Alcohol-based hand sanitizers are a key part of a strict approach to overall infection control, said Dr. Robert A. Weinstein.

Hospitals Must Resist The Rise of Superbugs

BY MIRIAM E. TUCKER
Elsevier Global Medical News

WASHINGTON — The only way for a hospital to address the problem of antimicrobial resistance is to adopt a culture of strict overall infection control, Dr. Robert A. Weinstein said at a press briefing sponsored by the National Foundation for Infectious Diseases.

Antimicrobial resistance has increased dramatically in hospitals in recent years and will continue to do so if left unchecked. In intensive care units nationwide, resistance rates in 2003 had increased, compared with 1998-2002, for nearly every antibiotic/bacteria combination looked at, from a rate of 1% for methicillin/coagulase-negative staphylococci to 47% for third-generation cephalosporins/Klebsiella pneumoniae (Am. J. Infect. Control 2004; 32:470-85).

For every infection caused by a resistant organism, hospital length of stay and hospital charges are increased by 1.0- to 1.7-fold and mortality by 1.3- to 5.0-fold, compared with infections caused by susceptible bacteria, translating to a cost differential of $6,000-$10,000. Not surprisingly, the difference in cost is even greater when patients infected with antimicrobial-resistant organisms are compared with patients without infection (Clin. Infect. Dis. 2006; 42[suppl. 2]:S82-9).

Available data suggest that efforts targeting overall infection control should be a priority, Dr. Weinstein said. "In 1999, we did a study and found that if you implement a comprehensive infection control program targeting overall infection control, you can reduce the risk of hospital admission due to ventilator-associated pneumonia by 35% in a multicenter study, researchers reported."

"This is the first intervention demonstrated to reduce ventilator-associated pneumonia incidence that does not require more effort or supervision from clinicians providing bedside care," said Dr. Marin H. Kollef, FCCP, of Washington University, St. Louis, and associates.

However, the reduced rate of pneumonia did not translate into decreased mortality, duration of intubation, duration of ICU stay, or duration of hospitalization, or frequency or severity of the adverse effects of intubation.

"In an editorial comment accompanying this report, Dr. Jean Chastre said that physicians should probably consider using silver-coated endotracheal tubes for "the subset of patients at very high risk of developing early-onset [ventilator-associated] pneumonia, such as neurologically impaired patients or trauma patients. But after controlling for the presence of the device for other patients, particularly those who might need prolonged ventilation, has not yet been clearly shown.

Dr. Kollef and associates compared the silver-coated endotracheal tube with standard tubes in a prospective trial sponsored by the device manufacturer, C.R. Bard Inc. A total of 1,509 patients requiring mechanical ventilation were included, and there were 99 pneumonias in 74 patients treated with silver-coated tubes compared to 150 pneumonias in the control group.

Patient demographics were similar in both groups, with the exception of some differences including a higher percentage of patients who were immunocompetent seniors dur-

Silver-Coated Endotracheal Tubes Cut VAP

BY MARY ANN MOON
Elsevier Global Medical News

Endotracheal tubes coated with silver, which has shown potent broad spectrum antimicrobial activity in vitro, reduced the incidence of ventilator-associated pneumonia by 15% in a multicenter study, researchers reported.

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VITAL SIGNS

Top 10 Reasons for Hospital Admissions for Children

Number of discharges

- Pneumonia 162,000
- Acute bronchitis 140,000
- Asthma 137,700
- Appendicitis 90,700
- Appendicitis 90,700
- Affective disorders 82,500
- Etiologic disorders 73,000
- Etiologic disorders 73,000
- Skin and subcutaneous tissue infections 69,500
- Skin and subcutaneous tissue infections 69,500
- Intestinal infections 67,200
- Intestinal infections 67,200
- Urinary tract infections 53,200
- Urinary tract infections 53,200
- Urinary tract infections 49,400

Note: Based on 2006 data; excludes newborn conditions. Source: Agency for Healthcare Research and Quality
CDC Guidelines Address Resistance

Hospitals • from page 1

Data support the efficacy of both guide- lines. In an analysis of CDC data reported at the 2008 meeting of the Society for Healthcare Epidemiology of America (SHEA) the authors noted that rates of MRSA bloodstream infections among ICU patients decreased from 1997 to 2001 but then declined steadily from 2002 to 2004, resulting in an overall 44.4% reduction in incidence during the period from 1997 to 2004. But such infections from methicillin-resistant S. aureus (MSSA) strains also declined during those 7 years, by 72.4%. Thus, although the proportion of infections caused by MRSA rose relative to susceptible strains, the in- fection rate dropped overall. “The percent isn’t as important as the number,” Dr. Weinstein commented.

Among 103 Michigan ICUs that adopted strategies based on those recommended by the CDC for prevention of intravascular catheter-associated infections, the median rate of such infections per 1,000 catheter- days decreased from 2.7 infections at base- line to 0 at 3 months after implementation of the study intervention, and the mean rate per 1,000 catheter-days dropped from 7.7 at baseline to 1.4 at 16-18 months of follow-up (N. Engl. J. Med. 2006; 355:2725-32).

Attention to the cleanliness of inanimate objects also has been shown to reduce in- fection rates. In a study presented in 2001 at an infectious disease conference, routine cleaning of surfaces in an ICU resulted in a 61% reduction in contamination of hos- pital workers’ hands and gloves with van- comycin-resistant enterococci (VRE).

And in another study for which Dr. Weinstein was a coauthor, routine daily bathing of medical ICU patients with cloths impregnated with chlorhexidine gluconate during November 2005–October 2006 reduced the rates of central venous catheter-associated bloodstream infections, compared with the baseline time period of September 2004–October 2005, from 5.31 to 0.69 per 1,000 catheter- days. Significant reductions were also seen in the rates of positive blood culture (from 10.26 to 5.17 per 1,000 patient-days) and of blood culture contamination (from 6.99 to 4.1 per 1,000 patient-days). In the surgical ICU, the number of positive blood cultures decreased from 10.05 to 6.04 per 1,000 patient-days. Those data were also reported at this year’s SHEA meeting.

Chlorhexidine gluconate eliminates what Dr. Weinstein calls the “focal vec- neer” that is common in ICU patients. “Basically they have stoel organisms all over their bodies. You use antiseptic to clean them. It’s just what your mother and grandmother would have told you.”

A more controversial method for re- ducing hospital rates of MRSA and VRE is the “search and destroy” system, involving active surveillance and isolation of MRSA patients. Widely used in the Netherlands, the system is also now mandated in four states and at all Veterans Affairs hospitals. Hospitals that are required to report infection rates will work to lower them.

But Dr. Weinstein believes there are the advantage of identifying asymptomatic indi- viduals and some studies do suggest it is beneficial, Dr. Weinstein believes there are several drawbacks. For one, nearly all the studies are “quasi-experimental,” while those that have used concurrent controls have been negative, he said, in an interview. In one such negative study he conduct- ed with associates in the Netherlands, sur- veillance cultures performed for 19 medical ICU patients during a 10-week pe- riod showed that 53 (54.8%) were colonized with MSSA and 9 (9.5%) with MRSA. Of those, 62 had been colonized before ad- mission to the hospital (53 with MSSA and 9 with MRSA). The other two appeared to have acquired MSSA in the medical ICU, but genotyping analysis determined that this was not the result of cross-acquisition (Clin. Infect. Dis. 2005;40:405-9).

Surveillance cultures and genotyping of MRSA and MSSA isolates demonstrated the absence of cross-transmission among patients in the MICU, despite ongoing in- troduction of these pathogens. Reporting culture results and isolating colonized pa- tients, as suggested by some guidelines, would have falsely suggested the success of such infection-control policies, the au- thor commented.

Moreover, patients in isolation might re- ceive less care. Dr. Weinstein added during the interview. In another study he con- ducted with his daughter, Dr. Kathryn B. Kirkland, health care workers were half as likely to enter the rooms of patients in con- tact isolation, although they were more likely to wash their hands after caring for these patients than after caring for patients not in isolation (Lancet 1999;354:1177-8).

Focusing solely on antimicrobial resistant organisms will not necessarily affect overall infection rates, particularly in hospitals where resistance rates are not excessively high. The “search and destroy” system “as- sumes one size fits all,” said Dr. Weinstein, adding that he believes that the state laws mandating the system are “ill-advised.”

