Fighting Tuberculosis in Siberia

BY HEIDI SPLETER
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.

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 “bronchoalveolar carcinoma.”

Rescue Combo Enough in Mild Asthma

BY ELIZABETH MECHCA
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...

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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, 268 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 (beclomethasone group).
- Placebo twice daily, with beclomethasone plus albuterol as 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. 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)62131-6]). He noted that the British Thoracic Society and NHBLI 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.
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 ritabutin, 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 prompt 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 deformations 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%).
Rule Identifies Newborns at High Risk of RSV

BY ELIZABETH MECHCA
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 outliers 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 sibs, 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 (Pediatics 2011;127:35-41). Using statistical analyses of the association between these predictors and the presence or absence of RSV LRTI, Dr. Michael Houwen of Wilhelminal 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 0 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 risk and low risk of RSV LRTI and subsequently can target preventive and monitoring strategies to children at high risk,”

ADVERSE EVENTS

BY ELIZABETH MECHCA
Elsevier Global Medical News

In a pilot study recommended as an adverse event difference from placebo, the incidence of headache was 22% in those taking sildenafil versus 17% in those not taking sildenafil. The incidence of nausea was 4% in those taking sildenafil versus 2% in those not taking sildenafil. No placebo patients had treatment-emergent visual loss.

Table 1. REVATIO All Causality Adverse Events in 3% of Patients and More Frequent (≥1%) Than Placebo

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Placebo (n=70)</th>
<th>REVATIO 20 mg TID (n=69)</th>
<th>Placebo-Subtracted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epistaxis</td>
<td>1</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>3</td>
<td>15</td>
<td>12</td>
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<tr>
<td>Dysuria</td>
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<td>13</td>
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<td>Myalgia</td>
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<td>Gastritis</td>
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<td>Rash</td>
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<tr>
<td>Headache</td>
<td>9</td>
<td>17</td>
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No fatal study-related adverse events were reported.

References

Homozygous and mosaic carriers of the PRKARIA allele for a rare form of congenital cataract should be identified and monitored because there is potential for a high rate of retinal pigment epithelial changes and subretinal fluid accumulation.

Table 2. Carbamazepine Metabolism

<table>
<thead>
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<tr>
<td>Carbamazepine</td>
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<tr>
<td>Phenytoin</td>
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Clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. Safety data were obtained from the 12-week, placebo-controlled clinical study and an open-label, 27-week extension study in patients with pulmonary arterial hypertension. In the placebo-controlled trial in pulmonary arterial hypertension, the adverse drug reactions occurring in ≥5% of REVATIO-treated patients at the recommended dose of 20 mg TID were 3% and was the same for the placebo group.

In the placebo-controlled trial in pulmonary arterial hypertension, the adverse drug reactions occurring in ≥5% of REVATIO-treated patients at the recommended dose of 20 mg TID and even more frequent in REVATIO patients than placebo patients, are shown in Table 1.

Table 1. REVATIO All Causality Adverse Events in 3% of Patients and More Frequent (≥1%) Than Placebo

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No fatal study-related adverse events were reported.
he and his coauthors concluded. They noted that to date, clinical prediction models have primarily 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 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 drops and throat swabs when their 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 under 2.5 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 weighing 4.2 kg at birth (1 point), and whose parents were 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 useful 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 to identify those at highest risk of RSV infection, most would come up with daily 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.’

Although he said 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.

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

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.

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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 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.”

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, 2006 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 26-151. 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 4.95 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.

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 wash 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.

Major Finding: Only use of mechanical ventilation and vasopressors were significantly associated with the development of pressure ulcers in the ICU (odds ratios of 4.95 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.

“Dr. Jeremy Pamplin, 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 lungs 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.

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.”

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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.”

Using 1990 census and hospital administration data, Dr. 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 ($P = 3$), 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.

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, 23 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 not need to be validated at other institutions and with additional studies.”

Dr. Fabian acknowledged that by design the study lacked clinical outcomes data and 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.

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

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 — harvested lungs, livers, and kidneys — performed just as well as lungs from cases who had not been protected from any form of lung injury.

