia. Even younger patients experienced limited benefits: For age groups between 0 and 64, the number of cases treated with antibiotics that would prevent pneumonia ranged between 96 and 119. The authors noted that only a relatively low number of antibiotic courses was required for the preventive effect.

TREATING 39 CASES OF CHEST INFECTION WITH ANTIBIOTICS IN PEOPLE AGED 65 YEARS AND OLDER WOULD PREVENT ONE CASE OF PNEUMONIA.

"There are legitimate concerns about the overuse of antibiotics in primary care and the development of resistance," wrote the researchers, led by Irene Petersen, statistician at University College London's Centre for Infectious Disease Epidemiology. "General practitioners should not base their prescribing for sore throat, otitis media, or upper respiratory tract infections on a fear of serious complications. In contrast, antibiotics substantially reduce the risk of a diagnosis of pneumonia after chest infection."

With lower respiratory tract infections, the researchers noted, it is difficult to distinguish between acute bronchitis, for which antibiotics are not recommended, and early pneumonia, for which antibiotics are recommended, without chest radiography, which is unavailable at many practices.

In an accompanying commentary, Dr. Samuel Coenen and Dr. Herman Goossens of the University of Antwerp wrote that while the research supports the recommendations against overprescribing of antibiotics, it does not help physicians make tough calls in the examination room.

"The available evidence does not provide clinicians with the guidance they need to prescribe antibiotics effectively for common infections in primary care, except maybe for acute otitis media," they wrote. "For lower respiratory tract infections in particular, clinicians cannot be confident about identifying who will benefit from antibiotics and who will not."

The researchers examined 3.36 million records of respiratory infections in the UK General Practice Research Database between July 1, 1991, and June 30, 2001. The records were used to identify patients who developed complications in the month following their diagnoses, excluding those recorded on the day of diagnosis, and to calculate the risks of complication based on prescription for antibiotics.

The researchers acknowledged that their methods may have influenced the findings. Patients with severe disease, and thus a greater risk of complications, may have been more likely to be prescribed antibiotics, which may have resulted in an underestimate of the protective effect of antibiotics, the researchers wrote.

In addition, patients with pneumonia are more likely to be treated in secondary care, so they might not have been recorded as part of the general practice database, which also could have led to an underestimation of the risk of complications.

However, the researchers added, cases of bronchitis may have been misclassified as pneumonia by physicians wishing to prescribe antibiotics, which may have led to an overestimation of the risk of pneumonia after chest infection and an overestimation of the protective effect of antibiotics.

Dr. Livermore and Dr. Johnson have contractual agreements with pharmaceutical companies that produce antibiotics. ■

Gene May Affect Cisplatin Response

Lung Cancer • *from page 1*

The data suggest that only 30% of the high expressors would still be alive at 40 months after surgery, while 70% of the low expressors would survive. By 60 months, the probability of survival drops to about 20% for those with high-BRCA1 primary tumors, but remains around 60% for the low expressors. Overall, having a high-BRCA1–expressing tumor doubled the hazard ratio for recurrence and mortality, compared with having a low-BRCA1–expressing tumor.

"BRCA1 was the only one of the genes that showed significant correlations with clinical outcome and the only independent prognostic variable other than tumor stage of IIIA or higher," Dr. Rosell said at the conference, which was sponsored by the Federation of European Cancer Societies.

He and his colleagues obtained very consistent findings in a validation cohort of 58 patients. They will publish a retrospective analysis before the end of this year, and they are actively developing a prospective trial to validate and quantify the predictive value of BRCA1 expression.

BRCA1 plays a central role in repair of DNA damage. Several earlier studies have shown that low levels of BRCA1 expression correlate well with cisplatin sensitivity, while increased BRCA expression is associated with treatment resistance.

"Since cisplatin is the gold standard drug for adjuvant chemotherapy in high-risk resected lung cancers, we think these findings could have significant therapeutic impact," he said. "Perhaps those patients with high-BRCA1–expressing tumors should just bypass cisplatin altogether, and go directly to taxane-based therapies."

Commenting on the presentation, Dr. Alexander Eggermont, president of the newly formed ECCO organization, said, "If this will be validated in future studies, it will really change the landscape of diagnostic testing and treatment decision making."

Dr. Rosell expects a long debate before practices change. Because cisplatin has been the standard of care for non–small cell lung cancer for so long, he explained, and because nearly all of the clinical trials for these cancers are cisplatin-based, there will likely be a fair amount of resistance to anything that challenges the preeminence of the drug or suggests that some patients would be better off without it. ■

Placenta No Barrier to H5N1 Avian Influenza

BY JONATHAN GARDNER
Elsevier Global Medical News

In humans, the highly pathogenic H5N1 avian influenza virus can spread beyond the lungs and also can cross the placenta to the fetus, according to research published in the Lancet.

Chinese researchers examined the postmortem tissues of two adults, a 35-year-old man from Jiangxi province and a 24-year-old woman from Anhui province who was 4 months' pregnant. Both individuals were confirmed as infected with H5N1 by the Chinese Centre for Disease Control and Prevention (Lancet 2007;370:1137-45).

Examination of tissues from the respiratory, digestive, and central nervous systems, and from other organs found viral genetic material and antigens to the virus. In the respiratory system, the researchers found signs that H5N1 had affected, among other tissues, the alveoli, in contrast to human influenza, which mainly targets the upper respiratory tract.

In the pregnant woman, the researchers found infected cells in the placenta and, in the fetus, they found viral sequences in the lungs, circulating mononuclear cells, and the liver.

The woman had been admitted after 6 days of fever, cough, and shortness of breath. She had handled ill birds 2 weeks before admission and died 2.5 days after, despite treatment with antibiotics and corticosteroids. No antivirals were given, the investigators noted.

The man died 27 days after developing fever and productive cough. Admitted to the hospital with a 6-day history of symptoms, he was first administered corticosteroids, followed by an antiviral, and then antifungal treatments.

The researchers said their findings help shed light on how H5N1 infections progress, which will be important for public health officials to watch because that strain of virus is feared as the most likely to result in a pandemic.

"Little is known about the specific effects in organs and cells targeted by the virus," wrote the researchers, led by Dr. Jiang Gu of Peking University in Beijing. "The infection initially seemed to be restricted to the lungs, but later reports have suggested that influenza A H5N1 could disseminate beyond the lungs," they said.

"These newly obtained data are important in the clinical, pathological, and epidemiological investigation of human H5N1 infection and have implications for public-health and health care providers," they added.

IN A PREGNANT WOMAN, RESEARCHERS FOUND INFECTED CELLS IN THE PLACENTA AND VIRAL SEQUENCES IN THE FETUS'S LUNGS AND LIVER.

In all, the researchers found viral genetic material and antigens in epithelial cells of the lungs and trachea, T cells of the lymph nodes, neurons of the brain, and Hofbauer cells and cytotrophoblasts of the placenta. They found viral genomic sequences but no antigens in the intestinal mucosa.

The route of infection for the central nervous system could be through the blood-brain barrier or through respiratory system nerves after replicating in tissues there, the researchers wrote.

For the intestines, the virus could be blood borne but could occur through the ingestion of respiratory secretions, they added.

How the vertical infection of the fetus would affect the fetus is unclear. Human influenza strains infecting a pregnant female have not been shown to affect the fetus, but since H5N1 also has effects on humans not seen in human strains, such as viremia, "the likelihood of virus reaching the uterus and placenta is probably higher in avian influenza than in human influenza," they wrote.

In an accompanying commentary, Dr. Wai Fu Ng of Princess Margaret Hospital in Hong Kong and Professor Ka Fai To of Chinese University of Hong Kong raise questions about the effects of the vertical infection route.

"The absence of pathological changes in the immunologically incompetent fetus is taken as evidence that viral replication itself is not pathogenic," they wrote. "Speculation about the fate of the fetus if the mother survived the infection is interesting.

"With the development of antibodies in the mother and their transplacental crossing into the fetus, pathological lesions in the fetus may result," they said. ■

Pages 4a—4b

Cardiac Troponin I May Signal Pulmonary Embolism Risk

BY BRUCE K. DIXON
Elsevier Global Medical News

CHICAGO — The measurement of cardiac troponin I should be routinely performed in all emergency department patients in whom pulmonary embolism is suspected, according to a study led by Dr. Hamid Shokoohi.