But he said he supports other types of recent legislation that are aimed at re- ducing the rates of hospital infections and their associated costs. For example, Medi- care’s policy to stop paying for eight health care-acquired infections as part of the Federal Deficit Reduction Act of 2005 be- gins Oct. 1, 2008. Included are intravenous catheter infections, mediastinitis after heart surgery, and catheter-associated uro- nary tract infections.

Medicare perceives these as pre- ventable ‘...Eventually, it will have an im- pact,’” Dr. Weinstein predicted.

Mandated public reporting of hospital infection rates—coupled with payment for “good” performance and penalties for “bad”—will also make a difference, he said. Although Dr. Weinstein is unconvinced that reporting hospitals are neces- sarily safer or that informed patients will obtain safer care, he does think that hos- pitals that are required to report infection rates will work to lower them.

Dr. Weinstein disclosed that he has re- ceived grant funding from the Centers for Disease Control and Prevention and from Sage Products Inc., which manufactures the disposable chlorhexidine-impreg- nated cloths that his group studied.

rates would virtually eliminate the prob- lem of antimicrobial resistance as well. “Resistance will disappear if there are no infections,” said Dr. Weinstein, professor of medicine at Rush University, Chicago.

In 2002, the Centers for Disease Control and Prevention issued two sets of guide- lines to address the issue of antimicrobial resistance in health care settings. One set, on hand hygiene, recommended the use of alcohol-based gel hand sanitizers among health care workers in order to improve compliance, because hand washing is often perceived as burdensome (MMWR 2002;51[RR16]:1-44).

The other CDC guideline, on prevention of intravascular catheter-related infection, advocated five principles: educating and training health care workers who insert and maintain catheters; using maximal ster- ile barrier precautions during central venous catheter insertion; using a 2% chlorhexidine alcohol-based gel hand sanitizers among health care workers in order to improve compliance, because hand washing is often perceived as burdensome (MMWR 2002;51[RR16]:1-44).

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Drug Combo Falls Short in Small Cell Lung Cancer

Irinotecan/cisplatin was no better than etoposide/cisplatin in a large study.

**BY KERRI WACHTER**
*Elsevier Global Medical News*

**CHICAGO**—Treatment with irinotecan and cisplatin was not significantly better than etoposide/cisplatin therapy in a phase III trial that sought to extend progression-free survival, overall survival, and response rates in patients with extensive-stage small cell lung cancer.

Median progression-free survival was 5.3 months for patients on irinotecan/cisplatin, and 1.2 months for those on etoposide/cisplatin (P = .07). Likewise, median overall survival was not much improved at 9.8 months for patients on irinotecan/cisplatin, compared with 9.1 months for those on etoposide/cisplatin (P = .71).

“This large North American trial failed to confirm the previously reported survival benefit with irinotecan/cisplatin in Japanese patients,” Dr. Ronald D. Natale said at the annual meeting of the American Society of Clinical Oncology, where he presented the disappointing findings. Progression-free survival and overall survival benefits had been seen in the Japan Clinical Oncology Group study 9511 (N. Engl. J. Med. 2002;346:85-91).

There are several possible reasons why the study failed to confirm the Japanese results, said Dr. Natale. Differences in tumor genetics may play a role, and the early stopping of JCOG 9511 may have resulted in the detection of a large treatment effect resulting from chance alone.

The trial’s sponsors and collaborators came from the National Cancer Institute, Southwest Oncology Group, North Central Cancer Treatment Group, and Cancer and Leukemia Group B.

Dr. Natale and his coinvestigators randomized 671 patients to receive irinotecan plus cisplatin (336 patients) or etoposide plus cisplatin (335). All were chemotherapy naive.

Patients in the irinotecan arm received 100 mg/m² of etoposide on days 1, 2, and 3, and 80 mg/m² of cisplatin on day 1 of a 3-week cycle. Both groups underwent four cycles.

In all, 324 patients in the irinotecan group and 327 patients in the etoposide group were evaluable for survival; 317 patients in the irinotecan group and 325 patients in the etoposide group were evaluable for toxicity, reported Dr. Natale, a medical oncologist at Cedars-Sinai Medical Center in Los Angeles.

The 1-year progression-free survival was similar between the two groups (7% in the irinotecan/cisplatin arm and 6% in the etoposide/cisplatin arm). Likewise, 1-year overall survival was comparable (41% with irinotecan/cisplatin and 34% with etoposide/cisplatin), said Dr. Natale.

The researchers also conducted exploratory analyses looking at the possible effects on outcome of age, gender, performance status, toxicity, extent of metastatic disease, weight loss, and lactate dehydrogenase. None of these factors predicted a better outcome with irinotecan than with etoposide.

In JCOG 9511, median progression-free survival in JCOG 9511 was 6.1 months for the irinotecan group and 4.8 months for the etoposide group. Median overall survival was 12.8 months for the irinotecan group and 9.4 months for the etoposide group.

As expected, etoposide produced greater hematologic toxicity; with grade 3/4 hematologic events occurring at the following rates with etoposide vs. irinotecan: absolute neutrophil counts (68% vs. 34%), thrombocytopenia (15% vs. less than 4.5%), and anemia (12% vs. less than 6%).

Conversely, some grade 3/4 gastrointestinal toxicities were greater with irinotecan than with etoposide, such as diarrhea (19% vs. 3%) and dehydration (16% vs. 8%).

Overall, grade 3/4 toxicities were seen in 64% of patients who were given etoposide and in 82% of those treated with etoposide.

Treatment-related deaths occurred in 4.6% of patients on etoposide and in 4.1% of those given irinotecan.

Given that ethnic differences are known to affect the metabolism of irinotecan, the researchers also conducted pharmacogenomic correlative studies on DNA collected from 67 patients who were given irinotecan and 75 patients who were treated with etoposide.

None of the genotypes was associated with efficacy outcomes, although associations were seen with toxicities.

The researchers found that grade 3/4 irinotecan-associated diarrhea was associated with the ABC transporter gene B1 (C3435T) T/T with an odd ratio of 3.9 (P = .01). Combined grade 3/4 neutropenia and diarrhea were associated with ABCB1 (C3435T)/T/T (OR, 5.0; P = .03) and UGT1A1 (G-3156A) A/A (OR, 7.6; P = .06).

Dr. Natale reported that he has been a consultant/advisor to Amgen Inc., AstraZeneca Pharmaceuticals LP, Eli Lilly & Co., Genentech Inc., Pharamon Corp., and Poniard Pharmaceuticals Inc., and that he has received honoraria from Eli Lilly and Genentech.

**Lymphocyte Test Identified Patients With Lung Cancer**

**BY NANCY WALSH**
*Elsevier Global Medical News*

**TORONTO**—Gene expression profiling of peripheral blood lymphocytes successfully identified lung cancer patients with an overall accuracy of 87% in a cross-sectional study of 230 subjects.

The new test, which is in the early development stage, had a sensitivity of 85% and a specificity of 87%, Dr. Anil Vachani reported at an international conference of the American Thoracic Society.

‘OUR APPROACH HAS INVOLVED PROFILING OF GENE EXPRESSION IN PERIPHERAL BLOOD MONONUCLEAR CELLS THAT ARE INVOLVED IN TUMOR IMMUNITY.’

The study included 140 subjects with lung cancer and 90 without.

“What we have shown in a preliminary fashion in collaboration with researchers from the Wistar Institute is that with a 24-gene signature we had 87% accuracy for distinguishing between cancer and controls,” Dr. Vachani of the University of Pennsylvania, Philadelphia, said in a press conference.

Lung cancer remains a very difficult cancer to diagnose, with many patients having lung nodules detected incidentally on chest x-ray or CT scan. The next step in diagnosis is problematic, as needle biopsy of the chest is difficult and bronchoscopy requires anesthesia and carries risks of bleeding and atelectasis. The nodule is often surgically removed, and a common outcome is that the nodule turns out to be benign and the patient did not have cancer at all, Dr. Vachani said.

Clearly, a blood test that could be used when patients are found to have lung nodules would be useful, and many research groups have worked on this. Most have focused on finding a signature protein, such as prostate-specific antigen, secreted by tumor cells into the bloodstream.

Unfortunately, lung cancer is a much more heterogeneous cancer than some others, and no single protein has been found to identify all types of lung cancer, said Dr. Vachani.

“Instead, our approach has involved profiling of gene expression in peripheral blood mononuclear cells that are involved in tumor immunity,” he said.

