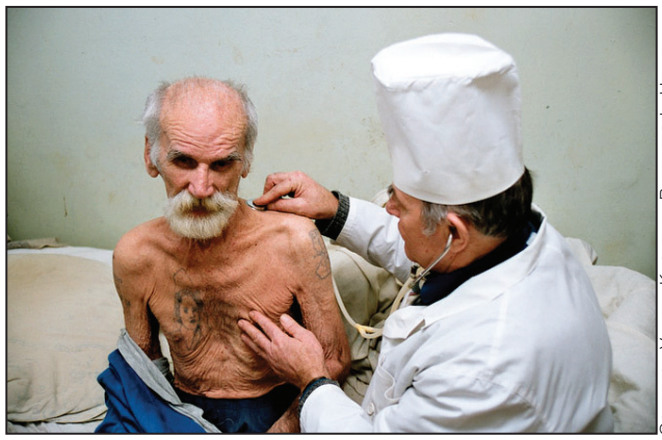
VOL. 6 • NO. 3 • MARCH 2011

CHEST Physician

THE NEWSPAPER OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS



COURTESY VALERY KASATKIN, PARTNERS IN HEALTH

A physician examines a tuberculosis patient in Russia, where MDR-TB is rampant. World TB Day is March 24.

Fighting Tuberculosis In Siberia

BY HEIDI SPLETE
Elsevier Global Medical News

Russia has one of the world's most persistent epidemics of multidrug-resistant tuberculosis.

The MDR-TB treatment program in the Tomsk region of Siberia, Russia, has been one of the long-term projects of the Boston-based medical service organization Partners in Health (PIH). Established in 2000, the program received a $1.5 million grant in November 2010 from the U.S. Agency for International Development to expand its services to five additional Russian regions: Novosibirsk, Altai Krai, Saratov, the Republic of Mari-El, and Voronezh.

Over the years, the project has evolved to address patient care needs more broadly, to train local health professionals, and to conduct research to improve treatment across Russia as a whole.

Today, through an exchange program created by PIH, Russian medical professionals can earn masters degrees in public health at Harvard University. The first graduates of the program are now sharing their knowledge as lecturers at the Moscow Medical Academy.

Dr. Alex Golubkov is the current medical director of the PIH program in Russia and Kazakhstan. He earned his medical degree in Russia in 1999, and then an MPH at Boston University in 2004. In the following interview, he discusses the MDR-TB program.

Why is MDR-TB such a problem in Russia?

The social situation in much of Russia lends itself to the development of TB and MDR-TB. Many patients that we treat in Russia are unemployed and homeless, and many of them suffer from alcoholism and HIV. In addition, high levels of imprisonment in Russia lead to the dissemination of TB and MDR-TB acquired in prisons to the civilian population. It is well known that imprisonment is one of the highest risk factors for TB, and if treatment was not provided in prison, resistance may be amplified, and these patients will develop drug-resistant TB.

See **Siberia** • *page 12*

Classification Revised for Lung Adenocarcinoma

Patient stratification improved.

BY SHERRY BOSCHERT
Elsevier Global Medical News

A joint effort by three medical groups has enabled a variety of specialists to join pathologists in revising the classification of lung adenocarcinoma, and they have made some major changes.

A new section addresses diagnosis and classification of non–small cell lung carcinoma (NSCLC) in small biopsies and cytology, including criteria to distinguish adenocarcinoma from squamous cell carcinoma.

The new classification also recommends performing epidermal growth factor receptor (EGFR) mutation testing in patients with advanced lung adenocarcinoma to help predict response to tyrosine kinase inhibitors.

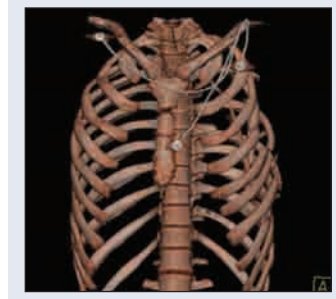
And it eliminates the term "bronchioalveolar carcinoma," while elsewhere in the document adding some new terms, including adenocarcinoma in situ and minimally invasive adenocarcinoma (J. Thorac. Oncol. 2011;6:244-85).

The International Association for the Study of Lung Cancer convened the multidisciplinary panel of experts to revise the previous World Health Organization classification of lung adenocarcinoma, with support and scientific oversight from the American Thoracic Society and the European Respiratory Society. Pathologists, oncologists, pulmonologists, radiologists, thoracic surgeons, and molecular biologists joined the effort.

The revisions should make it easier to stratify patients and to individualize treatment, Dr. William D. Travis, FCCP, chair of the expert panel, said in an interview.

See **Adenocarcinoma** • *page 16*

INSIDE



Rescue Combo Enough in Mild Asthma

BY ELIZABETH MECHCATIE
Elsevier Global Medical News

Rescue therapy with beclomethasone combined with albuterol reduced the risk of exacerbations requiring oral corticosteroid treatment, even without daily steroid use, according to a placebo-controlled study of children and teenagers with mild persistent asthma.

"Assessed from a risk-benefit point of view, our data suggest that, in children with mild persistent asthma, use of rescue inhaled corticosteroid could be an effective step-down alternative to discontinuation of such treatment after asthma control is achieved," said Dr. Fernando D. Martinez, of the Arizona Respiratory Center and the University of Tucson (Ariz.), and his associates.

This approach "could also be an alternative, step 2 therapeutic approach for mild persistent asthma in individuals who have not previously received a course of daily corticosteroid treatment," they added, although they noted

See **Asthma** • *page 2*

CHEST Physician
60 Columbia Rd.,
Bldg. B, 2nd flr.
Morristown, NJ 07960

CHANGE SERVICE REQUESTED

Presorted Standard
U.S. Postage
PAID
Permit No. 384
Lebanon Jct. KY

Daily ICS Use May Be Avoided

Asthma • *from page 1*

that the 44-month randomized, double-blind study was not designed to address this issue.

The TREXA study, funded by the National Heart, Lung, and Blood Institute (NHBLI), appeared online in the Lancet (doi:10.1016/S0140-6736[10]62145-9).

The study was conducted to determine whether discontinuing treatment with daily inhaled corticosteroids (ICS) in children with well-controlled mild persistent asthma increased the risk of exacerbations, and whether combining beclomethasone and albuterol as rescue therapy, with or without daily beclomethasone, was more protective against asthma exacerbations than was an albuterol-only rescue strategy.

In the study, 288 children and adolescents aged 5-18 years from five U.S. clinical centers, with mild persistent asthma during the previous 2 years, were randomized to one of four treatment groups:

► Beclomethasone twice daily, with beclomethasone plus albuterol as rescue (combined group).

► Beclomethasone twice daily, with placebo plus albuterol as rescue (daily beclomethasone group).

► Placebo twice daily, with beclomethasone plus albuterol as rescue (rescue beclomethasone group).

► Placebo twice daily, with placebo plus albuterol as rescue (placebo group).

Twice-daily beclomethasone treatment was one puff (40 mcg per puff) in the morning and evening; rescue beclomethasone treatment was two puffs of beclomethasone (80 mcg) for every two puffs of albuterol (180 mcg) needed for relief of symptoms. The primary outcome was the time to first exacerbation requiring treatment with oral corticosteroids.

Among those in the placebo group, who received only albuterol as rescue, the exacerbation rate was 49%, compared with 31% in the combined group, 28% in the daily group, and 35% in the rescue group. "Compared with the placebo group, the hazard ratios for asthma significantly lower in the daily beclomethasone group and the combined group, but the difference was not significant in the rescue beclomethasone group," they found.

The children in the two groups using daily beclomethasone also showed signs of less linear growth, a secondary end point: Children in these two groups grew a mean of 1.1 cm less than did those in the placebo group, a statistically significant difference. But the children in the rescue beclomethasone group (who received less than a quarter of the total daily ICS dose that the children in the combined and daily beclomethasone groups received) grew a mean of 0.3 cm less than did those in the placebo group, which was not a significant difference.

The two adverse events considered severe were a case of viral meningitis in the daily beclomethasone group and a case of bronchitis in the combined group.

The authors noted that children with mild persistent asthma should not be treated with rescue albuterol alone and that daily ICS is the most effective treatment to prevent exacerbations in this age group, and added that "our data suggest that inhaled corticosteroids used as rescue together with albuterol show benefits over rescue albuterol alone and avoids the growth effects associated with use of daily inhaled corticosteroids."

They added that to their knowledge, the study was the first to look at the use of ICS with albuterol as rescue therapy in school-aged children.

©DAGMAR HEYMANS/STOCKPHOTO.COM

"Inhaled corticosteroids used as rescue together with albuterol … avoids the growth effects associated with use of daily inhaled corticosteroids," the researchers said.

These results "have potentially important implications for the management of asthma," Dr. William Checkley wrote in an accompanying editorial (Lancet 2011 Feb. 15 [doi:10.1016/S0140-6736(10)62313-6]). He noted that the British Thoracic Society and NHLBI National Asthma Education and Prevention Program guidelines recommend daily ICS use as initial and step-up treatment for persistent asthma, and "step-down is possible if asthma symptoms are well controlled for at least 3 months."

The results of this study, however, "suggest that step-down from daily inhaled corticosteroids to such treatment as rescue in combination with rescue short-acting beta agonists could be a reasonable step-down strategy for patients with mild persistent asthma," wrote Dr. Checkley of the pulmonary and critical care division at Johns Hopkins University, Baltimore. This strategy would reduce the cumulative exposure to ICS "and obviate concerns about compliance with long-term controller treatment," he added, noting that more studies are needed.

Beclomethasone and the placebo inhalers were provided by Teva Pharmaceutical Industries, the manufacturer of a generic formulation of beclomethasone. Of the 20 coauthors, 12, including lead author Dr. Martinez, reported having been a board member and/or receiving consulting fees, honoraria, and/or pending grant support from various pharmaceutical companies, including AstraZeneca, GlaxoSmithKline, MedImmune, and Merck. The remaining authors had no disclosures. ■

IN THIS ISSUE

CHEST PHYSICIAN IS ONLINE

CHEST PHYSICIAN is available on the Web at www.chestnet.org/accp/chest-physician.

CHEST PHYSICIAN

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

The statements and opinions expressed in **CHEST PHYSICIAN** do not necessarily reflect those of the American College of Chest Physicians, or of its officers, regents, members, and employees, or those of the Publisher. The American College of Chest Physicians, its officers, regents, members, and employees, and Elsevier Inc. do not assume responsibility for damages, loss, or claims of any kind arising from or related to the information contained in this publication, including any claims related to products, drugs, or services mentioned herein.

Address Changes: Fax changes of address (with old mailing label) to 973-290-8245.

POSTMASTER: Send change of address (with old mailing label) to CHEST PHYSICIAN, 60 B Columbia Rd., 2nd flr., Morristown, NJ 07960.

CHEST PHYSICIAN (ISSN 1558-6200) is published monthly for the American College of Chest Physicians by Elsevier Inc., 60 B Columbia Rd., 2nd flr., Morristown, NJ 07960, 973-290-8200, fax 973-290-8250.

ELSEVIER SOCIETY NEWS GROUP, A DIVISION OF INTERNATIONAL MEDICAL NEWS GROUP

President, IMNG Alan J. Imhoff
Director, ESNG Mark Branca
Editor in Chief Mary Jo M. Dales
Executive Editors Denise Fulton, Kathy Scarbeck
Managing Editor Leanne Sullivan

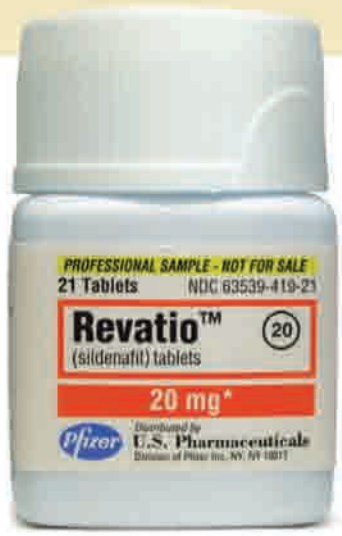
Circulation Analyst Barbara Cavallaro, 973-290-8253, b.cavallaro@elsevier.com
Executive Director, Operations Jim Chicca
Director, Production and Manufacturing Yvonne Evans Struss
Production Manager Judi Sheffer
Creative Director Louise A. Koenig
Display Advertising Manager The Walchli Tauber Group: 443-512-8899, fax 443-512-8909, greg.pessagno@wt-group.com

ADVERTISING OFFICES 60 B Columbia Rd., 2nd flr., Morristown, NJ 07960, 973-290-8200, fax 973-290-8250
CLASSIFIED ADVERTISING OFFICES The Walchli Tauber Group, 2225 Old Emmorton Rd., Suite 201, Bel Air, MD 21015, 443-512-8899
EDITORIAL OFFICES 5635 Fishers Lane, Suite 6000, Rockville, MD 20852, 240-221-4500, fax 240-221-2541

Did you know REVATIO samples are just a phone call away?

Order REVATIO Starter Samples by phone

Contact the REVATIO Sample Fulfillment Program by calling **1-866-833-9559**



Indication

REVATIO is indicated for the treatment of pulmonary arterial hypertension (WHO Group I) to improve exercise ability and delay clinical worsening. Delay in clinical worsening was demonstrated when REVATIO was added to background epoprostenol therapy. The efficacy of REVATIO has not been adequately evaluated in patients taking bosentan concurrently.

Important Safety Information

Do not use REVATIO in patients taking organic nitrates in any form, either regularly or intermittently. Consistent with its known effects on the nitric oxide/cGMP pathway, sildenafil was shown to potentiate the hypotensive effects of nitrates.

Before starting REVATIO, physicians should carefully consider whether their patients with underlying conditions could be adversely affected by the mild and transient vasodilatory effects of REVATIO on blood pressure. Pulmonary vasodilators may significantly worsen the cardiovascular status of patients with pulmonary veno-occlusive disease (PVOD) and administration of REVATIO to these patients is not recommended. Should signs of pulmonary edema occur when sildenafil is administered, the possibility of associated PVOD should be considered.

Caution is advised when PDE5 inhibitors, such as REVATIO, are administered with α-blockers as both are vasodilators with blood pressure lowering effects.

In PAH patients, the concomitant use of vitamin K antagonists and REVATIO resulted in a greater incidence of reports of bleeding (primarily epistaxis) versus placebo. The incidence of epistaxis was higher in patients with PAH secondary to CTD (sildenafil 13%, placebo 0%) than in PPH patients (sildenafil 3%, placebo 2%).

Co-administration of REVATIO with potent CYP3A4 inhibitors, eg, ketoconazole, itraconazole, and ritonavir, is not recommended as serum concentrations of sildenafil substantially increase. Co-administration of REVATIO with CYP3A4 inducers, including bosentan; and more potent inducers such as barbiturates, carbamazepine, phenytoin, efavirenz, nevirapine, rifampin, and rifabutin, may alter plasma levels of either or both medications. Dosage adjustment may be necessary.

Non-arteritic anterior ischemic optic neuropathy (NAION) has been reported post-marketing in temporal association with the use of PDE5 inhibitors for the treatment of erectile dysfunction, including sildenafil. It is not possible to determine if these events are related to PDE5 inhibitors or to other factors. Physicians should advise patients to seek immediate medical attention in the event of sudden loss of vision while taking PDE5 inhibitors, including REVATIO.

Sudden decrease or loss of hearing has been reported in temporal association with the intake of PDE5 inhibitors, including REVATIO. It is not possible to determine whether these events are related directly to the use of PDE5 inhibitors or to other factors. Physicians should advise patients to seek prompt medical attention in the event of sudden decrease or loss of hearing while taking PDE5 inhibitors, including REVATIO.

REVATIO should be used with caution in patients with anatomical deformation of the penis or patients who have conditions which may predispose them to priapism.

REVATIO contains sildenafil, the same active ingredient found in VIAGRA®. Combinations of REVATIO with VIAGRA or other PDE5 inhibitors have not been studied. Patients taking REVATIO should not take VIAGRA or other PDE5 inhibitors.

Patients with the following characteristics did not participate in the preapproval clinical trial: patients who have suffered a myocardial infarction, stroke, or life-threatening arrhythmia within the last 6 months, unstable angina, hypertension (BP >170/110), retinitis pigmentosa, or patients on bosentan. The safety of REVATIO is unknown in patients with bleeding disorders and patients with active peptic ulceration. In these patients, physicians should prescribe REVATIO with caution.

The most common side effects of REVATIO (placebo-subtracted) were epistaxis (8%), headache (7%), dyspepsia (6%), flushing (6%), and insomnia (6%). Adverse events of REVATIO injection were similar to those seen with oral tablets.

