

Biomarkers Show Promise

Nitric Oxide • from page 1

in children, Dr. Debley said. In contrast, eNO is a noninvasive biomarker of lower airway eosinophilic airway inflammation.

Levels of eNO are higher in asthma patients, compared with nonasthmatic patients, and levels decrease after corticosteroid treatment. The excess nitric oxide seen in asthma patients is primarily caused by an increase in the expression of the enzyme inducible nitric oxide synthase by airway epithelial cells.

In addition to helping diagnose asthma, eNO can be useful in predicting steroid responsiveness, said Dr. Debley. "It can also be used as a marker of compliance, to determine who is taking their medications."

Exhaled nitric oxide does have its limitations, as eNO levels do not always correlate with National Institutes of Health classifications of asthma severity, and eNO is not always associated with measures of airflow obstruction. Therefore, eNO should not be used by itself to assess asthma severity, but rather as a complement to spirometry.

Dr. Debley pointed out that eNO is used at his institution, and most children aged 6 years and older can perform the procedure. "Many 4- and 5-year-olds are also able to complete the test," he said. "It is easier

and more fun to perform than spirometry, and the kids don't seem to mind it."

Another promising future tool is the measurement of biomarkers in exhaled breath condensate (EBC), which is collected by cooling or freezing exhaled breath. It is then analyzed for the presence of inflammatory mediators, cytokines, and other proteins, which have been detected in EBC.

EBC is another area of interest, although the field is still in its infancy, compared with eNO, Dr. Debley said. In patients with asthma, leukotriene and interleukin-4 levels in EBC are reported to be higher, compared with those in healthy individuals. However, published literature has been inconsistent with regard to levels of leukotriene and other mediators in EBC between asthma and healthy patients, and in some cases, attempts to detect leukotrienes in EBC using commercially available assays have been unsuccessful.

Dr. Debley is currently conducting a longitudinal National Institutes of Health-funded study at Seattle Children's Hospital that is evaluating the use of eNO in wheezy toddlers and infants to identify which children with recurrent wheezing will respond to asthma medications and go on to develop persistent asthma. ■

Dr. LeRoy Graham, FCCP, comments:

Exhaled nitric oxide increasingly appears to be a valuable measure of airway inflammation. Clearly, limits in the reliability of symptom reports and technical limitations in both the performance and interpretation of spirometry, particularly in young children, suggest it is indeed a time for the reliable measurement of airway inflammation. Such measurement may well prove invaluable in assessing both disease severity and the response to anti-inflammatory therapy. The heterogeneity of the inflammatory response among individuals and the clinical evidence of varied response to various anti-inflammatory agents support the measurement of exhaled nitric oxide as a superbly discriminate tool in clinical management.

Flu Vaccine Called a 'Stopgap'

Avian Flu • from page 1

randomized, placebo-controlled phase I/II trial conducted by the National Institute of Allergy and Infectious Diseases in 452 adults aged 18-64 years.

Among the 103 patients who received the 90-mcg two-dose regimen, 45% developed an immune response expected to reduce the risk of contracting influenza—defined as at least a fourfold increase in the hemagglutinin inhibition immunogenicity titer 28 days after the injection. Although the remaining subjects did not reach this level of immunogenicity, data on other influenza vaccines "suggest that less than optimal antibody levels may still have the potential to help reduce disease severity and influenza-related hospitalizations and deaths," according to the FDA.

Dose-related injection-site reactions were the most common side effects, with 85% of those receiving 90-mcg doses having at least one such reaction. Systemic events were less frequent, with about 40% developing headache and 30% developing malaise.

These data were reviewed at a meeting

of the FDA's Vaccines and Related Biological Products Advisory Committee in February, during which the panel agreed that there were sufficient data to support the safety and effectiveness of the investigational vaccine during an avian flu pandemic or in situations of potential high-risk exposure. Studies of the vaccine in pediatric and geriatric populations are ongoing.

At the panel meeting, panelists and FDA officials referred to the vaccine as an "interim" or "stopgap" vaccine.

Whereas the dose of the vaccine is relatively high, compared with seasonal influenza vaccines, research is being done to develop a better vaccine, Dr. Baylor said during the press briefing. No one can predict what strains will be the cause of a pandemic if one occurs, but "we also know that from very preliminary and limited data, if the pandemic is an H5N1-like virus, this vaccine might provide some cross-protection," he said.

Information on U.S. pandemic flu preparedness is at www.pandemicflu.gov. ■

Infections Likely Concomitant

MRSA • from page 1

vaccine for the 2006-2007 season. Radiologic information, available for all 10 patients, demonstrated unilobar infiltrates in 3 and multilobar infiltrates in 7.

Particularly notable in the 10 cases was the short period between any respiratory symptom onset and either death or recovery of MRSA from the patient: Respiratory symptoms began a median of 3 days (range 2-6 days) before collection of specimens that grew MRSA. Of the six patients who died, the median period from respiratory symptom onset to death was 3.5 days (range 2-25 days), and four of the six died within 4 days of symptom onset.

These short durations suggest that the influenza virus and the MRSA infections probably occurred concomitantly, rather than the more classically described biphasic clinical course of CAP symptoms following flu illness, the CDC noted. ■

Dr. Doreen Addrizzo-Harris, FCCP, comments:

These cases highlight the importance of identifying patients with risk factors for Staphylococcus aureus, especially those with severe pneumonia during flu season. It is important to obtain a history of prior MRSA infections either in the patient or in a close contact.

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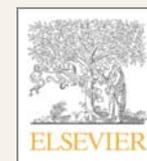
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GUEST EDITORIAL

TB Screening and Prevention Are Pediatric Issues

We shouldn't let the declining rate of tuberculosis in the United States lull us into missing opportunities for identifying and treating children who have latent infection or are at risk for the disease.

Happily, the tuberculosis rate in 2006 was the lowest recorded since national reporting began in 1953. The 13,767 reported cases last year, or 4.6 per 100,000 population, represents a 3.2% decline from the rate in 2005. However, the rate of decline in TB has slowed since 2000. From 1993 through 2000, the average annual percentage decline in TB incidence was 7.3% per year. Since 2000, that rate has been just 3.8% per year, according to the latest data from the Centers for Disease Control and Prevention (MMWR 2007;56:245-50).

Trends among children have been similar. In 2005, the latest year for which age-specific data are available, there were 863 cases among children aged 0-14 years, a rate of 1.4 per 100,000. Among those aged 15-24 years, the 1,542 cases represented a rate of 3.7 per 100,000. Both rates were slightly lower than in 2004 (1.6 and 3.8 per 100,000, respectively), and significantly less than the 2.9 and 5.0 rates seen in 1993. But, as with the entire population, the decline has slowed among children, too.

Although the highest TB rates in the United States are still among ethnic minorities in large urban areas, the disease is not limited to those populations. The proportion of TB cases among foreign-born individuals has increased each year since 1993; such cases now account for about one-fourth of all TB cases. In 2006, 56% of those were from just five countries: Mexico, the Philippines, Vietnam, India, and China.

Most of the foreign-born individuals in the United States who progress from latent TB infection to TB disease became

infected while abroad. These cases represent immigrants, internationally adopted children from countries with high TB rates, and children exposed during foreign travel.

For physicians in the United States who provide primary care for children, identifying children who are at risk for TB is critical. In 2004, the American Academy of Pediatrics (AAP), the American Thoracic Society (ATS), and the CDC issued a comprehensive set of guidelines we all should follow, entitled "Targeted Tuberculin Skin Testing and Treatment of Latent Tuberculosis Infection in Children and Adolescents" (Pediatrics 2004;114:1175).

The three organizations' Pediatric Tuberculosis Collaborative Group recommended four questions to be asked about every patient:

- ▶ Was the child born outside the United States? (If yes, ask in which country. If the child was born in Africa, Asia, Latin America, or Eastern Europe, place a tuberculin skin test [TST]).
- ▶ Has the child traveled outside the United States? (If yes, ask where. If the child stayed with friends or family in any of the above-mentioned areas for a week or longer, place a TST test.)
- ▶ Has the child been exposed to anyone with TB disease? (If yes, a series of questions should follow to determine if the person had TB or latent disease, when the exposure occurred, and the nature of the contact. If exposure is confirmed, place a TST test. If the child has been in contact with someone who has TB disease, notify local health authorities and consult with an infectious disease specialist.)
- ▶ Does the child have close contact with a person who has a positive TB skin test? (Ask the same follow-up questions as in the preceding.)

The only TB test now recommended is the intradermal injection of 5 tuberculin units of purified protein derivative from

Mycobacterium tuberculosis administered by the Mantoux technique.

The AAP/ATC/CDC guidelines define positive TST results in children and adolescents using three cutoff levels for the transverse diameter of the reaction: less than or equal to 5 mm, 10 mm, and 15 mm.

The 5-mm cutoff is used for children at high risk, including those in close contact with TB cases, those with positive findings on chest radiograph, or those with clinical evidence of TB disease.

The 10-mm cutoff is for those at moderate risk, including children less than 4 years of age, those with concomitant medical conditions, or those who were born in a country with a high TB prevalence.

The highest cutoff, 15 mm, is reserved for children aged 4 and older with no known risk factors.

Most physicians are familiar with the correct technique for TB testing, but fewer have had experience in interpreting the results. Guidelines suggest that the reaction must be read by a trained health care provider at 48-72 hours after placement. Interpretation should not be left to the parents. In fact, your office practice personnel may not be experienced either and, therefore, it may not be appropriate to place and read TST in the practice setting.

Evidence suggests that interpretation of TST even by health care providers may be fraught with error. In one study of 107 health care providers including 52 practicing pediatricians, 33 pediatric house officers, and 10 pediatric academicians, 93% identified a known tuberculin converter as tuberculin negative, based on their interpretation of the degree of induration. When presented with an induration of 15 mm, the group's median reading of its size was only 10 mm (Chest 1998;113:1175-7).

Live virus vaccines—measles, mumps, rubella, and varicella—can suppress the TST response. Also be aware that in patients treated with systemic corticosteroids or inpatients who have been

treated with the newer tumor necrosis factor antagonists, a false-negative test result can occur, while prior receipt of the BCG vaccine—given at birth in many TB-endemic countries—can produce a false-positive result. However, most children with a history of the BCG vaccine and a positive skin test result have latent tuberculosis. In these instances, consultation with your local infectious disease specialist will be helpful.

Perhaps most important, the identification of children with latent TB infection (LTBI) or tuberculosis disease (who rarely if ever are at risk to transmit TB when less than 10 years of age) is a sentinel event that should provoke an aggressive investigation targeting adult close contacts.

Here in Kansas City, we recently had a TB outbreak in a day care center, mostly among children born in the United States, which was related to their exposure to a foreign-born adult residing in the day care home. Epidemiologic details are being investigated; a combination of problems caused by language barrier, difficulty tracing contacts, and poor record keeping in an unlicensed facility complicate the process.

Treatment of LTBI and tuberculosis disease generally should involve the help of your local TB expert. While the proportion of TB cases resistant to both isoniazid and rifampin remained at 1.2% from 2004 to 2005, and isoniazid remains the standard drug for LTBI treatment, we can't be complacent.

In 2005, foreign-born individuals accounted for 81.5% of the 124 multidrug-resistant TB cases, and, according to the CDC, that percentage continues to grow. Treatment in such cases is more complicated, involving several drugs that are not generally used in the treatment of TB, and follow-up is important. ■

DR. JACKSON is chief of pediatric infectious diseases at Children's Mercy Hospital, Kansas City, and professor of pediatrics at the University of Missouri-Kansas City.



BY DR. MARY ANNE JACKSON

LETTERS

NPI Web Site Has Problems

Unfortunately, the article on the National Provider Identifier sounds more like a sales pitch for the Centers for Medicare and Medicaid Services than a balanced report ("National Provider Identifier Sign-Up Deadline Is May 23," March 2007, p. 2).

The NPI Web site, application process, and customer support are mediocre at best. Among the Web site's many problems are the following:

- ▶ There is a lack of clarity regarding which fields are optional and which are required.
- ▶ The application requires a Social Security number, yet there is no statement as to the security of the online process.
- ▶ It is unclear how many medical licenses need to be reported. There is no place for additional state licenses.
- ▶ You need to print every individual page for a hard copy. The CMS does not provide

a PDF format option for download, printing, and submission.

- ▶ The last statement notes, "I agree to keep the NPPES [National Plan and Provider Enumeration System] updated with any changes to data listed on this application form within 30 days of the effective date of the change." This places the submitting physician in an awkward position, because it is unrealistic to expect future updates of every piece of information within 30 days.
- ▶ The CMS does not state how the information will be shared and disseminated.

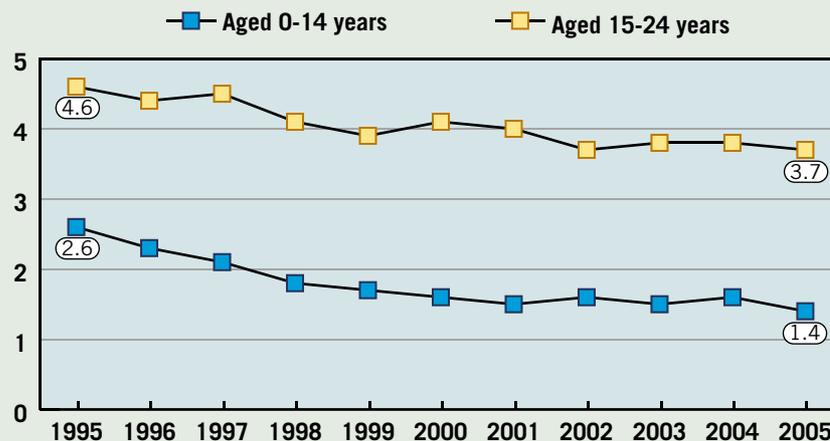
For all of the hype and importance of this major national initiative, you would think the online submission process would be a top-notch, elegant system. Quite the contrary.

Dr. Chris Patricoski
Anchorage, Alaska

DATA WATCH

U.S. Tuberculosis Rates Declining in the Young

(per 100,000 population)



Source: Centers for Disease Control and Prevention

TB Rates at All-Time Low, but Decline Has Slowed

Foreign-born individuals and racial/ethnic minority populations continue to be disproportionately affected.

BY MIRIAM E. TUCKER
Elsevier Global Medical News

The U.S. tuberculosis rate hit an all-time low in 2006, but the rate of decline has been slowing while drug-resistant cases continue to pose a threat, the Centers for Disease Control and Prevention said.

There were 13,767 TB cases reported in 2006, a rate of 4.6 per 100,000 population. That number represents a 3.2% decline from the 2005 rate, the lowest rate recorded since reporting began in 1953. However, the rate of decline has slowed recently: The average annual percentage decline in the TB incidence rate was 7.3% per year during 1993-2000, but the rate of decline dropped to just 3.8% per year during 2000-2006, the CDC said (MMWR 2007;56:245-50).

Foreign-born individuals and racial/ethnic minority populations continue to be

disproportionately affected by TB in the United States. In 2006, the TB rate among individuals born outside the United States was 9.5 times that of those born in the country, while the rates among blacks, Asians, and Hispanics were 8.4, 21.2, and 7.6 times higher than among whites, respectively.

The proportion of TB cases among foreign-born individuals has increased each year since 1993. In 2006, 56% of those cases were from just five countries: Mexico, the Philippines, Vietnam, India, and China. Most of the foreign-born individuals in the United States who progress from latent TB infection to TB disease initially became infected while abroad. Thus, "if the global TB pandemic remains unmitigated, eliminating TB in the United States will be increasingly difficult," the CDC said.

A total of 124 cases of multidrug-resistant TB (MDR TB) were reported in 2005, the most recent year for which complete

drug susceptibility data are available. The proportion of MDR TB cases—defined as resistance to at least two first-line therapies, isoniazid and rifampin—remained constant at 1.2% from 2004 to 2005. In 2005, foreign-born individuals accounted for 81.5% of the 124 MDR TB cases, the CDC said.

The number of extensively drug-resistant TB (XDR TB) cases didn't change substantially from 1993-1999 to 2000-2006, but the characteristics of cases shifted in parallel with the changing epidemiology of TB in general and of MDR TB in particular. During 1993-1999, 32 reported cases met the criteria for XDR TB (resistance to isoniazid and rifampin, and to any second-line fluoroquinolone and at least one injectable drug), compared with 17 during 2000-2006 (MMWR 2007;56:250-3).

As with the overall TB rates, the overall numbers declined while the proportion among foreign-born individuals rose, from 39% in the first period to 76% in the second. Other changes in XDR TB epidemiology included a decrease in the proportion of cases among HIV-infected

individuals and an increase in the proportion of patients who are Asian, they said.