The approach involves isolating lymphocytes from peripheral blood and performing global gene expression profiling on all 22,000 genes in the cell. Using advanced statistical algorithms, the researchers identified genes that are differentially expressed between patients and controls. They then went back to see if we can validate whether genes that are differentially expressed can actually predict which patients have cancer and which do not,” he said.

Although the results of his study were good, they need to get better, Dr. Vachani said. "The technology is in early development, and the study population will be expanded. External validation studies need to be done to see if the results from Pennsylvania can be replicated elsewhere, which has been problematic in some gene expression studies,” he said.

The expected role of this test would be as a second test following the identification of lung nodules on imaging studies.

**DATA WATCH**

Top 10 Causes of Death (age-adjusted mortality rate per 100,000 U.S. standard population)

| Disease of the heart | 210.3 |
| Malignant neoplasms | 183.8 |
| Cerebrovascular diseases | 46.6 |
| Chronic lower-respiratory diseases | 43.2 |
| Accidents | 38.1 |
| Diabetes mellitus | 24.5 |
| Alzheimer’s disease | 22.9 |
| Influenza and pneumonia | 20.3 |
| Renal diseases | 14.3 |
| Septicemia | 11.2 |

Source: 2005 preliminary data, Centers for Disease Control and Prevention
STEROID-RESISTANT PATIENTS HAVE BEEN FOUND TO HAVE PERSISTENT AIRWAY ACTIVATION, WITH ELEVATED INTERLEUKINS, DESPITE THE USE OF PREDNISONE.

In an accompanying commentary, Dr. Edward A. Belongia of the Marshfield (Wis.) Clinic Research Foundation, and Dr. David K. Shay of the influenza division, Centers for Disease Control and Prevention, agreed with the need for additional studies about the causes of pneumonia in elderly adults, particularly in highly vaccinated populations (Lancet 2008;372:352-4).

Calling the study by Dr. Jackson and his colleagues "well designed," they added that standard methods of comparing the effectiveness of flu shots in different seasons and in different populations are also needed.

The commentators also suggested that future studies of vaccine effectiveness should include other flu-related acute illnesses besides pneumonia and use sensitive and specific diagnostic tests, such as the polymerase chain reaction, for influenza.

"More studies and research are necessary to understand how well the vaccine prevents serious complications of the flu, such as pneumonia, in older seniors and those with chronic health problems."

"We have also investigated the mechanisms by which resistance develops. We have found that a key element in corticosteroid action is the ability to induce nuclear translocation of the glucocorticoid receptor from the cytoplasm into the nucleus," Dr. Leung said.

The anti-inflammatory effects of those drugs are mediated through the α (rather than the β) isoform of the glucocorticoid receptor, he explained.

Bronchoalveolar lavage samples from patients who have steroid-resistant asthma have been shown to have reduced α-receptor translocation in response to the drugs, as well as overexpression of its endogenous inhibitor, the β receptor.

"The inflammatory milieu in the airways of these patients is driving up the expression of the β receptor," Dr. Leung said.

Microbial superantigens also can induce T-cell resistance to steroids, suggesting a possible role for infection in the development of resistance, he added.

That superantigen-induced resistance can occur via a specific T-cell receptor signaling pathway involving the m1-activated protein kinase and the extracellular signal-regulated kinase, according to the authors of the study.

Previous studies have suggested that the glucocorticoid receptor itself might be a potential therapeutic target in resistant asthma, he noted.

Dr. Leung disclosed that he has no financial relationship with a commercial entity involved in this work.

In a recent study of patients with asthma, overexpression of components of the extracellular signal-regulated kinase and the tumor necrosis factor, despite the use of prednisone.

"The inability to enhance TIMP-1 production contributes to the abnormal MMP/TIMP ratio in steroid resistant patients."

Dr. Jackson noted that the study made it clear that ventriculoperitoneal shunting does not prevent airway remodeling, with structural changes such as angiogenesis, thickening of the basement membrane, and increase in smooth muscle.

In studies of those patients, steroid sensitivity is defined as a greater than 20% improvement in FEV1 (forced expiratory volume in 1 second) from baseline after a week of treatment with oral prednisone given in doses of 40 mg twice a day, whereas steroid resistance is a less than 15% improvement, Dr. Leung explained.

Investigations of patients who are steroid resistant found that they have blunted acute activation, with elevations in interleukin-2, -4, -5, -8, and -13, as well as tumor necrosis factor, despite the use of prednisone.

Those cytokines target different cell types, with IL-2 and IL-4 being capable of inhibiting TIMP-1 production, and IL-5 and IL-8 inducing resistance in neutrophils, and IL-13 inducing resistance in monocytes and macrophages, he said.

Recent studies have shown that steroid-resistant patients also have increased levels of matrix metalloproteinases (MMPs) and tissue inhibitors of metalloproteinases (TIMPs) in their bronchoalveolar lavage samples. Those molecules contribute to the remodeling of the airway wall matrix deposition, remodeling, and irreversible lung disease (J Allergy Clin Immunol. 2007;120:1065-72).

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Aggressive Program Cut Extensively Drug-Resistant TB

BY MARY ANN MOON
Elsevier Global Medical News

An aggressive management program cured 60% of patients with extensively drug-resistant tuberculosis in a resource-poor urban setting in Peru. And it cured 66% of those with drug-resistant disease.

The outcomes in this study of 651 patients with resistant tuberculosis—and a subgroup with extensively drug-resistant disease—were better than most results reported in the United States and Europe.

“This encouraging result constitutes a true change in the current perception of the disease as a virtual death sentence,” Dr. Mario C. Raviglione of the World Health Organization said in an editorial comment accompanying the report.

The challenge now is to scale up this program to cover an entire country, and to replicate it in countries with different social and economic conditions, Dr. Raviglione said (N. Engl. J. Med. 2008;359:636-8).

The retrospective study was conducted in patients who were referred for individualized, supervised outpatient care for TB in metropolitan Lima between 1999 and 2002, reported Dr. Carole D. Mitnick of Harvard Medical School, Boston, and her associates.

A total of 48 patients had extensively drug-resistant TB, which was defined as resistance to isoniazid, rifampin, any fluoroquinolone, and any second-line injectable agent (kanamycin, capreomycin, or amikacin), at a minimum. The remaining 603 patients had multidrug-resistant TB, defined as resistance to isoniazid and rifampin but not to both a fluoroquinolone and an injectable agent.

Individualized drug regimens were based on repeated drug-susceptibility testing, with a goal of keeping each patient on at least five antituberculosis agents that were likely to be effective. Patients took the highest doses they could tolerate, and treatment was protracted, lasting over 2 years in most cases. Aminocillin-clavulanate, clarithromycin, clofazimine, rifabutin, corticosteroids, and other drugs also were used extensively.


Health care workers delivered daily supervised treatment in patients’ homes and at health centers, free of charge. Psychosocial needs also were assessed and addressed continuously. Patients with high-grade resistance and localized disease underwent lung resection, even if they had restricted lung volume.

With this aggressive, comprehensive approach, 29 (60%) of the 48 patients with extensively drug-resistant TB were cured, as were 400 (66%) of the 603 patients with multidrug-resistant TB.

Conversion of sputum cultures from positive to negative took about 1 month longer for extensively drug-resistant TB than it did for multidrug-resistant TB, “yet the frequency of cure or relapse and the risk of death did not differ significantly” between the two groups of patients, Dr. Mitnick and her associates said.

THE CHALLENGE IS TO SCALE UP THE PROGRAM TO COVER AN ENTIRE COUNTRY, AND TO REPLICATE IT IN COUNTRIES WITH DIFFERENT CONDITIONS.

FYI
Nonmedical Use of Pain Relievers
A new report that compiled data from the 2004 to 2006 National Survey on Drug Use and Health shows that since 2002, the annual average number of people who used prescription pain relievers nonmedically for the first time has exceeded the number of new marijuana users. The report is available at download.ncadi.samhsa.gov/Prevlne/pdfs/nsduh08-0619.pdf.

Consumer’s Guide to Reporting
A Web site with detailed instructions on how to use the Food and Drug Administration’s consumer complaint system and MedWatch is available at www.fda.gov/consumer/updates/reporting061008.html. The site details which problems should be reported to whom, and how. A printer-friendly PDF is also available at www.fda.gov/consumer/updates/reporting061008.pdf.
Segmentectomy Promising for Stage I Lung Cancer

BY DOUG BRUNK
Elsevier Global Medical News

SAN DIEGO — Thorascopic segmentectomy for stage I non–small cell lung cancer is gaining momentum as an alternative to lobectomy. However, with the advent of CT screening protocols and the identification of earlier and smaller lung cancers, there has been a resurgence of interest in evaluating the use of limited sublobar resection—specifically anatomic segmentectomy.