A troponin (cTnI) level greater than 0.08 ng/mL should raise concern for central pulmonary vascular obstruction, especially in patients without overt clinical evidence of circulatory compromise, Dr. Shokoohi said at the annual meeting of the Society for Academic Emergency Medicine.

"Troponin has been shown to be of clinical benefit in prediction of in-hospital mortality and adverse outcome in pulmonary embolism," said Dr. Shokoohi, senior resident in emergency medicine at George Washington University, Washington.

Right heart failure is the usual cause of death from pulmonary embolism (PE), and right ventricular (RV) dysfunction may be an important warning sign of a bad outcome. "Cardiac echo is most frequently utilized to evaluate RV strain, but 2D echo is not available 24 hours a day, 7 days a week in most institutions," Dr. Shokoohi explained. The proximal level of PE is associated with the severity of PE determined by clinical, biochemical, and radiologic markers, he added.

The retrospective cohort study began with 179 emergency department patients diagnosed with PE over a 2-year period. After exclusion of patients who had not been tested for elevated troponin (52), those for whom a CT scan was not available (14), and other reasons, the final study sample was 104 patients.

To rule out chronic PE, only patients with a prior onset of symptoms of less than 2 weeks were accepted. The mean duration of symptoms among 20 patients with elevated troponin was 29 hours, compared with 44 hours among 84 patients with normal troponin.

Women made up 80% of patients in the elevated troponin group of patients, and were a 53% majority among those with normal troponin. The mean ages of the cohorts were 53 years and 51 years, respectively.

Diagnosis of PE was confirmed by spiral CT and high-probability ventilation perfusion scans.

The primary outcome measure was main pulmonary artery involvement; the secondary outcomes were ICU admissions, emergency department mortality, and the use of thrombolytic therapy.

The main pulmonary artery was involved in 70% of those patients with elevated troponin and only 14% of those with normal troponin. Lobar involvement was seen in 25% and 33% of each group respectively, Dr. Shokoohi reported.

"In determining the accuracy of cTnI to predict main pulmonary artery involvement, we had a sensitivity of 54%, a specificity of 92%, a negative predictive value of 86% and a positive predictive value of 75%," he said.

Increased troponin level also was highly correlated with ICU admission of patients with PE. A total of four patients with elevated troponin received thrombolytic therapy, versus none in the normal troponin group. There was a single ED death among the 20 patients with elevated troponin.

Dr. Shokoohi described several limitations of this study, including its single-institution retrospective nature, the exclusion of 36% of eligible patients because of a lack of a cTnI measurement or CT images, and possible physician awareness of troponin results and its potential effect on ICU admissions.

"But based on this study, if you have confirmed PE based on a CT scan and the patient has a negative troponin, he or she is less likely to have central pulmonary embolism," Dr. Shokoohi said.

Coauthors of the study included Dr. Robert Shesser, Dr. Jeffrey Smith, Dr. Michael Hill, and Dr. Robert Hirsh. ■

Dr. Keith Wille, FCCP, comments:
Dr. Shokoohi's results are further supported by a recent study (Circulation 2007;116:427-33) examining the prognostic value of troponins in acute pulmonary embolism (PE). In their meta-analysis, Becattini et al. reviewed 20 studies (1,985 patients) and found that 19.7% of patients with elevated troponin levels died, compared with 3.7% of patients with normal troponin levels. Elevated troponin levels were associated with higher short-term mortality (OR 5.24, 95% CI 3.28-8.38), death due to PE (OR 9.44, 95% CI 4.14-21.5), and adverse outcome events (OR 7.03, 95% CI 2.42-20.4). While these findings are intriguing, it is still unclear whether biological markers such as troponin may lead to better risk stratification, treatment decisions, and clinical outcomes for all PE patients.

IN THIS ISSUE

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MRSA's Toll 'Astounding'

Health Problem • *from page 1*

A total of 114 infections (1%) could not be classified. There were an estimated 18,650 deaths from invasive MRSA, giving a standardized mortality rate of 6.3 per 100,000.

The estimated incidence is "astounding," Dr. Elizabeth A. Bancroft commented in an accompanying editorial (JAMA 2007;298:1803-4). "To put this number into context, the estimated rate of invasive MRSA is greater than the combined rate in 2005 for invasive pneumococcal disease (14.1 per 100,000), invasive group A streptococcus (3.6 per 100,000), invasive meningococcal disease (0.35 per 100,000), and invasive *H[aemophilus] influenzae* (1.4 per 100,000)," said Dr. Bancroft, of the Los Angeles County Department of Public Health.

In addition, if the authors' projected mortality rate is accurate, "these deaths would exceed the total number of deaths attributable to human immunodeficiency virus/AIDS in the United States in 2005," added Dr. Bancroft.

The authors noted that their estimated incidence is higher than that of a recent CDC study (Emerg. Infect. Dis. 2005; 11:868-72). Compared with previously documented incidence rates (2001-2002) at two of the study sites, there was an increased incidence observed in Atlanta (from 19 to 33 per 100,000) and Baltimore (from 40 to 117 per 100,000). However, in the state of Connecticut, the 2005 incidence of 2.8 per 100,000 was relatively stable, compared with a 1998 incidence of 2.5 per 100,000, they wrote.

"Invasive MRSA disease is a major public health problem and is primarily related to health care but no longer confined to acute care," the study's authors concluded. ■

CHEST PHYSICIAN

CHEST PHYSICIAN, the newspaper of the American College of Chest Physicians, provides cutting-edge reports from clinical meetings, FDA coverage, clinical trial results, expert commentary, and reporting on the business and politics of chest medicine. Each issue also provides material exclusive to the members of the American College of Chest Physicians. Content for **CHEST PHYSICIAN** is provided by International Medical News Group and Elsevier Global Medical News. Content for NEWS FROM THE COLLEGE is provided by the American College of Chest Physicians.

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Bosentan Slowed Progression of Class II PAH

BY MITCHEL L. ZOLER
Elsevier Global Medical News

VIENNA — Patients with functional class II pulmonary arterial hypertension had significantly slower disease progression when treated with bosentan in a study with 185 patients, a finding that may shift the time to diagnose and start treatment of this disease.

The results support starting treatment of pulmonary arterial hypertension (PAH) "as soon as possible after the diagnosis is made because the majority of patients with PAH are in functional class II or III; the majority of PAH patients need treatment [with bosentan] according to these data," Dr. Nazzareno Galiè said at the annual congress of the European Society of Cardiology.

"In PAH it's very important to prevent deterioration, and that's what treatment with bosentan does," said Dr. Galiè. "The results show that PAH is a progressive disease, even in class II, highlighting the need for early diagnosis and treatment."

EARLY showed that in a pure cohort of class II patients, early treatment may delay PAH progression.
DR. RUBIN

The Endothelin Antagonist Trial in Mildly Symptomatic PAH Patients (EARLY) study "is the only study to focus on class II patients," and it included a strict definition of class II, said Dr. Galiè, professor of cardiology and head of the Pulmonary Hypertension Centre at the University of Bologna (Italy).

Based on these and other findings, applications have been filed with the Food and Drug Administration and similar agencies in other countries to expand bosentan treatment to patients with class II PAH. Bosentan (Tracleer) is already marketed for treating classes III and IV PAH by Actelion.

The new study was sponsored by Actelion, and Dr. Galiè is a speaker for and consultant to Actelion.

"The EARLY study results, and the results from [five] other studies that included class II PAH patients, support the benefit of treating patients with less-severe PAH. The added strength of the data from EARLY is that they demonstrated in a pure cohort of class II patients that early treatment may delay progression of the disease," commented Dr. Lewis J. Rubin, FCCP, a coauthor of the study and professor of medicine and director of pulmonary and critical care medicine at the University of California, San Diego. Dr. Rubin is a consultant to Actelion.

The study enrolled patients aged 12 years and older, mean age 44, with PAH rated as functional class II by World Health Organization criteria.

The disease could have been idiopathic (as it was in about 60% of patients), or caused by congenital heart disease (in about 17%), connective tissue disease (in about 18%), or HIV infection (in about 5%). The average duration of PAH was about 3 years.

Patients were randomized to treatment with either 62.5 mg bosentan b.i.d. for 4 weeks, followed by 125 mg b.i.d. for 5 months, or placebo.

After 6 months of treatment, the change from baseline in pulmonary vascular resistance, one of two primary end points, was increased by about 7% among 88 evaluable patients in the placebo group, and was decreased by about 16% in 80 patients in the bosentan group. The overall effect of bosentan treatment was to lower pulmonary vascular resistance by 23%, compared with placebo, a significant effect.