Effective treatment of MDR TB requires administration for 18-24 months of 4-6 drugs to which the infecting organism is susceptible, including multiple second-line drugs. Beginning in the 1980s, the use of second-line drugs increased substantially as physicians and TB control programs treated growing numbers of MDR TB cases. Increased use of these drugs resulted in MDR TB strains with extensive resistance to both first- and second-line drugs, the CDC said.

Progress has been made on several new drugs in the past year, with human testing currently being conducted with six agents in five different drug classes. The CDC's TB Trials Consortium, in collaboration with the Global Alliance for TB Drug Development, has completed two preliminary trials with moxifloxacin. Those studies are expected to lay the groundwork for a trial of a treatment-shortening regimen for TB. The consortium is also nearing completion of a trial of a 3-month rifapentine-based treatment for latent TB infection. ■

Use Caution in Diagnosing Asthma in Black Women

BY DOUG BRUNK
Elsevier Global Medical News

SAN DIEGO — Asthma may be overdiagnosed in many obese African American women who present with dyspnea, results from a small pilot study suggest.

The finding is important because the incidence rates of asthma and obesity have increased over the last 20 years, especially among African American women, Dr. Daniel Waggoner reported during a poster session at the annual meeting of the American Academy of Allergy, Asthma, and Immunology.

"If somebody gives you a very good history of asthma symptoms, sometimes it's a little bit easier to make the diagnosis," Dr. Waggoner, of the division of allergy and immunology at Creighton University, Omaha, Neb., said in an interview. "But if somebody comes in with rather nebulous symptoms, it's very important to get some objective testing to make a diagnosis [of asthma], because many medications [for it] have side effects, and they're expensive."

He and his associates evaluated 18 African American women aged 19-50 years who live in or near Omaha and who had a physician diagnosis of asthma for at least 3 months. All had a body mass index (kg/m²) of 30 or greater, an FEV₁ (forced expiratory volume in 1 second) value of 65% or greater, and symptoms of dyspnea.

Over the course of three office visits, the researchers performed the following measurements in each patient to verify the asthma diagnosis: spirometry with postbronchodilator values, exhaled nitric oxide (eNO), methacholine challenges, and full-body plethysmography. Each of the four tests was considered a positive criterion for the diagnosis of asthma.

Dr. Waggoner said that of the 18 patients, 8 (44%) had a positive methacholine challenge, 1 (6%) had demonstrated airway reversibility on spirometry, 10 (56%) had elevated eNO, and 6 (33%) had airflow obstruction as measured by plethysmography.

No patient met all four criteria for the diagnosis of asthma, and only 39% met two or more of the criteria.

"Only one patient did not have an albuterol prescription," Dr. Waggoner added. "I was really surprised that we didn't have at least a handful more [who] demonstrated reversibility with albuterol or a bronchodilator."

In their poster, the researchers concluded that in African American women who present with dyspnea, "an eNO and methacholine challenge should be considered to confirm or refute the diagnosis of asthma. Full-body plethysmography may provide clues to etiologies of dyspnea other than asthma, [such as physiologic air trapping] associated with obesity."

The study was funded by the State of Nebraska Tobacco Settlement. ■



In African American women with dyspnea, consider an eNO and methacholine challenge.
DR. WAGGONER

Twice as Many Women as Men Are Hospitalized With Asthma

BY DOUG BRUNK
Elsevier Global Medical News

SAN DIEGO — More women with asthma seek emergency care and are hospitalized for asthma-related symptoms than men, yet the markers of disease severity among hospitalized patients are similar between genders, results from a single-center study demonstrated.

One reason for the paradox may have to do with the fact that more women in the study had health insurance compared with men, Dr. Indu Warriar said during a poster session at the annual meeting of the American Academy of Allergy, Asthma, and Immunology.

"Men tend to be underinsured," Dr. Warriar, of the division of allergy and immunology at Wayne State University in Detroit, said in an interview. "That seems to be the case in any chronic disease. Men do the hit and miss thing. [They say] 'I'm feeling really sick; I'm going to the emergency department now' and come back. Women tend to be more proactive about their health care, and their insurance status seems to point to that."

Dr. Warriar and her associate, Dr. Alan Baptist, compared the demographic characteristics and markers of asthma disease severity from the medical records of 13,370 asthma patients who presented to the emergency department at Wayne State University (group 1) and 2,888 asthma patients who were admitted to the university's hospital (group 2) between Jan. 11, 1999, and Dec. 31, 2004. The median household income among patients in both groups was \$25,619.

Of the patients in group 1, 90% were black. The median age of women in the group was 40 years, while the median age of men was

33 years. More than half of the patients (58%) were women. A total of 53% of women vs. 58% of men had private insurance; 12% of women vs. 9% of men had Medicare; 16% of women vs. 7% of men had Medicaid, and 18% of women vs. 26% of men had no health insurance coverage.

Of the patients in group 2, 87% were black. The median age of women in the group was 47 years, while the median age of men was

46 years. More than two-thirds of patients (70%) were women. A total of 33% of women vs. 34% of men had private insurance; 22% of women vs. 21% of men had Medicare; 34% of women vs. 22% of men had Medicaid, and 11% of women vs. 23% of men had no health insurance coverage.

Women in group 2 had significantly longer hospital stays, compared with men (median of 3 days vs. 2 days, respectively), but markers of disease severity were not different between women and men, including the percentage who were admitted to the ICU (6.8% vs. 8.5%, respectively), the percentage who required intubation (4.5% vs. 5.2%, respectively), and the percentage who expired (0.4% vs. 0.9%, respectively).

"We need to figure out why women tend to get admitted more and address that issue," Dr. Warriar said. "Maybe it's because they have smaller airways or because their airway caliber is smaller. Maybe they're more symptomatic because of that."

Another implication from the study, she said, is a need to convince younger men with asthma to be more proactive about their medical care. "The older men get, the more they tend to come to the doctor. We need to target young men and see how we can make asthma care better [for them]." ■



Physicians need to convince younger men with asthma to be more proactive about their medical care.
DR. WARRIAR

Resistant Influenza B Virus As Virulent As Wild Type

A Japanese study shows a 'low but appreciable' rate of emergence of mutant influenza B strains.

BY MARY ANN MOON
Elsevier Global Medical News

Influenza B viruses with partial resistance to neuraminidase inhibitors have emerged during routine antiviral therapy and appear to be transmitted from person to person within communities as well as within families.

That finding emerged from a Japanese study.

So far, the rate of emergence of resistant influenza B viruses appears to be "low but appreciable" at 1.4%, and the mutant viruses appear to be as virulent as wild-type viruses, Dr. Shuji Hatakeyama and associates wrote.

In an editorial comment accompanying this report, Dr. Anne Moscona and Dr. Jennifer McKimm-Breschkin said that until now, the medical community has been somewhat complacent about resistant influenza B because little resistance of these viruses has been documented. Moreover, the few resistant strains that have emerged in animal and in vitro studies appeared to have compromised infectivity and transmissibility.

"This has led to the belief that significant transmission is unlikely to occur among humans," they wrote.

Now the findings of Dr. Hatakeyama and associates make it "strikingly clear" that resistant strains are already circulating among humans and that they induce infection with the same duration of symptoms, level of viral shedding, and clinical outcome as nonresistant strains.

These findings mean that "it is no longer possible to be confident that resistant strains will have little effect on epidemic or pandemic influenza," wrote the editorialists.

Dr. Hatakeyama of the University of Tokyo and associates tracked patterns of resistance and transmission during an influenza B outbreak in the winter of 2004-2005 that caused a widespread epidemic in Japan, the country with the highest use in

the world of neuraminidase inhibitors such as zanamivir and oseltamivir.

Pharyngeal or nasal swabs were obtained before and after antiviral therapy from one sample of 74 infected children and from another sample of 356 children (median age 5 years) and 66 adults (median age 34 years) with influenza B.

Seven subjects (1.7%) had strains with partial resistance to zanamivir, oseltamivir, or both, even though they had never been treated with antivirals.

There was evidence that identical strains of the virus had been transmitted among

'IT IS NO LONGER POSSIBLE TO BE CONFIDENT THAT RESISTANT STRAINS WILL HAVE LITTLE EFFECT ON EPIDEMIC OR PANDEMIC INFLUENZA.'

family members and among members of the same community (JAMA 2007;297:1435-42).

There were no differences in symptoms, clinical course, or viral shedding between subjects infected with resistant strains of the virus and those who had wild-type virus. This result indicated that these mutant viruses "do not lose virulence even though they have evolved to a status that is less sensitive to the drug," they noted.

In their editorial comment, Dr. Moscona of Weill Medical College of Cornell University, New York, and Dr. McKimm-Breschkin of Molecular and Health Technologies, Parkville, Australia, said, "Contrary to what had been hoped until now, some resistant variants are vigorous pathogens.

"The presence of low-level resistance sets the stage for selective pressure for development of high-level resistance," they noted (JAMA 2007;297:1492-3). ■

Flu Pandemic Fears Spur New Antivirals, Diagnostic Tests

BY BRUCE K. DIXON
Elsevier Global Medical News

KEYSTONE, COLO. — Health care professionals should prepare for a worldwide influenza outbreak that could be more devastating than the Spanish flu pandemic of 1918, which infected one-third of the world's population and killed half a million Americans, Dr. Gwen Huitt said at a meeting on allergy/clinical immunology, asthma, and pulmonary medicine.

At the locus of concern is H5N1, or avian influenza A, a strain against which the world population has no immunity, and which is resistant to established antivirals, said Dr. Huitt, director of infection control at the National Jewish Medical and Research Center, Denver.

"This new strain is highly pathogenic for humans, and although it remains largely confined to bird populations and has not been found to be highly transmissible in its current form, many experts believe H5N1 is only one small mutation away from being easily transmissible from person to person," she said at the meeting, sponsored by the National Jewish Medical and Research Center.

Dr. Huitt presented a depressing worst case scenario for the United States: An estimated 10 million hospitalizations, 2 million deaths, overwhelmed hospitals and public health services, the closing of schools for 3 months, workers unable to leave home, assigned grocery shopping days, and a devastated economy that could take years to recover.

And symptoms may be more severe than they were in the Spanish flu pandemic. "With H5N1, you start out with fever, cough, and myalgias, and ophthalmitis is commonly associated with this virus. Then we see rapid progression to pneumonia within 3-4 days, and the patient goes directly into adult respiratory distress syndrome, similar to [severe acute respiratory syndrome]," Dr. Huitt explained, adding that encephalitis may be an additional sequela.

At the end of 2006, the World Health Organization reported a total of 261 cases of H5N1 influenza with 157 deaths, which places the death rate from Avian flu at 60%. The death rate from ordinary seasonal flu is 3%.

Adding to the woes of a pandemic is the threat of methicillin-resistant *Staphylococcus aureus* (MRSA), Dr. Huitt said. "You survive the pandemic and then you get a severe MRSA pneumonia, which is known to come in and set up shop after our normal season. What happens then?"

The federal Department of Health and Human Services would activate the same National Response Plan used for terrorism, major disasters, and other emergencies so that transportation, communications, emergency management, mass care, housing, and human services are put to their best use.

Unfortunately, during a national

quarantine and the distribution of surgical masks to prevent droplet inoculation, Dr. Huitt remarked, the horse already will be out of the barn.

"All this would happen after the fact; we will already be behind the eight ball, because those who are in the early stages of infection are asymptomatic yet are shedding huge amounts of the virus," Dr. Huitt said, noting that H5N1 has an incubation period of up to 5 days.

A happier, less likely scenario has the coming pandemic resembling the 1958 Hong Kong flu, which killed about 34,000 Americans. However, experience with H5N1 suggests that we should be ready for the worst, Dr. Huitt warned. She urged all health care professionals to remain alert and follow strict infection control procedures, especially frequent hand washing.

"H5N1 can live on hard surfaces for up to 2 days," she said. "Transfer of the virus has been documented after it's been on a person's hands for 24 hours after that person touched a contaminated surface."

Not all the news is bleak. In partnership with the Centers for Disease Control and Prevention, the University of Colorado at Boulder is developing a diagnostic test called the Flu Chip, which can determine the genetic signatures of specific influenza strains from patient samples within hours.

"The Flu Chip has been almost 100% accurate in identifying the different types of influenza A, and that would be a huge advantage in a pandemic," Dr. Huitt said.

A promising DNA vaccine has profited about 80% immunogenicity in monkeys. The first trial in humans was launched in December. And because DNA vaccine manufacturing does not rely on the use of chicken eggs, it can be produced more quickly.

H5N1 is resistant to the antivirals amantadine and rimantadine, but Dr. Huitt discussed a new drug on the horizon called peramivir, a neuraminidase inhibitor that may have utility against H5N1.

In preclinical studies, avian influenza has been shown to be sensitive to peramivir, leading researchers to believe that in the proper formulation, the drug may be effective against the virus in humans. Dr. Huitt said the drug currently is available only in intramuscular and intravenous preparations, which would make large-scale administration impractical. "But critically ill people could be given this drug very quickly."

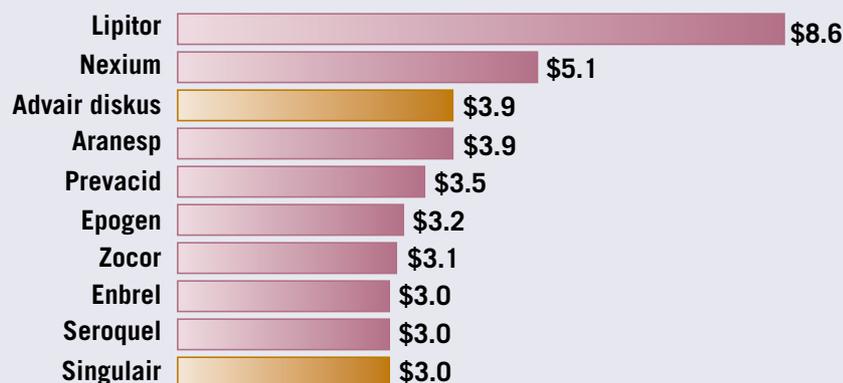
Dr. Huitt urged all health care practitioners to make frequent visits to WHO and U.S. government Web sites, including www.pandemicflu.gov and www.cdc.gov/flu. Once in the CDC site, click on "information for specific groups," then "health professionals."

Dr. Huitt is on the speakers' bureau and has consulted for Novartis, maker of a pandemic influenza vaccine, and is on the speakers' bureau for Hill-Rom Inc. ■

DATA WATCH

Top 10 Prescriptions by U.S. Sales

(in billions of dollars)



Source: 2006 data, IMS Health Inc.

Vaccine Cut Pneumonia Admissions by 39% in Children

BY MARY ANN MOON
Elsevier Global Medical News

The pneumococcal vaccine introduced in 2000 lowered pneumonia admission rates by nearly 40% within 4 years for children under the age of 2 years—the population specifically targeted by the vaccine program, reported Dr. Carlos G. Grijalva of Vanderbilt University, Nashville, Tenn., and his associates.

In 2004 there were approximately 41,000 fewer such hospital admissions than would have been expected without the vaccine, the researchers reported.

The seven-valent pneumococcal conjugate vaccine (PCV7) evidently conferred significant “herd immunity” as well, because pneumonia admissions for adults aged 18-39 years also fell significantly, by 26%. Most young adults were not vaccinated, but because this age group includes the parents of young children, it is likely that they benefited from reduced exposure

to pneumococci because their children were vaccinated, the investigators said.

Dr. Grijalva and his associates assessed the effects of the national PCV7 program because until now, the vaccine’s effect “on the burden of pneumonia in the general population has not been established.” They compared data collected in the Centers for Disease Control and Prevention’s Nationwide Inpatient Sample from the pre-PCV7 era (1997-1999) with that collected after the vaccine program was introduced. In 2004, this survey sampled an estimated 38,000 admissions to 1,004 hospitals in 37 states.

Rates of admission for all-cause pneumonia declined in children younger than age 2 years by 506 per 100,000 patients, a 39% reduction. Similarly, rates of admission for pneumococcal pneumonia dropped by 65% in this age group and by 75% in children aged 2-4 years, the investigators said (Lancet 2007;369:1179-86).

At the same time, rates of admission for

all-cause pneumonia declined by 26% and rates of admission for pneumococcal pneumonia declined by 30% in young adults. Historically, this age group has the highest proportion of pneumonia cases attributed to pneumococcal organisms, they noted.

No significant declines in either all-cause or pneumococcal pneumonia were noted in older adults.