Between 2002 and 2008, Dr. Matthew J. Schuchert and his associates compared the outcomes of 104 stage I lung cancer patients who had VATS with 121 patients who had anatomic segmentectomy. Primary outcome variables included hospital course, complications, mortality, recurrence patterns, and survival.

The mean age of patients was 70 years, the average tumor size was 2.3 cm, and the mean follow-up was 22 months. There were no significant differences between the two groups in gender, operative time, or estimated blood loss.

On average, the VATS patients had fewer lymph nodes harvested than did the open group (6 vs. 9, respectively), a shorter hospital length of stay (5 vs. 7 days), and a significantly decreased rate of overall pulmonary complications (26% vs. 34%). Specifically, the open group had significantly higher rates of pneumonia, need for bronchoscopy, respiratory failure requiring prolonged intubation or reintubation, and empyema, as well as need for infusion/drainage, than the VATS group.

There were no deaths in the VATS group, versus two in the open group, which represented an overall mortality rate of 0.9%.

Overall mortality was similar between the VATS and the open group, as were the rates of overall complications (26% vs. 24%, respectively), recurrence (16% vs. 24%), and overall survival (76% vs. 76% at 2 years).

Margin-to-tumor ratios less than 1 were associated with an increased rate of recurrence, which underscores the need for obtaining adequate margins during these resections,” he said.

He emphasized that lobectomy should still be considered as primary therapy for early-stage non–small cell lung cancer, especially when adequate margins are not obtainable. “Prospective studies will be necessary to better define the potential benefits and drawbacks of anatomic segmentectomy in the treatment of stage I non–small cell lung cancer,” he said.

“In lesions that are small and that are confined to a specific bronchopulmonary segment, we would consider performing anatomic segmentectomy in an effort to preserve function, especially in elderly patients or in patients where lobectomy may be considered a higher risk option,” he explained. “We generally prefer anatomic segmentectomy over a simple wedge resection because of concern regarding an increased local recurrence rate associated with wedges, compared with segments.”

Dr. Schuchert had no conflicts to disclose.

Dr. Robert Cerfolio, FCCP, comments: Although the concept of preserving pulmonary parenchyma is appealing, a minimally invasive approach is highly marketable, and patients and pulmonologists want it,” the thoracic surgeon needs to carefully evaluate prior to resection. Clinical mis-staging of integrated PET/CT scans are only documented well in patients who undergo careful oncologic resections.
Heart Groups Acknowledge Sleep Apnea-CVD Link

BY KERRI WACHTER
Elcrest Global Medical News

In the face of rising rates of obesity, hypertension, atrial fibrillation, and heart failure, physicians need to be mindful of the mounting evidence for a link between sleep apnea and cardiovascular disease when evaluating patients, according to Dr. Virend K. Somers, the joint statement writing committee.

"We feel it is important to alert the cardiovascular community to the implications of this emerging area of research. It is possible that diagnosing and treating sleep apnea may prove to be an important opportunity to advance our efforts at preventing and treating heart disease," Dr. Somers said in a press statement.

Dr. Somers chaired the joint statement writing committee.

Dr. Somers has received research support from Respironics and the ResMed Foundation; he is also a consultant to Respironics. Both companies make devices to treat sleep apnea. In addition, Dr. David P. White, committee co-chair, is the chief medical officer for Respironics.

Sleep-related breathing disorders are common among patients with established cardiovascular disease. Obstructive sleep apnea (OSA) affects a large proportion of patients with hypertension, coronary artery disease, stroke, and atrial fibrillation. Central sleep apnea (CSA), in contrast, occurs mainly in patients with heart failure.

Cardiologists are seeing more patients with sleep apnea diagnoses, according to Dr. Rita Redberg, director of women’s cardiovascular services at the University of California, San Francisco. “I have noticed an increase in the number of patients who tell me that they have a diagnosis of sleep apnea,” she said.

While the statement serves as something of a primer on the types of sleep apnea and its relevance to individuals who are at risk for, or who already have, cardiovascular disease, the authors acknowledge that there is much that is not known about the interactions between sleep apnea and cardiovascular disease. "We need to more clearly define the cause-and-effect relationship between sleep apnea and cardiovascular diseases and risk factors," Dr. Somers said.

Key questions include whether sleep apnea is a precipitating factor in the development of cardiac and vascular disease, whether sleep apnea accelerates cardiovascular disease progression, and if the treatment of sleep apnea results in clinical improvement, fewer cardiovascular events, and reduced mortality.

However, it will likely be difficult to disentangle the role of sleep apnea in the cardiovascular disease process because obesity is common among patients with sleep apnea, and this association "often obscures differentiation between the effects of obesity, the effects of OSA, and the effects of synergies between these conditions," the authors wrote. Also, cardiovascular disease is often among several comorbidities of OSA. Hence, it is "unclear whether abnormalities evident in the sleep apnea patient with cardiovascular disease are secondary to the sleep apnea, the cardiovascular condition, or both," the authors noted.

Given the number of unknowns about the interactions of sleep apnea and cardiovascular disease, and the limited number of randomized control trials, Dr. Redberg noted that she is unlikely to change her practice based on this scientific statement. "It’s unclear how this would help my patients," she said. She already encourages patients to make lifestyle changes aimed at reducing obesity, which is also strongly associated with OSA.

The statement authors noted that there are many challenges to the development of a best practices consensus for sleep apnea and cardiovascular disease. First, sleep medicine education is largely absent from cardiovascular training. And sleep apnea treatment options vary, are predominantly device based, and are not well tolerated by patients. Lastly, it’s unclear whether treating sleep apnea confers any real benefit in reducing cardiovascular events.

To complicate matters, there is no clear consensus on how to best quantify the severity of sleep apnea, nor is it known what threshold of severity should trigger therapy. It’s also not known if thresholds for treatment should be different for people with cardiovascular disease compared with healthy individuals.

For now, the statement recommends that patients be assessed on an individual basis. "Until we know the cause-and-effect relationship between sleep apnea and cardiovascular disease, it would be best to take a two-pronged approach and treat patients," the authors wrote.
CHEST 2008—Know Before You Go

CHEST 2008 is next month. Knowing a few things before you go will make your travel and meeting check-in “a snap.”

On-site travel has been made easy. Take advantage of rail, shuttle bus, and taxi services available between the airport and downtown Philadelphia. Look for signs for these services in the airport baggage claim area.

Complimentary shuttle service will be available to the convention center from Sheraton, Embassy Suites, Hampton Inn, and Ritz-Carlton. Complimentary shuttle service for morning and evening functions will be available to the Marriott Downtown from Sheraton, Embassy Suites, and Hampton Inn. Shuttle information will be posted at each hotel.

Everyone must check in at registration. Report to the ACCP registration area in the Pennsylvania Convention Center upon arrival. If you registered prior to September 23 and received a yellow registration packet, bring it with you for faster service. If you haven’t registered, there’s still time!

Online registration is available through Thursday, October 23. On-site registration begins Friday, October 24, at 6:00 PM. You can also register for CHEST 2009 at CHEST 2008 prices, and take advantage of other early registration offers for 2009.

While in the registration area, look for the ACCP Bookstore in this new location—now with longer, more convenient hours. New board review syllabi, ACCP-SEEK XVIII: Critical Care Medicine, and the first edition of ACCP-SEEK Sleep Medicine will be available, along with many other new and updated products.

Here’s a quick look at some meeting highlights:

- Hear the emerging biomedical and social science issues that can help you identify health-care disparities in your practice or community and overcome them. Don’t miss the keynote address, Monday, October 27, featuring Nicole Lurie, MD, MSPH.
- Attend any of the 16 literature review sessions to review the significant studies from the past year, presented by leading authorities. See your final program for session times and locations.
- Experience hands-on education in the ACCP Simulation Center. Practice the cognitive, technical, and behavioral skills needed to provide optimal patient care across a variety of situations. Preregistration is required to attend sessions—see www.chestnet.org for details.
- Enjoy the digital distribution of scientific abstracts and case reports, no longer produced in hard copy. Every attendee will receive them on CD-ROM.
- Participate in the new ACCP Clinical Case Puzzlers. Master clinicians, pathologists, and radiologists will present interesting or unusual cases and discuss the factors for making accurate diagnoses.
- View original science and meet with the researchers during two poster grand round sessions. Plan to attend Tuesday, October 28, and/or Wednesday, October 29, from 1:00 PM to 2:15 PM in the exhibit hall. Dessert will be served.
- Check out the latest products, technology advances, and information delivery systems relevant to your profession in the large exhibit hall. The exhibit hall will be open Monday through Wednesday, and free lunch will be served each day.