The second primary end point was change in exercise capacity, measured by distance walked in 6 minutes.

By this measure, bosentan was linked to a significant, 19-m boost in distance walked, compared with placebo, Dr. Galiè reported.

Bosentan treatment also led to significant improvements in time to clinical worsening, and a decrease in the percentage of patients whose condition worsened. Symptomatic progression of PAH occurred in 10% of patients on placebo, compared with 1% of the patients treated with bosentan.

With bosentan, Dr. Galiè said, "there is

more preservation of functional class."

Bosentan also led to significant improvements in self-rated quality of life, and a significant reduction in serum levels of NT-probrain natriuretic peptide (NT-proBNP). The drug was well tolerated, with an adverse event profile similar to that of the placebo group.

To boost the number of patients with PAH who start treatment early, Dr. Galiè suggested screening for PAH in groups that are known to have a relatively high prevalence of PAH. This includes patients with connective tissue diseases, such scleroderma, patients infected with HIV, and patients with congenital heart disease.

Three other reports at the meeting dealt with using bosentan to treat PAH; all three studies also were sponsored by Actelion.

One study enrolled 157 patients who had a specific, relatively common form of PAH, chronic thromboembolic pulmonary hypertension (CTEPH), which was inoperable or recurrent.

The results showed that treatment with bosentan was safe and led to improvements in pulmonary vascular resistance and other measures, Dr. Irene Lang, professor of vascular biology at the Medical University of Vienna, reported at the meeting.

The Bosentan Effects in Inoperable Forms of CTEPH (BENEFIT) study randomized patients to treatment with 62.5 mg bosentan b.i.d for 4 weeks, followed by 125 mg b.i.d. for 12 weeks or placebo. Their average age was 63 years.

Bosentan was linked with a significant, 24% reduction in peripheral vascular resistance in 66 evaluable patients, compared with 71 placebo patients. Treatment also significantly boosted cardiac index, and cut NT-proBNP levels and dyspnea scores. Bosentan treatment had no significant effect on 6-minute walk distance.

Another study assessed the acute hemodynamic effect of a single, 25-mg dose of sildenafil in 44 patients with PAH already on chronic bosentan treatment.

The results showed that the single sildenafil dose was safe, and after 60 minutes led to a significant drop in pulmonary vascular resistance, total pulmonary resistance, pulmonary artery pressure, and cardiac output.

The third study examined the phamacokinetics of a new formulation of bosentan designed for use in children. Results from 35 patients aged 2-11 years showed that the formulation led to reasonable serum levels and a good safety profile. ■

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Cochrane: Ibuprofen Can Slow Lung Deterioration in CF

BY TIMOTHY F. KIRN
Elsevier Global Medical News

With careful monitoring, high-dose ibuprofen treatment can slow progressive lung damage in patients with cystic fibrosis, particularly if begun before age 13 years, according to an updated Cochrane Library review.

In the previous review, conducted 2 years ago, the same reviewers concluded that there was only preliminary evidence that nonsteroidal anti-inflammatory drugs affected pulmonary deterioration, and they said that routine use could not be recommended. But the new review includes recent data from a large, Canadian cystic fibrosis (CF) trial conducted by one of the Cochrane reviewers—data that almost doubled the number of patients included in the latest analysis.

"High-dose ibuprofen can slow the progression of lung disease in people with CF, especially in children, and this suggests that strategies to modulate lung inflammation can be beneficial for people with CF," the reviewers stated.

This time, the reviewers had four trials to consider in their review, including the new Canadian one, said Dr. Larry C. Lands, director of pediatric respiratory medicine at Montreal Children's Hospital, and his colleagues. The new study was the Trans-Canadian trial, in which 142 patients aged 6-18 years were randomized to ibuprofen treatment or placebo and were followed for 2 years (J. Pediatr. 2007;151:249-54). Dr. Lands was the lead investigator.

The primary end point of the trial was the annual rate of decline in percent predicted forced expiratory volume in 1 second (FEV_1). Dr. Lands and his colleagues found no statistically significant difference in decline of FEV_1, although they did find apparent benefit to ibuprofen in a number of secondary end points.

In an editorial accompanying the study, Dr. Andrew Bush and Dr. Jane Davies of Royal Brompton Hospital, London, said the study authors "fail to convince us that they have shown a biologically likely benefit," they said. The study was underpowered

and failed to demonstrate a difference in its primary end point, the editorial's authors added (J. Pediatr. 2007;151:228-30).

Of the four trials analyzed in the Cochrane review, Dr. Lands and his colleagues relied mostly on the data from the Trans-Canadian trial and a 4-year trial with a similar design, which had 85 patients (N. Engl. J. Med. 1995;332:848-54). A third trial involved the use of piroxicam and could not really be compared, and the fourth trial was a dose-finding study (Cochrane Database Syst. Rev. 2007[Epub doi:10.1002/14651858.CD001505]).

Both of the trials on which the reviewers relied used twice-daily ibuprofen doses of 20-30 mg/kg a day, up to a maximum of 1,600 mg. The doses were adjusted to produce a peak plasma concentration of 50-100 mcg/mL, because ibuprofen may actually be proinflammatory at levels below that, Dr. Lands and his colleagues said.

The Trans-Canadian trial's researchers found no statistically significant difference in the annual rate of decline in percent-predicted FEV_1, but they did find a trend. The average annual rate of decline was 1.49% in the ibuprofen-treated patients, and 2.69% in the placebo-treated patients.

The other study on which the Cochrane review focused showed a significant difference in annual FEV_1 decline: an average percent-predicted decline of 2.17% for ibuprofen, compared with a 3.6% decline for placebo. Combining the trial data showed a difference in average decline of 1.20% in favor of ibuprofen, a difference that was "moderately" statistically significant, the reviewers said.

The second trial also demonstrated that the ibuprofen benefit was more pronounced in patients who were younger than 13 years. The average annual decline in percent-predicted FEV_1 in the younger patients was 1.49% for ibuprofen and 4.20% for placebo. In the older patients, the average annual decline was 3.13% for ibuprofen and 2.77% for placebo.

Both trials found an ibuprofen treatment benefit for forced vital capacity (FVC). The Trans-Canadian trial showed an average annual decline in percent-predicted FVC of 0.07% for ibuprofen, compared with 1.62% for placebo. The other trial demonstrated a mean annual FVC decline of 2.01% for ibuprofen, compared with 3% for placebo.

In general, the two studies showed no significant difference in intravenous antibiotics use between ibuprofen and placebo groups. However, the second study's researchers found that, in the fourth year of treatment, the percentage of patients using ibuprofen who needed intravenous antibiotic treatment was 29%, compared with 37% in the placebo group.

Dr. Lands and his colleagues noted that in the second study, a greater percentage of patients in the ibuprofen group had needed intravenous antibiotics before the study began (27%), and their rate of use remained relatively unchanged.

THE AVERAGE ANNUAL RATE OF DECLINE WAS 1.49% IN THE IBUPROFEN-TREATED PATIENTS AND 2.69% IN THE PLACEBO-TREATED PATIENTS.

Hospital admissions for respiratory exacerbations and hospital admissions in general didn't differ between the ibuprofen and placebo groups. However, the piroxicam study suggested ibuprofen treatment decreased the number of hospitalization days by 42%. The Trans-Canadian study showed that 70 patients in the ibuprofen group were hospitalized for a total of 248 days, while the 72 patients in the placebo group were hospitalized for 561 total days.

The four trials reviewed did not explicitly report data on major hemorrhage or allergic reactions. However, in all the trials, a greater proportion of ibuprofen-treated patients reported a decrease in abdominal pain and stool frequency. Neither group showed a difference in the presence of occult blood in the stool. ■

FYI

Adult Immunization Schedule Update

The Centers for Disease Control and Prevention released its 2007-2008 Adult Immunization Schedule in English in October, and expects to release it in Spanish later this year. To download the schedule or to obtain information on other vaccine-related topics, contact the CDC by visiting www.cdc.gov/vaccines/recs/schedules/adult-schedule.htm.

Preventive Service Recommendations

The Agency for Healthcare Research and Quality has published its 2007 "Guide to Clinical Preventive Services." It contains recommendations on 58 clinical preventive services that were made by the U.S. Preventive Services Task Force from 2001 to 2006 that can help clinicians determine which preventive medical tests are necessary for patients. To obtain copies of the guide, call 800-358-9295 or send an e-mail to ahrqpubs@ahrq.hhs.gov.