The most common side effects of REVATIO (placebo-subtracted) as an adjunct to intravenous epoprostenol were headache (23%), edema (14%), dyspepsia (14%), pain in extremity (11%), diarrhea (7%), nausea (7%), and nasal congestion (7%).

Revatio®
sildenafil
20 mg tablets
Start With Confidence™

Please see Brief Summary of Prescribing Information on the following pages.

www.REVATIO.com

Rule Identifies Newborns at High Risk of RSV

BY ELIZABETH MECHCATIE
Elsevier Global Medical News

In a study that identified independent risk factors for respiratory syncytial virus lower respiratory tract infections in a group of healthy term newborns, investigators in The Netherlands developed "a simple prediction rule" that they say can be used in clinical practice to identify healthy newborns who are at high risk for being treated as outpatients for these infections during the first year of life.

In the prospective birth cohort study of 298 healthy term babies born in two large urban Dutch hospitals between January 2006 and December 2008 who were followed for a year, the following were identified as independent predictors for respiratory syncytial virus (RSV) lower respiratory tract infections (LRTI): day care attendance and/or having siblings, high parental education level, birth weight over 4 kg, and birth from April to September.

The risk of RSV LRTI was 10 times higher for children with these four factors, compared with children without these factors (Pediatrics 2011;127:35-41).

Using statistical analyses of the association between these predictors and the presence or absence of RSV LRTI, Dr. Michiel Houben of Wilhelmina Children's Hospital, Utrecht, The Netherlands, and his associates derived the prediction rule, with scores ranging from 0 to 5. The absolute risk of having an RSV LRTI ranged from 3% for a child with a score of 2 or less (20% of the children) to 32% for a child with a score of 5 and all four of these factors (8% of the children).

"Clinicians can use these features to differentiate between children with high and low risks of RSV LRTI and subsequently can target preventive and monitoring strategies to children at high risk,"

he and his coauthors concluded. They noted that to date, clinical prediction models have been developed only for predicting hospitalization in preterm infants, and as far as they know, theirs is the first study that "attempts to predict the risk of nonhospitalized RSV LRTI for healthy newborns by using molecular detection of RSV."

The primary outcome measured in the study was development of RSV LRTI, which was based on a positive RSV polymerase chain reaction test result and symptoms of acute wheezing or a moderate/severe cough. Parents recorded their children's respiratory symptoms with daily logs and used nose and throat swabs when the child had a respiratory tract infection. During their first year of life, 42 (14%) of the 298 children had an RSV LRTI.

With the formula they derived, 1 point was assigned for a birth weight over 4 kg, 1 point for being born from April to September, 2 points for being in day care or having siblings, and 1 point for a high parental education level. In an example they provided, a baby born in July (1 point) who is in day care (2 points), weighed 4.2 kg at birth (1 point), and has parents who are not highly educated (0 points) would have a score of 4 points, corresponding to a "probability of developing a RSV LRTI of 23%," they wrote.

Because of the "extremely high" incidence of medically attended RSV infection, "children classified as being at high risk could be monitored more closely and lifestyle changes that reduce exposure could be applied," Dr. Houben and associates added.

If clinicians used this type of prediction rule in their practices, it would be used to identify those at the highest risk – with scores of 4 or 5 – rather than using a low score as a basis to advise parents not to worry.

Some of the factors that are in the formula are modifiable, and a score of 4 or 5 might influence parents to decide to take their children out of day care, said Dr. Lance Chilton, who is a pediatrician at the Young Children's Health Center at the University of New Mexico in Albuquerque.

Dr. Chilton, who was formerly the chair of the Center for Disease Control and Prevention's working group on RSV immunoprophylaxis, said that he is not aware of any clinicians who use a predictive scoring system to identify newborns at highest risk of RSV infection.

"If you asked a group of pediatricians what they used as a means of prediction as to who is at highest risk of RSV infection, most would come up with day care attendance and older siblings, and none of them would have guessed that higher educational achievement would be positively correlated with risk of a medically attended RSV infection," he said in an interview. "And most would say that they recommend that all babies stay away from coughing people and crowds of people during the winter virus season."

THE RISK OF RSV LRTI WAS 10 TIMES HIGHER FOR CHILDREN WITH THESE FOUR FACTORS, COMPARED WITH CHILDREN WITHOUT THESE FACTORS.

Although he said he thought the study appeared to be well done, he pointed out that there are major differences in hospitalization rates for RSV between United States and European epidemiologic studies, and that there are likely other differences, such as the use of emergency departments for treatment rather than general practices.

One concern he had was that the study might be used "as a means to suggest" that newborns with a score of 4 or 5 be given palivizumab (Synagis), "which would markedly increase costs without any proof of effectiveness, let alone cost-effectiveness."

One of the study authors received research funding and speaker's fees from Abbott International; the other authors indicated they had no relevant financial disclosures.

Dr. Chilton said that he had no relevant disclosures. ■

COMMENTARY

Dr. Burt Lesnick, FCCP, comments: This study is helpful in defining the additive nature of risk factors for lower respiratory tract infection in infants with RSV. What is surprising is that high birth weight was found to be a predictor of worse outcome. This is at odds with similar studies suggesting low birth weight is a significant risk factor.

Are Pressure Ulcers Really a 'Never Event'?

BY DOUG BRUNK
Elsevier Global Medical News

SAN DIEGO – The development of hospital-acquired pressure ulcers may be unavoidable in patients who present with respiratory and hemodynamic medical problems that impede optimal oxygenation to tissues, results from a study of more than 800 patients showed.

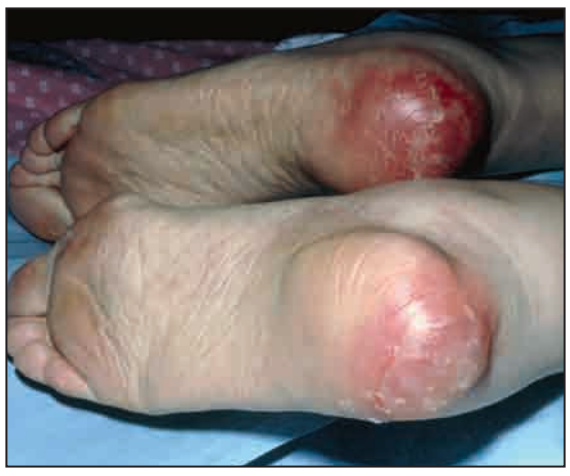
The findings challenge the position of the Centers for Medicaid and Medicare Services that pressure ulcers in this setting are a so-called "never event," said Margaret Mullen-Fortino, R.N., at the annual congress of the Society of Critical Care Medicine.

"They are categorized as a never event because it's believed that these are reasonably preventable through the application of evidence-based guidelines," said Ms. Mullen-Fortino, operations director of the surgical/trauma ICU at the Hospital of the University of Pennsylvania, Philadelphia. "The evidence-based guidelines include the acronym SKIN, with the S standing for surface selection such as low-air-pressure mattresses. The K stands for keep turning patients, the I stands for incontinence management, and the N stands for nutrition – making sure that patients are adequately nourished with enough protein."

However, she continued, "There is a large population of practitioners who believe that pressure ulcers are not a never event, that there are comorbidities that increase the chances of patients developing pressure ulcers. Much like a patient experiences a myocardial infarction because blood does not get to the heart muscle, we believe that pressure ulcers develop because adequate blood supply does not get to the skin, which is the largest organ in the body. Our hypothesis is that there is an association between the severity of illness and the development of pressure ulcers."

'Our hypothesis is that there is an association between the severity of illness and … pressure ulcers.'

MS. MULLEN-FORTINO



©Mike Devlin/Photo Researchers Inc

Use of mechanical ventilation and vasopressors were significantly associated with the development of pressure ulcers.

To test this hypothesis, Ms. Mullen-Fortino and her associates conducted a prospective cohort study of 824 patients who were admitted to the 20-bed surgical/trauma ICU at the Hospital of the University of Pennsylvania and to the 20-bed medical ICU at the Christ Hospital, Cincinnati, between Dec. 15, 2009, and Dec. 12, 2010. Variables assessed included age, length of stay, APACHE score, Braden score, readmission, and use of mechanical ventilation and vasopressors.

Ms. Mullen-Fortino reported that of the 824 patients studied, 221 (26.8%) developed pressure ulcers. Of these patients, 144 (65.1%) were ventilated and 67 (30.3%) required vasopressor support.

Among the entire study population, the median APACHE score was 74, with a range of 26-153. The median length of stay was 2 days, with a range of 1-91 days; the median Braden score was 14, with a range of 7-20; and the median patient age was 63 years.

All of the variables studied had a statistically significant association with the development of pressure ulcers with the exception of the use of vasopressors, "which was a surprise," Ms. Mullen-Fortino said.

She and her associates then performed logistic regression analysis limited to ICU length of stay, APACHE score, use of mechanical ventilation, and use of vasopressors. The Braden score was excluded "because that's a predictive model for skin integrity, not really for severity of illness," she explained. In this analysis, only use of mechanical ventilation and vasopressors were significantly associated with the development of pressure ulcers (odds ratios of 4.55 and 2.17, respectively).

Next, the researchers intend to prospectively examine the cohort using the Sequential Organ Failure Assessment, which quantifies the severity of the patient's illness based on the degree of organ dysfunction serially over time, "as opposed to the APACHE score, which provides you severity of illness on admission," Ms. Mullen-Fortino said. "We're hoping to see if the progression of the severity of illness correlates with the development of pressure ulcers. The compilation of this evidence will hopefully serve to inform future policy."

In 2007, she said, more than 250,000 hospitalized patients were reported to have stage 3 and 4 pressure ulcers. The cost of treatment is about $43,000 per pressure ulcer, and the condition demands "a tremendous amount of nursing resources and time," she said. ■

VITALS

Major Finding: Only use of mechanical ventilation and vasopressors were significantly associated with the development of pressure ulcers in the ICU (odds ratios of 4.55 and 2.17, respectively).

Data Source: A study of 824 patients who were admitted to the ICU at two separate hospitals during 1 year.

Disclosures: Ms. Mullen-Fortino said that she had no relevant financial conflicts.

COMMENTARY

Dr. Carl Kaplan, FCCP, comments: This article has significant relevance for policy makers in Washington, hospitalists, nurses, respiratory therapists, hospital administration, and the broader ACCP membership that includes medical, surgical, and trauma critical care physicians. The skin is likely an end organ such as the lung and kidneys in multiorgan dysfunction syndrome. The skin may be impacted by a two- or three-hit theory – that is, a series of events including the premorbid state, the pre-ICU state, and then the ICU standard of care that includes ventilator management.

Simple ICU Protocol Improved Handwashing Compliance

BY DOUG BRUNK
Elsevier Global Medical News

SAN DIEGO – Adding a simple question to the daily ICU checklist about handwashing before touching patients significantly improved handwashing compliance and was associated with a decreased rate of central line–associated bloodstream infections in a surgical intensive care unit over the course of 6 months.

"If you look at how people address hand hygiene compliance overall, most of the time it's with fairly elaborate and expensive educational and marketing campaigns," Dr. Jeremy Pamplin said in an interview after the study was presented during a poster session at the congress. "Inevitably, you improve hand hygiene compliance for a while. Then the campaign goes away and you start to have fading of the compliance."

As part of a process improvement project, Dr. Pamplin, medical codirector of the 20-bed surgical/trauma ICU at Brooke Army Medical Center, Fort Sam Houston, Tex., and his associates added the following question to their daily ICU checklist: "Has anyone seen anyone else touch the patient without washing their hands in the past 24 hours?" The question was asked during multidisciplinary ICU rounds for every patient, and only "yes" or "no" answers were allowed.

If respondents answered "yes," they were asked to provide the name of the offender, which was recorded. Compliance was measured by a third-party observer and was defined as washing hands or using hand sanitizer prior to touching a patient or the patient's immediate surroundings.

Dr. Pamplin and his associates collected data for 3 months before and 3 months after this question was added to the ICU checklist. Over that period, the rate of handwashing compliance significantly increased from 69% to 89%, while the rate of central line–associated bloodstream infections decreased from 13.7/1,000 central line days to 2.7/1,000 central line days, an improvement that did not reach statistical significance.

"Before we introduced this question to our checklist, it was very rare for a provider to tell another provider, 'Hey, I didn't see you wash your hands,' " Dr. Pamplin said. "After we introduced this question, people started doing it because we gave leadership and emphasis to it."

This resulted in a change of culture, he continued, "so if nurses, residents, or technicians saw someone walk into the room without washing their hands, they would stop them and say, 'Hang on a second; you didn't wash your hands.' Everyone knows that hand hygiene is an important part of infection control. The hard part is remembering to do it. It's a rare circumstance that someone gets upset by another health care provider who says, 'Hey, you forgot to wash your hands.' Because we have talked about hand hygiene compliance on rounds as a team, it has elevated that component of infection control so that everyone recognizes it as being important."

Dr. Pamplin said that he had no relevant financial disclosures to make. ■

COMMENTARY

Dr. Nirupam Singh, FCCP, comments: Even though hand hygiene remains the single most effective tool to prevent transmission of microorganisms, compliance remains a major issue. While Dr. Pamplin's data are yet to be published in a peer-reviewed journal, his approach appears simple and effective. More and more it is becoming clear that checklists work – as does empowering the entire team taking care of the patient. The MHA Keystone initiative significantly reduced catheter-related bloodstream infections using checklists and the bundle approach. Adding hand hygiene to the daily ICU checklist is a simple addition with the potential to have a big impact.

Poverty and Mortality in Critical Care Not Related

BY DOUG BRUNK
Elsevier Global Medical News

SAN DIEGO – There is no apparent relationship between neighborhood poverty rate, based on patient address, and mortality following critical care, results of a large, 10-year analysis showed.

"Our findings are in contrast to data in other arenas of health care that have established an inverse relationship between socioeconomic status and mortality," Sam Zager said at the annual congress of the Society of Critical Care Medicine. "The few studies that examine economic disparities and mortality in the critically ill are contradictory."

Neighborhood poverty rate was not significantly associated with mortality at 30 days or at 1 year post discharge.

MR. ZAGER

Using 1990 census and hospital administration data, Mr. Zager, a fourth-year student at Harvard Medical School, Boston, and his associates performed an observational study of 38,917 patients aged 18 years and older who received critical care at Brigham and Women's Hospital and Massachusetts General Hospital, both in Boston, in 1997-2007.

Neighborhood poverty rate was defined as the percentage of each neighborhood's residents with incomes below the federal poverty line, categorized as 5%-10%, 10%-20%, 20%-40%, or greater than 40%. They used logistic regression to examine death by day 30, 90, and 365 post ICU, as well as in-hospital mortality, and adjusted the data for age, sex, race, admission year, patient type (medical vs. surgical), Charlson-Deyo index, sepsis, CABG, myocardial infarction, hematocrit, white blood cell count, creatinine, and blood urea nitrogen.

The researchers also performed a sensitivity analysis for 1-year postdischarge mortality among patients discharged to home, as well as mortality among patients who lived less than 50 miles from the hospital of care.

The mean age of patients was 62 years, 42% were women, and 78% were white. After multivariable adjustment of the data, Mr. Zager and his associates found no statistically significant relationship between neighborhood poverty rate and all-cause 30-day mortality. The odds ratio was 1.05 for those who resided in neighborhoods in which 5%-10% of residents lived below the federal poverty line ($P = .2$), 0.96 for those who resided in neighborhoods in which 10%-20% of residents lived below the federal poverty line ($P = .5$), 1.08 for those who resided in neighborhoods in which 20%-40% of residents lived below the federal poverty line ($P = .2$), and 1.20 for those who resided in neighborhoods in which more than 40% of residents lived below the federal poverty line ($P = .2$).

Similar nonsignificant associations were observed for 90-day and 365-day mortality post ICU admission and for in-hospital mortality. In addition, neighborhood poverty rate was not significantly associated with 1-year postdischarge mortality in patients who were discharged to home or in patients who resided less than 50 miles from the hospital of care.

Study limitations included its observational design and inability to fully exclude patients who received critical care only in the emergency department. Also, "our study focuses on neighborhood poverty at the time of critical care initiation, which may not fully reveal the contribution of socioeconomic status to mortality risk," Mr. Zager said. ■

COMMENTARY

Dr. Carl Kaplan, FCCP, comments: This interesting and thoughtful observational study provides insight into what we believe, wish to believe, and need to believe; that is, the critical care medicine community provides unique and essential care that is dictated by immediate need, physiological parameters, and evidence-based science driven by a common "process of care delivery" by uniquely trained and dedicated physicians and a team of allied health professionals.

The postdischarge data are interesting regarding the maintenance of this mortality outcome benefit. Is it possible that critical care medicine is linked with more detailed outpatient support and medical care, or more focused and defined care needs once patients leave the hospital? There are a lot of interesting questions regarding why this study contrasts with some others in the medical literature.