More than 175 sessions presenting clinical updates in chest medicine are taking place throughout the week. To receive CME credit for the sessions you attend, complete the online CME process from any computer with Internet access. Look for dedicated computers on-site.

Select sessions will be available for purchase as electronic audio files. If you can’t make it to every session you’d like, look for the Digital Conference Provider booth.


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Don’t Miss These Sessions

- Instruction in Education: Walk Through Simulation-Enhanced Curriculum Development
  - September 25-26, 2008
  - Learn strategies for developing, implementing, and evaluating a clinical curriculum for pulmonary, critical care, or sleep medicine. Using a systematic approach to developing curricula, you will learn to incorporate the facilitator or educator, learners, teaching environment, and supplemental education materials to create learning plans with educational impact.

- Critical Care Fundamentals
  - February 13-15, 2009
  - This 3-day multimodal course will utilize various degrees of simulation to offer experiential learning in domains, including ventilator management, hemodynamic monitoring, and management of critically ill patient.

- Bronchoscopy Skills
  - February 20-22, 2009
  - This 3-day course will expose participants to the cognitive and psychomotor skills involved in utilizing bronchoscopy effectively in clinical practice.

- Difficult Airway Management
  - March 4-6, 2009
  - This 3-day simulation-enhanced workshop will provide hands-on experience with preparatory teamwork, and tools to manage common and complex airway situations.

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www.chestnet.org
Asthma and COPD: Evidence Supporting A Disease Continuum—Part 1

Physicians grapple with the question of the relationship between these two obstructive airway diseases.

Asthma and COPD represent two major global causes of disability and death. A global task force from the World Health Organization estimates that COPD will become the third most common cause of death by 2020. In addition, the worldwide prevalence of asthma continues to increase and will be close to 400 million by 2025.

Due to these disturbing statistics, physicians grapple with the question of the relationship (i.e., similarities and distinctions) between these two obstructive airway diseases. Are asthma and COPD two distinct clinical entities with little or no overlap? Or, do these conditions represent a continuum from mild to severe asthma in childhood that progresses to COPD in adulthood?

Many of the structural changes seen in COPD have been attributed to direct injury and inflammation from cigarette smoke components. Although the majority of cases of COPD occurs in current or former smokers, up to one-quarter of cases occurs in people who have never smoked (Behrendt. Chest 2005; 128:1239). This raises the possibility of other predisposing factors for the development of COPD, including remodelling and inflammatory effects of asthma.

In practical terms, however, separating these clinical entities is not straightforward. As more evidence is gathered, it becomes increasingly clear that spirometry testing, with or without bronchodilator response, is not sufficient for this purpose.

A vital question remains, as yet unanswered, as to whether early aggressive treatment of asthma in childhood will reduce the incidence of COPD in adulthood. This question has gained top priority, given the fact that recent studies show that a history of bronchiolitis, pneumonia, and asthma in early life is associated with a 57% greater risk for mortality from adult respiratory diseases and a twofold increase in COPD mortality (Galobardes et al. Thorax 2008; 63:423).

Table 1. Asthma and COPD: Challenging the Assumptions—Evidence for a Disease Continuum

<table>
<thead>
<tr>
<th>Asthma</th>
<th>COPD</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>May be smokers</td>
<td>Usually smokers</td>
<td>Up to 25% of cases of COPD present in nonsmokers (Behrendt. Chest 2005; 128:1239)</td>
</tr>
<tr>
<td>Reversible airway obstruction</td>
<td>Nonreversible airway obstruction</td>
<td>Almost half of adults with moderate to severe childhood asthma have irreversible airway obstruction (Limb et al. J Allergy Clin Immunol 2005; 116:1215)</td>
</tr>
<tr>
<td>Eosinophilic inflammation</td>
<td>Neutrophilic inflammation</td>
<td>Eosinophilia in mild COPD exacerbations; neutrophilia present in COPD and asthma exacerbations (Qiu et al. Thorax 2007; 62:475)</td>
</tr>
<tr>
<td>Bronchitis symptoms uncommon</td>
<td>Bronchitis symptoms common</td>
<td>Asthmatics at high risk for acquiring symptoms of chronic bronchitis (Silva et al. Chest 2004; 126:59)</td>
</tr>
</tbody>
</table>

The hypothesis of an interrelation between asthma and COPD is further supported by findings of Silva et al. (Chest 2004; 126:59). This group conducted a prospective observational study designed to evaluate the association between physician-diagnosed asthma and subsequent development of COPD in a large cohort of 3,099 adult subjects. Twelve periodic follow-up surveys were obtained, 1.5 to 2 years apart, over a total of 20 years.

Results showed a significant association between active asthma at initial survey and subsequent development of signs and symptoms consistent with COPD. Active asthmatics had a 10-times higher risk for acquiring symptoms of chronic bronchitis, 17-times higher risk for emphysema, and 12.5-times the risk for receiving a diagnosis of COPD, with Dlco (diffusing capacity of the lung for carbon monoxide) data included in the working definition of the latter two conditions. Vork et al. (Thorax 2003; 58:322) examined risk factors associated with the presence of irreversible airflow limitation and reduced transfer coefficient in 228 patients with asthma after 26 years of follow-up. Irreversible airflow limitation and reduced transfer coefficient are both lung function characteristics of COPD. At follow-up, 16% of patients had irreversible airway obstruction and 23% had a reduced transfer coefficient.

Of the patients with asthma who used anti-inflammatory medication, 80% still had airway obstruction, but irreversible airflow limitation developed less frequently. Smoking was associated with a reduced transfer coefficient but not with the development of irreversible airflow limitation. Interestingly, those patients with irreversible airflow limitation also developed COPD-like symptoms (cough, phlegm, dyspnea) at follow-up.

A continuation of this article will be published in the October 2008 issue of CHEST Physician.

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Associate Professor of Pediatrics
University of Louisville School of Medicine
Louisville, KY

Dr. Nemr Eid, FCCP
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Editor's Note

Dr. Eid and his associates raise provocative questions about the relationship between childhood asthma and adult irreversible obstructive airway disease. It is especially relevant that Dr. Eid is a pediatric pulmonologist. The continuum of lung growth and development from childhood into early adulthood makes the potential impact of inflammatory disease of the airways a crucial point of overlap between the pediatric and adult pulmonologist.

We should clearly be paying more attention to lung growth in children and adolescents who have asthma.
The ACCP Quality Improvement Committee (QIC) is committed to advocating for improved health-care outcomes for our patients by identifying, endorsing, implementing, and educating ACCP members on quality improvement (QI) strategies, measures, and products that have an impact on patient care. The QIC has been actively engaged in reviewing a number of National Quality Forum (NQF) and Physician Consortium for Performance Improvement (PCPI) performance measures for endorsement. These endorsed performance measures will be implemented by the Centers for Medicare and Medicaid Services (CMS) and other major payers. The QIC has well-defined processes and criteria for reviewing such measures to ensure they are clinically relevant, important, scientifically acceptable, usable, and feasible for the chest physician. This year, the QIC is inviting CHEST attendees to learn about QI strategies and initiatives that will impact their practice of medicine.

The following is a list of these activities:

- **Quality Improvement: Venous Thromboembolism—How Are Our Guidelines Being Implemented?**
  - Monday, October 27, 2008
  - 4:15 PM - 5:45 PM
  - This session will highlight the relationships of evidence-based guidelines and performance measures. There will also be a discussion about which recommendations from the new 8th edition of the ACCP antithrombotic guidelines may be amenable to performance measures and which will not.

- **ACCP Literature Review: Thoracic Imaging and Physician Performance Measures**
  - Tuesday, October 28, 2008
  - 10:30 AM - 12:00 PM

- **Quality Improvement: Transforming Hospitals—Designing for Safety and Quality**
  - Tuesday, October 28, 2008
  - 4:15 PM - 5:45 PM
  - This session will highlight the available evidence relating hospital design to patient outcomes, directly, through space and material usage, and indirectly through improved staff efficiency and satisfaction.