Researchers recorded the number of lungs that were suitable for transplantation when organ harvesting was ongoing after any ventilator disconnection was done with a ventilatory strategy that could serve as an adjunct to the gold standard for comparison.

“Worse than a lung that’s acceptable, I want a lung that’s perfect,” said Dr. Mark S. Roberts in an accompanying editorial (JAMA 2010;304:2643-4).

“This strategy 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 techniques, 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’Università Programma di Ricerca di Interesse Nazionale. No financial conflicts of interest were reported by the investigators.
When performing a lung cancer resection, thoracic surgeons performed lymphadenectomy significantly more often than did general surgeons and cardiac surgeons, making lymph node dissection the major determinant of stage, prognosis, and need for further therapy,” Dr. Michelle Ellis said at the annual meeting of the Society of Thoracic Surgeons.

“Furthermore, patients who have their lung resection performed by a board-certified cardiothoracic surgeon specialize 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 co-investigators reviewed 222,233 primary lung cancer cases from the Nationwide Inpatient Sample from 2000-2007 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 anatomic 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%, 4.4%, 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 also performed lymphadenectomy significantly more often (116% vs. 10% by cardiac surgeons and 113% 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. “We have 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 assessed.
Cardiothoracic Surgery

Rib Fixation in Flail Chest May Shorten Ventilation

By Patrice Wendling

Elverser Global Medical News

NAPLES, Fla. – Patients who underwent surgical rib fixation for flail chest spent on average 10 fewer days on mechanical ventilation than 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, 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 sepsis 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 mechanical ventilator is the last resort when the patient fails to wean from the ventilator, Doben pointed out that major trauma centers see roughly two flail chest cases per year. 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 PaO2/FIO2 (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, and is on the speakers bureau for, Acute Innovations, as well as a consultant to, and is on the speaker’s bureau for, Acute Innovations, a maker of thoracic surgery devices.

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 (FEV1), spirometric values. The physician can then evaluate remodeling in a more relative sense by analyzing how actively it compares with three additional airway obstruction components—acute asthmatic inflammation, airway hyperreactivity, and mucus formation.

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 collagen. Inflamed airway smooth muscle mass has been associated with a decline in FEV1 (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 lead[s] 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.

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.
MARCH 2011 • CHEST PHYSICIAN

In HIV-TB Coinfection, Treat HIV Soon After Tuberculosis

BY MITCHEL L. ZOLER
Elsavir Global Medical News

VIENNA — A quick start to anti-retroviral 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 thera- py] 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 Con- ference. Starting HAART within the first 2 weeks after starting TB treatment instead of waiting as long as 2 months "could potentially reduce overall mortality in 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 Anti-retrovirals (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 fol- lowed by antiretroviral therapy within 8 weeks. CAMELIA was sponsored by the French National AIDS research agency and U.S. National Institute of Health.

The study also focused on highly immunosuppressed pa- tients, enrolling only those with CD4 cell counts less than 200/mL, that is, 6% of adults. CD4 cell count of the 661 enrolled patients was 25/mL.

"The first diagnosis of HIV often occurs when patients pre- sent with TB, often with very low CD4 counts," commented Dr. Anton Pozniak, director of AIDS services at Chelsea and Westminster Hospital in Lon- don. "Half of our pa- tients with HIV and TB and in most UK units who present with TB are pretty convincing evi- dence; it’s fantastic re- sults," Dr. Pozniak said in an interview. But he noted that Dr. Blanc, that starting a TB and HIV regimen nearly si- multaneously was challenging. You need to give a whole lot of tablets all at once. The researchers said it’s okay to wait for 2 weeks, but 1 thing 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 with- in 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 antiretrovirals. Pozniak said that starting a TB and HIV regimen nearly simultaneously was challenging. You need to give a whole lot of tablets all at once. But we usually start within 2-3 days. The researchers said it’s okay to wait for 2 weeks, but 1 thing 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.”

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- 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.