The next step is to look for similar findings in other metropolitan urban areas that are not university medical school–based and in the suburban and rural communities of this country.

Lung Debris May Help Identify Surgical Margins

BY PATRICE WENDLING
Elsevier Global Medical News

CHICAGO – A novel technique utilizing stapled lung debris could help determine adequate and inadequate surgical margins in resected non–small cell lung cancer, results of a prospective study suggest.

Researchers at Albany (N.Y.) Medical College and the Hospital of St. Raphael in New Haven, Conn., are using cytology to analyze lung tissue taken from spent staple cartridges used during sublobar resection. The staple cartridge is simply mixed with 30 cc of normal saline and serves as the cytologic margin, Dr. Thomas Fabian, FCCP, explained at the Chicago Multidisciplinary Symposium in Thoracic Oncology.

"People have [observed] that certain staples used through cancers can potentially contaminate new tissue planes, so that is how the idea was born," he said in an interview.

Dr. Fabian and his colleagues prospectively compared staple-line cytology with traditional histopathologic evaluation of surgical specimens taken from 97 patients undergoing diagnostic sublobar wedge resection between November 2007 and September 2009. Of the 98 specimens retrieved, 30 were benign and 68 were malignant.

Staple-line cytology was 100% accurate when used in the evaluation of benign lesions and compared with histology, he said.

In the 68 malignant nodules, initial blinded cytologic evaluation was positive in 7, surgical pathology was positive in 6, and both were positive in 4.

Subsequent unblinded review of both specimens changed the final pathologic interpretation in 4 (6%) of the 68 cases, said Dr. Fabian, chief of thoracic surgery at the Albany Medical Center. The interpretation changed from a negative margin to a positive margin in three surgical specimens (7%) and in one staple-line cytology specimen (2%).

According to analysis of the unblinded data, staple-line cytology demonstrated an overall accuracy of 96%, with 88% sensitivity, 97% specificity, 70% positive-predictive value, and 99% negative-predictive value.

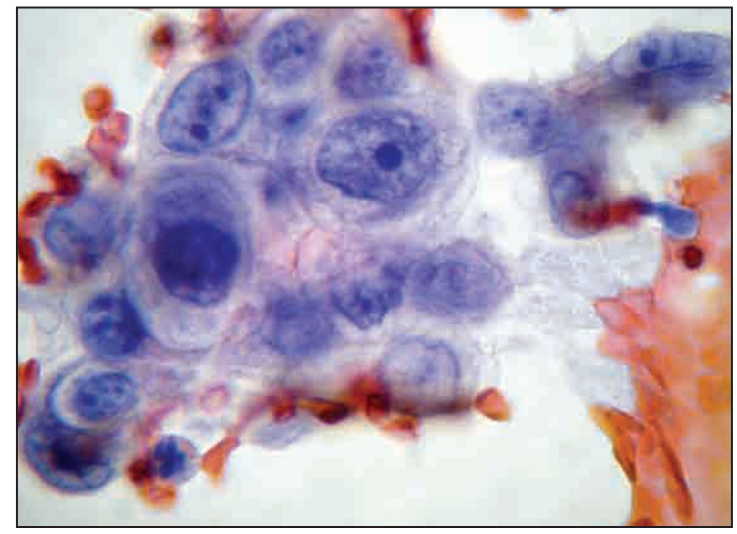
Dr. Fabian described staple-line cytology as a simple technique that could serve as an adjunct to the gold standard of histopathology, which he said is prone to inaccuracies including both false positives and false negatives.

"We need to reevaluate the techniques that allow us to accurately assess surgical margins – particularly in the setting of sublobar resections, given the growing interest in this technique," he said.

"The cytologic technique appears to be sensitive, specific, and accurate, but it does need to be validated at other institutions and with additional studies."

Dr. Fabian acknowledged that by design the study lacked clinical outcome data and said further evaluation is ongoing. The next step is to evaluate the technique in patients undergoing sublobar resection with curative intent.

Of the 68 malignant samples, 43 were diagnosed as adenocarcinoma, 7 were diagnosed as squamous cell carcinoma, 3 were diagnosed as large cell, 1 as small cell, 5 as carcinoid, and 9 as other histologies. ■



COURTESY DR. THOMAS FABIAN

Analysis of the unblinded data showed that staple-line cytology (above, adenocarcinoma) had an overall accuracy of 96%.

VITALS

Major Finding: Staple-line cytology demonstrated an overall accuracy of 96% when used to identify surgical margins in resected non–small cell lung cancer.

Data Source: Prospective study of 97 patients with non–small cell lung cancer undergoing sublobar wedge resection.

Disclosures: Dr. Fabian disclosed serving as a speaker for and receiving research funding and honoraria from Covidien. His coauthors reported no conflicts.

COMMENTARY

Dr. Richard Fischel, FCCP, comments: This report describes an interesting concept that I haven't seen before. However, if the cytology is positive and the surgical pathology is negative, how can the researchers assume the cytology is correct in demonstrating a positive margin when the gold standard for comparison is the surgical pathology results? Considering that there was a total of nine positive margins (seven determined by cytology, six by pathology, and four by both), and that seven of nine and six of nine are not very good results for tests used intraoperatively to make important decisions, the point may be that both approaches should be used to improve accuracy.

Strategy Protects Lungs for Transplantation

BY MARY ANN MOON
Elsevier Global Medical News

A strategy for protecting the lungs in potential organ donors nearly doubled the number of lungs that were suitable for transplantation, according to a report in JAMA.

The lung-protection strategy, which apparently forestalled much of the pulmonary damage associated with brain injury and mechanical ventilation, had no detrimental effects on other organs – hearts, livers, and kidneys – harvested from the same donors for transplantation, said Dr. Luciana Mascia of the departments of anesthesia and intensive care medicine at the University of Turin (Italy).

Potential organ donors who have relatively normal pulmonary function at the time of brain death often show marked declines in that function, so only 15%-20% of these lungs are suitable for transplantation when organ harvesting commences.

Dr. Mascia and her colleagues studied 118 patients with brain death who were potential organ donors and were being treated at 12 ICUs in Italy and Spain between 2004 and 2009. A total of 59 patients were randomly assigned to undergo conventional lung ventilation techniques, and the other 59 were assigned to a strategy of using lower tidal volumes, higher positive end-expiratory pressure (to prevent atelectasis), a closed system for any tracheal suctioning, alveolar recruitment maneuvers after any ventilator disconnections, and continuous positive airway pressure (CPAP) during apnea tests.

LUNGS WERE SUCCESSFULLY HARVESTED IN 27% OF THE CONVENTIONAL-CARE GROUP, COMPARED WITH 54% OF THE LUNG-PROTECTION GROUP.

After a mandatory 6-hour interval before brain death could be officially declared, there were 49 potential donors in the conventional-care group and 51 in the lung-protection group. The number of patients who then were found to meet lung-donor eligibility criteria had decreased with the conventional ventilation strategy by 29% to only 32 patients. In contrast, the number in the lung-protection group had increased to 56 patients, a significant difference.

This means that of the original potential donors, only 54% in the conventional-care group met eligibility criteria, compared with 95% in the lung-protection group, Dr. Mascia and her associates said (JAMA 2010;304:2620-7).

The ultimate number of lungs that were successfully harvested was 27% of the conventional-care group (16 lungs), compared with 54% of the lung-protection group (32 lungs), also a significant difference.

For the lung recipients, the median ICU length of stay was 12 days for patients who received lungs from the conventional-care group and 8 days for those who received lungs from the lung-protection group. Six-month survival was 69% for patients who received lungs from the conventional-care group and 75% for those who received lungs from the lung-protection group, a nonsignificant difference.

The number of other organs harvested did not differ between the two study groups, and 6-month survival of those recipients also did not differ significantly.

"Which of these [study] factors specifically improved respiratory functions is not certain," the researchers said. They speculated that recruitment of collapsed alveoli, prevention of end-expiratory collapse (obtained by the use of CPAP during the apnea test and of closed circuit for airway suction), and maintenance of recruited alveoli may have prevented the pulmonary damage caused by ventilators at low tidal volumes.

The Protective Ventilatory Strategy in Potential Lung Donors Study was stopped after 118 patients were enrolled, because of termination of funding.

"This study breaks important new ground in providing a solid evidence base for the care of potential organ donors and testing techniques of organ preservation," said Dr. Mark S. Roberts in an accompanying editorial (JAMA 2010;304:2643-4).

"The study [also] provides sobering evidence that conventional lung preservation practices, which have been used for many years, are remarkably inefficient in their task," added Dr. Roberts of the University of Pittsburgh School of Public Health.

This study was supported by the Ministero della Salute Programma Ricerca Finalizzata, the Regione Piemonte Programma Ricerca Finalizzata, and the Ministero dell'Universita Programma di Ricerca di Interesse Nazionale. No financial conflicts of interest were reported by the investigators. ■

Pages 8a—8b

Optimal Lung Resection Varies by Surgeon Specialty

BY DOUG BRUNK

Elsevier Global Medical News

SAN DIEGO – General surgeons perform the majority of lung resections for cancer in the United States, yet lung cancer resections performed by thoracic surgeons had significantly lower in-hospital mortality rates than did those performed by general surgeons and cardiac surgeons, according to results of a large analysis of national hospital data.

When performing a lung cancer resection, thoracic surgeons performed lymphadenectomy significantly more often than did general surgeons and cardiac surgeons. "Lymph node status in lung cancer is the main determinant of stage, prognosis, and need for further therapy," Dr. Michelle Ellis said at the annual meeting of the Society of Thoracic Surgeons. "The performance of lymphadenectomy at the time of lung cancer resection can be considered a process measure of quality."

Previously published studies have demonstrated that general surgeons perform the majority of thoracic cases in the United States, while surgeons who specialize in thoracic surgery have lower perioperative morbidity and mortality. "Furthermore, patients who have their lung resection performed by a board-certified cardiothoracic surgeon specializing in general thoracic surgery have longer overall and cancer-specific survival," said Dr. Ellis of Oregon Health and Science University, Portland. "We hypothesized that the completeness of intraoperative oncologic staging at the time of primary lung cancer resection varies by surgeon specialty, and may explain the observed differences in outcome."

To test the hypothesis, Dr. Ellis and her coinvestigators reviewed 222,233 primary lung cancer cases from the Nationwide Inpatient Sample from 1998 to 2007 who were treated surgically with limited lung resection, lobectomy, or pneumonectomy. The main outcome measure was the presence of lymphadenectomy or mediastinoscopy performed during the same admission.

Dr. Ellis reported that lung cancer resections were performed by general surgeons in 62% of cases, by cardiac surgeons in 35% of cases, and by thoracic surgeons in 3% of cases. The median annual case volume was 21 for thoracic surgeons, 23 for cardiac surgeons, and 8 for general surgeons.

In-hospital mortality rates for thoracic, cardiac, and general surgeons were 2.3%, 3.4%, and 4.0%.

DR. ELLIS

In-hospital mortality rates for thoracic, cardiac, and general surgeons were 2.3%, 3.4%, and 4.0%, respectively. This translated into an odds ratio for in-hospital mortality of 1.33 for cases performed by cardiac surgeons and 1.55 for those performed by general surgeons.

Thoracic surgeons performed lymphadenectomy significantly more often than did their counterparts (73% vs. 55% for both cardiac and general surgeons). Thoracic surgeons also performed mediastinoscopy significantly more often (16% vs. 10% by cardiac surgeons and 11% by general surgeons). "A patient was more than twice as likely to have a lymphadenectomy performed if the lung cancer resection was performed by a thoracic surgeon," Dr. Ellis said.

When the researchers assessed the impact of case volume on their multivariate model, they found that for every doubling of thoracic surgery case volume, there was a significant increase in the likelihood that a lymphadenectomy would be performed (OR, 1.28). On the other hand, for every doubling of general surgery case volume, there was a significant decrease in lymphadenectomy rates (OR, 0.95). Doubling of cardiac surgery case volume did not affect lymphadenectomy rates.

Dr. Ellis acknowledged certain limitations of the study, including the fact that it contains only single-admission information. "It also has limited cancer-specific data such as stage, and has no mechanism for long-term follow-up," she said. In addition, surgeons are anonymous in the database, so board certification could not be determined.

Dr. Ellis said that she had no relevant financial disclosures to make. ■

Rib Fixation in Flail Chest May Shorten Ventilation

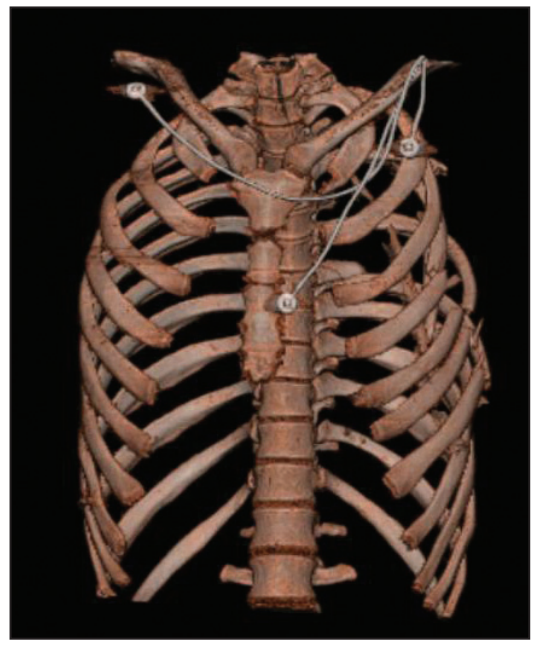
BY PATRICE WENDLING
Elsevier Global Medical News

NAPLES, FLA. – Patients who underwent surgical rib fixation for flail chest spent on average 10 fewer days on mechanical ventilation than did those managed traditionally in a single-center analysis of 21 patients with severe blunt chest trauma.

The total number of ventilator days was significantly lower in patients who underwent rib fixation, at a median of 4.5 days (range 0-30 days), compared with a median of 16 days (range 4-40 days) in those managed with pain control and respiratory therapy ($P = .04$).

Hospital length of stay was a median of 22 days in the nonsurgical group vs. 13 days in the surgical group, and ICU length of stay was a median of 18 days vs. 9 days, but those differences were not statistically significant. There was one postoperative seroma and no deaths in the surgical group.

Surgical rib fixation can be used as a rescue technique when the last resort is prolonged mechanical ventilation, but a large multicenter trial is needed to determine the best approach, Dr. Andrew R. Doben said at the annual meeting of the Eastern Association for the Surgery of Trauma.



COURTESY DR. ANDREW DOBEN

Patients with severe flail chest often require prolonged mechanical ventilation.

"This study provides some of the first data suggesting that surgical fixation may prevent prolonged ventilation in flail chest patients who initially do not require invasive mechanical ventilation," he said in an interview.

Dr. Doben pointed out that major trauma centers see roughly two flail chest injuries per month and that up to 60% of patients do not return to full-time employment. A prospective randomized trial showed benefits with surgical stabilization with Judet struts, compared with internal pneumatic stabilization (J. Trauma 2002;52:727-32), but that trial included only 18 fixation patients and all required invasive mechanical ventilation, he said.

Dr. Doben and his colleagues at the Medical University of South Carolina, Charleston, defined flail chest deformity as three consecutive ribs broken in two or more locations, and they initially focused on patients who failed to wean from the ventilator 5 days post injury, had isolated chest wall trauma, and had good neurologic status.

Surgical fixation using a combination of plates and intramedullary nails in three such patients produced positive results similar to those in the literature, but raised the question of whether mechanical ventilation could be avoided in patients who are failing, Dr. Doben said.

"Everybody's seen these patients – the 'in-betweeners' – they're not really failing, they're not yet vented, but they're heading that way," he said.

Dr. Doben highlighted the case of a 60-year-old man with seven total rib fractures including five segmental fractures and paradoxical chest wall motion, who had an epidural in place, was on oxycodone, NSAIDs, acetaminophen, and gabapentin, and was experiencing progressive pulmonary decline on bilevel positive airway pressure therapy for 3 days in the ICU. The patient underwent surgical rib fixation on hospital day 6, was mechanically ventilated overnight, and was extubated the following morning. He was discharged to home on hospital day 11, with no long-acting narcotics needed for pain, he said.

The retrospective chart review included the first 10 patients treated with surgical fixation from September 2008 to May 2010, matched with a previous group of 11 patients managed with standard therapy. Patients were required to have a Chest Abbreviated Injury Scale score of more than 3, a diagnosis of flail chest, and an ICU length of stay greater than 5 days. There were no surgical complications, and the average time on a ventilator after surgery was 1.5 days, said Dr. Doben, now with Baystate Medical Center in Springfield, Mass.

Invited discussant Dr. John C. Mayberry said no strong conclusions supporting flail chest repair can be drawn because of the small study size, but commended the authors for providing new data on its use in patients who do not require ventilation, but clinically worsen.