- **Quality Improvement: Surviving the Critical Care Performance Measure Onslaught**
  - Wednesday, October 29, 2008
  - 8:30 AM - 9:45 AM

This session will provide CHEST 2008 attendees with an understanding of what third party payers expect from clinicians and hospitals regarding adherence to and implementation of performance measures. On behalf of the ACCP membership, and together with the ACCP Health Affairs Division, the QIC participated in two multisociety efforts, engaging in separate dialogs with the Department of Health and Human Services (DHHS), Office for Human Research Protection (OHRP) and CMS.

  - The ACCP, together with the American Thoracic Society (ATS), Society of Hospital Medicine, American Association of Critical-Care Nurses (AACN), and the Society of Critical Care Medicine (SCCM), met with representatives of the DHHS and developed a policy statement regarding the role of IRBs in QI research and the impact of such regulations on future QI initiatives.

- **Hospital-Acquired Conditions (HACs)**
  - Together with the ATS, SCCM, AACN, NAMORC, and American Association of Respiratory Care, the ACCP composed a letter to CMS addressing proposed changes to the hospital inpatient prospective payment system. The letter specifically addressed a proposed policy for discontinuation of reimbursement for CMS-designated “serious preventable adverse events”, in particular, HACs. As a result of this effort, in the upcoming year, CMS is not classifying Ventilator-Associated Pneumonia, Iatrogenic Pneumothorax, or Delirium in the Critically Ill as preventable HACs. Furthermore, Deep Vein Thrombosis/Pulmonary Embolism will be considered a preventable HAC only when related to hip and knee replacements.

In the future, the QIC will develop a Webinar series that will inform participants of how QI initiatives will affect their practice of medicine and provide tools and resources to help chest physicians navigate the maze of performance measures. Additionally, the QIC is initiating a pilot registry to determine if such a tool will help chest physicians meet the demands of credentialing bodies and regulatory agencies, while providing the capability to benchmark individual physician practices against those of their peers.

For more information, contact Joyce Bruno Reitzner, MBA, MIPH, at jbruno@chestnet.org.

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**CHEST 2008 Faculty Honoraria Can Be Directed as a Charitable Contribution**

CHEST 2008 faculty members have the opportunity to contribute their honoraria to The CHEST Foundation. Contributing your honorarium is an easy way to participate as a donor and be a supporter of the four focus areas that The Foundation oversees—tobacco prevention, clinical research, humanitarian service, and critical care/end-of-life care.

Prior to the meeting, you can indicate on your online ACCP Faculty Form that you would like all, or a portion of, your honorarium to be made payable to The CHEST Foundation. The designated amount will automatically be given to The Foundation as a charitable contribution in your name. Any remainder that is due to you will be processed and mailed by the ACCP.

This donation clearly benefits The Foundation and may be a benefit to you by reducing your annual income at the end of the year. Canadian members donating in this way are allowed to donate US income and claim the eligible amount of the gift allowed on a US tax return, up to 75% of the net US income on a Canadian tax return.

There has been a steady increase in the number of members donating their honoraria each year. The variety of honoraria donated also has increased and includes participants at focus groups and roundtables at the ACCP spring board meetings, the year-round ACCP board review courses, and many types of miscellaneous reimbursements directed to The CHEST Foundation in lieu of payment.

The CHEST Foundation hopes that you will take advantage of this quick and easy way to contribute.

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**The CHEST Foundation Receives Matching Gift Challenge**

The CHEST Foundation has received an anonymous matching gift challenge for CHEST 2008. Every dollar that donors contribute to The CHEST Foundation’s Annual Fund during CHEST 2008 will be matched, dollar for dollar. The Foundation has set a goal of raising $35,000 at this year’s annual meeting, and this generous matching gift establishes the base contribution for achieving that goal.

The Foundation’s board and staff gladly accept this matching gift challenge, as it increases The Foundation’s general fund and provides an opportunity to make a real connection with donors. Historically, matching gift challenges have inspired ACCP members to give, and give generously, because they appreciate the fact that their donations count for more.

The CHEST Foundation considers this challenge an excellent opportunity for those interested in making their year-end contributions to The Foundation while at CHEST. All attendees at the meeting are encouraged to stop by The CHEST Foundation booth in ACCP Central to help us reach our goal and meet this challenge. While at the booth, you also can obtain information about any of the four focus areas your donation supports—tobacco prevention, clinical research, humanitarian service, and critical care/end-of-life care. We hope you will take some time to talk with the staff and share your ideas about The CHEST Foundation.
ACCP Set To Welcome a New President

Dr. James A. Mathers, Jr., FCCP, will be inducted as the new ACCP President in October during CHEST 2008 in Philadelphia. He is a partner with Pulmonary Associates of Richmond, VA, and has 27 years of private practice experience in pulmonary, critical care, and sleep medicine.

Dr. Mathers received his medical degree from the Columbia University College of Physicians and Surgeons in New York. He completed a medical residency at Maine Medical Center, Portland, then returned to Columbia University for his pulmonary fellowship.

Dr. Mathers has served the ACCP in numerous leadership roles, some of which include: two terms as Regent at Large on the Board of Regents, two terms on the Executive Committee of the Board of Regents, Trustee of The CHEST Foundation, and Chair of the Government Relations Committee.

In addition to his clinical practice, Dr. Mathers has worked with our sister societies, legislators, and regulatory agencies to remove barriers to appropriate care for patients with diseases of the chest. He believes that a shortage of chest physicians, in particular, those practicing critical care medicine, is a significant problem facing our membership and society.

We asked Dr. Mathers to share some of his thoughts on his upcoming presidential year.

A Letter to the Membership
I choose to enter the private practice of pulmonary and critical care medicine in Richmond, VA, in 1980, and the American College of Chest Physicians has been my home for postgraduate medical education ever since.

Over the years, my group practice has grown to 24 pulmonary, critical care, and sleep physicians—with a supporting staff of 80. Even though our group is large, I believe the issues confronting my practice are similar to those of the majority of community practices across this country. We are available 24 hours a day, every day of the year. We are often called to the emergency room or the ICU to evaluate and treat desperately ill patients and respond, regardless of their insurance status. We try to provide quality care and the best outcome for each patient.

Our goal in practice is the seamless implementation of state-of-the-art care for the benefit of our patients as defined by the scholarly products of the ACCP. In reality, however, one quickly finds that the process is often not seamless. In my practice lifetime, much has changed in the clinical arena. Those who have heard me speak for our group know that the process is often not seamless. In my practice lifetime, much has changed in the clinical arena. Those who have heard me speak for our group know that one of my favorite quotes is from the original legislation that established the Medicare program: “Nothing in this title shall be construed to authorize any Federal officer or employee to exercise any supervision or control over the practice of medicine or the manner in which medical services are provided.”

A substantial portion of the change in our practice environment has been brought about through federal legislation, passed by Congress, that has altered the initial Medicare program. These changes have affected our ability to care for individual patients in both the community and academic centers. An increasing array of rules and regulations has influenced patient access to a variety of medical therapies, as well as physician availability. Medical decision making now falls under the scrutiny of insurance companies, managed care organizations, pharmacy benefit programs, hospital management, independent review organizations, federal agencies, and consumer groups.

Similar to our clinical environment, the College is now faced with several new challenges. In addition to advancing our medical practice through products created by the membership and staff, the College, like many other societies, is confronted with increasingly stringent requirements for organizations that provide continuing medical education certification, increased scrutiny of industry relationships, new financial reporting requirements, and the increasing costs of operation with the prospect of flat or declining revenues. As a member-driven organization, we need the help of interested members with expertise in research, quality improvement, finance, education, advocacy, and ethics.

While we face complex issues in our environment, our profession has many personal rewards.

DR. MATHERS

The CHEST Foundation
Announces New Endowment

The CHEST Foundation has established the Forrest M. Bird, MD, PhD, ScD Endowment in Mechanical Ventilation. This endowment was created to honor Dr. Bird’s outstanding achievements as an inventor and scientist, as well as support innovation and education in the field of mechanical ventilation. The beneficiaries of the endowed fund are patients whose care has improved as a result of advances made in research and treatment of respiratory disease.