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

FDA Approves PDE-4 Inhibitor for COPD Flares

**By Michele G. Sullivan**

Elsivier Global Medical News

**R**oflumilast was approved by the Food and Drug Administration on 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-mg 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 13% 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 suicide 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 microbiological colonies surrounded by a layer of protective glyocalyx. 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 how to reduce 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 2 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 (Chew 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, affiliation 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.

Chronic Cough Often Caused by Multiple Factors

BY ROD FRANKLIN
Elsevier Global Medical News

KEYSTONE, Colo. – Physicians would do well to add habituation, neurological triggers, and laryngopharyngeal reflex 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 refractory cough include asthma, upper airway cough syndrome (postnasal drip), and gastroesophageal reflux disease. But looking beyond these common culprits and analyzing combining 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 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 reflex (LPR), he said. Physicians using both classic pH probes or impedance probes often interchange their diagnoses by missing clues, in large part because LPR is not specific in its presentation. The role LPR plays can be obscured by the presence of supraglottic edema or erythema, glottic abnormalities, epiglottic malformations, and lingual tonsillar abnormalities. They may have gastroesophageal reflux disease issues. Moreover, the coexistence of epiphelial 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 not prominent 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 obstructive pulmonary disease. 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 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, C peptidergic, 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 full-thickness and 30-minute clinical visits 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 obstructive pulmonary disease. 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.

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 $8,100. In the study, 20% was lost (38%) 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 16% in the Southeast. In all, 37% of patients had private insurance, 57% were covered by Medicare, and 6% had some other payer.

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 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 unspecified NSCLC who test positive for EGFR mutation are more likely to respond to treatment with tyrosine kinase inhibitors than are patients without mutation.

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.

“That 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 normal cytology may be 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 adenocarcinoma with some lepidic component. This conception 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 molecular diseases; the patients 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.
FROM THE DESK OF THE PRACTICE MANAGEMENT COMMITTEE

The Transition to ICD-10-CM

BY ROBERT DEMARCO, MD, FCCP, CHAIR; AND DONNA KNAPP BYBEE, FACEP, 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 physici

ans 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.

The 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 not been updated to be consistent with current clinical practices. Injuries will be grouped by anatomic 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.
News from the College

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 J. 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 to 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 $30,000 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.

Young 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 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.

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Don’t Miss These Sessions

- Ultrasonography: Fundamentals in Critical Care
  - April 15-17
  - Baltimore, MD
- Difficult Airway Management
  - July 22-24
  - Northbrook, IL
- Basic and Advanced Bronchoscopy Skills
  - August 5-7
  - Chicago, IL
- Focused Pleural and Vascular Ultrasound
  - September 22-23
  - Chicago, IL
- Critical Care Echocardiography
  - September 24-25
  - Chicago, IL
Third-Hand Smoke, Resuscitation, Disparities, Ethics

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 modific-

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 press 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 (DeReno et al. HEC Forum. 2006;18[4]:319; DeReno et al. Carb Q Healthc Ethics. 2006;15[2]:207; Empire 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 decrease 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 vari-

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 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 extra-

CHEST 2011 Opportunities

Call for Abstracts
Submit an abstract of your original investigative work for presentation. Submission is free.
- Gain international exposure by presenting to an audience of pulmonary, critical care, and sleep medicine specialists
- Compete for The CHEST Foundation investigative awards.

www.accpmeeting.org
Submission deadline: May 4

Call for Case Reports
Submit case reports for presentation during special sessions. Three types of case reports will be considered:
- Affiliate Case Reports
- Global Case Reports
- Clinical Case Puzzlers

www.accpmeeting.org
Submission deadline: May 4

The CHEST Foundation 2011 Awards Program
More Than $500,000 to Be Awarded
The tradition of recognizing and rewarding volunteer service, leadership, and clinical research continues in 2011. A variety of awards is available. See if you are eligible.

OneBreath.org
Application deadline: May 4
What's in a Name? Expansion and Diversification

BY DAVID D. GUTTERMAN, MD, FCCP

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 practitioners, physician assistants, pharmacists, and respiratory 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 brought down the horizon of care-unlimited 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 Chest Physicians Conference 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 all 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 practitioners 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 a 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

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: G6642 (the eligible professional works in a rural area without sufficient high-speed Internet access), G6643 (the eligible professional practices in an area without sufficient available pharmacies for electronic prescribing), or G6644 (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.