These findings indicate that *S. pneumoniae* was a major contributor to the burden of childhood pneumonia in the United States before the vaccine became available, they said.

The PCV7 vaccine “could have a large effect in less developed countries, where pneumococcal diseases cause not only substantial morbidity and health-care costs but also high childhood mortality,” Dr. Grijalva and his associates noted.

In an editorial comment accompanying this report, Dr. Orin S. Levine of Johns Hopkins Bloomberg School of Public Health, Baltimore, and Dr. Felicity T. Cutts

of La Londe les Maures, Provence, France, said the study findings show that “the preventable burden of pneumococcal disease is far higher than that estimated solely on the basis of statistics of invasive disease.”

“These findings are important because, in cost-effectiveness studies done before the launch of the vaccine, the estimated economic benefits of vaccination were limited to health impacts in vaccinated children. The reduction in all-cause pneumonia in vaccinated and unvaccinated populations illustrates again how the value of the vaccine has far exceeded expectations,” they noted (Lancet 2007;369:1144-45).

This study was funded in part by CDC agreements and a grant from the Agency for Healthcare Research and Quality. One of the investigators, Kathryn M. Edwards, has received grant support from Sanofi Pasteur, MedImmune, VaxGen, and Merck; she also has consulting agreements with MedImmune and Wyeth. All other authors declared no conflicts of interest. ■

Study Finds Link Between Obesity And Asthma Severity in Children

BY DOUG BRUNK
Elsevier Global Medical News

SAN DIEGO — Inner-city obese children with moderate to severe asthma require significantly more hospitalizations, more visits to the emergency department, and more steroid bursts than do their nonobese counterparts, Dr. Fatima Hassan reported during a poster session at the annual meeting of the American Academy of Allergy, Asthma, and Immunology.

The findings add to mounting evidence that suggests an association between obesity and the severity and frequency of asthma symptoms in children.

“It’s not only the asthma symptoms that are affected by obesity,” Dr. Fatima Hassan, a third-year pediatrics resident at Woodhull Medical and Mental Health Center, New York, said in an interview. “There are also effects on the general health profile, [such as children] who become depressed by their asthma symptoms and severity, and by the number of days they have to stay in the hospital.”

She and her associates at Children’s Hospital of Michigan in Detroit reviewed the medical charts of 109 inner-city children aged 6-18 years who were being followed in a high-risk clinic for people with moderate to severe asthma. They divided the children into obese and nonobese groups and compared their outcomes over a 2-year period. Obesity was defined as having a body mass index greater than or equal to the 95th percentile as determined by National Health and Nutrition Examination Survey

(NHANES) I age- and gender-specific data.

Of the 109 children, 43 were obese and 66 were not. Children in the obese group required significantly more hospitalizations than did children in the nonobese group (71 vs. 30, respectively), as well as more visits to the emergency department (194 vs. 30, respectively), and more steroid bursts (168 vs. 50, respectively).

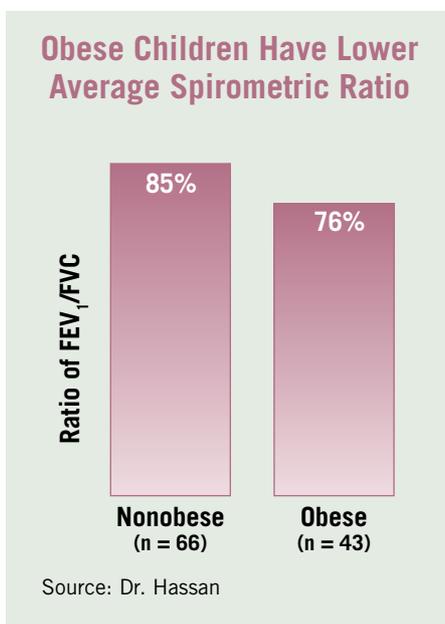
Obese children had a significantly lower average spirometric ratio of forced expiratory volume in 1 second (FEV₁) to forced vital capacity (FVC), compared with their nonobese counterparts (76% vs. 85%, respectively), but their average FEV₁ values were not statistically different from that of the nonobese children (83% vs. 87%, respectively). That discrepancy may have to do with other confounding factors such as obstructive sleep apnea and gastroesophageal reflux disease, they wrote.

Dr. Hassan noted that the prevalence of obesity among the study population was 39%, which is about twice as high as the prevalence in the general pediatric population, which ranges from 16% to 20%.

She acknowledged that advising obese children with asthma to lose weight can be tricky. “Some parents don’t believe that the children are obese and don’t see it as a problem,” Dr. Hassan said. Other parents “are really receptive when they see that the child is having problems.”

One limitation of the study was that it did not include children with the mild persistent form of asthma. The study was funded by the Michigan Department of Community Health. ■

Dr. LeRoy Graham, FCCP, comments: *Obesity is now well recognized as an important comorbid condition in childhood asthma. The current study suggests obesity is also related to physiologic severity in inner-city children with asthma. This is an important finding in a population characterized by disparate morbidity and mortality attributable to asthma. Clearly, additional study and the development of multidisciplinary disease management paradigms are sorely needed in this population. Previous assumptions that suggest that most of the disparity relates merely to nonadherence and lower socioeconomic status are no longer acceptable.*



Program’s Savings Pay For CF Screening

BY JONATHAN GARDNER
Elsevier Global Medical News

The United Kingdom’s new cystic fibrosis screening program for newborns can avert enough treatment costs to pay for itself, according to an analysis of treatment costs.

Compared with CF patients diagnosed clinically, newborns diagnosed through a measurement of immunoreactive trypsin on a dried blood spot were significantly less expensive to treat. Based on the analysis, the researchers estimate that a screening program would have cost slightly less than \$3 million in 2002 if it had been in place across the entire United Kingdom. The researchers estimate a mean drug-cost savings of \$3.4 million and a median of \$947,032 (Lancet 2007;369:1187-95).

“The argument that to wait until patients present with symptoms is potentially more cost effective than to diagnose early and presymptomatically, thereby saving the money that would otherwise have been spent on prophylactic and preventative treatment, does not hold true,” wrote Erika J. Sims, Ph.D., of the health economics group at the University of East Anglia, Norwich, England, and her colleagues.

In an accompanying editorial, Dr. Bridget Wilcken and Dr. Kevin Gaskin, of the University of Sydney, wrote that the analysis should buttress

earlier findings that screening for cystic fibrosis is cost effective.

The researchers analyzed treatment and cost data from 53 specialized centers and clinics contained in the U.K. Cystic Fibrosis Database.

Patients were divided into groups based on whether they were identified by screening within 2 months of birth or by clinical indications, with those presenting based on meconium ileus or family history excluded.

The researchers calculated the costs of long-term therapeutics and intravenous antibiotics, and extrapolated the costs of a Scottish screening program in place since 2002 across the entire United Kingdom, recalculating to U.S. dollars. They identified 184 patients diagnosed through screenings (53% homozygous for delta F508) and 950 clinically diagnosed (56% homozygous). From ages 1 to 9 years, the median treatment costs for those mixed phenotypes identified by screening were \$352 (mean \$7,228) a year, compared with median treatment costs for those clinically diagnosed of \$2,442 (mean \$12,008) a year.

For those homozygous patients, median treatment costs at age 1-9 years for those identified through screening were \$2,090 (mean \$6,302) a year, compared with \$2,516 (mean \$12,981) a year for those diagnosed clinically. ■

Pulmonary Perspectives

Timeliness of Care in Lung Cancer

Future research should seek to identify patient characteristics associated with more timely care.

Timeliness of care is one of six vital dimensions of health-care quality identified by the Institute of Medicine in their 2001 report entitled "Crossing the Quality Chasm" (Institute of Medicine. Washington, DC: National Academy Press, 2001). In lung cancer, delays in diagnosis and treatment potentially contribute to emotional distress in patients and their family members and may lead to missed opportunities for cure or effective palliation.

Expert consensus-based guidelines published by the British Thoracic Society recommend that patients with suspected lung cancer be evaluated by a respiratory specialist within 2 to 7 days, that results of diagnostic tests be communicated to patients within 2 weeks, and that treatment be initiated within 2 weeks (chemotherapy and curative radiotherapy) to 8 weeks (surgical resection) of diagnosis (BTS. *Thorax* 1998; 53:S1).

Performance measures developed by the

RAND Corporation, also using expert consensus-based methods, specify that a diagnosis should be established within 2 weeks of presentation, and that treatment should be initiated within 6 weeks of diagnosis (Quality of Care for Oncologic Conditions and HIV. RAND 2000).

Available evidence suggests that the timeliness of care in current lung cancer practice often falls short of these targets.

Most studies of timeliness of care in lung cancer have been performed in Europe and Japan. Two of these studies, both performed in Northern Europe, reported a median delay of approximately 3 weeks between the onset of symptoms and contact with a general practitioner (Koyi et al. *Lung Cancer* 2002; 35:53; Dische et al. *Thorax* 1996; 51:1262). The results of these studies should be interpreted with caution, however, because of the possibility of recall bias.

The time interval between first contact with the health-care system and diagnosis has been examined, and most often it was reported that the median time to diagnosis was between 2 and 6 weeks, although time to diagnosis was over 12 weeks in one study from Sweden (Mansson and Bengtsson. *Scand J Prim Health Care* 1994; 12:39).

Others have examined the time interval between first contact with the health-care system and initial treatment, or the time interval between hospitalization and initial treatment. Most reported a median time between first contact and treatment of approximately 3 months, although median time to treatment was as short as 5 weeks in a study that described a rapid access investigation service in the United Kingdom (Laroche et al. *Thorax* 1998; 53:445). Median time between hospitalization and treatment ranged from 3 weeks to 3 months.

Few published studies have attempted to identify predictors of more timely care.

While several reported that age was not

associated with delays in diagnosis or treatment, one small study (n=83) found that patients younger than age 45 were less likely to seek evaluation within 3 months of the onset of symptoms (Bourke et al. *Chest* 1992; 102:1723). No study, to my knowledge, has exam-

ined the relationship between the timeliness of care and other patient factors (eg, race/ethnicity, comorbidities, etc) or institutional characteristics.

Only a few studies have examined the relationship between timely care and survival, and the results of these studies have been mixed.

Two studies from Japan reported worse survival in patients who experienced longer delays after suspicious nodules were detected by lung cancer screening. In one study, median survival was approximately 35 months for patients with diagnostic delays less than 4 months, compared with 20 months for patients with longer delays ($p<0.05$) (Kanashiki et al. *Oncol Rep* 2003; 10:649).

Likewise, another study found that, after adjusting for age, gender, histology, stage, and treatment, the hazard of death was twice as high in patients who had a 1-year delay in diagnosis because the radiographic abnormality was seen only in retrospect (hazard ratio [HR] 2.2, 95% CI 1.4 to 2.8) (Kashiwabara et al. *Lung Cancer* 2003; 40:67). These studies are limited by small sample sizes, arbitrary cut points for defining diagnostic delays, and the possibility of lead time bias, as the authors did not specify the point in time from which survival was measured.

Another uncontrolled study from Scotland examined the effect of delay on tumor growth, an intermediate outcome (O'Rourke and Edwards. *Clin Oncol* 2000; 12:141). The median time between a

diagnostic CT scan and a follow-up CT scan for radiotherapy planning was 54 days (range 18 to 131 days). During this time interval, median tumor cross-sectional diameter increased by 19% (range 0 to 373%).

Several studies of patients with surgically treated lung cancer (Billing and Wells. *Thorax* 1996; 51:903; Aragonese et al. *Lung Cancer* 2002; 36:59; Pita-Fernandez et al. *J Clin Epidemiol* 2003; 56:820) reported no association between more timely care and survival.

In the only non-European study, Quarterman et al (*J Thorac Cardiovasc Surg* 2003; 125:108) retrospectively reviewed the records of 83 veterans who underwent resection for stage I or stage II non-small cell lung cancer (NSCLC) at the San Francisco VA Hospital between 1989 and 1999. Median time from initial contact to surgical treatment was 82 days. In an unadjusted analysis, there was no difference in the hazard of death for patients who did and did not receive surgery within 90 days (HR 1.06, 95% CI 0.87 to 1.3).

The results of this small study, like those of the other three studies in surgical patients, are potentially confounded by the exclusion of patients who did not undergo surgery. It is possible that some patients were systematically excluded because they had long delays in care and, therefore, had disease that progressed to a stage not treatable by surgery. These studies did not control fully for other factors that might confound the relationship between timeliness and survival, such as tumor size and the presence of symptoms at the time of presentation.

One study from Sweden examined timeliness of care and survival in a relatively large (n=466) and heterogeneous sample of patients with NSCLC (Myrdal et al. *Thorax* 2004; 59:45). Median time from symptom onset to treatment was 4.6 months (interquartile range [IQR] 3.0 to 7.1 months), and median time from hospitalization to treatment was 1.6 months (IQR 0.9 to 2.4 months). Predictors of longer times to treatment included older age, less advanced TNM stage, and surgical treatment.

With regard to survival, longer time to treatment was associated, paradoxically, with a reduced hazard of death. Even after adjusting for age, gender, tumor histology, TNM stage, and surgical treatment, the hazard of death was still lower in patients who experienced longer delays in treatment (adjusted HR 0.80, 95% CI 0.6 to 1.0).

Obviously, lung cancer patients do not improve over time while awaiting treatment, so the paradoxical results of this study are most likely due to selection bias. Specifically, it is likely that patients with more aggressive tumors had more severe symptoms and signs, sought medical attention sooner, were diagnosed and treated relatively promptly, and then promptly died.

This "confounding by selection" makes it difficult to study the effect of more timely care on survival and other lung cancer outcomes. It would not be ethical to randomly assign lung cancer patients to groups that receive care that is more or less timely. Natural experiments and sophisticated observational study designs may or may not be able to provide a definitive answer.

It is also likely that some delays in care are not avoidable—a natural tension exists between timeliness and other important dimensions of the quality of care, including safety and effectiveness. It does not make sense to skip a potentially time consuming perioperative evaluation in a patient who is a borderline surgical candidate for the sake of providing timely care alone.

However, future research in US health-care settings should seek to identify patient characteristics and institutional factors that are associated with more timely lung cancer care, and interventions should be designed to improve timeliness without compromising other dimensions of health-care quality. ■

Dr. Michael K. Gould, FCCP
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Stanford School of Medicine,
Stanford, CA

**ONLY A FEW STUDIES
HAVE EXAMINED THE
RELATIONSHIP BETWEEN
TIMELY CARE AND SURVIVAL,
AND THE RESULTS OF
THESE STUDIES HAVE
BEEN MIXED.**

DR. GENE L. COLICE, FCCP
Editor,
Pulmonary Perspectives

Editor's Insight

As the debate about screening for lung cancer in asymptomatic patients continues, often ignored are issues relevant to the care of patients who do have lung cancer.

Dr. Gould raises many important questions about the timeliness of care in these patients: What symptoms, especially in patients with underlying lung disease, should prompt general practitioners to consider the diagnosis of lung cancer? How quickly should general practitioners and their

pulmonary consultants move in establishing the diagnosis of lung cancer? Once the diagnosis of lung cancer is confirmed, will expeditious staging and treatment improve outcomes?

There is an obvious lack of recent information addressing these questions. Further research on ways to improve the timely identification and treatment of lung cancer patients, as Dr. Gould correctly points out, should be a priority.

—Editor

NEWS FROM THE COLLEGE



PRESIDENT'S REPORT

Capitol Hill Caucus: Part II—ACCP Goes to Washington

Last month, I discussed the attitudes of Americans regarding health care. Polls from both political parties agree that most Americans identify rising health-care costs, declining access to care, and the 46 million Americans with no health insurance as the most important domestic issues today.

At the 14th Annual ACCP Capitol Hill Caucus in March, 81 ACCP members and staff met with members of Congress and their staffs to discuss issues that are important to our patients and our profession. Most of us don't get courses in lobbying during medical school or residency, so on Monday afternoon, we learned some of the basics.

Knowing that you have about 15 minutes to make your points before being ushered out and another group comes in to express their concerns, you have to be organized and stay rigorously on message.

We were prepared with our talking points and instructed to keep three things in mind: (1) Be brief. (2) Be accurate. (3) Say something new. A personal story about a specific patient was recommended as a particularly effective tactic to get the Legislative Aids (LA) interested. And, the LAs do run the agenda.

Finally, we were instructed to be sure to make the "ask," and we had two high-priority "asks."

The first was to fix the "sustainable growth rate" (SGR) formula for Medicare physician reimbursement. We followed the same script as last year but had to come back because this problem seems too sticky to get fixed in the current political climate.