Dr. Mayberry, with Oregon Health and Science University in Portland, asked whether the study protocol evolved over time, and whether the 10 fixation patients represent the authors' first experience with the technique. This line of questioning was continued by an audience member who asked what kind of course work prepared the authors to perform rib fixation.

Dr. Doben responded that he had limited experience with chest repairs as a general surgery resident in Maine, but that these were indeed the first 10 rib fixation patients in Charleston. The surgeries in both Maine and Charleston were performed in conjunction with cardiothoracic and orthopedic surgeons who had expertise in hardware insertion, he noted.

With respect to the study protocol, Dr. Doben said initially the authors were very strict and only treated patients on mechanical ventilation, as suggested in the literature, but expanded the scope to include those on nonmechanical ventilation. The analysis excluded patients with a Glasgow Coma Scale score of 8 or less for 5 days, all in-hospital deaths in the control group, and two 80-year-olds with "do not intubate" orders who declined surgery.

Finally, audience members asked why ICU times were not lower in the surgical group and how the authors addressed pulmonary contusions, since previous reports suggest either no benefit or worsened morbidity in patients with a significant underlying pulmonary contusion who undergo fixation for flail chest.

Dr. Doben said length of stay was likely not lower because they delayed surgery in a number of patients until their chest became their primary medical issue. He called for studies to address the issue of flail chest and contusions, but said that he and his colleagues have performed fixation in these patients reasonably early on, at 2 or 3 days into the course of their contusion, when their PaO_2/FIO_2 (P/F) ratio was markedly improved.

"Really, what kept them on the vent was more their mechanics and not their P/F ratios, and I think that's a pretty definable time period," he said.

Dr. Doben and his coauthors reported having no conflicts of interest. Dr. Mayberry has grant/research support from, serves as a consultant to, and is on the speakers bureau for, Acute Innovations, a maker of thoracic surgery devices. ■

COMMENTARY

Dr. Richard Fischel, FCCP, comments: Flail chest injuries have mostly been treated with nonsurgical intervention, often with disastrous results. This study nicely describes improved results in a select population using surgical rib/chest wall fixation. Such data may lead to increasingly aggressive therapy for flail chest or at least further studies to determine if an aggressive approach to fixation is reasonable. The team approach involving surgeons with fixation experience should be emphasized.

Assess Airway Remodeling to Guide Asthma Therapy

BY ROD FRANKLIN
Elsevier Global Medical News

KEYSTONE, COLO. – It doesn't take a long stretch of the imagination to surmise that chronic airway remodeling has an impact on airway obstruction in persistent asthma. But to what degree? And should steroid dosing be adjusted to mediate its progression at younger ages?

Biopsies alone don't adequately address these questions. The impact of airway narrowing is more of a "reasonable correlation" that physicians must formulate by evaluating asthma-related damage and epithelial tissue thickening over time, then comparing it to airway constriction in the patient, said Dr. Anthony N. Gerber of the University of California, San Francisco.

"What [physicians] are forced to do is perform biopsies and correlate the amount of airway smooth muscle thickening or the quantity of basement membrane thickening with the severity of airway obstruction," he said at a meeting on allergy and respiratory diseases, which was sponsored by National Jewish Health. "I don't know if it's really possible to deconvolute the precise amount that airway remodeling is contributing to airway obstruction."

Correlating CT scans with bronchial biopsies and histologic analysis sets the stage for a comparison of findings with forced expiratory volume in 1 second (FEV_1) spirometric values. The physician can then evaluate remodeling in a more relative sense by analyzing how actively it conspires with three additional airway obstruction components – acute asthmatic inflammation, airway hyperreactivity, and mucus formation.

Some patients may 'have more symptoms from the remodeling than they ever had from acute asthma attacks.'

DR. GERBER

The central hallmarks of chronic remodeling are increased airway smooth muscle mass and subepithelial fibrosis, or thickening in the lamina reticularis from dense fibrotic responses as a result of accumulated collagens. Inflamed airway smooth muscle mass has been associated with a decline in FEV_1 (Am. J. Respir. Crit. Care Med. 2010;182:317-24) and is characterized by abnormal cell turnover and proliferation, presumably in response to the chronic inflammatory stimuli that trigger the patient's asthma. The proliferating cell nuclear antigen (PCNA) is an acknowledged marker for this part of the process, with patients more likely to demonstrate higher levels of PCNA-positive cells as their asthma severity scores increase, Dr. Gerber said.

In addition, subepithelial fibrosis progression may be chronic, with increased smooth muscle narrowing seen in older patients (Am. J. Respir. Crit. Care Med. 2000;162:663-9).

"Should we treat people with airway remodeling differently than you would treat a typical asthmatic, where you're just trying to manage their symptoms? … We really don't know enough about the natural history of airway remodeling. Nor do we know enough about the effects of giving high doses of inhaled corticosteroids to potentially reverse airway remodeling," the pathologist said. "But I do think that there's evidence to maybe give pause to the idea that we should try and find the lowest corticosteroid dose that effectively controls symptoms."

So does persistent asthma bring on airway remodeling, or does remodeling worsen an existing case of asthma?

"In general, asthma comes first and leads to remodeling over time," he said in an interview. "However, some people appear more prone to develop remodeling than others. And for some, they may eventually have more symptoms from the remodeling than they ever had from acute asthma attacks."

Only after quantifying the impact of airway remodeling can the physician make an informed decision on adjustments to steroid therapy. Glucocorticoid use remains something of a gamble, as many of the genes that glucocorticoids act on to control catabolism are not inflammatory regulators. But some early findings have identified KLF15 as a possible glucocorticoid target and regulator of airway remodeling, he said.

Dr. Gerber sits on the advisory board and consults for Breathe Technologies. ■

COMMENTARY

Dr. Darcy Marciniuk, FCCP, comments: The more we learn about asthma, the less we seem to understand. The practical issue of quantifying airway remodeling in the clinical setting is difficult. However, as highlighted by Dr. Gerber, it appears more important to ensure optimal asthma management and control in our patients, rather than to solely pursue the lowest inhaled corticosteroid dosage.

MDR-TB Persistent in Russia

Siberia • *from page 1*

MDR-TB is a subset of regular TB that takes at least 2 years to treat successfully. Patients usually need four second-line drugs at a minimum, and many patients need five or six drugs.

How and why did PIH get involved in Russia?

There was no protocol anywhere in the world for how to treat MDR-TB. PIH developed a protocol in Peru in 1994, and then they built on the success of that protocol in Russia. Members of the PIH team approached the Russian Minister of Health for permission to start a program because of the number of people at risk there. We set up the program in Tomsk because there was already a program in place to treat regular TB, and we expanded it to include MDR-TB. We have received funding from several sources, including the Open Society Institute and the Eli Lilly & Co. Foundation.

In 2004, we worked with the Tomsk TB Services to apply for a grant from the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM). Upon receiving the funds, PIH was asked to become the principal recipient-manager of the grant, and it has supported our training and treatment efforts in addition to treatment of 950 MDR-TB patients in both civilian and prison sectors. This year's grant from USAID allows us to expand our collaboration with Russian medical facilities in five different regions.

What is unique about providing treatment for MDR-TB in Russia?

We have to provide treatment through our local partners, because PIH-Russia would need a medical license to treat patients in Russia. So we don't directly treat patients, but we provide technical assistance and training to the doctors in Tomsk about how to treat them. A patient with lab-confirmed MDR-TB is enrolled into the program and reviewed by a clinical committee. A PIH staff physician is always present at the committee to provide advice. Each patient gets a personalized work-up and a prescription for medications. The committee decides on the regimen and where to start treatment.

If the patient lives far from a city, he or she can stay in the larger city TB hospital for the first few months of treatment and then switch to a local facility. About 80% of the patients stay in the hospital for intensive treatment for 3-4 months and up to 6 months, especially if they come from a rural area.

In a city, there might be several outpatient facilities. For example, we have TB dispensary offices in Tomsk where patients can come every day, and also a day care hospital, where 160 patients are treated daily without staying overnight.

What strategies have helped you reach this high-risk population?

One of the key challenges in treating MDR-TB in this population is finding and treating them every day, because they don't always know where they are going to be from one day to the next. Some patients don't have identification cards, and they may come from socially marginalized groups, so they are afraid of government institutions and are trying to hide.

One of the ways we've dealt with that is through a program called Sputnik that provides free home-based care for TB and MDR-TB patients. PIH hires and trains local nurses to follow up and locate patients and deliver medications as well as meals, psychological, emotional, and social support. The team works 12 hours every day. Each nurse works on a 6-hour rotation, and they aim to educate the patients and build trust, in order to bring them back into the medical system. Each day, they ask patients where they will be the next day so that they can contact them to maintain treatment. Patients in the program are thoroughly checked by the doctor for drug-related side effects, and they receive lab tests results once a month.

We are trying to promote treatment outside of the hospital to reduce the risk of hospital-associated infections, so it is safer and much easier in many cases for patients to stay at home.

Also, the weather is quite severe in Siberia, especially in the winter, when it is –22°F, and it is hard for patients to get out and get medications at a TB facility. In Tomsk, we provide daily food packages to about 80% of our TB patients, and to all our MDR-TB patients, to provide additional nutrition for them and their families. The Red Cross helps us provide food packages, and they support the medical staff, which provides home visits.

What are the outcomes of your program so far?

We have enrolled more than 1,700 MDR-TB patients from 2000 to 2010, and the cure rate on average is 75%, based on 2-year treatment results. For the prison sector, it is 85%-88%, mainly because it is much easier to manage patients in the prison environment. Unfortunately, some patients are very sick at the start of treatment and they die, especially if they have advanced disease or a high level of drug resistance known as XDR-TB, that is resistant to 5-9 different TB medications. The problem in treating TB is that no new medications have been available in 40 years, so we have to treat our patients with medications that were not created to combat MDR-TB. These medications cause a lot of side effects, and the treatment takes 2 years. We hope that with new medications, now in clinical trials, we can look forward to treatment regimens that are much stronger and take less time.

But our results have been good. We track the status of all major TB indicators, including TB mortality, and we are proud that Tomsk has the lowest TB mortality rate of all regions in Russia, and the lowest incidence rate among Siberian regions. Tomsk TB Services, in collaboration with PIH, treats about 1,000 TB and 3,000 MDR-TB patients annually, and the results have led to the overall decrease of TB in the region.

When we started our Sputnik project, the adherence rate among high-risk patients was 40%, and now it is about 80%-85%.

What are the next steps for PIH in Russia?

Similar programs are under development in five additional regions. We will need to train the medical personnel there, because setting up the treatment plans and managing high-risk TB and MDR-TB patients is new to them. In addition, we would like to start screening people who are at high risk for TB, including the relatives and friends of our patients, in order to initiate an appropriate treatment for them as soon as possible. ■

For more information about the Partners in Health MDR-TB program in Russia, visit www.pih.org/pages/russia.

In HIV-TB Coinfection, Treat HIV Soon After Tuberculosis

BY MITCHEL L. ZOLER
Elsevier Global Medical News

VIENNA – A quick start to antiretroviral therapy in patients coinfected with tuberculosis and HIV saved lives in a randomized study with over 600 patients.

"Mortality was reduced by [a relative] 34% when HAART [highly active antiretroviral therapy] was introduced at 2 weeks, compared with 8 weeks after the onset of TB therapy," Dr. François-Xavier Blanc said at the 18th International AIDS Conference. Starting HAART within the first 2 weeks after starting TB treatment instead of waiting as long as 2 months "could potentially save 150,000 annual HIV-TB deaths" worldwide, said Dr. Blanc, a physician at Bicêtre (France) University Hospital.

Dr. Blanc and his associates designed the Cambodian Early vs. Late Introduction of Antiretrovirals (CAMELIA) trial to address an issue raised by 2010 recommendations of the World Health Organization, which said that in coinfected patients, TB treatment should start first followed by antiretroviral therapy within 8 weeks. CAMELIA was sponsored by the French national AIDS research agency and U.S. National Institutes of Health.

Starting HAART within 2 weeks of TB therapy 'could potentially save 150,000 annual HIV-TB deaths' worldwide.

DR. BLANC

The study also focused on highly immunosuppressed patients, enrolling only those with CD4 cell counts less than 200/mcL; the median CD4 cell count of the 661 enrolled patients was 25/mcL.

"The first diagnosis of HIV often occurs when patients present with TB, often with very low CD4 counts," commented Dr. Anton Pozniak, director of AIDS services at Chelsea and Westminster Hospital in London. "Half of our patients with HIV and TB and in most U.K. units present with TB. This is pretty convincing evidence; it's fantastic results," Dr. Pozniak said in an interview. But he noted, as did Dr. Blanc, that starting a TB and HIV regimen nearly simultaneously was challenging.

"You need to give a whole lot of tablets all at once," said Dr. Pozniak. "Starting TB medication can cause nausea and vomiting and hepatitis, and people are a little concerned if they give antiretrovirals on top. But we usually start within 2-3 days. The researchers said it's okay to wait for 2 weeks, but I think it will likely be interpreted to mean start within the first 2 weeks, once a patient is settled on the TB drugs." During his talk, Dr. Blanc agreed that "starting within the first 2 weeks is okay."

"It's a very important study; it's something we didn't know the answer to," commented Dr. Joseph J. Eron Jr., director of the Center for AIDS Research at the University of North Carolina in Chapel Hill. "You try to start the TB treatment first because of its transmissibility. I think it then makes sense to wait 10-14 days, or some number of days, to make sure the patient tolerates the TB medications" and then start antiretroviral therapy.

CAMELIA ran at five sites in Cambodia during January 2006–May 2010. The patients averaged 35 years old, and two-thirds were men. All patients began on the same multidrug therapy for TB and then randomized into two HIV treatment arms, with 332 patients starting antiretroviral therapy at 2 weeks and 329 starting at 8 weeks. All patients also received the same HIV regimen.

The study's primary end point was death during follow-up. The early-treatment group had 59 deaths, a rate of 8/100 person-years, while 90 patients died in the delayed HIV treatment group, a rate of 14/100 person-years. The difference was statistically significant. At 3 years follow-up, the mortality rate was 18% in patients who started at 2 weeks and 30% in those who started at 8 weeks.

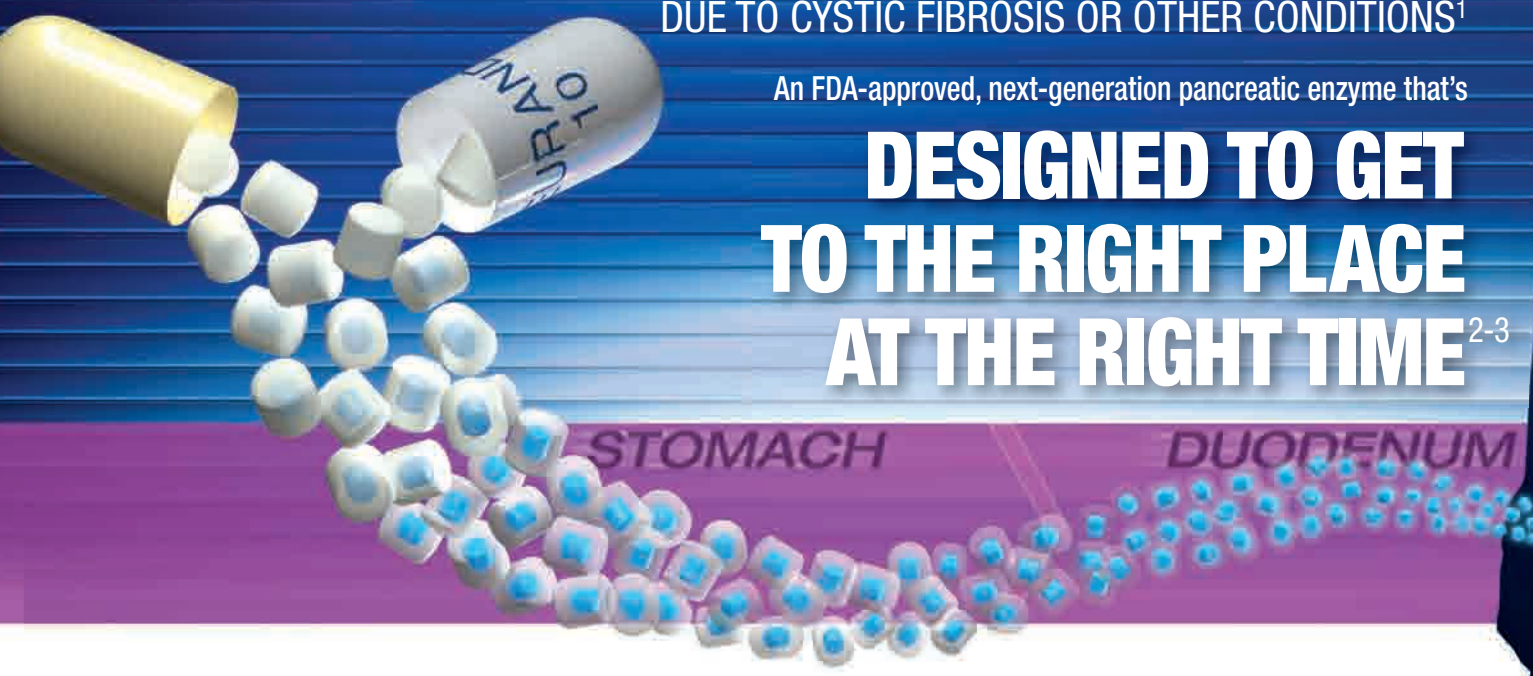
In a multivariate analysis that controlled for baseline CD4 cell count, body mass index, and other factors, a late start to treatment was linked with a 52% increased risk of death.