Pulmonary Perspectives

The Perils of Pseudo-Compounded Medications

Physicians have a major responsibility to ensure the safety of their patients' medications.

Recently, there has been a significant rise in public concern about drug safety. The concern encompasses FDA-approved pharmaceuticals and, even more troubling, imported drugs that are not well regulated. Many less heavily publicized pharmaceuticals are mass-manufactured drugs prepared in the United States that masquerade as traditionally compounded products. These drugs should be of great concern to clinicians and their patients. Physicians who specialize in respiratory diseases need to be especially vigilant, because many of these medications are used in nebulizers. Hormones and dermatologic preparations are other commonly "compounded" drugs.

The age-old practice of compounding drugs is when a pharmacist prepares a pharmaceutical by mixing ingredients, in response to a physician's prescription, to meet the needs of a specific patient. This is an invaluable service rendered for patients who require special drug combinations that are not commercially available, people who may be allergic to inactive ingredients in FDA-approved products, and children who may need flavors added to encourage them to take a medicine.

However, so-called "compounding pharmacies" exist that are engaged in the mass manufacturing of drugs under the guise of a traditional compounding practice. They produce millions of doses of their product in anticipation of a physician's order. The problems with this practice are that the drugs are not FDA-approved and that the FDA does not regulate the manufacturing process. Pharmacists running these operations take the position that compounding is supposed to be regulated at a state level by state pharmacy boards. Yet the FDA can intervene, and has intervened, when it can prove that there is mass manufacturing taking place.

There are several consequences of the compounding practice that are very troubling. States do not have the resources necessary to inspect compounding pharmacies, and some states have only a handful of inspectors to cover the entire state, which allows for some extremely shoddy practices by the "compounders." The raw materials used for their preparations are not FDA-approved, so it is impossible to determine their provenance, purity, or potency. Manufacturing processes are often not sterile, and preparations have been unevenly potent, causing the overtreatment or undertreatment of patients. In addition, plastic ampules of drugs for nebulizer formulations have paper labels with ink that can leach into the solutions, unlike FDA-approved preparations where the labeling is embossed in the plastic, to avoid this problem. There are well-documented instances of each of these problems where patient injury has resulted.

The FDA states that it knows of 200 adverse events involving 71 compounded products since 1990 (US FDA. Consumer Update, May 3, 2007: The Special Risks of Pharmacy Compounding. Available at www.fda.gov/consumer/updates/compounding053107.html), despite the fact that pharmacies are not required to report adverse events like commercial drug manufacturers. Examples of these adverse events include: (1) three patients who died of infections acquired by cardioplegic solutions during open-heart surgery; (2) two patients whose eyes were damaged by infected solutions during cataract surgery; (3) three patients who died of Serratia-infested injectable beclomethasone; and (4) 18 cases of *Serratia marcescens* in several states due to contaminated magnesium sulfate IV solution (Sunenshine et al. *Clin Infect Dis* 2007; 45:527). A particularly egregious and instructive case involved a Kansas City, MO, pharmacy that prepared 4,000 L of respiratory solutions to be used for nebulization and distributed them nationwide to 18,000 patients. These medications were contaminated with *Pseudomonas cepacia*. The pharmacy never notified doctors or patients about the contamination and destroyed critical records. It was ultimately disciplined by the state Board of Pharmacy, which, in Missouri, is more aggressive and effective than in many other jurisdictions (Missouri Board of Pharmacy Takes Action Against Kansas City Company [press release]. Jefferson City, MO, March 10, 2003).

In some instances, "compounding" manufacturers claim that they have generic versions of drugs, which are, in fact, not FDA-approved; therefore, they are not available in this country. An example is the medication budesonide, for use in nebulizers. The only approved form of this drug is Pulmicort Respules (AstraZeneca; Wilmington, DE), a special formulation that is aqueous-soluble. Budesonide is notoriously insoluble in water, so these "compounders" dissolve it in high concentrations of ethanol. Their preparations are then sold and administered to patients, including children, via nebulization. Ethanol is very irritating to the lungs and, in these cases, is being given to patients who already have inflammatory lung disease.

These drugs are marketed in ways that are deceptive to physicians and patients. In one marketing method, suppliers of durable medical equipment link up with the mass manufacturers. When a patient submits an order for a nebulizer, the supplier will offer a free nebulizer if the patient gets his medication from the supplier, which is delivered to his home. The supplier bills the insurance company or Medicare, and the medication is virtually cost-free. This sounds like a good deal, except for the fact that the medications are unreliable and can even be dangerous.

Physician approval for compounded drugs may also be obtained deceptively. The request for approval is faxed to the physician from the pharmacy; however, frequently, the form does not make it clear that a substitution is being requested. In addition, the form does not indicate that these drugs are not FDA-approved, and that many other combination drugs offered are available in FDA-approved versions. A major example of this is the albuterol/ipatropium combination, available as DuoNeb (Dey, L.P.; Napa, CA), which seems to be a favorite of mass manufacturers. Another example is budesonide, as previously noted. Physicians may be unaware that they are signing off on drugs that are not FDA-approved and of inferior quality. One could speculate that the "compounding" manufacturers and distributors are counting on physicians being too busy to scrutinize what they are signing.

PHYSICIANS WHO SPECIALIZE IN RESPIRATORY DISEASES NEED TO BE ESPECIALLY VIGILANT, BECAUSE MANY OF THESE MEDICATIONS ARE USED IN NEBULIZERS.

Is there any peril to physicians if a patient becomes ill as a result of taking such a medicine? In fact, it is the physician who becomes liable for the adverse events. Once the physician approves the medication, the pharmacist preparing the drug is no longer at risk for liability.

One might ask what is being done to protect patients and physicians from these unscrupulous pharmacies. The FDA issued a Compliance Policy Guide in 2002 outlining the circumstances that would trigger its intervention. To the extent the FDA can intervene with limited resources, it has intervened. This list also is instructive in identifying the behaviors of these pharmacies that put them in conflict with proper manufacturing practices. These behaviors include:

- Compounding drug products that have been pulled from the market because they were found to be unsafe or ineffective.
- Compounding drugs that are essentially copies of a commercially available drug.
- Compounding drugs in advance of receiving prescriptions, except in very limited quantities relating to the amounts of drugs previously compounded based on valid prescriptions.
- Compounding finished drugs from bulk active ingredients that are not components of FDA-approved drugs, without an FDA-sanctioned, investigational new drug application.
- Receiving, storing, or using drug substances without first obtaining written assurance from the supplier that each lot of the drug substance has been made in an FDA-registered facility.
- Failing to conform to applicable state law regulating the practice of pharmacy (US FDA. Consumer Update, May 3, 2007: The Special Risks of Pharmacy Compounding. Available at www.fda.gov/consumer/updates/compounding053107.html).

Compunding has been a major concern for patient advocacy groups and specialty societies. Allergy and Asthma Network/Mothers of Asthmatics took the lead in forming a coalition of patient groups, specialty societies, and pharmaceutical companies to address this problem. The coalition, called Consumer Health Alliance for Safe Medications, has helped raise public awareness through lobbying, education programs, and media events. It has brought the problem to the attention of the Centers for Medicare and Medicaid Services and, as a result, Medicare is no longer providing reimbursement for medications not approved by the FDA. Attempts to secure federal legislation are ongoing.

Consumers can protect themselves by ensuring that the medication they get from pharmacies or durable medical equipment companies is FDA-approved. They should check with their physicians and pharmacies.

Physicians have a major responsibility to ensure the safety of their patients' medications. They must read all their faxes for prescriptions before they sign them. They also need to read the fine print to ensure that the concentrations of combination medications are the same as in their commercial preparations. They must insist that the medications they prescribe are dispensed as written and their patients' medications are FDA-approved. They need to be aware that, if their patients are not doing well using their nebulized medication, the problem could be that the medication was obtained from a compounding pharmacy and underpotent.