Briefly, the SGR is intended to link Medicare payments to the gross domestic product (GDP). However, when growth in medical care expenditures per beneficiary exceeds the growth rate of the GDP, then physician payments get reduced.

Practice costs have risen at rates higher than the GDP and inflation for several years, and the SGR formula called for cuts in reimbursement every year. Congress allowed a 5% cut in 2002 but froze the cut every year since and added small positive updates in 2003 to 2005 (but not matching inflation).

At the end of 2006, Congress froze Medicare payments, postponing the 5% cut until the end of 2007, when physicians are facing a 10% payment cut if no action is taken. With the costs of practice rising out of physicians' control, a 10% reduction in payment will force many to stop seeing Medicare

patients. And worse, since Medicare payments are tied to the entire health-care sector, these effects will be amplified through private, Medicaid, and military reimbursement formulas. So, there is nothing "sustainable" or "growing" about the SGR, except for, maybe, the hardship it causes practicing physicians.

Our proposal (along with most of our colleagues) is to scrap the SGR formula and replace it with payments linked to the Medicare Economic Index (MEI), which tracks increases in practice costs over time. We believe this is reasonable, and also fair, as physicians are the only providers subject to the impossible SGR formula.

The problem is that implementing another system will cost billions of dollars, and as we all know, that is a tough "ask" in the current climate. And whoever said life is fair?

Our other major issue relates to the current and worsening shortage in the critical care workforce. Briefly, there are already too few critical care clinicians of all disciplines (nurses, respiratory therapists, pharmacists) to provide proper care for patients already in our ICUs, and the numbers of providers are not projected to increase fast enough to keep pace with the aging of the population who will require intensive care.

Largely through efforts of the ACCP, in close collaboration with the American Association of Critical-Care Nurses, American Thoracic Society, and Society of Critical Care Medicine, we worked with Senator Richard Durbin (D-IL) and Senator Mike Crapo (R-ID) to draft the Patient-Focused Critical Care Enhancement Act (S.718), introduced in the Senate on February 28, 2007.

This proposed legislation represents a first step to address this workforce shortage by funding \$5 million for research and \$4 million for demonstration projects on ICU practice and organization, coordinated community and regional approaches, family assistance programs, and the use of telemedicine technology, especially in rural areas underserved by the critical care workforce.

In addition, it calls for the recruitment of at least 50 intensivists yearly into the National Health Service Corps Loan Repayment Program. (The bill and other materials related to the critical care workforce shortage can be found at www.chestnet.org/practice/gr/CCWorkforce.php.)

On Tuesday morning, we heard from one Senator and four Representatives,

two of whom were physicians. They all agreed that the problems of the uninsured and rising health-care costs were dire, and that the SGR sorely needs fixing.

To me, the most thoughtful and compelling of the group was Representative Tom Allen of Maine. Full disclosure: yes, I am a registered Democrat, and no, I do not live in Maine and have not, nor will I conceivably ever, vote for him. Living in Maine is not my destiny.

He identified the central issue: What is the role of government in health care? Is it to improve the lives and health of our citizens, or is it to stay out of the way and let the market take care of it? He pointed out correctly that somehow other free and affluent societies like ours cover everyone at two-thirds the cost of the United States, with the same outcomes.

Medicare and Medicaid will not survive if the SGR is not changed and providers stop participating.

He even offered some constructive and feasible solutions, including subsidizing small business to provide health insurance for employees, covering all children, and allowing everyone to buy into Medicare, with a subsidy if they need one. He also was a sponsor of the Pulmonary and Cardiac Rehabilitation Act (S.329/H.R.552) that provides a pulmonary rehabilitation benefit for all Medicare recipients. This is obviously important to our patients and to ACCP members and worthy of serious support by all of us.

In the afternoon, we all were scheduled to meet in the offices of our respective members of Congress. A few

met with the Senators and Representatives personally but most with the health-care LAs.

Speaking for myself, the LAs of my Representatives and Senators knew all about the SGR problem and would love to fix it. After all, I'm from New York, the bluest of blue states, where we think spending money on health care is OK, even if taxes go up some. But nobody quite knows how to fix SGR, especially in the current political and economic environment.

We suggested linking it to the Medicare Economic Index, but they replied that it would cost billions, and we countered that it was necessary. They agreed a fix was needed, and they would transmit our message to

their boss. They didn't know about the workforce legislation, but we provided the verbal and written support, and they promised to look it over and bring

it to their boss. I was impressed by their grasp of health-care issues, and sorry for them because there was a line of people with other passionate concerns behind us, and they would have to be as polite and attentive as they were to us.

But, I also believe that all of the members of Congress would get all of our messages, and, maybe the messages will have a positive impact. Besides, the ATS has a caucus too, and the ACCP will be back next year to Congress to remind them about these issues, along with some new ones. ■

Photos from the 2007 ACCP Capitol Hill Caucus can be found at www.chestnet.org/practice/gr/index.php.



BY DR. MARK J. ROSEN, FCCP

KNOWING THAT YOU HAVE 15 MINUTES TO MAKE YOUR POINTS BEFORE BEING USHERED OUT, YOU HAVE TO BE ORGANIZED AND STAY RIGOROUSLY ON MESSAGE.

PRACTICE MANAGEMENT

CMS Opens the Online Doors to Its New DOQ-IT University

The Centers for Medicare and Medicaid Services (CMS) has announced the national launch of DOQ-IT (Doctor's Office Quality Information Technology) University, or DOQ-IT U, to support health information technology in physicians' offices.

The new interactive learning tool educates physicians in the adoption and implementation of electronic health records and care management practices.

DOQ-IT U is an interactive,

Web-based tool designed to provide solo and small-to-medium-sized physician practices with the education for successful health information technology adoption, including lessons on culture change, vendor selection, and operational redesign, along with clinical processes. The nationally available e-learning system is available at no charge.

To view the entire press release, please go to: www.cms.hhs.gov/apps/media/press_releases.asp. ■

Healthy Work Environments: True Collaboration

BY DEBRA GERARDI, RN, MPH, JD

The AACN *Standards for Establishing and Sustaining Healthy Work Environments* require that “every team member embrace true collaboration as an ongoing process and invest in its development to ensure a sustained culture of collaboration.”¹

The creation of cultures in which everyone is accountable for achieving common goals, respectful professional conduct, integration of diverse viewpoints, and engagement in difficult conversations requires us to focus on skills and processes currently underrepresented in our clinical work environments. Expanding our capacity to collaborate with colleagues at each of these levels enhances our ability to partner with patients and families in meaningful ways.

Collaborating across professions is challenging. Recent studies reveal that physicians and nurses have different perceptions regarding levels of collaboration, cooperation, and conflict. In a

survey of intensive care nurses and physicians, 73% of physicians believed that collaboration with nurses was high or very high, while only 33% of nurses in the same units believed that to be

true.² A 2001 study looked at how hospital professionals handle cooperational conflicts.³ The researchers found that, before recognizing conflict, physicians tolerate

more stress and disagreement than members of other professional groups. Improving interprofessional collaboration requires that we develop shared meaning around these concepts before developing skills to improve how we engage with each other.

To collaborate effectively and navigate the space where trust, respect, reputation, and integrity lie, we must master four basic skills: to be present in the moment, listen openly, problem-solve together, and

make the other person look good. Expanding our capacity to focus and be present when communicating with colleagues is an essential first skill. Listening openly requires that we approach

interactions with curiosity rather than certainty. Being open and listening below the surface to what is really

being said saves time and builds trust.

Professional training often reinforces the myth that we are solely responsible for patient care. Interdependencies are integral to complex environments, and developing the ability to problem-solve together expands our capacity for developing more effective and accurate solutions.

To do no harm, we must work together. Complexity dictates that no one has enough information to care individually for the patient. Coming together is the only way to consistently prevent harm to patients. Strategies for fostering collaborative work environments include:

- ▶ Creation, use, and evaluation of processes that define accountability for collaboration
- ▶ Skills training in communication, teamwork, negotiation, and conflict resolution
- ▶ Expanded opportunity for interprofessional partnerships and joint decision making
- ▶ Organizational commitment to provide time needed to address and resolve disputes
- ▶ Creation of codes of conduct and universal agreements to behave professionally and respectfully
- ▶ Creation of processes that support

conflict resolution at all levels of the organization and that make use of trained facilitators or mediators within or external to the organization when appropriate

▶ Consistently address behaviors that disrupt the work environment or lead to unsafe care

Collaboration occurs at the intersection between self-reflection and active engagement; it is simultaneously a conscious act by individuals and the product of group wisdom. Collaboration requires time and commitment; in return, we gain understanding, build trust, discover common purpose, and expand possibility. Collaboration is our means for working better together and not just working side-by-side.

For more information, go to www.aacn.org/hwe.

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Ms. GERARDI is Chair, Program on Health Care Collaboration and Conflict Resolution, Werner Institute for Negotiation and Dispute Resolution, Creighton University School of Law. She can be reached at debragerardi@creighton.edu.



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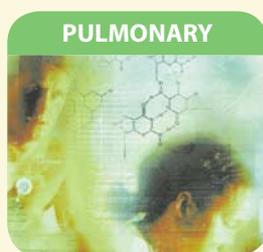
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ACCP PRODUCT OF THE MONTH COPD: Emerging Trends in Treatment Options—Podcast

As chronic obstructive pulmonary disease (COPD) becomes more prevalent and associated mortality rates continue to rise, the need for better treatment options and different delivery systems is high.

This virtual symposium podcast from the CHEST 2006 satellite will provide the most current information regarding diagnostic tools and treatment opportunities. Drs. Neil R. MacIntyre, FCCP, Stephen C. Lazarus, FCCP, and Fernando J. Martinez, FCCP, will review advanced studies and ideas for future treatments and other pharmacologic options in their presentations. To view the virtual satellite symposium

podcast, please visit the ACCP online education site at www.chestnet.org/education/online/index.php, and click on the podcast link.



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Contest closes May 31.

NEWS FROM THE COLLEGE



SLEEP STRATEGIES

Management of Obstructive Sleep Apnea: The Patient's Perspective

What do patients want and need from physicians, and where do the problems and pitfalls lie?

In September 2006, the ACCP Sleep Institute sponsored a 1.5-day conference with the aim of developing a continuity of care model for long-term management of obstructive sleep apnea (OSA). We invited pulmonary/sleep medicine specialists, primary care physicians, home-care company representatives, continuous positive airway pressure (CPAP) and other sleep-related equipment manufacturers, insurance company representatives, and, perhaps, most importantly, four patients with OSA.

The patient spokesperson was Dave Hargett, a retired Sears manager who lives in the Chicago suburbs, about 40 miles from the ACCP headquarters in Northbrook, IL. He was such an exceptionally articulate and passionate spokesperson for the patient perspective, I wanted to give him another venue to share his message about OSA.

I interviewed Dave recently about his experience with OSA, what patients want and need from their physicians, and where the problems and pitfalls lie in developing a strong

and successful partnership between patient and physician. We also talked about what possible solutions might exist to improve patient-physician partnering and patient outcomes.

Charles Atwood: Dave, thanks for agreeing to be interviewed for *Sleep Strategies*.

Dave Hargett: You're welcome.

Atwood: If you are willing to talk about your experience with sleep apnea, I think it would be a good place to start.

Hargett: I was diagnosed with OSA in 1994. I read a newspaper story about sleep apnea and thought I had all the symptoms mentioned in the article and should get checked out. Six months later, I talked to my primary physician about it. Admitting he knew nothing about sleep, he referred me to a sleep specialist.

After a few insurance hassles, I had a diagnostic sleep study. The study showed severe OSA. My apnea-hypopnea index was 82, with desaturations as low as 52%. The night my sleep physician received the results, I started receiving CPAP at a temporary setting

of 8 cm. Ultimately, pressure went to 13 cm, but, even at the initial setting of 8 cm, I felt tremendously better after a week of use. I was able to cut out my 2-hour Saturday and Sunday naps after only 4 days! I still use CPAP today at a pressure of 12 cm.

While I've had cardiac bypass surgery, an open cholecystectomy, and other health issues, I still feel better today at age 58 than I did with untreated severe apnea at age 45. To paraphrase a country song, "I was much too young to feel that damn old!"

Atwood: What is your connection now to the sleep field?

Hargett: I'm an apnea patient turned sleep activist and advocate. I'm serving my 4th year as Chairman of the American Sleep Apnea Association (ASAA). I also volunteer in the Chicago area as an A.W.A.K.E. group leader, where I run two separate A.W.A.K.E. groups.

Atwood:

A.W.A.K.E. (Alert, Well, And Keeping Energetic) groups are sleep apnea patient support groups fostered by the ASAA.

Hargett: That's right. A.W.A.K.E.

groups provide a way to offer patient education and compliance tips. We're always looking for more sleep centers to start up and to sponsor groups. I also respond to e-mail questions that come through the ASAA Web site. I answer 250 to 300 e-mails per month from patients who have questions about diagnosis and therapy. I spend hours each month talking to patients on the phone. I also do public speaking on sleep apnea.

Atwood: From your viewpoint as a very knowledgeable patient and patient advocate for sleep medicine, what do you see as some of the problems that patients face in getting help for OSA?

Hargett: The first and most serious problem is that many physicians just do not know very much about sleep disorders or they don't take them seriously.

My own family physician is a very good doctor, but he does not have a single question about sleep on his office health questionnaires. He knows that I have sleep apnea and asks me about it regularly now, but I have no idea how often he recognizes it in other patients—probably not enough.

Atwood: What do your friends in A.W.A.K.E. meetings tell you about their experiences?

Hargett: They are confused. Their primary care physician may have referred them to a sleep laboratory for testing, but the sleep laboratory staff has no long-term connection with the patient

still in educating patients about their disorder and therapy options.

Once the prescription is written for CPAP or the patient is passed on to an apnea dentist or a surgeon, many of the specialists lose track of their patients. No one is following up to ensure compliance with therapy.

Personally, I believe that patients who have severe sleep apnea, as I do, need a competent specialist to help manage this problem. Because sleep apnea touches on so many other aspects of health, severe disease can really be distressing. Having a good sleep specialist on your medical team

is important.

My sleep specialist is a pulmonary physician who is board-certified in sleep medicine. He has been very helpful, and I see him once a year.

Atwood: The ACCP is currently implementing a primary care education program directed at "front-line" physicians—family physicians, general internists, and others who work in primary care. What can we do to better educate patients about sleep apnea? What do patients want to know about this condition?

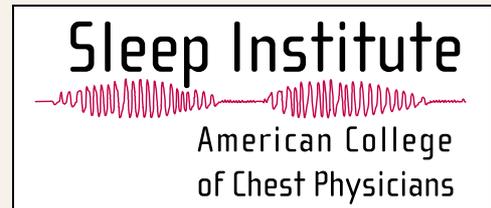
Hargett: Patients ask me all the time: "What is sleep apnea?" These questions come from people diagnosed with apnea and already receiving therapy. Patients are hungry for information about their diagnosis and what therapy is best. Physicians should take the time to explain things up front so that the patients can understand the issues and be more comfortable with the chosen therapy.

Patients receiving CPAP also need to be reassured that CPAP therapy is very manageable. Too often, I hear people say "I can't wear a mask" or "I can't use that machine the rest of my life."

I tell patients it's like wearing glasses. You need glasses to see and you need the CPAP to breathe when you sleep. Glasses have to be adjusted when they slip on your nose slightly; just like a CPAP mask at night. They have to be cleaned regularly, just like your mask and headgear. Occasionally, you need to see your eye doctor to get your prescription checked, just as you may need a follow-up titration study.

Compared with the benefits gained, the hassle of therapy is not that much.

Atwood: Thanks, Dave, for your time and insights into how patients deal with and feel about sleep apnea. ■



because they are mainly there to do sleep studies. Patients may work with a home-care company who provides their CPAP machine, but the home-care company is paid for equipment, not follow-up care. Many companies do the best they can to provide support, but there is a limit.

Some patients I know have never seen a physician knowledgeable about sleep medicine. They have been diagnosed with a serious disorder, one associated with serious consequences to quality of life, heart disease, risk of car crashes, etc. They have a therapy prescribed and then are left without anyone really to help them.

I often tell people that for patients with sleep disorders, managed health care means "manage your own health care." Ask questions. Learn. Find help. Manage your own care.

Atwood: What are physicians weakest at in the OSA diagnosis and treatment process?

Hargett: At the primary level, recognition of sleep disorders is improving, but it is still the weakest point. Patients are frequently in denial about sleep problems. They don't mention all their symptoms, and physicians don't put together all the clues.