ACCP members who have been fortunate enough to work with Dr. Bird, or who have benefited from his innovations as students or practitioners, will recognize his remarkable contributions to the field of pulmonary medicine. The Foundation is asking all members to help establish the Forrest M. Bird, MD, PhD, ScD Endowment in Mechanical Ventilation. Your tax-deductible contribution to this fund will help to ensure that advances in research and treatment of respiratory disease will have the support they need now and in future generations.

To make a contribution, please visit The Foundation’s Web site at www.chestfoundation.org to download an endowment brochure for mailing in your donation or make a secure online donation directly.

The ACCP and The CHEST Foundation will be honoring Dr. Bird with a special tribute during CHEST 2008 in Philadelphia, PA, at the 16th Annual Making a Difference Awards Dinner on Saturday evening, October 25, 2008, at the Marriott Downtown Hotel. Join your ACCP colleagues and friends for this celebration. Pre-registration for this event is required. To register online for the Making a Difference Awards Dinner, please visit The CHEST Foundation’s Web site at www.chestfoundation.org.

To obtain more information about donating to the Forrest M. Bird, MD, PhD, ScD Endowment in Mechanical Ventilation, your tax-deductible contribution to this fund will help to ensure that advances in research and treatment of respiratory disease will have the support they need now and in future generations, please visit The CHEST Foundation’s website at www.chestfoundation.org or (847) 498-8308.

This Month in CHEST—Editor’s Picks

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

▶ The Language of Breathlessness Differentials Between Patients With COPD and Age-Matched Adults. By Dr. Marie Williams, et al.

▶ A Randomized Trial of CT Fluoroscopic-Guided Bronchoscopy vs Conventional Bronchoscopy in Patients With Suspected Lung Cancer. By Dr. David Ott, FCCP, et al.

▶ The Carbon Monoxide Diffusing Capacity: Clinical Implications, Coding, and Documentation. By Dr. Alan L. Plummer, FCCP.

▶ Sleep Loss and Sleepiness: Current Issues. By Dr. Thomas J. Balkin, et al.


www.chestjournal.net
Diagnosis and Evaluation of OSA in Children

Sleep fragmentation from obstructive sleep apnea may result in impaired daytime performance.

Children with obstructive sleep apnea (OSA) may present with nocturnal and/or diurnal symptoms. The patient history is best obtained from parents or siblings who share the same bed, because children are often unaware of what happens when they are asleep.

Nocturnal Symptoms
Snoring is the most common presenting complaint of children with OSA. At night, the child may be snoring loudly with gasping, gurgling, or choking. Twelve percent of all children snore “on most nights,” and it is estimated that up to 3% of school-aged children have frank OSA. It occurs equally in both sexes. Parents may notice frank apneas in their children. They may describe restless sleep because of movement of the chest and abdomen. They may describe restless sleep, but sometimes the only manifestation of restless sleep is finding the bedclothes askew in the morning. Children with OSA are at higher risk for enuresis, which may resolve when the OSA is adequately treated.

Daytime Symptoms
Children with OSA may describe daytime sleepiness. More commonly, they display behavior problems or difficulties in school. They may have difficulty paying attention in class and may be mislabeled with attention deficit disorder. They may have “micro-sleeps” that are misinterpreted as daydreaming or absence seizures. All of these may result in poor academic performance.

Physical Examination
Normal findings on physical examination do not exclude a diagnosis of OSA in children. These children may fail to thrive, perhaps due to increased work of breathing, or they may be obese. Their tonsils may be large, and they may have adenoid facies and hyponasal speech. They may have a small jaw, large tongue, and/or a high arched palate. Any craniofacial or neurologic defect that may affect upper airway size or motor tone also may predispose children to OSA.

Diagnostic Methods
There have been many attempts to diagnose OSA in children by clinical criteria. A recent review of the biomedical literature (Bretzke et al. Arch Otolaryngol Head Neck Surg 2004; 131:827) found that “clinical history and physical examination are not reliable for diagnosing OSAHS.”

Less than half of the children who are referred to sleep centers because of a clinical suspicion of OSA meet polysomnographic criteria for the disorder.

Questionnaires alone have been unable to differentiate OSA from primary snoring. Clinical scores that include factors such as difficulty breathing during sleep, observed apneas, and snoring have been suggested to differentiate children with OSA but have not been useful in diagnosing polysomnographically proven OSA in children who have been referred to a pediatric sleep center.

Analysis of a 15-min audiotape improved the sensitivity of a clinical score from 0.46 to 0.71, but the authors concluded that audiotapes are not sufficiently specific to reliably distinguish primary snoring from OSA. Adding a “sleep tape” to reinforce clinical criteria resulted in a sensitivity of 0.92, but the specificity was only 0.29 with a positive predictive value of 0.5.

Home Studies
Because of the expense and inconvenience of laboratory-based polysomnography (PSG), there have been attempts to use simpler, more limited studies in the diagnosis of OSA in children.

Studies in the home have the advantage of a more natural sleeping environment, but fewer channels result in less precise measurement. In addition, there is no technologist available to solve technical problems, so a certain percent of home studies will need to be repeated. Pulse oximetry can only detect apneas, and fewer respiratory events than adults and a high proportion of hypopneas, so the studies must be scored and reviewed with great care. In adults, obstructive apneas 10 s or longer are scored; however, in children, who have a faster respiratory rate, a respiratory event of two missed breaths is scored.

Summary
Obstructive sleep apnea is common in children, and the resulting sleep fragmentation may result in impaired daytime performance. The children may be misdiagnosed with absence seizures or attention deficit disorder. Snoring is the most common presenting symptom, but the diagnosis should be confirmed with overnight PSG in a laboratory that has expertise in dealing with children. The PSG results can define the severity of the disorder so that proper treatment and monitoring can be instituted.

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Dr. Len J. Brooks, FACC
University of Pennsylvania
Division of Pediatric Pulmonology and Sleep Medicine
The Children’s Hospital of Philadelphia
Philadelphia, PA
During CHEST 2008, the CHEST Foundation will hold its annual Making a Difference Awards Dinner on Saturday, October 25, 2008. This is the tenth year for the Humanitarian Awards Program and the Foundation will bestow $25,000 in grants to ACCP members for their pro bono service. This year, there are nine winning projects in three categories: four project development grants, four recognition awards, and one Ambassadors Group humanitarian award.

The ACCP and CHEST Foundation will be paying special tribute to Forrest M. Bird, MD, PhD, ScD. Dr. Bird is being recognized specifically for his development of the first mass-produced mechanical ventilators for acute and chronic cardiopulmonary care. The ACCP Industry Advisory Council also will present their annual monetary award to community outreach event partners, Penn Alexander Elementary School and Steppingstone Scholars, Inc.

The Making a Difference Awards Dinner will be held at the Marriott Downtown hotel, in the Grand Ballroom, 1201 Market Street, Philadelphia, PA. The open reception will take place from 7:00 PM to 7:45 PM, and dinner and ceremonies are from 8:00 PM to 10:30 PM. Invitations to the Making a Difference Awards Dinner will be mailed after Labor Day. Tickets price is $150 per person ($25 of the ticket price is tax deductible). The $500 level are entitled to one complimentary ticket.

The CHEST Foundation’s 10th Annual Making a Difference Awards Dinner sponsors, to date, are AstraZeneca, LP; Boehringer Ingelheim Pharmaceuticals, Inc.; Eisai, Inc.; GlaxoSmithKline; Merck & Co., Inc.; and Sepracor, Inc.

Women’s Health Network Meets at CHEST 2008

The Women’s Health Network (WHN) invites CHEST 2008 attendees to attend the WHN Luncheon on Tuesday, October 28, 2008, at 11:45 AM – 1:00 PM, and the WHN Open Meeting immediately following from 1:00 PM – 2:15 PM. Seating is limited to the first 250 guests at the luncheon.

Keynote speaker Stephen M. Winter, MD, FCCP, will give a presentation, and the Boehringer Ingelheim Pharmaceuticals, Inc. Clinical Research Awards in Women’s Pulmonary Health will be granted. Also featured will be sections of a new video developed by The CHEST Foundation and Ambassadors Group members. The WHN luncheon is supported exclusively by an educational grant from Merck & Co., Inc.