Physicians must insist that whatever medication their patients inhale, ingest, or apply, it conforms to the highest possible manufacturing standards and that "compounded" products are not surreptitiously substituted for FDA-approved medications. ■

Dr. Gene L. Colice, FCCP
Editor,
Pulmonary Perspectives

Dr. Daniel Ein
Chief, Division of Allergy
and Clinical Professor of Medicine
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Washington, DC

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PRESIDENT'S REPORT

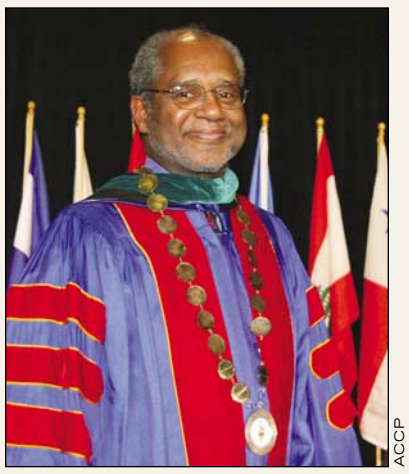
Welcoming a New ACCP President

Dr. Alvin V. Thomas, Jr., FCCP, assumed the role of ACCP President during Convocation ceremonies at CHEST 2007.

Dr. Thomas is Associate Professor of Internal Medicine and Pulmonary Medicine and Chief of the Pulmonary Division at Howard University in Washington, DC.

He also serves as Graduate Faculty Representative on the Howard University Board of Trustees.

Dr. Thomas has been a member



ACCP

DR. ALVIN V. THOMAS, JR., FCCP

of the ACCP since 1973 and has been active in ACCP leadership, serving on several committees, including the Continuing Education Committee.

In addition, he was a Trustee of The CHEST Foundation (1999-2003), Chair of the ACCP Scientific Program and Abstracts Committee (2000-2001), and Scientific Program Chair for CHEST 2002.

His scholarly and research interests are in pulmonary vascular disease, particularly sickle cell acute chest syndrome and pulmonary hypertension in sickle cell disease.

We asked Dr. Thomas to briefly discuss some of his plans for the upcoming presidential year.

Q. What would you like to accomplish as President of the ACCP?

I intend to focus on the issue of disparities in health and health care, particularly among minorities and the poor and underserved in this country.

These are issues that are being increasingly discussed at a national level and in the general medical literature, but there has been minimal discussion of the issues in the pulmonary, critical care, and sleep literature.

My goal is to have the issue of disparities be a part of the "cultural fabric" of the College. The issue is relevant to all ACCP activities—education, research, and advocacy.

An additional goal is to have the ACCP (and The CHEST Foundation) become national thought leaders on disparity issues in pulmonary, critical care, and sleep medicine.

Q. What do you consider to be the greatest strengths of the ACCP and how will you build upon them?

By far, the greatest strengths of the College are the members and the staff (including the executive

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management). Since my very first time of involvement with the College, I have been totally impressed with the professionalism, dedication to excellence, motivation, and willingness to help that the entire staff (without exception) has shown.

My experience has been the same with the College's executive management, including the Executive Vice President and CEO, who sets the expectations and standards for the organization.

Over the years, as I have been increasingly involved in leadership activities within the ACCP, I have experienced the same attitude of dedication and commitment by members of the College.

Whenever a specific task needs to be completed, without exception, a member (or members) steps forward to volunteer his or her time and talent, despite a full plate of commitments at home base.

I have never worked with any other organization where people so willingly volunteer their time and talent.

This culture of service to the College, by staff and members, is what makes the ACCP so special and so successful. It is truly a "family."

Q. What is the greatest challenge facing the College and how will you address it?

The challenges that the College faces are several, including the issue of standards of quality medical care for the profession and the evaluation of physician medical care and pay for performance.

However, among the most urgent is the nature and role of medical education in our discipline, including adherence to increasingly stringent continuing medical education guidelines by the Accreditation Council for Continuing Medical Education (ACCME).

Associated with this issue is the nature of our changing relationship with the pharmaceutical industry.

These two later issues have and will have enormous impact on the nature and financial support of the College's educational efforts.

The College's Education Committee has developed and continues to develop innovative approaches to many of the ACCME guidelines. Several are being implemented at CHEST 2007. College staff and physician leadership are actively involved with efforts to respond to ACCME guidelines on pharmaceutical support.

I will be discussing these and other issues in future editions of our *CHEST Physician* newspaper.

Q. And finally, what is your charge to the members and new Fellows of the ACCP?

My charge to members and new FCCPs is to get involved in the activities of the College. Join a NetWork of your choice. Participate in the many educational opportunities offered by the College (including board reviews and educational courses), and attend annual CHEST meetings, including CHEST 2008 in Philadelphia.

The ACCP is a dynamic and responsive organization. Make us part of your professional life. ■

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EDUCATION INSIGHTS

Publishing and Promoting Evidence-Based Guidelines

BY DR. SANDRA ZELMAN LEWIS
ACCP Assistant Vice President, Health and Science Policy

The Health and Science Policy (HSP) Committee and ACCP staff have had a prolific 2007 and anticipate more publications in 2008. Three evidence-based clinical practice guidelines were published in the current year, along with a policy paper. Next year will see the publication of several more guidelines. In addition, the ACCP had a chance to promote our guideline development work at an international conference this past summer.

In May, *Pulmonary Rehabilitation: Joint ACCP/AACVPR Evidence-Based Guidelines* was published as a supplement to *CHEST*. Dr. Andrew Reis, FCCP, chaired the panel of nine authors and one methodologist. The importance of pulmonary rehabilitation in the care and management of patients with COPD has grown as the scientific literature on this topic has expanded, leading to the need for a set of guidelines.

Under the supervision of the guideline chair, Dr. Lewis Rubin, FCCP, "Pulmonary Arterial Hypertension Medical Therapies Update" was published in June's issue of *CHEST* to incorporate important recent evidence and revise the recommendations and medical treatment algorithm from the 2004 supplement, *Diagnosis and Management of Pulmonary Arterial Hypertension: ACCP Evidence-Based Clinical Practice Guidelines.*

The *Diagnosis and Management of Lung Cancer: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (2nd Edition)* was published in September as a supplement to *CHEST*. Dr. Michael Alberts, FCCP, and Dr. Gene Colice, FCCP, led a panel of nearly 100 multidisciplinary lung cancer experts. The Evidence-Based Practice Center at Duke University performed the literature review and analyses to guide the development of the recommendations in five treatment areas. In addition, five areas that received the *de novo* review in the first edition were updated with new literature and revised recommendations. Three new chapters address pathology, integrative oncology, and bronchioloalveolar lung cancer. These guidelines received considerable media attention in both the lay and medical press. Dr. Robert Milroy penned an editorial that was published in the same month's issue of *CHEST:*

"The ACCP lung cancer guideline project group most certainly have achieved their goal to produce updated, evidence-based, clinically relevant guidelines for physicians and other healthcare providers managing the care of patients with lung cancer and those who are at risk for lung cancer. There is no doubt that publication of the Second Edition of these lung cancer guidelines … represents an important addition to the lung cancer guidelines armamentarium, and will result in further improvements in the processes of care, treatments, and outcomes for lung cancer patients, not only in the United States but throughout the rest of the world."

Continuing in the tradition of publicizing HSP processes and advancements, "ACCP Evidence-Based Guideline Development: A

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Successful and Transparent Approach Addressing Conflict of Interest, Funding, and Patient-Centered Recommendations" was published online in May and in print in September in *CHEST*. This paper proffers the key HSP processes from topic submission to dissemination of the final products. This ACCP guideline development methodology, forever a work-in-progress, received praise in an accompanying editorial by Dr. Carolyn Clancy, the Director of the Agency for Healthcare Research and Quality (AHRQ), and Jean Slutsky, PA, MSPH, the Director, Center for Outcomes and Evidence, AHRQ.

Dr. Ian Nathanson, FCCP, and Dr. Sandra Zelman Lewis attended the Guidelines International Network (GIN) meeting in Toronto, Ontario, Canada, in August. This was the first time this international group met on the North American continent. Dr. Nathanson displayed a poster and addressed questions from a thoughtful audience about an implementation project at the Nemours Clinic utilizing the ACCP grading system. Dr. Lewis presented a session on the ACCP guideline development process, which was well received by this international community of evidence-based medicine scholars.