Primary physicians also need to do a better job following up with their patients with sleep apnea. I realize a primary care physician may not know very much about sleep apnea or treatment options, but at least they could encourage their patients to follow up with knowledgeable specialists or even home-care companies if they have problems with therapy.

This is not happening. Primary care physicians are not asking how CPAP therapy is going or if patients are even using it regularly. On the other hand, patients should be more proactive in discussing their apnea with their primary physicians.

Most sleep specialists are great at diagnosis, but I see major weakness

Dr. Charles W. Atwood, Jr., FCCP
Section Editor, Sleep Strategies

NETWORKS
Benefits to Fellows-in-Training, Response to CMS Posting
Affiliate

If you are a fellow-in-training and an ACCP affiliate member, I have to congratulate you. The Affiliate NetWork is committed to you successfully completing fellowship and is looking for ways to optimize that educational experience. Our mission is to help you develop into great clinicians and world leaders in all fields of cardiopulmonary, critical care, and sleep medicine.

Your Affiliate NetWork provides the forum to showcase your work and opportunities to share and learn with your colleagues, become more involved in the College, and have fun. These are exclusive oppor-



tunities that come with your special status as an affiliate member:

- ▶ **Get that job you want after graduation.** At our CHEST 2007 Affiliate NetWork Luncheon on October 22, we will show you what private practice groups are looking for when interviewing candidates.
- ▶ **Take "The CHEST Challenge."** Practice board-review-type questions online for free. Do well and WIN A FREE TRIP TO CHEST 2007. In Chicago, you and two other fellows from your program compete as a team in game-show-style rounds for cash prizes.

Visit www.chestchallenge.org. CHEST Challenge is supported by AstraZeneca LP (Play-offs) and ALTANA Pharma US, Inc – a NYCOMED Company (Championship).

- ▶ **Use our world stage.** Only affiliate members are invited to submit case reports to the annual CHEST meeting. Cash awards are given for the best presentations, and all presented case reports are published in a *CHEST* supplement.

- ▶ **Fast track to College leadership.** You have the opportunity to run for open positions on the Affiliate NetWork Steering Committee. If elected, you will help choose case reports and plan for the annual CHEST meeting. Information about the election process will be e-mailed to Affiliate NetWork members in the coming weeks.

MAJ William F. Kelly, MC, USA, FCCP
 Vice-Chair, Affiliate NetWork

Pulmonary Vascular Disease

The Pulmonary Vascular Disease NetWork invites you to visit its newly updated Web pages at www.chestnet.org/networks/pvd/index.php. The steering committee is committed to further developing the con-

tent and anticipates that it will become a premier instructive site for patients and physicians.

Among the resources provided is a regularly updated curriculum of current articles and published papers on pulmonary

vascular disease. The NetWork is also compiling a list of physicians treating pulmonary hypertension to serve as a resource for members. An online questionnaire will be posted on the Web page. The NetWork recently conducted a survey on the

Help us explore the way we look at idiopathic pulmonary fibrosis (IPF)

IPF has been associated with increased levels of endothelin (ET), a 21-amino acid peptide with diverse biological functions and pathological effects.¹ Patients with IPF demonstrate elevated ET plasma concentrations and ET expression in the lung tissue,² and ET concentration has been found to correlate with disease activity.³ Through ongoing research we are exploring the link between ET and the disease of IPF.



NEWS FROM THE COLLEGE

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Description of Current Practices Related to the Follow-up of Patients with Pulmonary Arterial Hypertension. The primary objective of the survey is to determine the pattern of follow-up testing used by physicians who treat patients with PAH and to explore what short-term and long-term differences physicians feel are clinically important for selected objective outcomes.

E-mail the NetWork Chair at Namita.Sood@osumc.edu.

Pulmonary Physiology, Function, and Rehabilitation

The Centers for Medicare and Medicaid Services (CMS) posted on their Web site a National Coverage Application for pulmonary rehabilitation (CAG-00356N) for review and comment. In addition, CMS requested information on several other aspects of pulmonary rehabilitation.

The ACCP (through this PPRF NetWork), in collaboration with the Ameri-

can Thoracic Society, the American Association of Cardiovascular and Pulmonary Rehabilitation, and the National Association for Medical Direction of Respiratory Care, addressed issues in the NCA posting, including a definition of pulmonary rehabilitation, the components of pulmonary rehabilitation, patient outcomes, and the evidence for evaluating health outcomes in the Medicare population.

In addition, a response to the recently

released AHRQ Technology Assessment (*Pulmonary Rehabilitation for COPD and other Diseases*, released November 21, 2006) was provided by the group. A copy of this response can be found on the CMS Web site. A response from CMS is expected within 6 months.

The NetWork will be assisting with the simulation experience at CHEST 2007. For the first time, a simulation experience in pulmonary function testing will be available for CHEST attendees.

All are welcome to attend the NetWork Open Meeting at CHEST 2007 to learn more about the activities of the NetWork and how to become involved. ■

This Month in CHEST: Editor's Picks

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

► **ICU-Acquired Weakness.** By Dr. W. Schweickert and Dr. J. B. Hall, FCCP

► **Statins Reduce the Risk of Lung Cancer in Humans: A Large Case-Control Study of US Veterans.** By Dr. V. Khurana, et al

► **Effects of Hypercapnia on BP in**

Hypoalbuminemic and Nagase Analbuminemic Rats. By Dr. J. L. Gómez, et al

► **Burden of Potentially Avoidable Anticoagulant-Associated Hemorrhagic and Thromboembolic Events in the Elderly.** By Dr. C. van Walraven, et al

► **Radial Artery Pulse Pressure Variation Correlates With Brachial Artery Peak Velocity Variation in Ventilated Subjects When Measured by Internal Medicine Residents Using Hand-Carried Ultrasound Devices.** By Dr. J. M. Brennan, et al

► **World Trade Center Sarcoid-Like Granulomatous Pulmonary Disease in New York City Fire Department Rescue Workers.** By Dr. G. Izbicki, MD, et al

► **Systemic Effects of Smoking.** By Dr. D. G. Yanbaeva, et al

► **The Ethical Foundations of Professionalism: A Sociological History.** By Dr. H. C. Sox

► **Pulmonary Rehabilitation: Joint ACCP/AACVPR Evidence-Based Clinical Practice Guidelines.** By the ACCP/AACVPR Pulmonary Rehabilitation Guidelines Panel: Dr. A. L. Ries, FCCP (Chair), et al (CHEST Supplement)

www.chestjournal.org

A landmark IPF morbidity and mortality trial is under way

Patients are now enrolling in a new IPF trial called BUILD-3.

Inclusion criteria include age over 18 years, biopsy-proven IPF diagnosis, and disease duration less than 3 years. Exclusion criteria include interstitial lung disease due to conditions other than IPF, and severe restrictive lung disease.

Visit www.BUILD-3.com to find the trial site nearest to your practice.

Refer patients ■ Enroll patients ■ Build the future

Visit www.BUILD-3.com or www.clinicaltrials.gov to learn more.

(Identifier # NCT00391443)

BUILD³

1. Fagan KA, McMurtry IF, Rodman DM. Role of endothelin-1 in lung disease. *Respir Res.* 2001;2:90-101. 2. Uguccioni M, Pulsatelli L, Grigolo B, et al. Endothelin-1 in idiopathic pulmonary fibrosis. *J Clin Pathol.* 1995;48:330-334. 3. Giaid A, Michel PP, Stewart DJ, Sheppard M, Corrin B, Hamid Q. Expression of endothelin-1 in lungs of patients with cryptogenic fibrosing alveolitis. *Lancet.* 1993;341:1550-1554.

EDUCATION INSIGHTS

ACCP To Attend Guidelines International Network Conference

BY CARLA T. HERRERIAS, MPH;
SANDRA ZELMAN-LEWIS, PHD;
AND JULIA HEITZER, MS

This summer, a member of the Health and Science Policy (HSP) Committee and HSP staff will be attending the 4th Guidelines International Network (G-I-N) conference in Toronto, being held in North America for the first time.

The themes of this conference are as follows: setting standards in guideline development; translating knowledge and implementation of guidelines; and evaluating the impact of guidelines. This conference will bring together both members and nonmembers of the G-I-N, guideline developers and adapters, clinicians, policy makers, and many others.

The G-I-N is an international not-for-profit association of organizations and individuals involved in the development and use of clinical practice guidelines. G-I-N seeks to improve the quality of health care by promoting systematic practice guidelines and their application into practice.¹

The ACCP, through the HSP Committee, has submitted two abstracts for the conference. The first focuses on the ACCP guideline methodology, including an overall summary of our grading system and how it was developed. It also addresses resource allocation and patient preferences. The second abstract describes a project at Nemours Clinical Management Program, Orlando, FL, to measure standards of care in pediatrics through the development of critical data elements,

identified by linking content experts to experts in evidence-based medicine. Critical data elements can be valuable tools for measuring standards of care. The Nemours project utilizes the ACCP grading system.

Furthermore, the HSP Committee has made a decision to address the implementation of ACCP clinical practice guidelines. Through its continuing association with the Agency for Healthcare Research and Quality, specifically Translating Research Into Practice, the ACCP has learned about implementation techniques that are in use at various institutions here and abroad. The Guidelines Implementation Subcommittee was formed in late 2006, with the initial goal of assessing which formats ACCP members would find useful for implementation tools

that could be incorporated into practice in their local settings. This subcommittee is developing a session on implementation of guidelines for CHEST 2007. Watch for more information on upcoming guidelines and implementation tools on the HSP Web site, at www.chestnet.org.

Attendance at this conference and membership in the G-I-N provides the ACCP a valuable opportunity to network and develop relationships, both nationally and internationally, with other guideline developers and those who focus on dissemination and implementation of clinical practice guidelines. ■

1. Guidelines International Network Web site. Available at: www.g-i-n.net. Accessed March 30, 2007

ACCP WORLDWIDE The 7th ACCP Central America Pro Bono CME Course

BY DR. UDAYA B. S.
PRAKASH, FCCP

The 7th Annual ACCP Central America pro bono CME course on March 27-28, 2007, was successfully concluded as part of the XXI Congreso de la Federación Centroamericana y del Caribe de Neumología y Cirugía del Tórax, March 27-30, 2007, San Pedro de Macoris, República Dominicana. The 5-day congress was attended by more than 420 physicians from 20 countries. The 1.5-day ACCP course was attended by approximately 145 physicians.

The ACCP pro bono faculty included: Dr. Carlos M. Alvarado-Galvez, FCCP (Tegucigalpa, Honduras); Dr. V. Theodore Barnett, FCCP (Milwaukee, WI); Dr. Naresh A. Dewan, FCCP (Omaha, NE); Dr. Rodolfo C. Morice,

FCCP (Houston, TX); Dr. Udaya B. S. Prakash, FCCP (Rochester, MN); and Dr. Sandra K. Willsie, FCCP (Kansas City, MO). The ACCP scientific program director was Dr. Udaya B. S. Prakash, FCCP. The co-director and president of the Federation congress was Dr. Eduardo Gautreau de Windt.

The scientific program included formal lectures and a workshop on bronchoscopy. The topics were selected by the organizers and included asthma, pleural effusions, sleep-disordered breathing, ACCP lung cancer guidelines, pulmonary complications of AIDS, and more.

The 8th ACCP Central America pro bono CME course is scheduled (pending approval from ACCP leadership) for March 4-5, 2008, at the Intercontinental Hotel, Managua, Nicaragua. ■

CHEST 2007 and Chicago: A Tourist's To-Do List

As "The City That Works," Chicago certainly provides all of the amenities necessary for a top-notch meeting, such as CHEST 2007. But, the city has so much more to offer! Whether by foot, bus, or boat—on land, lake, river, or in the sky, here are just a few of the must-see and do's while visiting Chicago.



Perhaps one of the best ways to see the city is from 1,000 feet straight up, made possible by visiting the Sears Tower Sky Deck or the John Hancock Observatory. From your perch, you'll be able to see many of Chicago's famous attractions, like Navy Pier, Buckingham Fountain, the Millennium Park Bean, and the Lincoln Park Zoo, to name a few.

But, if you prefer being a little closer to the ground, many year-round tours are available by bus and boat. Your hotel's concierge is the perfect place to make arrangements.

Some of the city's finest hidden gems include local art galleries and small performing arts studios, but Chicago also offers some of the world's finest and largest museums. A quick trip over to Museum Campus offers the opportunity to choose from three of Chicago's best—the Field Museum, Shedd Aquarium, or Adler Planetarium. And, just down the road in either direction, you'll find the Museum of Science and Industry or the Art Institute of Chicago. If you plan on visiting more than one,

consider purchasing the CityPass, which includes admission to a number of museums for a flat fee.

With all there is to see and do, it'll be a wonder if you can fit it all in—but that doesn't mean you shouldn't try. Everything this city has to offer, from its famous landmarks to world-renowned attractions,

are just a few of the reasons why Chicago is our kind of a town and the perfect place for CHEST 2007!

For more information about Chicago, visit www.choosechicago.com/default.html.

Stay tuned for more details about CHEST 2007, October 20-25, coming soon! ■



ACCP faculty at the 7th Annual ACCP Central America pro bono CME course (L-R): Drs. Morice, Prakash, Dewan, Alvarado-Galvez, Willsie, and Barnett.



NEWS FROM THE COLLEGE

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Making a Difference Society: New Category Introduced

The Making a Difference Society debuted at CHEST 2006 and 50 ACCP members committed to being Difference Makers by becoming Charter Members of the Society at the \$1,000+ level. Making a Difference Society donors are annual contributors giving in the \$1,000 to \$25,000 range.

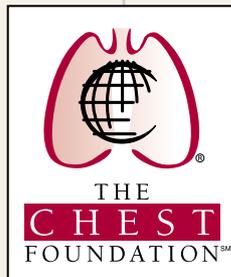
The debut of this Society created an interest among new fellows (up to 5-years out of training), as well as among affiliate and allied members. The second phase of the Making a Difference Society-New ACCP Members has been launched. The giving levels for New ACCP Members have been reduced to allow for participation that may be more attainable. This new program's tax-deductible contributions will range from \$100 to \$1,000 annually.

Benefits shared by both types of Making a Difference Society donors will be a listing in The CHEST Foundation's Annual Report and complimentary Making a Difference Award Dinner tickets for annual giving of \$500 (one ticket) and \$1,000 (two tickets).

In addition, donors will receive special recognition as Medallion Difference Makers for those contributing at the highest level within their respective giving level.

These annual gifts allow The Foundation's work to continue in the four focus areas that ACCP members are already familiar with: tobacco prevention, critical care and family assistance, clinical research, and humanitarian awards. Our goal has been consistent: helping you help your patients live and breathe easier.

You may make your Making a Difference Society donations by credit card online at www.chestfoundation.org. If you prefer, mail a check to the attention of Marilyn Lederer at The CHEST Foundation, 3300 Dundee Road, Northbrook, IL 60062. If you would like to have more information about the Making a Difference Society, please contact Teri Ruiz at truiz@chestnet.org.



Don't Miss the Making a Difference Awards Dinner

This year's Making a Difference Awards Dinner will be held during CHEST 2007 on Saturday, October 20, 2007, 7:00 PM to

10:30 PM, at the architecturally significant Chicago Cultural Center.

Join your ACCP colleagues and friends in honoring the distinguished career of ACCP Past President, Dr. Thomas L. Petty, Master FCCP. The

CHEST Foundation, along with lead sponsor, Boehringer Ingelheim Pharmaceuticals, Inc., has established an endowment in his honor. The Thomas L. Petty, MD, FCCP, Endowment in COPD Research will fund COPD research and other activities to improve care for patients with COPD.

This is the ninth consecutive year that The CHEST Foundation will recognize ACCP members' important pro bono service around the world. Grant and award monies total \$150,000 and will support 14 outstanding sustainable community projects. There will be four winning Humanitarian Project Development Grants, nine winners of the Humanitarian Recognition Award, and one Ambassadors Group Humanitarian Recognition Award winner.

Registration will be available online starting July 2, 2007, at www.chestfoundation.org. Price per ticket is \$150. Making a Difference Society Members at the \$500 and \$1,000+ levels will be provided with one or two tickets, respectively. Contact Teri Ruiz at truiz@chestnet.org.