Dr. Blanc had no disclosures. Dr. Pozniak and Dr. Eron said that they had no disclosures relevant to this topic. ■

FOR THE TREATMENT OF EXOCRINE PANCREATIC INSUFFICIENCY DUE TO CYSTIC FIBROSIS OR OTHER CONDITIONS[1]

An FDA-approved, next-generation pancreatic enzyme that's

DESIGNED TO GET TO THE RIGHT PLACE AT THE RIGHT TIME[2-3]



Designed to deliver improved fat absorption[4]...

- Mean coefficient of fat absorption (CFA) was 88.3% for patients treated with ZENPEP vs 62.8% for patients treated with placebo (primary endpoint) in the pivotal trial of patients aged ≥7 years[4]
- 91% (n=29 of 32) of patients achieved a CFA >80%[4]
- Results were achieved without the use of concomitant agents such as PPIs, H_2-antagonists, and motility agents[4]

...with improved symptom control, even when switched from a previous enzyme[4]

- 100% (N=19) of children with PI due to CF switched to ZENPEP from a previous unapproved pancreatic enzyme had improved or maintained their level of symptom control (secondary endpoint)[4]
  - In this open-label, uncontrolled trial of patients aged 1 to 6 years, parents/guardians reported that 47% of patients switched to ZENPEP had improved symptom control (n=9) and 53% maintained symptom control (n=10)[4]*
  - ZENPEP is not interchangeable with any other pancrelipase product, and requires a new prescription

Important Safety Information

- Exercise caution when prescribing ZENPEP to patients with gout, renal impairment, or hyperuricemia and when administering pancrelipase to a patient with a known allergy to proteins of porcine origin
- Fibrosing colonopathy is a rare serious adverse reaction associated with high-dose use of pancreatic enzyme replacement products and most commonly reported in pediatric patients with CF. Exercise caution when doses of ZENPEP exceed 2500 lipase units/kg of body weight per meal (or greater than 10,000 lipase units/kg of body weight per day)
- To avoid irritation of oral mucosa or inactivation of enzymes, do not chew ZENPEP capsules or beads or retain in the mouth
- There is theoretical risk of viral transmission with all pancreatic enzyme products, including ZENPEP

Please read Brief Summary of Prescribing Information on adjacent page and provide Medication Guide to patients prescribed ZENPEP.

*Reports were subjective and recorded in a daily diary form.[4]

References: 1. ZENPEP [package insert]. Yardley, PA: Eurand Pharmaceuticals, Inc.; 2010. **2.** Data on file MED-0151, Eurand Pharmaceuticals, Inc., Yardley, PA. **3.** Data on file MED-0152, Eurand Pharmaceuticals, Inc., Yardley, PA. **4.** Wooldridge JL, Heubi JE, Amaro-Galvez R, et al. EUR-1008 pancreatic enzyme replacement is safe and effective in patients with cystic fibrosis and pancreatic insufficiency. *J Cyst Fibros.* 2009;8(6):405-417.

EURAND

Zenpep®
(pancrelipase)
Delayed-Release Capsules

PRECISELY THE WAY IT SHOULD BE™

 Printed in USA. ZEN 03203 1/11

FDA Approves PDE-4 Inhibitor for COPD Flares

BY MICHELE G. SULLIVAN
Elsevier Global Medical News

Roflumilast was approved by the Food and Drug Administration March 1 to decrease the frequency of exacerbations in patients with severe chronic obstructive pulmonary disease associated with chronic bronchitis and a history of exacerbations.

The drug is the only PDE-4 inhibitor approved for this indication, according to Forest Pharmaceuticals, which developed the agent. It will be marketed as Daliresp and is expected to be commercially available later this year.

Roflumilast will be available in 500-mcg pills to be taken daily for the prevention of COPD exacerbations in patients with severe disease, according to the agency.

Its efficacy and safety were evaluated in eight clinical studies comprising 9,394 adult patients, of whom 4,425 took the drug, according to a statement issued by Forest. Two of these studies were 1-year placebo-controlled trials that together enrolled more than 3,100 patients. Those treated had a history of COPD associated with chronic bronchitis and had experienced an exacerbation of the disease during the 12 months before beginning treatment. All patients were taking concomitant medications, including long- and short-acting beta-2 agonists, and/or short-acting anticholinergics.

Overall, the drug reduced the rate of moderate or severe exacerbations by 15% in one trial and 18% in the other, compared with placebo. The drug also improved prebronchodilator lung function.

Among the eight trials, most common adverse reactions in those taking the drug included diarrhea, weight decrease, nausea, headache, back pain, influenza, insomnia, dizziness, and decreased appetite. Of patients taking roflumilast, 14% withdrew from the studies because of adverse events: 5% for gastrointestinal upset and the rest for other problems. Serious adverse events occurred in 14% of those taking placebo and 13% of those taking roflumilast. Death from COPD occurred in 20 patients in the roflumilast group and 22 in the placebo group – not a significant difference.

The company also noted that weight change occurred more often in those taking the drug. It occurred mostly in obese rather than underweight patients and caused no increased morbidity relative to placebo. However, the company warned in a 2010 FDA presentation, "Patients and physicians should be informed that weight loss is associated with roflumilast and weight should be regularly monitored."

The drug is contraindicated in patients with moderate to severe liver impairment (Child-Pugh class B or C), according to the company's statement.

Other safety warnings that will appear on the packaging include:

► Roflumilast is not a bronchodilator and should not be used for the relief of acute bronchospasm.

► Psychiatric events including suicidality are associated with its use, occurring in 5.9% of treated patients compared with 3.3% of those taking placebo. Three patients experienced suicide-related adverse reactions, with one completion and two attempts, compared with one suicidal ideation in one placebo-treated patient.

► The drug should not be used in conjunction with strong P450 enzyme inducers and used with caution in patients taking inhibitors of the CYP3A4 or CYP1A2 enzymes.

► Roflumilast should not be used by pregnant women unless the risks and benefits are carefully weighed, and should not be taken during labor and delivery.

The drug's mechanism of action is not fully understood, the company noted. "It is thought to be related to the effects of increased intracellular adenosine monophosphate." ■

COMMENTARY

Dr. Darcy Marciniuk, FCCP, comments: COPD exacerbations are a leading cause of hospitalization and mortality. We've had no new and effective therapeutic agents in COPD for years – this medication represents an important step forward. While the exact role roflumilast in the comprehensive management of COPD remains to be fully understood, any agent that further improves lung function and reduces exacerbations is welcome.

Biofilm Stage Linked to In-Hospital Pneumonia

BY PATRICE WENDLING
Elsevier Global Medical News

NAPLES, FLA. – The presence of an advanced-stage biofilm in an endotracheal tube, and not duration of intubation, was significantly associated with pneumonia in a cohort of 32 critical care patients.

Biofilms are complex and dynamic polymicrobial colonies surrounded by a layer of protective glycocalyx. The bacteria cannot be identified with standard culturing methods, and antibiotics have a minimal effect. The concept of biofilm formation and related infections is becoming more widely accepted, with much of the early work coming from the dental field, Dr. Alison M. Wilson explained at the annual meeting of the Eastern Association for the Surgery of Trauma.

Biofilms have been identified on the surface of and within various medical devices and orthopedic hardware in both pediatric and adult patients, but little is known about what causes them to grow.

"It's very unpredictable who will form an advanced biofilm," she said. "We've had patients who were intubated for only 2 hours and had a stage IV biofilm, and others [who were] intubated for 21 days with a stage I biofilm."

Dr. Wilson, chief of the division of trauma, emergency surgery, and surgical critical care at West Virginia University in Morgantown, and her colleagues demonstrated in a previous study that biofilms on extubated endotracheal tubes significantly increase airflow resistance and that performance of these tubes may be comparable to that of new tubes one to four sizes smaller (Chest 2009;136:1006-13).

In the current analysis, the researchers used light microscopy to identify biofilm presence and scanning electron microscopy to delineate biofilm architecture in endotracheal tubes within 2 hours of extubation from 32 adult trauma and general surgery patients. Staging was performed by a microbiologist expert in biofilms blinded to all patient data.

In a stage I biofilm, the bacteria are loosely adhering to each other and to the surface, and can be removed mechanically or treated with antibiotics. In stage II, there is very robust adhesion between the microcolonies, which are surrounded by extracellular polymeric substances, affectionately known as slime, Dr. Wilson said. The bacteria cannot be treated effectively with antibiotics. In stage III, the polymicrobial colonies are completely covered by extracellular polymeric substances and 3-D matrices that recruit bacteria to the biofilm. In stage IV, there is sloughing and shedding of the biofilm and embolization of the live microcolonies to distant sites, she said.

Patients in the study had a mean age of 50 years (range, 13-81 years). The average ICU stay was 13 days, and average intubation duration was 7.4 days. All of the endotracheal tubes were found to have a biofilm, Dr. Wilson said.

Half of the patients developed pneumonia while intubated. Pneumonia occurred in 2 of 6 patients with a stage I biofilm, 3 of 8 patients with a stage II biofilm, 3 of 8 with a stage III biofilm, and 8 of 10 with a stage IV biofilm.

The duration of intubation was not related to biofilm stage; the average length of intubation was 4.3 days for stage I biofilm patients, 9.5 days for stage II, 8.1 days for stage III, and 7.1 days for stage IV.

Invited discussant Dr. Amy N. Hildreth said that although the study would have been strengthened by the inclusion of illness severity data, it "provides a significant contribution to the growing body of literature suggesting that ventilator-associated pneumonia should instead be termed endotracheal tube–associated pneumonia."

Dr. Hildreth, a surgeon with Wake Forest University Baptist Medical Center in Winston-Salem, N.C., asked what the authors think causes more rapid development of stage IV biofilm in some patients, and whether any particular organisms are associated with biofilm stage.

Dr. Wilson said the development of an advanced biofilm seems to be fairly random in terms of time, but that certain organisms, notably yeast, may provide scaffolding for biofilm development.

An audience member asked what clinicians can do to prevent biofilm formation. Dr. Wilson said she would not recommend changing the tubes, and noted that several novel approaches are being studied, including inhalation agents and different types of tubes such as silver tubes. She added that in vivo test is needed to detect biofilm, to help clinicians determine whether their patient is failing because of a biofilm or something else.

Dr. Wilson, her coauthors, and Dr. Hildreth disclosed no relevant financial disclosures. ■

COMMENTARY

Dr. Marcos Restrepo, FCCP, comments: The results of this very interesting study are striking and concerning if we consider zero VAP a feasible goal. These results suggest that zero VAP is not possible; however, this study was done on critical care patients from a trauma/surgical ICU, who have one of the highest rates of VAP overall, so perhaps the results cannot be extrapolated to the general population. In addition, the clinical characteristics of the patients are not clearly defined in this report until the final peer review is available; there is no information regarding the VAP preventive strategies that were used in the mechanically ventilated patients; the definition of VAP was not described; and it is unclear if microbiology-proven VAP occurred. The authors did not observe a difference in the four stages of biofilm formation and the incidence of VAP. However, the presence of biofilm in all of the patients supports prior research using the silver-coated endotracheal tube in order to prevent VAP. In conclusion, this is a provocative study, but many issues will require further research in order to clarify the association between biofilm and VAP.

Chronic Cough Often Caused by Multiple Factors

BY ROD FRANKLIN
Elsevier Global Medical News

KEYSTONE, COLO. – Physicians would do well to add habituation, neuropathic triggers, and laryngopharyngeal reflux to the list of factors they assess when tracing the origins of a cough that has persisted for longer than 8 weeks, advised a Colorado pulmonary specialist.

The usually recognized initiators of chronic refractory cough include asthma, upper airway cough syndrome (postnasal drip), and gastroesophageal reflux disease. But looking beyond these common culprits and analyzing combined etiologic factors on a case-by-case basis may be necessary, emphasized Dr. Ronald C. Balkissoon of the division of pulmonary and critical care medicine at National Jewish Health in Denver.

"Most people who have chronic cough have at least two or more underlying problems that are contributing to it," Dr. Balkissoon said at a meeting on allergy and respiratory diseases, which was sponsored by National Jewish Health. "Often [physicians] will just try to treat one issue like acid reflux and it doesn't work, so they presume that's not part of the problem. But you really have to have a multidisciplinary approach and consider all the relative contributing factors."

An especially underappreciated complication is laryngopharyngeal reflux (LPR), he said. Physicians using both classic pH probes or impedance probes often shortchange their diagnoses by missing clues, in large part because LPR is not specific in its presentation. The role LPR plays can be obfuscated by the presence of supraglottic edema or erythema, glottic abnormalities, epiglottic malformations, and lingual tonsillar hypertrophy, among other factors.

Moreover, the cobblestoning of epithelial tissue, an obvious sign of LPR, is not exclusive to that disease. It is also seen in cases where chronic cough derives mostly from a postnasal drip. Bronchoscopy will often reveal a transformation of tissue from normal columnar epithelium into squamous epithelium, even when the reflux is nonacidic, but beyond that, finding the proper context for tissue changes such as cobblestoning and ruling out non-LPR origins can be a challenge.

Chronic cough has a detrimental effect on the lives of many, with almost 30 million clinical visits reported annually in the United States. Females demonstrate a higher cough reflex sensitivity than do males, and the condition is driven by several additional originating factors that range from ACE inhibitor use to chronic bronchitis and bronchiectasis.

The learned and neuropathic origins of persistent cough stand as additional elements that may be more important in the big picture than many clinicians realize.

"Habituation, I think, is a very, very big part of what happens to people who have chronic cough," Dr. Balkissoon said. "They may have postnasal drainage issues. They may have gastroesophageal reflux disease issues and even ongoing asthma, but by the time they develop this cough that's been going on for 15 or 25 years, there's clearly habituation."

At another level, neuropathic manifestations of chronic cough are due to the irritant receptors that thrive in the lungs and throat. These include nociceptive C fibers, G protein, transient receptor potential vanilloid 1, and transient receptor potential A1.

The jury is still out on newer receptor antagonists, as well as surgical procedures such as fundoplication and other nonpharmacologic management approaches. But a diagnosis that acknowledges the likelihood of a more complex group of reasons for chronic cough may be the most logical way to seek better-tailored therapies.

"Most of the people who have chronic cough really have the common etiologies, but understanding that they're often in combination and they have one or more reasons for it being refractory is the most important point," Dr. Balkissoon said.

Dr. Balkissoon disclosed speaking on behalf of AstraZeneca, Boehringer Ingelheim, Genentech, GlaxoSmithKline, and Novartis. ■

COMMENTARY

Dr. Darcy Marciniuk, FCCP, comments: Chronic cough is a nemesis of every pulmonologist and the list of causes continues to grow. A distressing symptom for so many of our patients, this report highlights the often multifactorial etiology for chronic cough. Until the hope of new advances and therapies is fulfilled, a systematic diagnostic and therapeutic approach is the clinician's most effective tool.

Bevacizumab May Extend Lung Cancer Survival

BY PATRICE WENDLING
Elsevier Global Medical News

CHICAGO – Bevacizumab maintenance after first-line chemotherapy for advanced non–small cell lung cancer was associated with longer overall survival in a retrospective study of 403 patients treated in outpatient community settings.

Median NSCLC disease progression was 10.3 months among patients who continued on bevacizumab (Avastin) until disease progression after they received first-line chemotherapy plus bevacizumab, compared with 6.5 months for those who discontinued the monoclonal antibody after chemotherapy.

Median overall survival reached 20.9 months vs. 10.2 months, respectively, Dr. Eric Nadler reported in a poster at the Multidisciplinary Symposium in Thoracic Oncology.

It is standard practice in clinical trials to continue giving patients bevacizumab until disease progression, but recent assessments of treatment patterns showed that bevacizumab is often discontinued when chemotherapy ends. Price has been an issue, with the typical monthly cost of bevacizumab for advanced lung cancer placed at about $8,800 in 2006. Only 38% (or 154) of the 403 patients in the study received bevacizumab until disease progression.