Looking forward, HSP is anticipating the publication of several guidelines in 2008, including the following:

- 8th edition of the Antithrombotic and Thrombolytic Guidelines
- A new topic, Management of Dyspnea in Advanced Lung Disease and Congestive Heart Failure
- The first nonclinical guideline topic, Continuing Medical Education

For more information about the HSP projects and products, contact Dr. Sandra Zelman Lewis at slewis@chestnet.org. ■

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NEWS FROM THE COLLEGE

NETWORKS

Of Surveys, Stents, and CMS Challenges

Affiliate

The goal of the Affiliate NetWork is to provide an avenue for presentation at national meetings, leadership opportunities within the ACCP, and direction for both education and career development. ACCP Affiliate membership is available to all physicians-in-training who have been accepted to, or are currently participating in, a fellowship, residency, or equivalent program of clinical cardiopulmonary medicine, surgery, critical care, sleep, or one of the closely related specialties. Membership dues are discounted to allow all interested physicians-in-training to participate.

At CHEST 2007, there were 146 scheduled case presentations, following a record 367 submissions. All presentations are moderated by an Affiliate member and feature a guest expert in the particular area of focus. Also at CHEST 2007, two Affiliate members were given the opportunity to participate in "Stump the Stars," a session conducted in a clinical/radiologic/pathologic case report format. Dr. Julian Williams from Coney Island Hospital in Brooklyn, NY, and Dr. Nazar Almakki from Howard University Hospital in Washington, DC, were selected to present interesting, unknown cases to esteemed professors Dr. Marvin Schwarz, FCCP, and Dr. Jeffrey Myers, FCCP.

Ideas for NetWork activities and Web page content (www.chestnet.org/networks/affiliate/) are welcomed and can be e-mailed to networks@chestnet.org.

Airways Disorders

In mid-2006, the US Food Drug Administration (FDA) posted a "black-box" warning on the use of long-acting beta-agonists (LABAs), based on data that suggested there could be an increase in mortality when certain populations receive this medication. The Airways Disorders NetWork embarked on a project to obtain information about what US physicians understand about the potential risks and benefits of LABA use for their patients, as well as to understand the LABA-prescribing patterns across various groups of physicians. The NetWork recently designed and distributed a survey to more than 8,000 practicing physicians. The working group, chaired by Dr. Jill Karpel, FCCP, plans to prepare an abstract and distribute the findings in the coming months. For more information about the Airways Disorders NetWork, send an e-mail to networks@chestnet.org.

Interventional Chest/Diagnostic Procedures

Central airway obstruction is a devastating process caused by both malignant and benign etiologies. The development of self-expanding metallic airway stents (SEMS) made this therapy available to a wider population of pulmonologists.

Coincident with the advancing technology, multiple publications revealed the significant and immediate benefits for many patients. The results were inspiring, but complications always exist. There has been a history of concern about the risk-to-benefit ratio of SEMS in patients with benign airways disease. Removal of long-standing metallic stents is known to be problematic and associated with serious complica-

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tions. These issues led the FDA to publish an advisory on the use of metallic stents in patients with "benign airway disorders" in 2005 (US Food and Drug Administration Web site. Available at: www.fda.gov/cdrh/safety/072905-tracheal.html. Accessed September 18, 2007).

The FDA advisory recommended that physicians always review the indications, warnings, and precautions for appropriate patient selection. Metallic tracheal stents should be used in patients with benign airway disorders only after thoroughly exploring all other options. Bridging therapy with metallic tracheal stents is not recommended, because removal of the metallic stent can result in serious complications. If a metallic tracheal stent is the only option for a patient, insertion should be done by a physician who is experienced in metallic stent placement and removal. If removal is necessary, the procedure should be performed by a physician who is experienced in removing metallic stents.

The ACCP Interventional Chest/Diagnostic Procedures NetWork Steering Committee recently prepared and published an editorial addressing this issue. The editorial, "Airway Stenting for Patients With Benign Airway Disease and the FDA Advisory: A Call for Restraint," was published in *CHEST* (2007; 132:1105) and fully supports the FDA advisory. The NetWork Steering Committee believes that all physicians who utilize endoluminal airway therapies should be familiar with the ACCP and the American Thoracic Society/European Respiratory Society consensus statements (see "Recommended Reading" below).

Unfortunately, there are no consensus suggestions for the use of SEMS in patients with benign central airway obstruction.

Dr. Mark E. Lund, FCCP
Interventional Chest/Diagnostic Procedures Steering Committee Member

Recommended Reading

1. Ernst A, Silvestri GA, Johnstone D, et al. Interventional pulmonary procedures: guidelines from the American College of Chest Physicians. *Chest* 2003; 123:1693-1717
2. Bolliger CT, Mathur PN, Beamis JF, et al. ERS/ATS statement on interventional pulmonology. European Respiratory Society/American Thoracic Society. *Eur Respir J* 2002; 19:356-373

Pulmonary Physiology, Function, and Rehabilitation

On June 27, 2007, the Centers for Medicare & Medicaid Services announced that it did not have the statutory authority to cover pulmonary rehabilitation programs. One month later, the US House of Representatives' Committee on Ways and Means and Committee on Energy and Commerce recommended Medicare legislation that does not include HR 552, a bill that would formally establish pulmonary and cardiac rehabilitation as a Medicare benefit. The Senate has S 329, a bill identical to the House bill HR 522, which has gained significant sponsorship from at least 33 members of the Senate. At the time of this writing, a final decision regarding the bill is still pending. Members of the NetWork, along with members of the Government Relations Committee, have been working with members of other organizations, including the American Thoracic Society, the American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR), and NAMDRC, to attempt to gain further support for this Senate bill.

The Pulmonary Rehabilitation: Joint ACCP/AACVPR Evidence-Based Clinical Practice Guidelines were published in the May 2007 issue of *CHEST* (2007; 131:4S). These guidelines were a project originating with the NetWork and include an update of the 1997 guidelines, as well as new guidelines on the topics of exercise maintenance following pulmonary rehabilitation, nutrition, supplemental oxygen therapy, and diseases other than COPD. These guidelines further strengthen the scientific basis for the effectiveness of pulmonary rehabilitation. ■

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NEWS FROM THE COLLEGE

ACCP Fellow Is Named New Dean of LSU Medical School

Dr. Steve Nelson, FCCP, has been appointed the new Dean of the School of Medicine of the Louisiana State University Health Sciences Center in New Orleans by Center Chancellor Dr. Larry Hollier.

Joining the faculty in 1984, Dr. Nelson was named as Professor of Medicine in 1994 and the John H. Seabury Professor of Medicine in 1995. Since 2000, Dr. Nelson has served as Director of one of only five National Institutes of Health-awarded comprehensive alcohol research centers in the nation. He served as Vice-Chair of Research in the Department of Medicine and was named Chief of the Section of Pulmonary Medicine in 2005.

DR. STEVE NELSON, FCCP

Dr. Nelson's major clinical interests include lung immunology, pneumonia, adult cystic fibrosis, and sepsis. His research interests are primarily directed toward understanding normal pulmonary host defense mechanisms; defining how disease states undermine and disrupt these defense mechanisms; and determining the potential of biological response modifiers, including gene therapy, to provide innovative approaches to the prevention and treatment of pulmonary infections.

Dr. Nelson received the 2006 Edward C. Rosenow III, MD, Master FCCP Honor Lecture Award from the ACCP for outstanding contributions to mentorship and training of chest physicians. He also is a reviewer for *CHEST* and several other medical journals. ■

Product of the Month: PCCU

In the two new second editions of *Best of PCCU*, you will find some of the best critical care and pulmonary articles from recent PCCU volumes to provide you with current information and management strategies related to the care of critically ill and pulmonary patients.

PCCU
PULMONARY AND CRITICAL CARE UPDATE

The articles provide the entire critical care and pulmonary medical teams with a thorough review of information that can be used to prepare for the critical care or pulmonary subspecialty examinations or to review relevant topics in the critical care and pulmonary fields.

In the critical care and pulmonary editions, several of these lessons have been updated with new material and references, including the addition of the ACTH (Cortrosyn) stimulation test to the low systemic vascular resistance lesson in the critical care edition and the addition of the AASM scoring guidelines to the polysomnography lesson in the pulmonary edition.

Each article ends with poststudy questions, so you can test your comprehension and compare your results to the correct responses found at the end of the book.

The ACCP is certain that the current information and management strategies presented in the second updated editions of the *BEST of PCCU Critical Care* and the *Best of PCCU Pulmonary* will enhance the care you provide for your patients.