Critical Learning for Critical Care Teams

Noninvasive and Home Mechanical Ventilation: ICU and Beyond 2007

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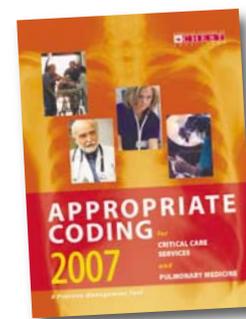
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Oral Care Regimen Halved VAP Rate in Burn Unit Patients

BY DOUG BRUNK
Elsevier Global Medical News

SAN DIEGO — An oral care regimen administered every 4 hours significantly decreased the rate of ventilator-associated pneumonia in a population of pediatric burn patients, Debbie Chapyak, R.N., said at the annual meeting of the American Burn Association.

Although oral hygiene is considered standard nursing care, “it is often neglected,” said Ms. Chapyak of the Shriners

FIFTY PERCENT OF PATIENTS IN THE CONTROL GROUP DEVELOPED VAP, COMPARED WITH 28% OF PATIENTS IN THE NEW PROTOCOL GROUP.

Hospitals for Children—Northern California. “Due to the presence of the endotracheal tube, traditional tooth brushing is difficult.”

She and her associates evaluated the impact of a new oral care protocol on the rate of ventilator-associated pneumonia (VAP) in 70 acute burn patients—all of whom required more than 48 hours of ventilator support—admitted to the hospital over a 2-year period.

Before the new protocol was introduced, the researchers used swabs to administer Nystatin solution 5 mL to the oral cavity every 6 hours and Peridex 5 mL every 12 hours.

No tooth brushing or suctioning of subglottal secretions was done.

The new protocol consisted of administering the Q-Care Oral Care Cleansing System by Sage Products.

With this product, the teeth and surface of the gum are brushed with a suction swab and antiseptic rinse every 4 hours. Each package contains enough oral care for 24 hours.

Of the 70 patients, 30 underwent oral care before the new protocol was introduced (controls) while 40 underwent oral care with the new protocol.

There were no differences in mean age or VAP risk factors between the two groups, but patients in the new protocol group had larger burns and a higher percentage of full-thickness burns than did the controls.

Ms. Chapyak reported that 15 patients in the control group (50%) developed VAP, compared with 11 patients in the new protocol group (28%).

This represented a drop from 28 cases of VAP per 1,000 ventilator days in controls to 14 cases of VAP per 1,000 ventilator days in the new protocol group, a difference that was statistically significant.

Limitations of the study included the small sample size and the use of historical controls.

“We were unable to account for possible protocol lapses, and we were unable to assess the frequency of actual oral care before the protocol,” she said.

The investigators reported no financial ties to Sage Products.

Ventilator-associated pneumonia, the second most common nosocomial infection in pediatric patients, affects about one-quarter of all critically ill children. ■

Biomarkers Shed Light on Acute Brain Dysfunction in Critically Ill Patients

BY MARY ELLEN SCHNEIDER
Elsevier Global Medical News

ORLANDO — Certain biomarkers of inflammation and coagulopathy are altered in critically ill patients with acute brain dysfunction, according to preliminary research presented by Dr. Timothy D. Girard of Vanderbilt University, Nashville, Tenn.

Markers indicating inflammation and abnormally increased coagulation were associated with an increased number of days of delirium or coma in critically ill patients, Dr. Girard said at the annual congress of the Society of Critical Care Medicine.

Dr. Girard and his colleagues evaluated 139 mechanically ventilated patients in the ICU, all of whom were enrolled in a clinical trial studying daily spontaneous breathing with or without spontaneous awakening.

The researchers collected plasma on days 1 and 5 of the study to test for biomarkers indicating systemic inflammation and dysregulated coagulation.

In addition, all patients were prospectively evaluated daily regarding their level of arousal with the Richmond Agitation-Sedation Scale and for the presence of delirium with the Confusion Assessment Method for the ICU.

The research was supported by the National Institutes of Health and the Saint Thomas Foundation.

The 139 patients involved in the biomarker study were predominantly older, with a mean age of 65 years.

About half of the patients were women, and the population was critically ill with a median APACHE II score of 27. About half of the patients in the cohort

had sepsis or acute respiratory distress syndrome.

The researchers used multivariate analysis to determine the association between biomarker concentrations and the duration of delirium after adjusting for age, severity of illness, sepsis, baseline cognitive impairment, and total dose of sedative and analgesic drugs given in the ICU.

Among all 139 patients, multiple biomarkers were associated with duration of acute brain dysfunction, but that analysis can be complicated by the early death of some patients, Dr. Girard said.

Among the 96 survivors, however, soluble tumor necrosis factor receptor 1 (TNFR1), neutrophil gelatinase-associated lipocalin (NGAL), D-dimer, and protein C were each independently and significantly associated with the total duration of delirium.

As concentrations of the markers indicating increased inflammation—TNFR1 and NGAL—increased, patients were more likely to have prolonged delirium.

The same was true of rising D-dimer concentrations, which indicate abnormally increased coagulation. As protein C concentration increased, however, indicating normal coagulation, the duration of delirium decreased.

The results indicate that inflammation and coagulopathy are important contributors to the development of brain dysfunction in ICU patients.

“These markers are not specific to brain dysfunction, however, and our next step will be to identify novel markers of critical illness-associated brain dysfunction,” Dr. Girard said. ■

Minocycline-Rifampin-Coated Catheters Beneficial in Burn Unit

BY DOUG BRUNK
Elsevier Global Medical News

SAN DIEGO — The introduction of minocycline-rifampin-impregnated catheters was associated with a significant reduction of catheter-related bloodstream infections in burn intensive care unit patients and a significant drop in health care costs, Dr. Nichole S. Meissner reported during the annual meeting of the American Burn Association.

According to the National Healthcare Safety Network, an average of seven catheter-related bloodstream infections per 1,000 line-days occur in the burn intensive care unit, compared with four infections per 1,000 line-days in the medical-surgical ICU. “Many burn centers have adopted a policy of routine changes to keep these rates at acceptably low levels,” said Dr. Meissner, a resident in the department of surgery at the University of California, Irvine Medical Center.

“However, this consumes time and resources, and places the patient at increased risk with each procedure.”

She added that the minocycline-rifampin-impregnated catheters have lower rates of infection, compared with chlorhexidine-silver sulfadiazine-impregnated catheters, and lower rates of colonization compared with silver-platinum-carbon-impregnated catheters. “An optimal catheter policy will reduce the risk of catheter-related bloodstream infection [and] at the same time reduce the patient exposure to risk associated with catheter insertion,” she said.

During the study’s preintervention period (May 2000 through June 2003), she and her associates changed the indwelling catheters in burn ICU patients every 3-4 days via new puncture.

During the intervention period (July 2003 through June 2006), the researchers used minocycline-rifampin-impregnated catheters on all patients in the burn ICU

who required catheterization. They allowed the catheters to remain in place for 7 days during the first 6 months, and for up to 14 days during the rest of the study period. The lines could be removed at any time based on the attending’s discretion.

‘AN OPTIMAL CATHETER POLICY WILL ... REDUCE THE PATIENT EXPOSURE TO RISK ASSOCIATED WITH CATHETER INSERTION.’

An infection-control nurse who made rounds with the medical center’s burn team monitored the rate of infections.

Dr. Meissner reported that the preintervention rate of catheter-related bloodstream infections was 11.9 per 1,000 catheter-days. After the intervention, it

dropped to 4.7 per 1,000 catheter-days. “We were able to prevent 57% of infections, which equated to seven catheter-related bloodstream infections,” she said. “If each infection is estimated to cost between \$12,300 and \$56,000 per infection, then we saved between \$86,100 and \$392,000 during the study period.”

In the postintervention period, there were nine catheter-related bloodstream infections in 1,837 catheter-days. Six of these were from minocycline-rifampin-impregnated catheters, two from peripherally inserted central catheter lines, and one from a cordis catheter. The average indwelling time was about 9 days.

All nine infections occurred in critically ill patients who had an average age of 54 years. Their average total body surface area burned was 43%, and their average hospital length of stay was 73 days. There were three deaths, none directly associated with catheter-related bloodstream infection. ■

Enzyme Speeds Subcutaneous Fluid Infusion Rate

BY BRUCE K. DIXON
Elsevier Global Medical News

SALT LAKE CITY — Recombinant human hyaluronidase makes it possible to safely hydrate patients subcutaneously with a gravity line feed at flow rates approaching 500 cc/hour, according to a preliminary study presented at the annual meeting of the American Academy of Hospice and Palliative Medicine and the Hospice and Palliative Nurses Association.

Administering parenteral fluid subcutaneously has obvious advantages over using the intravenous route, but clinical use has been limited by concerns about flow rate and discomfort. Recombinant human hyaluronidase (Hylenex) addresses those concerns, Dr. Jay Thomas said.

"We were able to deliver Ringer's solution in a clinically relevant time frame without a pump and in a way that was very well tolerated, and we can start thinking about replacing some of our [intravenous] hydration," said Dr. Thomas, clinical medical director of the Center for Palliative Studies at San Diego Hospice, which is affiliated with the University of California, San Diego.

Hylenex recombinant injection was approved by the Food and Drug

Administration in 2005 as an adjuvant agent to increase the absorption and dispersion of other injected drugs and remains the only FDA-approved hyaluronidase from a recombinant human source.

This prospective, double-blind, randomized, placebo-controlled trial, known as INFUSE-LR (Increased Flow Utilizing Subcutaneously Enabled Lactated Ringer's), recruited 54 volunteers. Each volunteer received subcutaneous injections simultaneously in both upper arms through 24-gauge catheters connected to 500-cc bags of Ringer's lactate solution hung from scales so that their weight could be monitored.

A pharmacist prepared injections of either 1 cc of Hylenex of varying doses or saline, after which the intravenous bags were opened to gravity, Dr. Thomas said.

"In the arms that received hyaluronidase, flow rates were increased fourfold, compared to placebo arms," he said, adding that the overall mean flow rate for subcutaneous infusion with Hylenex was 464 mL/hr vs. 118 mL/hr with placebo.

The subcutaneous infusion rate, when preceded by Hylenex, was closer in flow to a standardized intravenous infusion rate than to the subcutaneous infusion rate with placebo, based on flow rates in five participants in the pilot phase of the



Increased edema is evident in the subject's right arm, which received an infusion without Hylenex, compared with the left arm, which received the enzyme.

study, according to data furnished by Halozyme Therapeutics Inc. and Baxter Healthcare Corp., makers of Hylenex.

In addition, there was visible distortion of the arms that did not receive Hylenex. Edema was quantified as mild, moderate, or severe. Gross edema was dramatically decreased by the enzyme, and

severe edema occurred only in placebo arms, he said.

There were no major adverse systemic events, and based on the adverse event profile, Hylenex was at least as well tolerated as placebo, he added.

Dr. Thomas disclosed no relevant financial relationships.

PHOTOS COURTESY DR. JAY THOMAS

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2007

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Ventilation 2007
Montréal, Québec, Canada

June 22 - 25
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August 24 - 27
Sleep Medicine Board
Review Course 2007
Phoenix, Arizona

August 24 - 28
Critical Care Board
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August 28
Lung Pathology 2007
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Opioid Medication Errors Common in Hospitals

BY BRUCE K. DIXON
Elsevier Global Medical News

SALT LAKE CITY — Opioid administration and prescribing errors are common in hospitals, and frequently result in uncontrolled pain as well as overdoses, according to a retrospective study presented at the annual meeting of the American Academy of Hospice and Palliative Medicine and the Hospice and Palliative Nurses Association.

"Most of the issues were due to administration by nurses, and underdoses were frequently reported as medical errors in these hospitals," Dr. Sydney Morss Dy said.

The investigators mined 6 years of data from MED-MARX, an anonymous national medication error reporting database used by about 850 hospitals, and quantitatively described all harmful opioid errors that occurred on regular patient care units that did not involve devices such as patient-controlled analgesia.

Free text error descriptions also were analyzed, added Dr. Dy, of the department

of health services research division, Johns Hopkins University, Baltimore.

Of 644 harmful error reports from 222 facilities, 60% were route of administration errors, and 20% were prescribing errors. "Most of the errors were related to faulty communication, lack of knowledge, performance deficits, or not following protocol," Dr. Dy said.



Of 644 harmful error reports from 222 facilities, 60% were route of administration errors.

DR. DY

One-fourth of the errors caused underdosing, and half caused overdosing, she added. Improper dose and prescribing errors were significantly more common with morphine (47%) or hydromorphone (42%) than with the other opioids included in the study: meperidine, oxycodone, and fentanyl.

"Some of these errors were due to the physician writing the prescription in milligrams and the nurse giving an intravenous dose in milliliters," said Dr. Dy.

Omission errors were most common with oxycodone (23%) and fentanyl patches (35%), and wrong route of administration was most common with meperidine (34% vs. 3% for morphine), the investigators reported.

In the quantitative analysis, the researchers found that common problems included:

- ▶ Starting intravenous morphine at a dose that was too high, or starting hydromorphone at a dose that would have been appropriate for morphine.
- ▶ Confusing immediate-release oxycodone with sustained-release oxycodone.
- ▶ Neglecting to change or remove fentanyl patches.
- ▶ Administering meperidine intravenously instead of intramuscularly.

These study findings already have prompted discussion of improvements at Johns Hopkins Hospital, where plans are underway to change educational procedures to include starting doses and to

change practice guidelines to, among other things, recommend that prescriptions be written in units of both milligrams and milliliters.

"These patterns of errors should be considered when prescribing, administering, and dispensing opioids, and should be incorporated into pain guidelines, education, and quality improvement programs," Dr. Dy said.

The study was limited by the absence of data on the relative frequency of opioid use in the hospitals, so there could be no determination about which of the five opioids caused the most harm. Also, there was no ability to check on the validity of the error reports, and all findings pertained only to the hospital setting, she said. ■

Hospice Patients Not Getting Full Benefit of Inhalers

BY BRUCE K. DIXON
Elsevier Global Medical News

SALT LAKE CITY — Hospice practitioners are not adequately trained in the use of inhaled medications, according to a study presented at the annual meeting of the American Academy of Hospice and Palliative Medicine and the Hospice and Palliative Nurses Association.

The study, presented at a poster session, revealed knowledge gaps in patient assessment, pharmacology, and pharmacokinetics of inhaled medications and inhalation-delivery technique among a study group of 50 hospice nurses, according to Laura T. Scarpaci, Pharm.D.

It's evident that formal education of hospice practitioners regarding the delivery of inhaled bronchodilator and anti-inflammatory medications is needed, said Dr. Scarpaci, manager of clinical education at ExceleRX Inc. in Philadelphia.

The nurses completed a written questionnaire that gathered demographic data, as well as information about previous training with an inhaler device, administration, pharmacokinetics, mechanism of action, patient assessment, and nursing technique.

Additionally, each nurse demonstrated the use of a metered-dose inhaler, a spacer (a supplementary device that eliminates the need to inhale simultaneously with device actuation), a dry powder inhaler, and a nebulizer, while being observed by a pharmacist trained in the use of inhalers.

The percentage of steps completed correctly by the nurses ranged from 35% with the dry powder inhaler to 77% with the metered-dose inhaler. (See box.) For a dyspnea patient, 52% of the nurses said they would perform symptom assessment; only 2.5% said they would ask the patient to rate his dyspnea severity.

Dr. Scarpaci and her coinvestigator Mary McPherson, Pharm.D., said that all hospice patients using metered-dose inhalers should be encouraged to use a spacer.

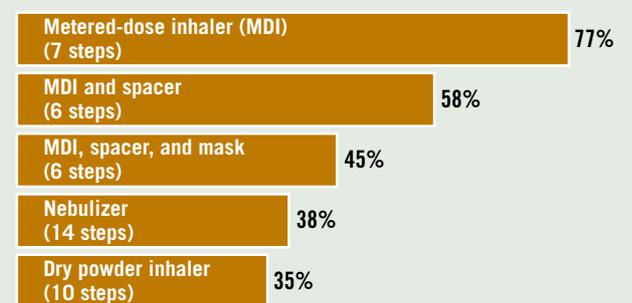
"Controlled breathing is difficult for patients with a terminal illness, and a metered-dose inhaler with a spacer, in addition to allowing the patient to breathe more normally, provides the same drug delivery as using the more invasive and expensive nebulizer," said Dr. McPherson, a professor at the University of Maryland School of Pharmacy, Baltimore.

This study followed a pilot study that suggested that instructing hospice patients in the proper use of inhalers improved dyspnea, Dr. McPherson explained in an interview. "It led us to wonder why patients were doing such a bad job with their inhalers."

In one hospice studied, of the 1,300 patients admitted over a 1-year period, 20% were using an inhaled medication. "So it's important that patients know how to use these devices because over 80% of people with terminal illness develop dyspnea," said Dr. McPherson.