The industry-sponsored study identified patients with nonsquamous NSCLC from an electronic health records system that contains data from 884 community-based oncologists in US Oncology Inc.–affiliated practices or clinics in 20 states.

Patients were treated from July 2006 through June 2008, with 31% located in the Southwest and 30% in the Southeast. In all, 37% of patients had private insurance, 57% were covered by Medicare, and 6% had some other payer.

The maintenance group tended to have better pre- and postchemotherapy performance status scores and a greater number of completed chemotherapy cycles (median, six vs. four). Overall, 56% of the maintenance group and 39% of the no-maintenance group received a second-line therapy.

To control for survivorship and selection bias, researchers excluded patients with disease progression or death within 30 days of chemotherapy completion; landmark analyses were conducted at 18, 21, and 26 weeks from initial treatment.

Among those who were alive and progression free at 18 weeks, bevacizumab monotherapy until disease progression was associated with a 46% reduced risk of death (hazard ratio, 0.54), reported Dr. Nadler of the Texas Oncology–Baylor Sammons Cancer Center in Dallas. The association between bevacizumab and longer residual overall survival persisted among the patients who remained progression free and alive at 21 weeks (HR, 0.58) and 26 weeks (HR, 0.61).

Bevacizumab monotherapy was associated with longer progression-free survival at 18 weeks (HR, 0.73), but the association was no longer observed at 21 weeks (HR, 0.82) and 26 weeks (HR, 0.79).

Although the nonrandomized nature of the study precludes making any conclusions about causality, the authors concluded that the findings provide "significant insights into real-world patterns of care and associated outcomes and provide important evidence on which to base future comparative effectiveness research."

In a separate national survey, Dr. Nadler and associates at Tufts University in Boston reported that 84% of oncologists say that patients' out-of-pocket spending influences treatment recommendations, even though only 43% frequently or always discuss costs with patients. Among the 787 oncologists surveyed, 79% favored more comparative effectiveness research and 80% supported more cost-effectiveness data, but only 42% felt well prepared to interpret it (Health Aff. [Millwood] 2010;29:196-202). ■

COMMENTARY

Dr. W. Michael Alberts, FCCP, comments: A doubling of median overall survival in those who continued to receive bevacizimab after receiving first-line chemotherapy until progression is noteworthy. One must remember, however, that this study was retrospective and nonrandomized.

EGFR Testing Recommended

Adenocarcinoma • *from page 1*

The changes also could significantly influence the next revision of the TNM (tumor, node, metastases) staging system, "not only for pathologic staging but also for clinical staging," said Dr. Travis, a thoracic pathologist at Memorial Sloan-Kettering Cancer Center, New York.

The new section on small biopsies and cytology specimens is especially important because 70% of lung cancers are diagnosed in samples like these, the consensus panel's statement said. New criteria for diagnosing adenocarcinoma vs. squamous cell carcinoma include the use of special stains in difficult cases, and emphasize the importance of preserving tissue for molecular studies.

COMMENTARY

Dr. W. Michael Alberts, FCCP, comments: An assembled group representing three societies with an interest in lung cancer proposed major changes in the classification of lung adenocarcinomas. Recent advances in treatment, immunohistochemistry, and molecular biology prompted the effort. While merely recommendations at this time, the case for the proposal is well outlined and referenced. Interestingly, this document recommends that the term "bronchoalveolar cell carcinoma" be abandoned. Effecting such a change may prove to be challenging as "BAC" is well entrenched in the lexicon of lung cancer.

Dr. Travis outlined three important clinical reasons to distinguish cases of adenocarcinoma from squamous cell carcinoma, especially in advanced disease:

- Patients with advanced lung adenocarcinoma or unspecified NSCLC who test positive for EGFR mutation are more likely to respond to treatment with tyrosine kinase inhibitors than are patients without mutation.
- Patients with adenocarcinoma or unspecific NSCLC are more likely to respond to pemetrexed (Alimta) than are patients with squamous cell carcinoma.
- Bevacizumab is contraindicated in patients with squamous cell carcinoma because it can lead to life-threatening hemorrhage, he said.

The statement attempts to banish the term bronchioloalveolar carcinoma from histopathology because it is used in ways that confuse five distinct categories: adenocarcinoma in situ; minimally invasive adenocarcinoma; lepidic predominant adenocarcinoma; adenocarcinoma that is predominantly invasive with some nonmucinous lepidic component; and invasive mucinous adenocarcinoma.

"Adenocarcinoma in situ" and "minimally invasive adenocarcinoma" appear in the classification for the first time for small solitary adenocarcinomas with either pure lepidic growth or predominant lepidic growth and no more than 5 mm invasion, because these terms identify patients who have nearly a sure shot at disease-free survival after complete resection.

The statement recommends a new approach for classification of resected invasive lung adenocarcinomas using comprehensive histologic subtyping and classification according to the predominant histologic subtype.

"This allows for improved stratification of patients compared to the 2004 WHO classification, and allows for identification of subtypes that have prognostic significance and that can be correlated with molecular findings," Dr. Travis said.

Introducing the concept of in situ carcinoma raised the consideration that tumor size measured according to the size of the invasive component may be a better approach than measuring total tumor size in predicting survival for patients with small solitary adenocarcinomas with a lepidic component. This concept potentially could affect both pathologic and clinical staging in the next TNM, he said.

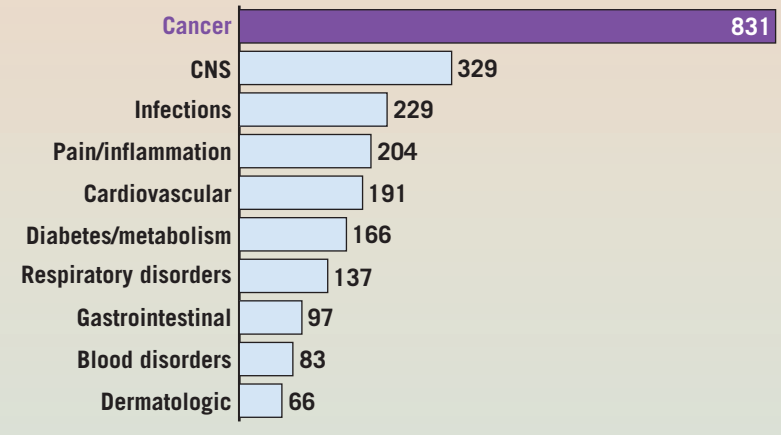
Using CT, prognosis may be better predicted by the size of the solid component in partly solid nodules rather than by total tumor size including the ground-glass component, Dr. Travis explained.

"Hopefully, this will be investigated by lung cancer groups around the world in the next 5 years, so the TNM committee can address this issue in developing the eighth edition of TNM based on validated data," he said.

One of the consensus committee members, Dr. Giorgio Scagliotti, has received honoraria from Sanofi-Aventis, Roche, Eli Lilly, and AstraZeneca. Another committee member, Dr. David Yankelevitz, is a named inventor on some patents related to the evaluation of diseases; the patents are licensed to General Electric and may produce compensation if they are commercialized. The rest of the committee reported having no financial conflicts of interest. ■

DATA WATCH

Cancer Drugs Fill Pharmaceutical Pipeline



Note: Includes drugs in phase I, phase II, and phase III or awaiting FDA approval for the top 10 areas of development in 2009.
Sources: Medco 2010 Drug Trend Report; R&D Directions 2009;15:4-89

ELSEVIER GLOBAL MEDICAL NEWS

FROM THE DESK OF THE PRACTICE MANAGEMENT COMMITTEE

The Transition to ICD-10-CM

BY ROBERT DEMARCO, MD, FCCP, CHAIR; AND DONNA KNAPP BYBEE, FACMPE, VICE-CHAIR

The International Classification of Diseases (ICD) is the international standard coding language for classifying morbidity and mortality. The current version being utilized for morbidity classification is ICD-9-CM, which was clinically modified (CM) for use in the United States. ICD-9-CM will be phased out and replaced by ICD-10-CM and ICD-10-PCS (Procedural Coding System) on October 1, 2013.

ICD-10-CM will be the new standard for all HIPAA transactions, including physician and nonphysician patient encounters for outpatient, inpatient, and physician office utilization. If HIPAA transactions are not coded using the correct ICD-10-CM code on and after October 1, 2013, the Centers for Medicare & Medicaid Services (CMS) will reject claims for payment and other transactions, resulting in additional work for practice administration and the delay of reimbursement.

ICD-9-CM consists of three volumes. The first two volumes (diagnostic codes) will be replaced by ICD-10-CM, which will be utilized by all health-care providers in every health-care setting. The third volume (procedure codes) will be replaced by ICD-10-PCS, which will only be used for hospital claims for inpatient hospital procedures. *Current Procedural Terminology* (CPT®) will continue to be the standard for physician claims procedures and services.

Several major reasons necessitate the transition to ICD-10-CM. ICD-9-CM lacks the level of detail and specificity that modern medicine demands and is out of date on some terminology. Also, ICD-9-CM coding convention is running out of space for new diagnoses.

National Center for Health Statistics (NCHS) provides industry with a code to code(s) translation reference dictionary known as general equivalence mappings (GEMs), which is available on the CMS Web site. Ninety-five percent of ICD-9-CM codes correspond to one or more ICD-10-CM codes. According to CMS, "GEM files attempt to organize [the differences between ICD-9 and ICD-10] in a meaningful way, by linking a code to all valid alternatives in the other code set from which choices can be made depending on the use to which the code is put." Some ICD-9 codes have a one to one relationship to ICD-10 codes, but many have one to many relationships, since ICD-10 has a higher level of specificity.

GEMs from ICD-10-CM to ICD-9-CM provide a temporary but reliable mechanism for mapping records containing ICD-10 diagnosis codes to "reimbursement equivalent" ICD-9 diagnosis codes, so that while systems are being converted to process ICD-10 claims directly, the claims may be processed by this legacy system. Keep in mind that a medical record that will be processed and stored as ICD-10 data should always be coded directly using ICD-10-CM.

ICD-9-CM consists of approximately 13,500 diagnostic codes with three to five characters (the first being either alpha or numeric, with the rest being numeric). ICD-10-CM has about 68,000 alphanumeric codes that are three to seven characters long (the first character being alpha, the second numeric, and the rest either alpha or numeric). In general, ICD-10-CM codes are more specific, conveying a greater level of information regarding the corresponding diagnosis.

Similar to ICD-9-CM, ICD-10-CM has a hierarchical code structure. The first three characters represent the category; the next three characters represent the "etiology, anatomic site, and severity"; and the seventh digit is an "extension" for obstetrics, injuries, and external causes for injuries. The terminology used for ICD-10 coding has been updated to be consistent with current clinical practices. Injuries will be grouped by anatomical site rather than the type of injury. Some diseases are being reclassified to different chapters.

When deciding on an electronic health-care record (EHR) system for your practice, be sure to ask vendors whether their systems will be able to handle the transition to the ICD-10 standard. If your practice has already purchased an EHR system, ask your current vendor what system upgrades or replacements will be necessary to accommodate the transition, and get written confirmation.

Preparation for ICD-10 by pulmonary, critical care, and sleep practices will require significant planning, training, and system upgrades. Practices need to begin preparing for the transition. ■

For additional information, see Chest. 2010;138(1):188-192.

Applications Now Being Accepted Through May 4

Third GlaxoSmithKline Distinguished Scholar in Thrombosis Award

The CHEST Foundation's Distinguished Scholar Program provides an opportunity for ACCP members to extend their impact in clinical practice. This year, The CHEST Foundation will give the Third GlaxoSmithKline Distinguished Scholar in Thrombosis Award. The 3-year, $150,000 award will be presented to an ACCP member who proposes a thrombosis-related project and/or service that does one or more of the following:

- Investigates alternatives for treatment
- Educates patients about options for diagnosis and treatment
- Disseminates new knowledge about diagnosis and treatment
- Addresses family, legislative, and regulatory issues
- Defines new mechanisms leading to innovations and improvements in treatment

Henry I. Bussey, PharmD, FCCP, was selected as the Second GlaxoSmithKline Distinguished Scholar in Thrombosis in July 2008. The objectives of his project, "A Superior Method of Oral Anticoagulation Management to Substantially Reduce Event Rates, Improve Quality of Life, and Reduce Health-care Costs" are to develop and demonstrate a new method of oral anticoagulation management that will reduce stroke, MI, death, and major bleeding by 30% to 60% compared with current management.

OneBreath™ Clinical Research Award in Lung Cancer

The CHEST Foundation is pleased to announce the 2011 OneBreath™ Clinical Research Award in Lung Cancer. ACCP members who have completed at least 2 years of pulmonary or critical care fellowship or a thoracic surgery residency and are within 7 years of completing training are encouraged to apply.

"The newly established OneBreath™ Clinical Research Award in Lung Cancer represents the continuation of a long tradition of The CHEST Foundation's support of clinical research in lung cancer. The strength of this award is in its focus on junior investigators who often have a difficult time obtaining grant funding and need this type of award to get their careers off the ground. It is our hope that qualified young investigators take advantage of this great opportunity," says Gerard Silvestri, MD, FCCP, Co-Chair, Award Review Committee.

Projects focused on medical and/or surgical detection and treatment of lung cancer based on clinical and/or translational research will be considered. A grant of $100,000 with payments of $50,000 each year for 2 years will be awarded. ■

Read about all of the 2011 awards at OneBreath.org, *or go to* mc.manuscriptcentral.com/chest2011 *to submit an application. Contact Lee Ann Fulton at* lfulton@chestnet.org *with questions regarding the awards.*

Youth Ambassador Spreads Healthy Lungs Message

As a sophomore-year student at Saratoga High School, in Saratoga, CA, Youth Ambassadors Group member, Nikhila Janakiram, began her "Breath of Life" program. She felt compelled to share the knowledge she had obtained through The CHEST Foundation's Lung Lessons℠ to bring an awareness of the ill effects of smoking to children in elementary and middle school in northern California. Through taking the initiative to contact principals and librarians in her local community, she has offered her program to hundreds of students from both Foothill and Argonaut elementary schools and patrons of the libraries in Milpitas and Pleasanton, CA.

Nikhila's presentations incorporate visual materials provided by The CHEST Foundation's lending library, such as a jar of tar, showing how a year's worth of smoking pollutes a person's lungs. The jar of tar has made a "big impact" on her audience, triggering numerous questions and making the students more determined to resist smoking.

When asked why she makes these presentations, Nikhila said, "The increase in lung cancer over recent years concerns me, which was the motivating factor for me to get involved and start my program to educate children in my own community."

As Nikhila's mother shared in a letter to The CHEST Foundation, "Her ambition is to be a practicing physician, and this opportunity has only reinforced her passion for this profession." The Ambassadors Group is very lucky to have such a dedicated youth member engaged in promoting its antitobacco and healthy lungs message. ■

NETWORKS
Third-Hand Smoke, Resuscitation, Disparities, Ethics

Occupational and Environmental Health

A Third-Hand Look at Smoking

Third-hand smoke, the residual particulate matter of tobacco smoke remaining after a cigarette is extinguished, may represent an additional serious health hazard, particularly in the home. It has been found on surfaces, including furniture, carpeting, clothing, and even on an individual's hair. The residual nicotine in this contamination has been found to react with atmospheric nitrous acid, forming carcinogenic substances referred to as tobacco-specific nitrosamines (Sleiman et al. *Proc Natl Acad Sci USA*. 2010;107[15]:6576). Third-hand smoke contains over 250 products, including the known toxins of butane, carbon monoxide, cyanide, ammonia, toluene, arsenic, lead, chromium, cadmium, and radioactive polonium-210 (Winickoff et al. *Pediatrics*. 2009;123[1]e:74). It therefore represents an insidious danger well after active smoking has stopped. For instance, nonsmokers moving into a home of a previous smoker had higher levels of skin nicotine and urine cotinine, even after the home had been vacant for 2 months (*Tobacco Control*. 2001;20:1-8).

Young children are particularly vulnerable to the effects of third-hand smoke exposure because they crawl or place contaminated objects in their mouths. A high serum cotinine level in children has been shown to be associated with lower scores in reading, mathematics, and block design skills (*Environ Health Perspect*. 2005;113[1]:98).

Although many individuals are aware of the health risks associated with first- and second-hand smoke, few are aware of third-hand smoke and its resultant danger. The knowledge that third-hand smoking is harmful was found to be an independent variable to home smoking bans (Winickoff et al. *Pediatrics*. 2009; 123[1]:e74). Patient education about third-hand smoke is an important way to counsel smokers on the multiple dangers of tobacco exposure and will help reduce the threat of tobacco-related diseases in our most vulnerable population.