For more information and to purchase the newly updated *Best of PCCU* editions, please visit the ACCP Store online at www.chestnet.org and click on the ACCP Store icon, at the top right side of the page. ■

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2007-08

November 15 - 18, 2007
2007 Pulmonology Update: A joint meeting of the SPOI, SATS, and ACCP
Cape Town, South Africa

November 30 - December 4, 2007
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SLEEP STRATEGIES

Portable Monitoring for Sleep Apnea: An Update

The diagnosis of sleep apnea, once a relatively straightforward proposition, is getting more complicated each year.

In the past, polysomnography was the only test available for diagnosing sleep apnea. However, over the last decade, recording technology has advanced to where it is relatively easy to make high quality recordings of multiple physiologic signals simultaneously in just about any setting, including the home. The use of this technology is slowly changing the discussions about sleep apnea, if not the face of the disease quite yet.

For the last 10 years, portable testing for sleep apnea has been "just around the corner." The future may be coming soon, depending on the results of a meeting held September 12, 2007, at the headquarters of the Centers for Medicare & Medicaid Services (CMS) in Baltimore, MD.

At the present time, sleep apnea must be diagnosed in a sleep laboratory facility in order for the subsequent provision of continuous positive airway pressure (CPAP) therapy to be reimbursed by insurers.

This has always been the position of Medicare. Most private insurers institute their policies according to the large federal insurer. This means that most insurers will not pay for CPAP therapy on the basis of sleep apnea diagnosed with a portable sleep apnea monitor in a patient's home.

Over the last decade, sleep recording equipment manufacturers have developed portable sleep apnea monitors that many physicians in the sleep apnea field believe are sufficiently accurate for use, at least in some cases, in diagnosing sleep apnea outside of a sleep laboratory setting.

CMS last examined this issue in 2004. At that time, CMS asked its Medical Care Advisory Committee (MCAC) to consider adopting new rules that would allow CPAP to be paid for by Medicare and Medicaid based on a portable sleep study performed outside of a sleep laboratory facility.

At this 2004 meeting, the MCAC did not recommend approval to this requested change in CMS regulations. The MCAC did encourage those individuals in the sleep apnea field to continue to develop a higher quality of evidence showing the benefits of portable sleep apnea monitors, especially in the elderly and those who are disabled—groups of patients CMS typically serves.

Fast forward to 2007: At the request of the American Academy of Otolaryngology, CMS decided to revisit this question. The MCAC was asked to consider expanding CMS regulations to include CPAP coverage for Medicare beneficiaries when the diagnosis is based on a non-facility-based sleep study.

To analyze this topic further, the Agency for Healthcare Research and Quality commissioned a state-of-the-science review from the Evidence-Based Practice Center (EPC) at Tufts–New England Medical Center.

The work of the EPC work was completed in early 2007 and distributed to various reviewers and stakeholders for comment. Many readers interpreted the comments as giving a cautiously optimistic view of portable sleep apnea monitoring with level 3 monitors, which are capable of recording airflow, respiratory effort, pulse-oximetry, and heart rate.

On behalf of the ACCP, Dr. Richard Castriotta, FCCP (Chair, Sleep Medicine NetWork) and I (Chair, Sleep Institute) attended the CMS meeting. We prepared comments for the meeting several weeks prior to attending.

Sleep Institute
American College of Chest Physicians

Our position was similar to the position the ACCP has held since the first MCAC meeting in 2004. We stated that the ACCP was in favor of expanding non-facility-based testing with certain precautions in place to prevent misuse of the technology.

We told the MCAC, and at least 70 attendees, that "our goal is not to turn every bedroom in America into a sleep laboratory," but that thoughtful and careful use of portable sleep apnea testing may improve the availability of testing for patients with a high likelihood of obstructive sleep apnea. These patients may not have a sleep laboratory available for testing or insurance coverage for sleep laboratory services.

Our comments also stressed the importance of restricting the use of portable sleep apnea testing to physicians who are knowledgeable about sleep apnea and appropriately trained in the use of these devices. We also stressed the need for making facility-based sleep laboratories available for patients who have equivocal or nondiagnostic studies.

Others at the MCAC meeting took a similar position. The American Thoracic Society emphasized the need for more research on alternative ways of diagnosing sleep apnea and initiating therapy, stating that portable sleep apnea monitoring was promising but not completely proven. The American Academy of Otolaryngology, which initiated this request for review of current CMS policy, came out strongly in favor of portable monitoring, as did several speakers associated with various portable testing technologies or patient advocacy groups. The National Association for Medical Direction of Respiratory Care (NAMDRC) supported increasing coverage for portable monitors, as well as some needed changes to current polysomnography policy.

As was the case at the 2004 MCAC meeting, the American Academy of Sleep Medicine (AASM) presented the view that portable testing is not ready for widespread use; therefore, CMS should make no change to the current regulations. The foundation of the AASM has initiated a study examining one particular approach to portable monitoring and recommends waiting until that study is completed.

After comments were heard and a brief general discussion was held, in which the MCAC members asked questions of the speakers and the audience, the committee members voted on a series of questions about the possible role of portable sleep apnea testing developed by CMS prior to the meeting.

My impression of the MCAC deliberation was that they were interested in the *idea* of portable sleep apnea testing but had concerns about how it could be put into practice.

It was clear from their subsequent open discussions that they were impressed with a recent study published earlier this year by Mulgrew and colleagues (Mulgrew et al. *Ann Intern Med* 2007;147:157) from the University of British Columbia. The study compared clinical outcomes from a cohort of patients with rather severe sleep apnea, who were randomly assigned to either traditional in-lab diagnosis and treatment or autotitrating CPAP,

Continued on following page

AMERICAN COLLEGE OF CHEST PHYSICIANS

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This Month in *CHEST*: Editor's Picks

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

▶ **Family Satisfaction in the ICU: Differences Between Families of Survivors and Nonsurvivors.** *By Dr. R. J. Wall, et al.*

▶ **Daytime Cheyne-Stokes Respiration in Ambulatory Patients With Severe Congestive Heart Failure Is Associated With Increased Mortality.** *By Dr. T. Brack, FCCP, et al.*

▶ **Topics in Practice Management: Split-night Polysomnography.** *By Dr. N. P. Patel, et al.*

Portable Monitors in the Diagnosis of Obstructive Sleep Apnea. *By Dr. M. Ahmed, et al.*

▶ **Recent Advances in Chest Medicine: Preoperative Evaluation of the Patient With Pulmonary Disease.** *By Dr. S. R. Bapoje, et al.*

Organ Allocation in Lung Transplant. *By Dr. S. Q. Davis; and Dr. E. R. Garrity, Jr.*

▶ **Chronic Bronchitis in Women Using Solid Biomass Fuel in Rural Peshawar, Pakistan.** *By Dr T. Akhtar, et al.*

▶ **Effective Written Communication for Patients With Limited-English-Proficiency.** *By Dr. T. Oshimi*

Papers Associated With the Global Themes Issue:

▶ **Indoor Air Pollution: A Poverty-Related Cause of Mortality Among the Children of the World.** *By Dr. A. Emmelin; and Dr. S. Wall*

▶ **Socioeconomic Status and Lung Function.** *By Dr. M. J. Hegewald, FCCP; and R. O. Crapo, FCCP*

▶ **Information Technology for Health in Developing Countries.** *By Dr. F. Bukachi; and Dr. N. Pakenham-Walsh*

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following questionnaires and a portable, sleep apnea test in the home that demonstrated significant sleep apnea. Dr. Frank Ryan, the senior author of the paper, presented the results of the study to the conferees.

In the end, the voting on the portable monitoring questions was mostly in the middle of the possible range: 3s out of a range of 1 to 5, where higher scores reflect more enthusiasm for portable sleep apnea monitoring.

In my opinion, this gives the Coverage Advisory Group of CMS (the CMS group that recommends changes in coverage decisions) "room to maneuver" when deciding whether to make changes to their current coverage decision about this contentious technology.

CMS plans to announce its coverage decision in December of this year. Some industry watchers believe that the MCAC's lack of a strong "no" vote means that portable monitoring will likely be approved. It may be just as likely that CMS will await the results of two clinical trials, currently underway or being planned in the United States, that will examine clinical outcomes more fully than prior studies.

In either case, portable sleep apnea monitoring is here to stay and will almost certainly remain controversial. ■

Dr. Charles W. Atwood, Jr., FCCP
University of Pittsburgh School of Medicine
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FDA May Call for Label Changes

Cold Meds • *from page 1*

group. The week before the meeting, however, manufacturers of cough and cold products voluntarily took products with references to infants off the market, and the Consumer Healthcare Products Association (CHPA) and its member companies recommended to the FDA that the "ask a doctor" statement on the labels of these products be changed to "do not use" in children under age 2.