"The physician, the nurse, and the pharmacist may all believe that the other person is instructing patients in the proper use of their inhalers. Instead of making that assumption, all those involved in the care of hospice patients should take the initiative and provide counseling and education," Dr. Scarpaci said in an interview. ■

Average Percentage of Steps Completed Correctly By Nurses Demonstrating Delivery Devices



Note: Data based on a study group of 50 hospice nurses.
Source: Dr. Scarpaci



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Pulmonary Segmentectomy Makes a Comeback

Studies suggest outcomes are equivalent to those of lobectomy for some early-stage lung tumors.

BY BRUCE JANCIN
Elsevier Global Medical News

SAN DIEGO — Thoroscopic pulmonary segmentectomy is a safe and technically feasible operation that gets patients out of the hospital an average of 2.5 days earlier than open segmentectomy, Dr. Broadus Z. Atkins said at the annual meeting of the Society of Thoracic Surgeons.

“Thoroscopic pulmonary segmentectomy is a sound option for lung-sparing anatomic resection for experienced thoroscopic surgeons,” according to Dr. Atkins of Duke University, Durham, N.C.

“This approach appears to have distinct advantages compared to open procedures,” he said.

Pulmonary segmentectomy was a thoracic surgery mainstay for more than half a century before falling into disfavor more than a decade ago, after an influential randomized trial by the Lung Cancer Study Group showed that it resulted in higher local recurrence and mortality rates than lobectomy in patients with early-stage non-small cell lung cancer (*Ann. Thorac. Surg.* 1995; 60:615-22).

But the last several years have brought renewed enthusiasm for the procedure.

The potential advantages of sublobar resection include preservation of lung function and greater flexibility in resecting metastases to the lung from extrapulmonary primary tumors.

Evidence from several studies suggests that outcomes are equivalent to those with lobectomy for early-stage lung tumors less than 2 cm in diameter.

For these reasons, a multicenter trial is underway comparing segmentectomy to lobectomy in early-stage lung cancer, Dr. Atkins noted.

Use of thoroscopic lobectomy has become widespread over the past several years because of evidence for less postoperative pain, shorter chest tube duration, and fewer complications, as well as faster return to full activity than with open lobectomy.

However, there have been few reports on thoroscopic segmentectomy published in the literature.

To address this shortcoming, Dr. Atkins reported on 77 consecutive segmentectomies performed since the year 2000 at Duke; 48 were done thoroscopically, while 29 were open procedures. During the same time period, Duke surgeons performed about 1,500 lobectomies.

Patients in the thoroscopic and open segmentectomy groups were similar with respect to age, gender, smoking history, and preoperative spirometry values.

A greater number of patients in the thoroscopic segmentectomy group had primary lung cancer; metastatic lung tumors were more common in the open surgery group.

The average operative time of about 135 minutes was similar in both groups, as were estimated blood loss, the number of

THE POTENTIAL ADVANTAGES INCLUDE PRESERVATION OF LUNG FUNCTION AND GREATER FLEXIBILITY IN RESECTION OF METASTASES TO THE LUNG.

mediastinal lymph node stations sampled, and chest tube duration.

However, length of hospital stay averaged 4.3 days in the thoroscopic group, compared with 6.8 days for open surgery patients.

At least one postoperative complication occurred in about one-third of patients in each group. Complications in the two study arms were similar in nature and severity.

Patients in the thoroscopic segmentectomy group had lower 30-day and long-term mortality rates and fewer distant metastases; however, audience members downplayed the significance of these findings because the study was nonrandomized and selection bias appeared to be at work.

They noted that disease beyond stage I was five times more common in patients in the open segmentectomy group, and the size of their removed tumors was significantly greater as well. In addition, a higher mortality rate might be expected in the open segmentectomy group because of their greater prevalence of metastatic disease.

The possibility that segmentectomy may have unfairly gotten a bad rap in the last couple of decades was raised by Dr. Joseph Locicero III, FCCP, who described an unexpected twist to one of the previous negative trials.

“It turns out on interviewing a number of the surgeons involved that they didn’t actually perform a segmentectomy; they performed a generous wedge resection or completed a segmentectomy with a stapler.

“In those cases we’re really not sure if an anatomic procedure was performed,” said Dr. Locicero, director of surgical oncology at Maimonides Medical Center, New York. ■

Obesity Didn’t Boost Morbidity Risk After Pulmonary Surgery

BY BRUCE JANCIN
Elsevier Global Medical News

SAN DIEGO — Contrary to conventional surgical wisdom, obesity doesn’t increase the perioperative morbidity or mortality associated with major pulmonary surgery, according to two studies presented at the annual meeting of the Society of Thoracic Surgeons.

The studies involved large patient populations: one undergoing anatomic resection for non-small cell lung cancer, the other pulmonary transplantation.

“The results of our study are provocative and challenge the assumptions about outcomes following thoracic surgery in obese patients. Our results suggest that it is unwarranted to avoid surgical intervention in obese patients who are otherwise appropriate candidates for resection of lung cancer,” observed Dr. Philip W. Smith of the University of Virginia, Charlottesville.

Obesity used to be uncommon in lung cancer patients. Not any longer.

“In our recent institutional experience, about two-thirds of lung cancer patients are overweight and one-quarter are obese prior to resection,” explained Dr. Smith, who predicted the trend is likely to accelerate.

“With childhood and teenage obesity on the rise, the epidemic of obesity will continue to expand, and thoracic surgeons will see increasing numbers of obese patients with lung cancer,” he said.

He compared outcomes in 127 obese and 372 overweight or normal-weight

patients in a consecutive series undergoing anatomic resection for non-small cell lung cancer.

In contrast to his working hypothesis, obesity wasn’t associated with greater morbidity or mortality.

Indeed, the 30-day overall mortality of 1.4% was similar in both groups. Average hospital length of stay and 30-day re-admission rates were also similar.

One or more complications occurred in 33% of nonobese and 31% of obese patients.

Most intriguingly, respiratory complications occurred in 22% of nonobese pa-

‘OUR RESULTS SUGGEST THAT IT IS UNWARRANTED TO AVOID SURGICAL INTERVENTION IN OBESE PATIENTS WHO ARE ... APPROPRIATE CANDIDATES.’

tients but only 14% of obese patients, a difference that barely missed statistical significance.

Dr. Smith didn’t conduct a cost analysis, but he said that even without any increase in complications, obese patients require more use of health care resources, including specialized equipment, demands upon staff, longer operating room times, and increased medication requirements.

Dr. Smith’s report met with a degree of skepticism.

“I think we should send all our obese patients to Charlottesville,” quipped session cochair Dr. G. Alexander Patterson, FCCP, the Evarts A. Graham Professor of Surgery and chief of the division of cardiothoracic surgery and section of general thoracic surgery at Washington University, St. Louis.

“I don’t believe your study. It can’t be true,” the surgeon added with a smile.

But audience member Dr. Carolyn E. Reed, FCCP, hastened to reassure Dr. Smith that she believes it is true.

Dr. Reed and her colleagues at the Medical University of South Carolina, Charleston, recently reviewed their esophagectomy outcomes in obese vs. nonobese patients and were similarly surprised by the results.

“Our findings absolutely mimicked yours,” said Dr. Reed, professor of surgery and chief of general thoracic surgery at the university.

She added that she suspects but can’t prove the explanation is that obese patients undergoing thoracic surgery are managed more aggressively at the first sign of any problem.

Elsewhere at the meeting, Dr. Ricardo S. Santos of the University of Pittsburgh reported that preoperative weight had no impact upon lung transplantation outcomes in 517 patients who underwent the procedure there. It is the largest series reported to date.

Mean length of stay and 90-day and 10-year mortality rates were similar in the 68 obese patients, the 51 underweight ones, and normal-weight patients.

There was a suggestion of a survival benefit in the obese patients through the first 5 years that’s “difficult to explain,” he said in an interview.

“It’s important to say we didn’t change our recommendations: If patients are underweight, they should gain weight, and if they’re obese, they have to lose weight. But we don’t make these conditions a contraindication for lung transplantation or a reason for delay,” Dr. Santos continued.

“Some of our patients come from other centers where they were declined for lung transplantation because their BMI [body mass index] was 32 or 33 kg/m²,” he explained. “We’ll accept them for evaluation and proceed with lung transplantation if they don’t present any other major comorbidities.”

Using BMI as the sole criterion to preclude transplantation “is not acceptable,” Dr. Santos concluded. ■

Dr. Robert Cerfolio, FCCP comments: *Smith and colleagues have provided a timely report given the epidemic of obesity not only in the United States but also worldwide.*

Increased weight and body mass index, just like advanced age, should not be a reason to deny a patient an operation that has the potential to provide benefit or cure.

Although these patients do require some special postoperative considerations, the vast majority—if motivated—can safely undergo surgical resection of any type.

Size Matters in Talc Poudrage for Pneumothorax

BY BRUCE JANCIN
Elsevier Global Medical News

SAN DIEGO — The key to complication-free videothoroscopic talc poudrage for primary spontaneous pneumothorax is to use talc of relatively large particle size, Dr. Giuseppe Cardillo asserted at the annual meeting of the Society of Thoracic Surgeons.

This is the treatment of choice for recurrent and complicated primary spontaneous pneumothorax, he said. In his series of 861 patients treated during a 9-year period—the largest by far ever reported—the treatment success rate was in excess of 98% with a postoperative morbidity rate of 3.4%.

Talc is inexpensive, readily available, and provides better efficacy and fewer recurrences than any other agent available for chemical pleurodesis, added Dr. Cardillo of Carlo Forlanini Hospital, Rome, and the University of Rome La Sapienza.

There are no controlled trials to provide guidance as to optimal dosage. Some surgeons administer as much as 10 g. His own practice is to nebulize 2 g of talc into the pleural cavity.

Primary spontaneous pneumothorax is chiefly a disease of otherwise healthy young men. The incidence has been

placed at 18-28 cases per 100,000 population per year in men—peaking in their 20s—and at 1.2-6 cases per 100,000 per year among women. The diagnosis is readily made by chest x-ray.

Smoking plays an important role in this form of lung disease. The lifetime risk of primary spontaneous pneumothorax in otherwise healthy male smokers has been estimated at up to 12%; that's more than 100-fold greater than the risk in non-smoking men.

Smoking also figures prominently in the recurrence risk after talc poudrage. In fact, smoking is the only identifiable risk factor for recurrence. In Dr. Cardillo's series, the recurrence rate was 2.5% in smokers, compared with 0.6% in non-smokers.

Like most experts, he advocates treating a first episode of primary spontaneous pneumothorax by simple intercostal chest drainage. Surgery is best reserved for a recurrent episode or a complicated first episode marked by bilateral involvement or failure of the lung to fully reexpand after chest drainage.

He and his colleagues perform the video-assisted thoracic surgery under general anesthesia, and tailor the procedure to the results of intraoperative staging using Vanderschueren's classification. Stage I

disease, with no endoscopic abnormalities, is treated by talc poudrage only. For stage II, marked by pleuropulmonary adhesions, the surgeons lyse all adhesions and perform talc poudrage. For stages III and IV, they staple the blebs and bullae in addition to doing talc poudrage.

In their 861-patient series, the 3.4% complication rate was manifested mainly by localized pleural effusion, prolonged air leak, and subcutaneous emphysema, all of which resolved spontaneously.

The mean hospital stay was 5.6 days. Two-thirds of patients returned to work within 21 days, and 91% returned within 30 days. At discharge, 13% of patients reported moderate to severe paresthesia, which resolved spontaneously within 6 months in all cases.

The median particle size of the asbestos-free talc preparation used by the Italians is 25.6 mc. Only 11% of the particles are smaller than 5 mc, compared with 50%-80% in samples reported from the United States and South America. Dr. Cardillo is convinced that the large particle size protects against adult respiratory distress syndrome and empyema, neither of which occurred in his series.

Audience members expressed some concern about the unknown long-term adverse effects of talc poudrage in young

patients with many decades of life remaining. Dr. Cardillo replied that no problems have emerged with up to 9 years' follow-up thus far in his series. The results of repeated pulmonary function tests in a 26-patient subset have been normal. He conceded, however, that reentering the chest in the event of future thoracic surgery "will be a big problem."

Dr. Robert Cerfolio, FCCP, comments:
Dr. Cardillo has reported his experience on using talc for benign disease. Although we agree that firm data are lacking to support "problems" with talc in young patients with benign disease, the jury is out and will be for another 50 years in these patients. Because the natural long-term history of talc in these patients is unknown and because so many physicians worry about it causing constriction and maybe even cancer, we still prefer to use mechanical pleurodesis with VATS pleurectomy and intentionally apply a staple line on the apex of the lung and in a few other areas that are buttressed with strips that help create adhesions between the lung and chest wall. This technique also works in 98%-99% of patients as well, and avoids talc. The article is important, however, and the size and amount of talc is also important. The long-term follow-up (25-50 years) on these patients will provide important information to all of us.

Medication Error Rates Are Highest in Perioperative Areas

BY ELIZABETH MEHCATIE
Elsevier Global Medical News

ROCKVILLE, MD. — More than 11,000 perioperative medication errors were reported to a national database of hospital medication errors between 1998 and 2005. Of these, 5% resulted in harm, according to a report issued by the U.S. Pharmacopeia.

The database, known as MEDMARX, is operated by the USP and is the largest national database of hospital medication errors in the United States, receiving about 15,000 new reports every month.

The 11,239 perioperative medication errors reported by more than 500 hospitals in 7 years were divided into four settings: outpatient surgery (30% of the total reports), the preoperative holding area (7%), the operating room (34%), and the postanesthesia care unit (29%). The proportion reported in the preoperative holding area was lower because this category was added to the database in 2003.

The 5% rate of harmful errors is about threefold higher than the proportion of medication errors resulting in harm in all other areas of the hospital combined. The proportion of perioperative medication errors that resulted in harm was higher among patients under age 17 than among older patients.

Among the medication errors that resulted in harm, there were four deaths, including one pediatric patient, according to Diane D. Cousins, a registered pharmacist and vice president of the Center for the Advancement of Patient Safety at the USP.

A total of 739 drug products were involved in errors, the most common of

which were the antibiotics cefazolin and vancomycin; the analgesics morphine, fentanyl, and meperidine; the sedative midazolam; and heparin, Ms. Cousins said. There were 165 drugs (22%) involved in harmful errors, most commonly morphine, fentanyl, and cefazolin.

Errors included administering the wrong medication or the wrong amount of medication, administering medication at the wrong time, omitting a medication or a dose, or administering medication incorrectly.

In the operating room, omission and wrong drug administration were the most common mistakes, she said. For example, a surgeon called in an order for a dose of ampicillin to be given during surgery that was scheduled a week later, but the order was never recorded. As a result, the patient (a child) never received the drug.

In the postanesthesia care unit setting, the most typical errors involved prescribing and administering incorrect amounts of drugs, she said. After an elderly patient was discharged from the postanesthesia care unit to an inpatient unit, it was discovered that the patient was receiving an excessive amount of heparin because of a programming error made in the postanesthesia care unit.

The results were announced during a press briefing sponsored by the USP, which released the report in partnership with the Uniformed Services University of the Health Sciences (USUHS), the Association of Perioperative Registered Nurses (AORN), and the American Society of PeriAnesthesia Nurses (ASPAN). Published by the USP Center for the Advancement of Patient Safety, the report is the largest

known national analysis of medication errors related to surgery, Ms. Cousins said during the press conference.

The findings were also provided in a briefing to 11 national organizations and agencies, with the intention of calling them to action.

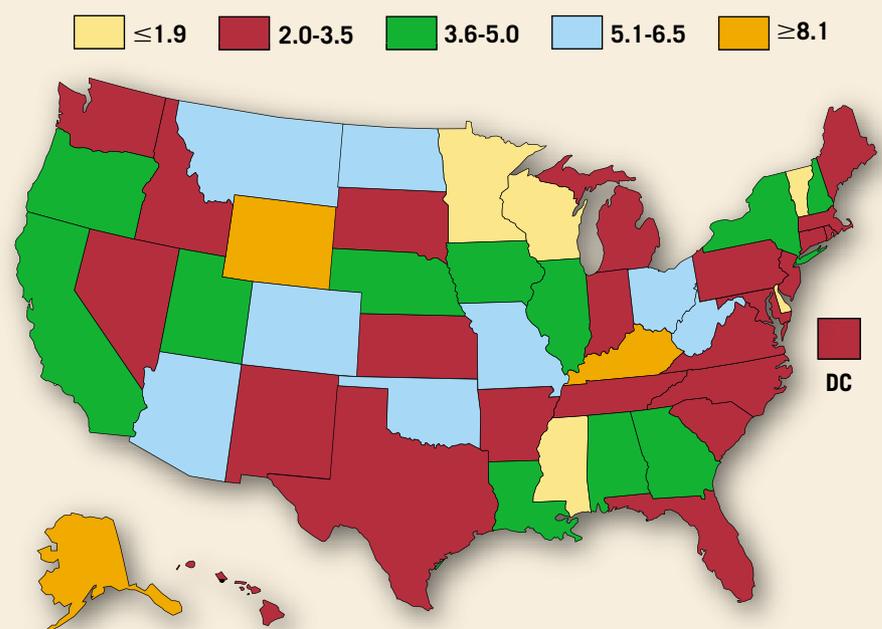
The 47 recommendations issued in the report include implementing strategies that improve communication among all

perioperative team members, designating a pharmacist to coordinate medication safety, working to ensure that medications are administered on time, "and calling on manufacturers to provide products in ready-to-use, sterile packaging, especially for drugs administered to children."