Dr. Timothy B. Coyle; and
Dr. Daniel A. Gerardi, FCCP
NetWork Chair

Pediatric Chest Medicine

New PALS Guidelines Available

Community training centers around the country will be rolling out the new Pediatric Advanced Life Support 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care.

Recently published as a special report in the November 2010 issue of *Pediatrics,* the new guidelines review advances in resuscitation science and best practice. Over the past 20 years, improved survival rates have been reported with in-hospital resuscitations for infants and children; however, survival rates to discharge with extramural cardiac arrests have remained at approximately 6%.

Respiratory events continue to be the primary etiology of cardiopulmonary arrests in children. Rapid response teams available to inpatient facilities with infants and children at increased risk for respiratory failure significantly decrease risk of arrest by early identification and intervention. Primary cardiac events, however, both in-patient and extramural events, continue to carry higher mortality. Manual defibrillators with pediatric-sized paddles and adjustable energy doses are preferred for use in children, particularly infants less than 12 months of age.

Family presence during resuscitation is becoming a more common occurrence. Studies report that these families identified benefits to and comfort from being present during resuscitation. The guidelines are careful to add that a staff member should be assigned to be with the family during the process to provide support and information as needed.

Online programs are available for Pediatric Advanced Life Support (PALS). Further information can be accessed on the American Heart Association Web site: www.americanheartassociation.org.

Dr. Mary E. Cataletto, FCCP
Steering Committee Member

Women's Health

Health Disparities and Women's Health: Today's Evidence, Tomorrow's Agenda

The First Periodic Health Disparities and Inequalities Report was released by the Centers for Disease Control and Prevention (CDC) in January 2011. Health disparities are the differences in health outcomes between groups that reflect inequalities. The CDC highlights health disparities by gender, race and ethnicity, income, education, disability status, and other social characteristics in the United States. This report presents the harsh reality. Despite considerable work and progress in recent years, health disparities continue to exist in our nation. The majority of preventable deaths are in women. The need for continued aggressive work, particularly in women's health, couldn't be more emphasized.

The report provides the two most critical aspects required to address the issues of health disparity. In-depth analysis of the recent trends and ongoing variations in health indicators provide today's evidence compelling action, while the recommendations and important steps in encouraging actions and facilitating accountability provide tomorrow's agenda to reduce modifiable disparities by using interventions that are effective and scalable. The CDC, once again, gives a powerful vehicle to enhance awareness and understanding of vulnerable populations. It is the challenge to the individuals, society, and associations to implement the necessary tools to best address health disparities and inequalities in our nation.

To read the report, go to www.cdc.gov/Features/HealthDisparitiesReport.

Dr. Daya Upadhyay
Steering Committee Member

Palliative and End-of-Life Care

Early Ethics Intervention in ICUs: Learning What Works

Patients in a hospital ICU present complex ethical challenges. Because 10% to 20% of ICU admissions can be expected to die during that admission or upon discharge to their next level of care (Zimmerman et al. *Crit Care Med*. 1998;26[8]:1317), staff can have difficulties shifting gears when all technically feasible care may no longer be clinically meaningful. Because the death rate is high, moral distress can take its emotional toll on staff (Hameric et al. *Crit Care Med*. 2007;35[2]:422), and communications with families can be conflicted. Families of ICU patients may lack trust, and an increasing subset of families want decisional control (Johnson et al. [published online ahead of print Oct 29, 2010]. *Am J Respir Crit Care Med*. doi:10.1164/rccm.201008-1214OC).

Clinical ethicists may help prevent and resolve ethical complexities that produce conflict and distress through early ethics interventions (DeRenzo et al. *HEC Forum*. 2006;18[4]:319; DeRenzo et al. *Camb Q Healthc Ethics*. 2006;15[2]:207). Empiric data (Schneiderman et al. *Crit Care Med*. 2000;28[12]:3920; Schneiderman et al. *JAMA*. 2003;290[9]:1166) show that early ethics contact with families (Scheunemann et al. *Chest*. 2011; 139[30]:543) may reduce conflict and distress among families and clinicians.

To increase understanding of how early ethics intervention might reduce conflict and distress, we are beginning a project that will look at an array of variables that may predict ethics complexities and early ethics interventions that could reduce communication problems, reduce length of stay and, ultimately, reduce liability. As our clinical ethics hunches are supported or refuted, we will use these data to design future studies and early ethics interventions to contribute to improving the quality of critical care delivered at our hospital.

Nneka O. Mokwunye, PhD; and
Evan G. DeRenzo, PhD
Steering Committee Member

BY DAVID D. GUTTERMAN, MD, FCCP

PRESIDENT'S REPORT

What's in a Name? Expansion and Diversification

For more than 75 years, the name "American College of Chest Physicians" has become synonymous with excellence in education, innovation in guideline development, and leadership in the management of diseases of the chest. The ACCP takes pride in providing the majority of practicing pulmonologists in the United States with these opportunities. As we have grown through the years, our success has piqued interest from a broader constituency of care providers. We have always been inclusive of other chest physicians, including cardiologists, cardiac and chest surgeons, radiologists, pediatricians, emergency medicine specialists, and others. We have also expanded our programs to match the scope of pulmonary practice as it incorporated both critical care and sleep medicine.

But at an even higher level, the ACCP has become more encompassing and more integrated by embracing a broader group of chest practitioners. For some time now, the ACCP has also included among its members, the important community of health-care professionals who provide frontline support for patients with chest-related illnesses. This important and growing component of our membership allows us to be more inclusive, and, in doing so redefines the "P" in ACCP to include nurse 'P'ractitioners, 'P'hysician assistants, 'P'harmacists, and res'P'iratory therapists, among others. This is critical to our strategic focus on educational efforts that involve health-care teams engaged in the increasingly multidisciplinary approach to patient care.

An expansion is also taking place at the other end of our name. We have always been an international society, since the "A" in ACCP has been inclusive of the US and Canada for many years. We have close ties to the Canadian Thoracic Society. Many Canadian practitioners have dual membership, we regularly host our annual meeting in Canada, and just last year, a Canadian physician was elected into the Presidential line of the ACCP.

However, this is just the tip of the iceberg. Our world is becoming more connected through technology and more accessible with cheaper travel. As Thomas Friedman's best-seller title indicates, "The World Is Flat." Global connectivity in the Internet era has broadened our horizons and eliminated obstacles to communicating with colleagues on other continents. There is no better example of this flattening than our experience with the *CHEST* journal. With its electronic accessibility for international members, growing popularity, translation into other languages, highly clinically relevant content, and climbing impact factor, it is no wonder that the *CHEST* brand is more widely known than ACCP, the organization that publishes it.

As a result of greater global connectivity, the past decade has brought a steep rise in international requests of ACCP for meeting endorsements and participation abroad. A specific committee has been set up to handle these requests and organize our global efforts. As a result, we have witnessed record numbers of international attendees at the annual CHEST meeting (over 30% in 2010) and an evolution of our international education efforts to now include multiyear contracts for simulation, postgraduate seminars, and enduring education products.

This initiative represents an important strategic opportunity and commitment for ACCP—to support chest physicians across the world as we do in North America. As a result, we also derive benefit from collaborations with a diverse group of colleagues sharing novel approaches to care delivery and bringing a unique patient mix to complement and enrich everyone's educational experience. To this end, we are introducing the inaugural Global Case Reports session at CHEST 2011 in Hawaii, where interesting cases from around the world will be presented and discussed in one venue during Sunday's program. This all occurs at the first meeting of CHEST to be held off the North American continent. Thus the "A" in ACCP could be redefined to include 'A'll countries in which CHEST medicine is practiced.

Having a membership that is interdisciplinary (inclusive of nonphysician practitioners) and geographically diverse results in cultural, professional, and personal enrichment of our programs, leadership, and education offerings. To be sure that we capture that diversity and employ it in support of the College, I announced last fall plans to create a Presidential Task Force on Diversity. It gives me great pleasure to announce that this task force has been created and is being led by two icons in the field: Marilyn Foreman, MD, MS, FCCP, from Morehouse School of Medicine; and Sola Olopade, MD, MPH, FCCP, from the University of Chicago Pritzker School of Medicine. They co-chair a broad-based group of senior ACCP members and staff to review current ACCP approaches to diversity and promotion of health equity. The charge of the task force is to develop an encompassing, enduring plan to ensure optimal integration of diversity throughout the activities and structure of the ACCP. This approach will help define new opportunities when applied to the international arena and when used to link our broad membership of care providers in a multidisciplinary fashion. The ACCP is one of only a few societies making diversity and attention to disparities such a high priority. Being on this forefront allows us to provide greater value to our members and to their patients.

I welcome your comments and invite you to access the Presidents' blog at http://www.chestnet.org/accp/blogs/presidents to reflect on this article or express your thoughts about the ACCP or related topics. ■

Electronic Prescribing Incentive Program (eRx) and Noncompliance Penalty

The Electronic Prescribing Incentive Program (eRx) is an incentive program for physicians (and other eligible professionals) who are successful electronic prescribers as defined by the Medicare Improvements for Patients and Providers Act of 2008 (MIPPA). The eRx incentive payment for 2011 and 2012 is 1.0% of total estimated allowed charges per year. For 2013, the incentive payment will be reduced to 0.5%.

Beginning in 2012, there will be a penalty for not participating in eRx. The penalty will be a reduction in Physician Fee Schedule payments by 1.0% in 2012, 1.5% in 2013, and 2.0% in 2014. **In order to avoid a penalty in 2012, an eligible physician or group practice must have 10 unique eRx events between now and June 30, 2011.** To avoid a penalty in 2013, an eligible physician must have 25 unique eRx events in calendar year 2011 e-prescribed.

To both qualify for the incentive and avoid the penalty, physicians must possess and use a qualified eRx system and also report on his or her adoption and use of the eRx system. The physician must also meet the criteria for successful electronic prescriber specified by the Centers for Medicare & Medicaid Services (CMS) for a particular reporting period. Finally, at least 10% of a successful electronic prescriber's Medicare Part B covered services must be made up of codes that appear in the denominator of the eRx measure.

Reporting eRx participation only involves reporting a single Quality-Data Code, **G8553**, which signifies that at least one prescription created during the encounter was generated and transmitted electronically using a qualified eRx system.

Some physicians can qualify for hardship exemptions from the eRx penalty by requesting exemption from the payment adjustment by submitting one of the following codes: **G8642** (the eligible professional practices in a rural area without sufficient high-speed Internet access), **G8643** (the eligible professional practices in an area without sufficient available pharmacies for electronic prescribing), or **G8644** (the eligible professional does not have prescribing privileges).

Unlike the PQRS and EHR programs, little time buffer exists for avoiding the eRx penalty. Your practice must submit a minimum of 10 unique eRx events by June 30, 2011, or all of your Medicare Physician Fee Schedule Part B payments will be reduced by 1% at the beginning of next year. A minimum of 25 unique eRx events must be submitted by the end of this year, or your practice would also be penalized in 2013. It has not yet been announced whether or not 2012 eRx submissions will count against incurring a 2013 penalty. At present, the only existing way of avoiding a 2013 penalty is by submitting a minimum of 25 unique eRx events by the end of 2011. ■

Need assistance? Contact the ACCP coding and reimbursement consultant staff, Diane Krier-Morrow, MBA, MPH, CCS-P, at (847) 677-9464 or dkriermorr@aol.com*; or contact QualityNet Help Desk at* qnetsupport@sdps.org *or (866) 288-8912. For the CMS eRx Web page, go to cms.gov/ERxIncentive.*

SLEEP STRATEGIES

Posttraumatic Stress Disorder, Sleep, and Breathing

Dr. James Parish, FCCP
Section Editor,
Sleep Strategies

The clinical syndrome now known as posttraumatic stress disorder (PTSD) has a long history. Very similar conditions were called soldier's heart during the American Civil War, shell shock during the First World War, and combat fatigue during World War II. In nonmilitary contexts, the child abuse syndrome, battered woman syndrome, and railroad spine (among survivors of railroad accidents) presumably represent the same sort of reaction to traumatic events. It has been estimated that PTSD will affect 8% to 9% of the US population at some point in life. This condition may be manifest in a wide variety of victims of traumatic events, including children, as well as men and women of all ages. Survivors of critical illnesses may be at risk for manifestations of PTSD. PTSD is highly prevalent in veterans of the war in Vietnam, the Persian Gulf War, and recent military actions in Iraq and Afghanistan.

Clinical Manifestations: Criteria for Diagnosis

The term "posttraumatic stress disorder" emerged during the 1970s and was defined in the *Diagnostic and Statistical Manual of Mental Disorders-III* (American Psychiatric Association; 1981); it has remained in subsequent revisions in the nosology. Current diagnostic criteria require that symptoms in three clusters including intrusive recollection of events, avoidance/emotional numbing phenomena, and hyperarousal, be present following life-threatening exposures for more than 1 month and result in functional consequences. These criteria have defined unique features of PTSD, but the range of symptoms experienced by these patients is much broader, albeit nonspecific. Symptoms include vivid and intrusive memories, flashbacks, and intense emotional and physical reactions to reminders of the events. At the same time, it is often difficult to remember specific aspects of the events, and reminders can occur unpredictably. PTSD sufferers may lose interest in social and family life, feel emotionally detached, and have a sense of limited future happiness or success. These individuals are often irritable and subject to sudden outbursts of anger, hypervigilance, and difficulty concentrating. They may have feelings of guilt, self-blame, shame, mistrust, and betrayal. They typically feel depressed, hopeless, and alienated. Substance abuse and suicidal ideation and action are all too common.

The neuroendocrine, neurochemical, neuroanatomic, and genetic basis for development and expression of PTSD remain subject to much controversy. Clinical polysomnography may be insensitive to the neurobiological disease responsible for this condition. There is an urgent need for further investigations using more sophisticated technology. Treatment with a range of pharmacologic agents and behavioral techniques has been shown to be effective, but many therapeutic challenges remain. Sleep disturbances are very prominent in the morbidity of PTSD.

PTSD and Insomnia

The prevalence of insomnia is related to the nature of the traumatic exposure. As many as 70% to 91% of patients with PTSD report difficulty falling asleep or staying asleep. Many studies suggest that insomnia is frequently predictive of development of psychiatric and medical problems, as well as substance abuse.

PTSD and Nightmare Disorder

Repetitive dreaming with recall of traumatic events is considered to be part of the cluster of intrusive recollections. Disturbances in REM sleep mechanism are often cited as a hallmark of PTSD. These patients may "act out" their dreams, often violently, in a manner difficult to distinguish clinically from so-called REM sleep behavior disorder. This latter condition is characterized by dysfunction in REM-induced atonia and is often associated with subsequent development of degenerative neurologic disorders. Much of the literature related to management of nightmare disorder is based on PTSD-related nightmares; 19% to 71% of patients report nightmares, depending on the severity of PTSD and their exposure to physical aggression. An evidence-based review found that image rehearsal therapy could be recommended for treatment of nightmare disorder. In addition, treatment with adrenergic blocking agents, such as prazosin, has been shown to improve PTSD-related nightmares (Aurora et al. *J Clin Sleep Med*. 2010;6[4]:389).

PTSD and Periodic Limb Movements

There are limited data that suggest a high prevalence of periodic limb movements during sleep in patients with PTSD. It has been suggested that these movements contribute to awakenings, insomnia, and daytime sleepiness. Unfortunately, these studies have not included adequate control groups. Furthermore, standards for diagnosis of clinically significant limb movements of sleep have become more rigorous, particularly with regard to the presence of restless legs symptoms. It may be that leg movements are a reflection of the lower threshold of arousal. Additional investigations in this area are needed.

PTSD and Sleep Apnea

A background of hyperarousability in patients with PTSD creates instability of sleep continuity. This instability probably contributes to the development of both obstructive sleep apnea (OSA) and central sleep apnea. In a recent study of active duty servicemen, Dodson et al (*Chest*. 2010;138[4]:616A) found that 73% of randomly selected patients with PTSD demonstrated OSA on standard polysomnography. The mean age of these patients was 34 years. Many complained of daytime sleepiness, with a mean Epworth sleepiness score of 14, and tended to be overweight, with a mean BMI of 29 kg/m^2. At the other end of the age spectrum, Yesavage and colleagues (Sleep-disordered breathing in Vietnam veterans with posttraumatic stress disorder [published online ahead of print June 2010] *Am J Geriat Psychiatry*) studied 105 Vietnam veterans with PTSD using unattended sleep studies and found that 69% had an apnea-hypopnea index greater than 10 events/h.