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Let CHEST keep you updated any way that is most convenient for you. Get cutting-edge, clinically focused content delivered in an array of formats tailored to your day-to-day needs.
Posttraumatic Stress Disorder, Sleep, and Breathing

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 veterans 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/m². At the other end of the age spectrum, Yasavaghe and colleagues (Sleep-disordered breathing in Vietnam veterans with posttraumatic stress disorder [published online ahead of print June 2010] Am J Geriatr Psychiatry) studied 105 Vietnam veterans with PTSD using unattended sleep studies and found that 69% had an apnea 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 (Kracow 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 problem-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 pathophysiological 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, FACC
Chair, ACCP Sleep Network
Professor of Medicine, University of Cincinnati College of Medicine
Chief, Sleep Medicine Services
Cincinnati Veterans Affairs Medical Center
Cincinnati, OH

This Month in CHEST: Editor’s Picks

- 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.

Fixed Airflow Limitation in Asthma
By Dr. E. Rand Sutherland, FCCP

Biological Therapy for Asthma
By Dr. Sheharyar R. Durrani; and Dr. William W. Bause
First iPad/iPhone Diagnostic Imaging App Cleared for Use

BY ROBERT FINN
Elsevier Global Medical News

The FDA cleared the app, named Mobile MIM, for viewing 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 radiology images on Apple’s iPad and iPhone in the absence of a standard workstation. The agency cautioned that it is not intended to replace standard workstations, and should only be used when one is not available. The app can measure distance on the image as well as image intensity; it can also display measurement lines, regions of interest, and annotations.

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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 FDA has cleared a mobile app for viewing radiology images on an iPad or iPhone. The FDA cleared the app, named Mobile MIM, for viewing radiology images on Apple’s iPad and iPhone in the absence of a standard workstation. The agency cautioned that it is not intended to replace standard workstations, and should only be used when one is not available. The app can measure distance on the image as well as image intensity; it can also display measurement lines, regions of interest, and annotations.

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**PRACTICE TRENDS**

**Growth in Medical Spending Lowest in 50 Years**

*By Alicia Ault*  
Eisegor Global Medical News

**March 2011**  
*Chest Physician*

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**Medical spending** continued on the decline in 2010 for the first time in at least a half-century. According to the most recent data from the Centers for Medicare and Medicaid Services (CMS), national medical spending increased by 3.9% in 2010 (compared to 7.3% in 2009) — the smallest increase from one year to the next since medical spending data has been compiled since 1960. The reasoning behind the decline in medical spending is multifaceted and was caused, in part, by a reduction in private health insurance enrollment. In 2009, the nation’s total health tab was $2.5 trillion, or $8,86 per person, according to the annual analysis of a federal data set called the National Health Accounting Expenditures 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.

The recession depressed the GDP and thus allowed health care to gobble up a larger share, said the federal analysts at a press conference held to discuss 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. According to Anne Martin, an economist at the CMS Office of the Actuary, said, “In 2009, the impact was almost immediate, according to Ms. Martin. Of the nation’s health care spending, 71% was paid for by private health 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 off-setting the slowdown by other payers, Ms. Martin said. More children and working-age adults enrolled in Medicaid as the economy went south, she said, and also because of provisions of the stimulus bill, or American Recovery and Reinvestment Act. There was a 7.4% increase in the number of enrollees 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, at $503 billion in 2009. The 4% increase from 2008 was the slowest rate of growth since 1996 — partly a result of fewer Americans going to the doctor. The analysts cited data showing that 36% of Americans 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 other services, category, grew at double the rate of physician services.

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**Tygacil (Tigecycline) Brief Summary**

For further product information and current package insert, please visit www.tygacline.com or call our medical communications department toll-free at 1-800-934-5556.
TYGACIL is indicated for the treatment of adults with:

- **Complicated skin and skin structure infections** caused by *Escherichia coli*, *Enterococcus faecalis* (vancomycin-susceptible isolates), *S. 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), *S. 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.