The report is available (for purchase) at www.usp.org/products/medMarx.

DATA WATCH

State Medical Boards' Serious Disciplinary Actions (per 1,000 physicians)



Note: Rate is calculated by averaging the rates from 2003 to 2005.
Source: Public Citizen

Competitive Bidding to Debut for Medical Equipment

BY ALICIA AULT
Elsevier Global Medical News

Starting in April 2008, retailers and suppliers in 10 metropolitan areas who sell certain durable medical equipment will have to become accredited and enter a competitive bidding process, according to a final rule issued by the Centers for Medicare and Medicaid Services.

Unlike other entities, physicians may opt out of competitive bidding and accreditation, but they will still have to accept a single payment for the durable medical equipment (DME) item instead of a fee schedule-based payment, Acting CMS Administrator Leslie Norwalk said in a briefing with reporters.

The new competitive bidding program was developed to reduce Medicare's substantial DME expenditures and to decrease the out-of-pocket burden for beneficiaries, who are liable for copayments of 20%.

"The final rule we are announcing today is focused on improving both service delivery and the quality of care, while getting savings for beneficiaries and taxpayers," Ms. Norwalk said in a statement.

She estimated that Medicare could shave \$1 billion a year off its DME tab by the time the program is fully implemented in 2010.

The final rule will apply initially only to 10 categories of supplies and only to suppliers in 10 competitive bidding areas (CBA) that have been established by CMS. Physicians, hospitals, and other entities that sell DME, prosthetics, orthotics, and certain other supplies will be required to submit bids to CMS proposing charges for the items.



Wheelchairs, CPAP devices, and respiratory assist devices are among the items that will be subject to a bidding process.

Bidding will probably be open from late April until late June. CMS will evaluate the bids and then, probably in December, the agency will award contracts to a certain number of bidders in each CBA, Ms. Norwalk said in the briefing.

Beginning in April 2008, Medicare will pay a single amount for each item in those areas instead of basing payments on a fee schedule, as it has in the past.

CMS will expand the program to 70 bidding areas in 2009, and to more CBAs, and to cover more DME items after that, Ms. Norwalk said.

The new process was required by the Medicare Prescription Drug Improvement and Modernization Act of 2003. CMS outlined its intentions in a proposed rule in August 2006. It also gathered data from two pilot studies that ran from 1999 to 2002 in San Antonio and in Polk County, Fla., Ms. Norwalk said. After incorporating public comments and experience

from the pilot, CMS published the final rule in the Federal Register.

Suppliers in the following 10 areas will be the first who are subject to the new requirements: Charlotte-Gastonia-Concord, N.C./S.C.; Cincinnati-Middletown, Ohio / Ky. / Ind.; Cleveland-Elyria-Mentor, Ohio; Kansas City, Mo./Kans.; Dallas-Fort Worth-Arlington,

Tex.; Miami-Fort Lauderdale-Miami Beach, Fla.; Orlando-Kissimmee, Fla.; Pittsburgh; Riverside-San Bernardino-Ontario, Calif.; and San Juan-Caguas-Guaynabo, Puerto Rico.

The locations were selected because they are 10 of the largest Metropolitan Statistical Areas in the United States and because each area had high costs and/or high utilization of DME items in the 10 focus categories. Although New York, Los Angeles, and Chicago are among the largest Metropolitan Statistical Areas and have high costs and utilization, CMS decided to exclude those areas initially to simplify the process, Ms. Norwalk said.

The 10 categories include oxygen supplies and equipment; standard power wheelchairs, scooters, and accessories; complex rehabilitative power wheelchairs and accessories; mail-order diabetes supplies; enteral nutrients, equipment, and supplies; continuous positive airway

pressure devices, respiratory assist devices, and supplies and accessories; hospital beds and accessories; negative pressure wound therapy pumps and supplies and accessories; walkers and related accessories; and support surfaces (group 2 and 3 mattresses and overlays).

In most CBAs, only nine categories will be subject to bidding in 2008. All 10 will be covered in the Miami and the San Juan areas.

Since 60% of diabetic supplies are delivered by mail-order, CMS decided to require those suppliers to be subject to competitive bidding. Thus, patients with diabetes will continue to have the option of mail-order and it should be less costly, according to CMS. Payment for supplies obtained at a pharmacy or elsewhere will still be covered under the old Medicare fee schedule, even in the 10 CBAs, the agency said.

Blood glucose monitors are not subject to competitive bidding.

To qualify to bid, suppliers have to be accredited by 1 of 10 agencies certified by CMS. Those include the Joint Commission on Accreditation of Healthcare Organizations, the Board of Orthotist/Prosthetist Certification, and the Accreditation Commission for Health Care Inc. Generally, bidders also have to be in good standing with Medicare, have an active National Supplier Clearinghouse number, agree to service an entire bidding area, regardless of where a beneficiary may be located.

Of the winning contract slots, 30% are set aside for small suppliers—those with annual gross revenue of \$3.5 million or less. ■

The accrediting bodies, bidding criteria, and other details are listed at www.cms.hhs.gov/CompetitiveAcqforDMEPOS.

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Periodic Limb Movements Do Not Equal Restless Legs

BY JANE SALODOF MACNEIL
Elsevier Global Medical News

SCOTTSDALE, ARIZ. — Periodic limb movements are common during sleep and should not be confused with restless legs syndrome, Dr. Barbara A. Phillips, FCCP, warned at a meeting on sleep medicine sponsored by the American College of Chest Physicians.

Counting lots of periodic limb movements does not add up to a diagnosis of restless legs syndrome (RLS), according to Dr. Phillips, medical director of the sleep center at Samaritan Hospital in Lexington, Ky. RLS must be diagnosed with a clinical interview.

As many as 85% of RLS patients have periodic limb movement during sleep, but so do many people with other sleep disorders and healthy people with no sleep issues, said Dr. Phillips, a professor of pulmonary and critical care medicine at the University of Kentucky, Lexington. About half the patients tested in a sleep laboratory will have periodic limb movement.

"It doesn't predict anything. It doesn't correlate with anything useful. Treating it doesn't improve patient outcome," she said, describing the clinical significance of

periodic limb movement as controversial.

RLS is real, with a prevalence of 3%-15% in the general population, Dr. Phillips reported. Studies have associated it with poorer quality of life, excessive daytime sleepiness, and depression and anxiety. Current thinking holds that insufficient brain iron causes abnormalities in dopamine function in the brain and spinal cord. These abnormalities, in turn, cause RLS.

Most primary cases of RLS are hereditary, Dr. Phillips said, but iron-deficiency anemia, end-stage renal disease, medications (selective serotonin reuptake inhibitors, tricyclics, dopamine antagonists, and antihistamines), diabetes, rheumatoid arthritis, and peripheral neuropathy can be secondary causes.

About 25% of pregnant women develop RLS, she noted. It has not been shown to cause fetal harm, but approved medications for RLS are contraindicated during pregnancy.

Dr. Phillips emphasized that diagnosis of RLS is based on four core symptoms:

► Patients have an urge to move their limbs. This urge is "usually accompanied

or caused by uncomfortable and unpleasant feelings in the limbs."

► Symptoms start or become worse with rest or inactivity.

► Discomfort is relieved when patients get up or move about.

► Symptoms appear or become worse in the evening or at night.

In addition, Dr. Phillips said family history of RLS, response to dopaminergic therapy, and the presence of periodic limb movements can support a diagnosis but are not diagnostic by themselves.

She suggested the International RLS Rating Scale and Scoring Sheet (www.mdvu.org/library/ratingscales/rls) as a tool for assessing symptom severity. Laboratory testing should include serum ferritin levels and percent of iron saturation.

She also recommended a neurologic assessment, if peripheral neuropathy is suspected, as it can mimic RLS. Likewise, she said children and patients suspected of having coexisting obstructive sleep apnea or narcolepsy should be sent for polysomnography. Differential diagnosis

also should include akathisia in patients on a dopamine antagonist and muscle cramps.

Two dopamine agonists are approved for RLS treatment: pramipexole and ropinirole. She recommended that patients with frequent RLS symptoms take one or the other nightly 30-90 minutes before bedtime. Average doses are 0.25 mg/day of pramipexole and 2 mg/day of ropinirole.

Carbidopa and levodopa also are used off label, but Dr. Phillips said neither is likely to be approved for RLS. About 80% of patients develop augmentation in which symptoms become worse with long-term use. Nonetheless, Dr. Phillips said occasional off-label as-needed use could help patients who have infrequent symptoms.

Other treatment strategies address factors that aggravate RLS. Dr. Phillips said many patients find that sleep deprivation, alcohol, caffeine, and smoking can make RLS worse, as can too much or too little exercise.

Treating secondary causes such as proven iron deficiency and renal disease also can help. Although Dr. Phillips said to consider discontinuing medications that can worsen RLS, she added that she has never taken a patient off a selective serotonin reuptake inhibitor. ■



Periodic limb movement 'doesn't predict anything. It doesn't correlate with anything useful.'

DR. PHILLIPS

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Sleep Apnea Did Not Predict Metabolic Abnormalities

BY SARAH PRESSMAN LOVINGER
Elsevier Global Medical News

Obstructive sleep apnea was not associated with an increased risk of metabolic abnormalities in patients with sleep-disordered breathing, according to the results of a new study.

However, obesity was associated with a greater risk of obstructive sleep apnea and metabolic abnormalities.

"We did not find any independent correlation between [apnea-hypopnea index] and metabolic abnormalities," stated Dr. S.K. Sharma of the division of pulmonary and critical care medicine, All India Institute of Medical Sciences, New Delhi, and colleagues (Sleep Med. 2007;8:12-7).

The researchers evaluated 120 people in

a cohort study lasting from April 2003 to March 2005. Using polysomnographic data, they compared lipid parameters in 40 obese apneic participants (apnea-hypopnea index 32.2, range 13-52.8) with 40 obese nonapneic controls (AHI 1.3, range 0-2.5) and with 40 normal-weight controls without apneic breathing (AHI 0.7, range 0-1). The parameters included serum lipids, fasting blood sugar, serum insulin, insulin resistance, leptin, and adiponectin levels.

Patients with a body mass index (BMI) of at least 25 kg/m² were considered

obese, the definition used by the World Health Organization for Southeast Asia. The ratio of male to female participants was 1.1:1, and the average age was 42.5 years. The researchers excluded subjects with diabetes, acromegaly, chronic renal failure, and those on chronic steroid therapy or hormone replacement medication.

The results revealed no significant differences in fasting blood sugar, insulin resistance, leptin, and adiponectin levels between the obese group with obstructive sleep apnea (OSA) and the obese control

group. The patients in the OSA group had higher lipid levels than did those in the control group, but the difference was not statistically significant.

The investigators did find that obesity as determined by BMI, waist circumference, and waist-hip ratio was independently associated with OSA. They also found significant differences in serum insulin, insulin resistance, leptin, and HDL and LDL cholesterol levels in the nonapneic obese group, compared with the normal-weight control group. ■

FYI

Cancer Facilities Guide Available

The top treatment facilities and specialists for different cancers, plus financial tips, drug trial information, and success stories, are available in a new guidebook, "Patient Resource: A Cancer Treatment and Facilities Guide for Patients and Their Families." The book is available for free to physicians and costs \$6.95 for patients to purchase directly. The guide is available at www.patientresource.net/place-order.htm.

Quality Reporting Questions Answered

More than 50 frequently asked questions about the Physician Quality Reporting Initiative are available on the Web site of the Centers for Medicare and Medicaid Services. Visit www.cms.hhs.gov/PQRI, scroll down to "Related Links Inside CMS," and click on "All PQRI FAQs."

Free Rx Savings Card

The Together Rx Access Card is a free prescription savings card for people who are legal residents of the U.S., are not eligible for Medicare, do not have prescription drug coverage, and meet certain income levels. Most card holders will save 25%-40% on more than 300 brand-name prescription products. Savings also are available for generic products. For more information, visit www.togetherrxaccess.com.

Prescription Assistance Fact Sheet

The National Council on Patient Information and Education is distributing a fact sheet to advise consumers who lack health insurance or prescription drug coverage about prescription assistance programs and prescription savings/discount programs. For more information, read the fact sheet at www.talkaboutrx.org/documents/paps.pdf.



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 ≤ 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/m² basis. **Use 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/m² basis) or to mice at doses up to 1200 mg/kg (2 times the recommended maximum human dose calculated on a mg/m² basis) or to rabbits at a dose level of 100 mg/kg (approximately equal to the recommended maximum human dose calculated on a mg/m² 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 recommend-

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

ed 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

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

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

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

*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 some 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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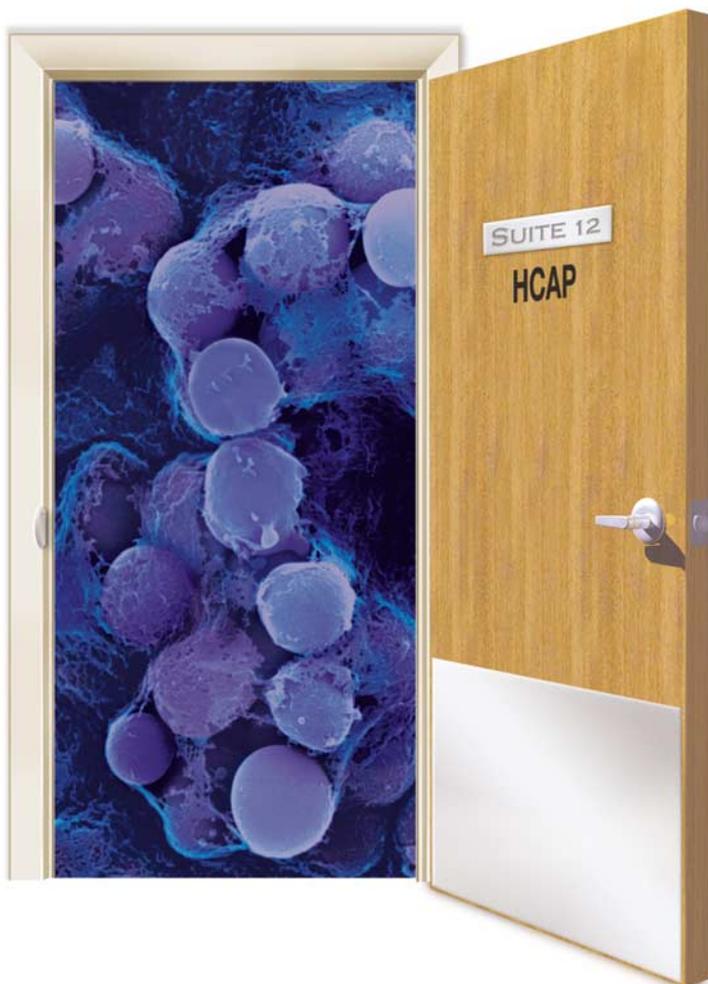
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knock, knock.



Gram-positive infection?

WE'RE THERE, TOO.*



*For gram-positive infections due to susceptible strains of indicated organisms in treating moderate-to-severe pneumonia or febrile neutropenia.

MAXIPIME is contraindicated in patients who have shown an immediate hypersensitivity reaction to MAXIPIME, cephalosporins, penicillins, or any other β -lactam antibiotics.

In North American clinical trials of MAXIPIME at a dose of 0.5 to 2 g IV q12h, the most common adverse events were local reactions (3%), including phlebitis (1.3%), pain and/or inflammation (0.6%); rash (1.1%). 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 administration of antibacterial agents.

HCAP defined as: healthcare-associated pneumonia.

Please see brief summary of prescribing information on adjacent page.



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