Poor Tolerance of CPAP for Sleep-Disordered Breathing

Some investigators have suggested that treatment of sleep-disordered breathing with continuous positive airway pressure (CPAP) may be helpful in the management of PTSD-related insomnia (Krakow et al. *J Trauma Stress*. 2001; 14[4]:647). More recent studies demonstrate that CPAP therapy may be very difficult for these patients. El-Soth and colleagues (*Sleep*. 2010;*33*[11]:1435) investigated response to CPAP in a population of 148 veterans with PTSD and OSA with control subjects matched for age, gender, BMI, and OSA severity. They found that the patients with PTSD were much less able to successfully utilize CPAP over a relatively short-term interval. Adherence was 41% compared with 70% in the control group. Of note, Vietnam veterans are particularly likely to develop problematic sleep-disordered breathing because of the cumulative effects of obesity, smoking, substance abuse, and the common development of metabolic syndrome. In addition, these veterans are approaching the age of onset of neurodegenerative disease that may also involve dream-enacting behavior as a feature of REM sleep behavior.

The pathophysiologic basis for the confluence of PTSD and sleep apnea syndrome is far from clear. It is possible that there is simply a coexistence of two rather common conditions. Nevertheless, this coincidence creates management difficulties that one suspects will be a challenge for the foreseeable future, particularly if it is unrecognized.

Kenneth R. Casey, MD, MPH, FCCP
Chair, ACCP Sleep NetWork
Professor of Medicine, University of Cincinnati College of Medicine
Chief, Sleep Medicine Services
Cincinnati Veterans Affairs Medical Center
Cincinnati, OH

PCCSU Lessons for March

▶ **Fixed Airflow Limitation in Asthma**
By Dr. E. Rand Sutherland, FCCP
▶ **Biological Therapy for Asthma**
By Dr. Sheharyar R. Durerani; and Dr. William W. Busse

PCCSU
Pulmonary, Critical Care, Sleep Update

This Month in *CHEST*: Editor's Picks

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

▶ **International Classification of Diseases Coding Changes Lead to Profound Declines in Reported Idiopathic Pulmonary Arterial Hypertension Mortality and Hospitalizations: Implications for Database Studies.** *By Dr. J. Link et al.*
▶ **Survival Following Lobectomy and Limited Resection for the Treatment of Stage I Non-small Cell Lung Cancer Less Than or Equal to 1 cm in Size: A Review of SEER Data.** *By Dr. M. Kates et al.*
▶ ***Reported Pneumonia in Patients With COPD: Findings From the INSPIRE Study.*** *By Dr. P. M. A. Calverley et al.*
▶ **Ventilator-Associated Tracheobronchitis in a Mixed Surgical and Medical ICU Population.** *By Dr. J. Dallas et al.*

New! Listen to a podcast discussion on this article at http://chestjournal.chestpubs.org

MEDICAL ETHICS

▶ **A Brief Historical and Theoretical Perspective on Patient Autonomy and Medical Decision Making: Part I. The Beneficence Model.** *By J. F. Will, JD.*

First iPad/iPhone Diagnostic Imaging App Cleared for Use

BY ROBERT FINN
Elsevier Global Medical News

The Food and Drug Administration on Feb. 4 gave its first clearance to an application that will allow physicians to review radiology images on Apple's iPad and iPhone in the absence of a standard workstation.

The FDA cleared the app, named Mobile MIM, for viewing images and making diagnoses using computed tomography, magnetic resonance imaging, and nuclear medicine technology such as positron emission tomography. The agency cautioned that it is not intended to replace standard workstations, and should only be used when one is not available.

©MIM Software Inc.

The FDA has cleared a mobile app for viewing radiology images on an iPad or iPhone.

The app can measure distance on the image as well as image intensity; it can also display measurement lines, regions of interest, and annotations.

The FDA noted that the luminance displayed by a mobile device can vary greatly, even among identical models. The image's luminance also can vary based on ambient lighting. The app includes an interactive contrast test that will allow a user to determine whether he or she can properly distinguish subtle differences in contrast.

The Mobile MIM app was created by Cleveland-based MIM Software Inc. The company said on its Web site Mobile MIM should be available in Apple's App Store the week of Feb. 7. ■

'Know the Label' Program Underway

The Doctors Company and the PDR Network have launched a national campaign to help "educate physicians and improve their knowledge of ever-changing FDA-approved medication labeling."

The "Know the Label" program will allow physicians to earn free continuing medical education credit for reading full Food and Drug Administration–approved medication labeling online at www.PDR.net.

About one-third of medical malpractice cases include some "drug-related aspects of the complaint," and "in those cases the then-current FDA-approved drug labeling is most often the standard to which physicians or other prescribers are held by the courts," according to a statement published on www.PDR.net.

Last year, more than one-quarter of drugs had "a material labeling change," the statement said.

For more information about the program, go to www.pdrnetwork.com or www.thedoctors.com. ■

CLASSIFIEDS

Also available at www.imngmedjobs.com

PROFESSIONAL OPPORTUNITIES

2011 CLASSIFIEDS

Chest Physician Rates
4 Column Classified Ads
From 1" to 12"
Sizes from 1/48th of a page to a full page

For Deadlines and More Information Contact:
Rhonda Beamer
Walchi Tauber Group, Inc.
2225 Old Emmorton Road, Suite 201
Bel Air, MD 21015
443-512-8899 Ext 106
FAX: 443-512-8909
Email: rhonda.beamer@wt-group.com

Metro Alabama

An excellent healthcare system needs a board certified or board eligible Pulmonary physician. Join a well established group that recognizes and values your ability and contribution. Take your career to the next level with full hospital support, referrals, onsite office, and a call schedule that provides for living. The area offers excellent schools, recreational activities, and is one of the fastest growing areas in the state. Easy drive to the Smoky Mountains or Gulf beaches. Competitive salary, benefits and possible student loan assistance. For more information, please send CV to medplanjj@aol.com or via fax to 205-870-7061.

Pulmonary/ Critical Care

Exceptional opportunity to join a well established, private group including two pulmonologists, three hospitalists, two internal medicine physicians and several allied health professionals. Call would be 1:3. Group is offering a competitive salary and benefit package with early partnership track. The group's new medical office building is located adjacent to the hospital. Upper Valley Medical Center (UVMC) is a thriving state-of-the-art hospital located on a 130 acre campus conveniently located on I-75 minutes north of Dayton and within an hour's drive to Columbus and Cincinnati. Enjoy practicing at ***one*** hospital offering behavioral health services, dialysis center, long term care facilities, a four bed sleep lab, a Cancer Care Center, and much more! UVMC is affiliated with Premier Health Partners, a comprehensive health system serving southwest Ohio. Area communities offer excellent public and private schools, numerous parks, golf courses, two country clubs, cultural centers, indoor ice arena, nature preserves, and a vast array of housing options.

For information contact: **Wendy Castaldo, Director of Medical Staff Development, Upper Valley Medical Center, 1-800-772-3627, FAX: 937-440-8549, wcastaldo@uvmc.com. (J-1 Visa waiver not available)**

Pulmonology and Critical Care Medicine

Forbes and Fortune Small Business Magazine rank Billings, Montana - the Best! Practice medicine in a city ranked as one of the **Best Small Places for Business and Careers** (*Forbes*, 2009) and the **Best Small City in which to start a business** (*Fortune Small Business Magazine*, November 2009). St. Vincent Healthcare in Billings, Montana seeks a well-trained, compassionate physician for **Pulmonology and Critical Care Medicine**

- Great practice with maximum flexibility that focuses on quality lifestyle
- Full time or part time position available
- ICU service call: 1:4
- Outpatient Pulmonology clinic: low overhead practice
- Hospitalist program available
- Pediatric Intensive Care Unit staffed 24/7 with Board Certified Pediatric Intensivists
- SVH is staffed for 250 beds
- Regional destination hospital: serves a four-state area and more than 900,000 people each year
- AASM accredited sleep center; Level II Trauma Center; HELP Helicopter and Fixed Wing air transport program with specialty transport teams
- SVH invests in the latest technology
- SVH is ranked Best for Heart Attack Care and #15 for Quality in the nation
- Thriving medical community in a family-oriented suburban location
- Excellent School System
- Abundant recreational activities year round – hiking, skiing, fishing, biking and camping
- Excellent Benefits and Competitive Salary Structure, based on MGMA
- Sign-on Incentives, Moving Allowances, and CME reimbursement. Will consider loan forgiveness.

Contact: Colleen Martin at
Colleen.Martin@svh-mt.org
or 406-237-4003

Metro South Carolina

Hospital employed joining well established nine physician Pulmonary/CC group in desirable Blue Ridge Metro area two hours to Atlanta and Charlotte associated with a growing 450 bed hospital system. 1-10 call. Excellent negotiable salary, bonus and benefits. DONOHUE AND ASSOCIATES
800-831-5475 F: 314-984-8246
E/M: donohueandassoc@aol.com

Moving?

Look to Classified Notices for practices available in your area.

Disclaimer

Chest Physician assumes the statements made in classified advertisements are accurate, but cannot investigate the statements and assumes no responsibility or liability concerning their content. The Publisher reserves the right to decline, withdraw, or edit advertisements. Every effort will be made to avoid mistakes, but responsibility cannot be accepted for clerical or printer errors.

Growth in Medical Spending Lowest in 50 Years

BY ALICIA AULT
Elsevier Global Medical News

Health care spending grew at its slowest rate in 50 years in 2009, as the recession caused Americans, especially those with lower incomes and less insurance coverage, to cut back on their use of physician, hospital, and other health services, according to a report by federal analysts.

The data indicated that Americans reduced their physician office visits in 2009.

The overall 4% rate of health spending growth followed an increase of 4.7% in 2008. In 2009, the nation's total health tab was $2.5 trillion, or $8,086 per person, according to the annual analysis of a federal data set called the National Health Expenditure Accounts by economists and statisticians at the Centers for Medicare and Medicaid Services (CMS).

The analysts found that even with a low rate of health care spending growth, health care spending increased as a share of the nation's gross domestic product. Health care costs accounted for 17.6% of the GDP, up a record 1% from the previous year.

EVEN WITH A LOW RATE OF HEALTH CARE SPENDING GROWTH, HEALTH CARE SPENDING INCREASED AS A SHARE OF THE NATION'S GDP.

The recession depressed the GDP, and thus allowed health care to gobble up a larger share, said the federal analysts at a press briefing announcing their findings, which were published in the journal Health Affairs (2011;30:11-22).

The economists and statisticians painted a picture of a nation stunned by job loss and declining incomes. In the past, there has been a lag between a recession and any impact on health care costs, largely because it has been thought that people will always need health care, Anne Martin, an economist at the CMS Office of the Actuary, said.

But in 2009, the impact was almost immediate, according to Ms. Martin.

Of the nation's health care spending, 71% was covered by insurance from private or public payers, according to the report. Medicare spending remained steady from 2008 to 2009, but there was a large reduction in spending by private insurers. The government analysts said that this was due in part to a reduction in private coverage. They estimated that private insurance enrollment declined by 6.3 million people (3.2%).

Medicaid, on the other hand, saw its rate of spending grow by 4%, in part offsetting the slowdown by other payers, Ms. Martin said. More children and working-age adults enrolled in Medicaid as the economy continued to flatten, she said, and also because of provisions of the stimulus bill, or American Recovery and Reinvestment Act. There was a 7.4% increase in enrollment in 2009, compared with a 3% increase in 2008. The federal government bore most of the burden for the spending increase, she said.

Americans also vastly curbed their out-of-pocket spending on health care – another reflection of the poorly performing economy, the federal analysts noted.

Hospital care continues to be the largest segment of health care spending. At $760 billion, it accounted for at least a third of the nation's health bill. The growth rate in hospital spending for private insurers was only 3% in 2009, down from 6% in 2008. Medicaid's spending growth accelerated from 3% to 10%, in part because enrollees used emergency departments for primary care, said the analysts.

Physician spending was the second-biggest category, at $505 billion in 2009. The 4% increase from 2008 was the slowest rate of growth since 1996 – partly a result of fewer Americans going to see the doctor. The analysts cited data showing that 36% of Americans said they had fewer health professional visits in 2009.

Instead, they might have gone to outpatient or retail clinics, according to the report. Spending for "clinical services," which is included in the physician services category, grew at double the rate of physician services. ■

TYGACIL is in the 2009 IDSA/SIS guidelines for cIAI and the 2009 SIS guidelines for cSSSI.[1,2]

Expanded broad-spectrum coverage[3]* is on your side

***TYGACIL does not cover *Pseudomonas aeruginosa*.**

TYGACIL is indicated for the treatment of adults with:

- **Complicated skin and skin structure infections** caused by *Escherichia coli, Enterococcus faecalis* (vancomycin-susceptible isolates), *Staphylococcus aureus* (methicillin-susceptible and -resistant isolates), *Streptococcus agalactiae*, *Streptococcus anginosus* grp. (includes *S. anginosus, S. intermedius*, and *S. constellatus*), *Streptococcus pyogenes*, *Enterobacter cloacae*, *Klebsiella pneumoniae*, and *Bacteroides fragilis*
- **Complicated intra-abdominal infections** caused by *Citrobacter freundii*, *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Enterococcus faecalis* (vancomycin-susceptible isolates), *Staphylococcus aureus* (methicillin-susceptible and -resistant isolates), *Streptococcus anginosus* grp. (includes *S. anginosus*, *S. intermedius*, and *S. constellatus*), *Bacteroides fragilis*, *Bacteroides thetaiotaomicron*, *Bacteroides uniformis*, *Bacteroides vulgatus*, *Clostridium perfringens*, and *Peptostreptococcus micros*
- **Community-acquired bacterial pneumonia** caused by *Streptococcus pneumoniae* (penicillin-susceptible isolates), including cases with concurrent bacteremia, *Haemophilus influenzae* (beta-lactamase negative isolates), and *Legionella pneumophila*

Important Safety Information

- TYGACIL is contraindicated in patients with known hypersensitivity to tigecycline
- Anaphylaxis/anaphylactoid reactions have been reported with nearly all antibacterial agents, including tigecycline, and may be life-threatening. TYGACIL should be administered with caution in patients with known hypersensitivity to tetracycline-class antibiotics
- Isolated cases of significant hepatic dysfunction and hepatic failure have been reported in patients being treated with tigecycline. Some of these patients were receiving multiple concomitant medications. Patients who develop abnormal liver function tests during tigecycline therapy should be monitored for evidence of worsening hepatic function. Adverse events may occur after the drug has been discontinued
- The safety and efficacy of TYGACIL in patients with hospital-acquired pneumonia have not been established
- **An increase in all-cause mortality has been observed across phase 3 and 4 clinical studies in TYGACIL-treated patients versus comparator-treated patients. The cause of this increase has not been established. This increase in all-cause mortality should be considered when selecting among treatment options**
- **TYGACIL may cause fetal harm when administered to a pregnant woman**
- **The use of TYGACIL during tooth development may cause permanent discoloration of the teeth.** TYGACIL should not be used during tooth development unless other drugs are not likely to be effective or are contraindicated
- Acute pancreatitis, including fatal cases, has occurred in association with tigecycline treatment. Consideration should be given to the cessation of the treatment with tigecycline in cases suspected of having developed pancreatitis
- *Clostridium difficile*-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including TYGACIL, and may range in severity from mild diarrhea to fatal colitis
- Monotherapy should be used with caution in patients with clinically apparent intestinal perforation
- TYGACIL is structurally similar to tetracycline-class antibiotics and may have similar adverse effects. Such effects may include: photosensitivity, pseudotumor cerebri, and anti-anabolic action (which has led to increased BUN, azotemia, acidosis, and hyperphosphatemia). As with tetracyclines, pancreatitis has been reported with the use of TYGACIL
- To reduce the development of drug-resistant bacteria and maintain the effectiveness of TYGACIL and other antibacterial drugs, TYGACIL should be used only to treat infections proven or strongly suspected to be caused by susceptible bacteria. As with other antibacterial drugs, use of TYGACIL may result in overgrowth of non-susceptible organisms, including fungi
- The most common adverse reactions (incidence >5%) are nausea, vomiting, diarrhea, abdominal pain, headache, and increased SGPT
- Prothrombin time or other suitable anticoagulant test should be monitored if TYGACIL is administered with warfarin
- Concurrent use of antibacterial drugs with oral contraceptives may render oral contraceptives less effective
- The safety and effectiveness of TYGACIL in patients below age 18 and lactating women have not been established

Please see brief summary of Prescribing Information on adjacent page.

References: 1. Solomkin JS, Mazuski JE, Bradley JS, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. *Clin Infect Dis.* 2010;50:133-164. **2.** May AK, Stafford RE, Bulger EM, et al. Treatment of complicated skin and soft tissue infections. *Surg Infect.* 2009;10:467-499. **3.** TYGACIL® (tigecycline) Prescribing Information, Wyeth Pharmaceuticals Inc.

Pfizer

Tygacil® tigecycline IV

Expanded broad-spectrum coverage