The committees called for industry to conduct efficacy studies in children over age 2, not just pharmacokinetic studies.

Among the other recommendations made by the committees were that statements that a product was "pediatrician recommended," or similar statements on the front panel of these products be eliminated and that all ingredients, with their concentrations and strengths, be listed on the front panel.

The committees also unanimously agreed that clinical studies in children were needed to establish efficacy, with clinical end points that are the symptoms for which the products are marketed.

The ingredients under review are decongestants, first-generation antihistamines, antitussives, and expectorants, which are regulated by a monograph, under which they are classified as "generally recognized as safe and effective," based on advisory committee recommendations from 30 years ago.

After the meeting concluded, Dr. John Jenkins, director of the FDA's office of new drugs, said that because these products are regulated under a monograph, making formal changes to the recommended uses and labeling of these products involves a rule-making process, with a comment period, a laborious process that can take from 1 to several years to finalize.

Therefore, the agency will review the recommendations and comments of the committees, and will issue interim recommendations to the public about the safe and effective use of these products "in the near future," he said.

The recommendations would not necessarily lead to a ban on these products, but might result in labeling that says they should not be used in children under age 6, for example, Dr. Jenkins said.

The review of these products was prompted by a Citizen Petition filed last year, by Dr. Joshua Sharfstein, a pediatrician and Baltimore City Health Commissioner, with chiefs of pediatric departments at Baltimore medical institutions, which referred to reports of serious injuries and deaths associated with the use of these products in young children.

In the petition, they said that although these products were considered safe by parents and pediatricians, their misuse has been associated with serious adverse effects in children under age 6.

The petition requested that the agency issue a statement to the public that OTC antitussive, expectorant, nasal decongestant, and antihistamine cough and cold products have not been shown to be safe and effective in treating coughs and colds in children under age 6, and that the labeling be changed to state that they should not be used for treating coughs and colds in children under age 6.

The petition also asked the agency to notify manufacturers of these products that marketing with labels that used terms such as "infant" or "baby" with pictures of children under age 6 is not supported by scientific evidence.

Dr. Sharfstein said at the meeting that while there was no evidence that the products were safe and effective in children aged 6 to under 12, they felt that there was more urgency regarding the use of these products in children younger than 6 years of age.

An FDA review of serious adverse events reported in association with cough and cold products in children younger than age 6 years concluded that the use of these products has been associated with serious adverse events, including deaths in this age group, often related to overdoses that were accidental, intentional, or a result of a medication error. Most involved products that contained multiple ingredients.

After the meeting ended, Dr. Sharfstein said in an interview that "finally, these products were held to a standard of science, and they didn't pass."

A statement issued by CHPA said that the industry would work with the FDA to design "appropriate pediatric clinical efficacy studies." ■

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Asthma Survey Casts Doubt on Hygiene Hypothesis

BY FRAN LOWRY
Elsevier Global Medical News

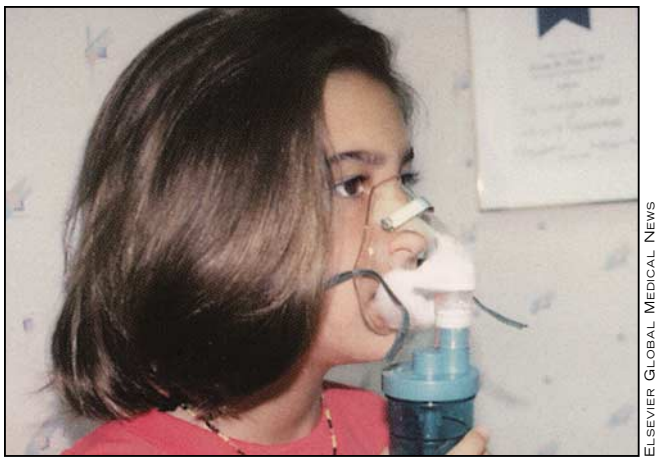
Preventing common respiratory and gastrointestinal tract illnesses in young children does not make them more prone to develop allergic disorders when they reach their teenage years, Danish researchers reported.

The finding casts doubt on the hygiene hypothesis, first proposed in 1989, which states that a lack of early childhood exposure to infectious agents increases the susceptibility to allergic diseases later in life.

The researchers, led by Dr. Teija Dunder of the University of Oulu (Finland), surveyed a group of adolescents who had participated in a randomized infection prevention trial 12 years earlier.

That trial, also conducted by Dr. Dunder and her colleagues, found that efforts to reduce common infections in child day care centers resulted in 24% fewer prescriptions for antibiotics and 16% fewer days with symptoms of infections among the children randomized to the infection prevention arm.

In this follow-up study, which was undertaken to eevaluate the effect of the researchers' success in reducing those infections on the later development of allergic diseases, the rates of asthma, allergic rhinitis, and atopic dermatitis were the same in the group that received the hygiene intervention and the group that did not (Arch. Pediatr. Adolesc. Med. 2007; 161:972-7).



ELSEVIER GLOBAL MEDICAL NEWS

Child using a steroid inhaler. Teens with fewer infections in early childhood were no more likely to develop asthma.

They surveyed 481 teens from the hygiene intervention group, who had markedly fewer infections, and 447 controls. Asthma was diagnosed in 48 teens (10%) in the intervention group and in 46 teens (10%) in the control group.

Also, there were no differences seen in the numbers of teens who had developed allergic rhinitis or atopic dermatitis as diagnosed by a physician, or who had reported asthma, allergic rhinitis, or atopic dermatitis symptoms, the researchers wrote.

The respondents from both groups were similar with regard to their family history of atopic diseases, duration of breastfeeding, and number of siblings.

The mean ages at which the children were diagnosed with asthma were similar: 4 years in the intervention group and 4.3 years in the control group. They also were similar at the onset of atopic dermatitis (0.8 years in the intervention group and 0.9 years in the control group) and the onset of seasonal allergic rhinitis (3.8 years in the intervention group and 3.7 years in the control group).

The researchers said that "the magnitude of the reduction in infections and the duration of the intervention in our randomized hygiene intervention trial should have led to an increase in asthma rates if the hygiene hypothesis were to apply to common childhood infections. … As our intervention lasted 15 months, we believe that this duration would have been long enough to show at least some effect on the occurrence of asthma, but this was not seen."

They added that in a previous observational study, attendance at day care during the first 6 months of life protected against the development of asthma, as did the presence of one or more older siblings at home (N. Engl. J. Med. 2000;343:538-43).■

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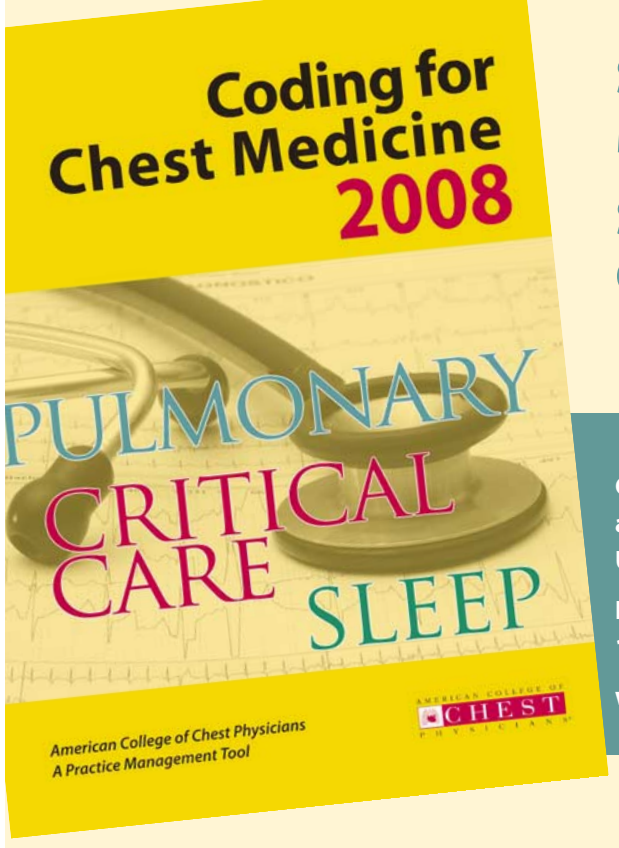

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