The WHN Open Meeting will review issues and events from the past year’s accomplishments, consider opportunities for the dissemination of the Make the Choice: Tobacco or Health? Speakers Kit, and will have a panel presentation from the WHN Clinical Research Award in Women’s Health recipient.
Pulmonary/Critical Care Faculty Position
Wake Forest University School of Medicine

The Section on Pulmonary, Critical Care, Allergy and Immunologic Diseases is seeking two BC/BE physicians at the Assistant/Associate Professor level. The principal clinical and teaching focus of these positions will be Critical Care. For candidates interested in a significant research component, opportunity for protected time will be encouraged to support the development of independent and integrated research activities. Currently, the section is an ARDS Network study site and has over 3.3 million in NIH funding, and consists of 22 faculty members (MDs and PhDs). The Section at Wake Forest will continue significant expansion as the result of multiple ongoing research and clinical programs. Winston-Salem and the surrounding Piedmont region of NC provide a unique opportunity for faculty to enjoy work, family and outdoor activities. All inquiries should be submitted to: Eugene Bleckley, MD, Chief, Division of Pulmonary, Critical Care, Allergy and Immunologic Diseases, Wake Forest School of Medicine, Wake Forest University School of Medicine is an Equal Opportunity, Affirmative Action Employer.

Northern California Hospitalist Opportunity

Sutter Medical Group is seeking a BE/BC Pulmonary Critical Care physician in Auburn, CA. Good call schedule. Option for hospitalist work if desired.

Sutter Auburn Faith Hospital is a medium sized hospital with a 24/7 hospitalist program, open ICU, high resolution CT scan, cardiac cath lab, full nuclear medicine department, bronchoscopy suite and a pulmonary function laboratory.

Auburn is centrally located in the Sierra Nevada foothills between Sacramento and Lake Tahoe. Auburn is close to shopping and restaurants, and offers a variety of outdoor activities.

Pulmonary Critical Care Sleep Optional

Enjoy the benefits of an employed position.

Wonderful opportunity to practice your profession. Four season activities, excellent schools and easy access to a Regional Airport. Will sponsor J1 Visa. Contact Linda Shulman, Alpha Physician Search 800-504-3441. lshulman@alphamg.com View additional opportunities, www.aphsps.com

Intensivist

Northern, New Jersey: Desirable location within a short drive from New York City. Located in the rolling hills of northern New Jersey is a fully renovated community hospital. Intensivist needed to join a successful single specialty practice offering partnership in twenty-four months. Submit CV to Chest#84, P.O. Box 996, Abingdon, MD 21009.

Suburban Pittsburgh

Pulmonary and Sleep Medicine Physician needed in suburban Pittsburgh, PA. Excellent salary and fringe benefits. Equal Opportunity Employer. J1 Visa consideration. Please send CV to Chest #84, P.O. Box 996, Abingdon, MD 21009.

Mesothelioma

HELP YOUR PATIENTS COPÉ WITH THIS DIAGNOSIS.

We are a nationally recognized plaintiffs’ asbestos law firm and built our reputation representing those diagnosed with mesothelioma, and other asbestos diseases. We can help your patients understand the legal implications of their diagnosis. Our website has been recognized as “providing useful information for patients and their families.” (Robinson et al, Malignant Mesothelioma. The Lancet, 2000; Vol. 356:397-408.) KAZANLAW.COM Helping Asbestos Victims Since 1974. Kazan, McClain, Abrams, Lyons, Greenwood & Harley, A Professional Law Corporation - 171 Twelfth Street 3rd Floor, Oakland, CA 94607, 1-877-995-6372 - www.kazanlaw.com email: skazan@kazanlaw.com

Southern California

Sleep Optional

The community of Auburn is nestled in the Sierra Nevada foothills approximately 35 miles northeast of Sacramento. Auburn is known for its family-oriented atmosphere and for its excellent schools. Residents enjoy year-round outdoor recreations such as golfing, hiking, biking, and white water rafting.
DORIBAX™ (doripenem for injection) for Intravenous Infusion

Contraindications
DORIBAX™ is contraindicated in patients with known serious hypersensitivity to doripenem or to other drugs in the same class or in patients who have demonstrated anaphylactic reactions to beta-lactams.

Warnings and Precautions
Serious and occasionally fatal hypersensitivity (anaphylactic) and/or serious skin reactions have been reported in patients receiving beta-lactam antibiotics. These reactions are more likely to occur in individuals with a history of sensitivity to multiple allergens. Before therapy with DORIBAX™ is instituted, careful inquiry should be made to determine whether the patient has had a previous hypersensitivity reaction to other beta-lactams, cephalosporins, penicillins or other allergens. If this product is to be given to a penicillin- or other beta-lactam-allergic patient, caution should be exercised because cross-hypersensitivity among beta-lactam antibiotics has been clearly documented.

If an allergic reaction to DORIBAX™ occurs, discontinue the drug. Serious acute hypersensitivity (anaphylactic) reactions require emergency treatment with epinephrine and other emergency measures, including oxygen, IV fluids, IV antihistamines, corticosteroids, pressor amines and airway management, as clinically indicated.

Interaction with Sodium Valproate: Carbapenems may reduce serum valproic acid concentrations to subtherapeutic levels, resulting in loss of seizure control. Although the most common adverse reactions to DORIBAX™ were predominantly Gastrointestinal (GI) in the three phase 3 clinical studies, the most common adverse reactions to DORIBAX™ were GI disturbances (nausea, diarrhea, vomiting, abdominal pain) in over 20% of patients. Gastrointestinal adverse events may be dose-related and occur more frequently at higher doses.

Table 1: Adverse Reactions†† Having Clinically Important Differences in Incidence Rates (%) of DORIBAX™ Relative to Comparator

<table>
<thead>
<tr>
<th>System</th>
<th>DORIBAX™ 500 mg q8h</th>
<th>Comparator</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous system disorders</td>
<td>Headache</td>
<td>16</td>
<td>5</td>
</tr>
<tr>
<td>Vascular disorders</td>
<td>Palpitations</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Gastro-intestinal disorders</td>
<td>Nausea</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Blood and Lymphatic System</td>
<td>Disorders</td>
<td>1</td>
<td>10</td>
</tr>
</tbody>
</table>

*An adverse drug reaction was defined as an undesirable effect, as part of its pharmacological action or may be unpredictable in its occurrence.
††An adverse drug reaction was defined as an undesirable effect, as part of its pharmacological action or may be unpredictable in its occurrence.

Use in Specific Populations
Pregnancy: Category B: DORIBAX™ was not teratogenic and did not produce effects on ossification, developmental delays or fetal weight in rats treated with doripenem. Doripenem was not teratogenic and did not produce effects on ossification, developmental delays or fetal weight in rats treated with doripenem. Doripenem was not teratogenic and did not produce effects on ossification, developmental delays or fetal weight in rats treated with doripenem. Doripenem was not teratogenic and did not produce effects on ossification, developmental delays or fetal weight in rats treated with doripenem. Doripenem was not teratogenic and did not produce effects on ossification, developmental delays or fetal weight in rats treated with doripenem. Doripenem was not teratogenic and did not produce effects on ossification, developmental delays or fetal weight in rats treated with doripenem. Doripenem was not teratogenic and did not produce effects on ossification, developmental delays or fetal weight in rats treated with doripenem. Doripenem was not teratogenic and did not produce effects on ossification, developmental delays or fetal weight in rats treated with doripenem. Doripenem was not teratogenic and did not produce effects on ossification, developmental delays or fetal weight in rats treated with doripenem. Doripenem was not teratogenic and did not produce effects on ossification, developmental delays or fetal weight in rats treated with doripenem. Doripenem was not teratogenic and did not produce effects on ossification, developmental delays or fetal weight in rats treated with doripenem. Doripenem was not teratogenic and did not produce effects on ossification, developmental delays or fetal weight in rats treated with doripenem. Doripenem was not teratogenic and did not produce effects on ossification, developmental delays or fetal weight in rats treated with doripenem. Doripenem was not teratogenic and did not produce effects on ossification, developmental delays or fetal weight in rats treated with doripenem. Doripenem was not teratogenic and did not produce effects on ossification, developmental delays or fetal weight in rats treated with doripenem.

Uses: Use in pediatric patients have not been established.

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DORIBAX™ is indicated as a single agent for the treatment of complicated intra-abdominal infections caused by susceptible strains of E coli, K pneumoniae, P aeruginosa, B caccae, B fragilis, B thetaiotaomicron, B uniformis, B vulgatus, S intermedius, S constellatus, or P micros.

† DORIBAX™ is indicated as a single agent for the treatment of complicated urinary tract infections caused by susceptible strains of E coli, including cases with concurrent bacteremia, K pneumoniae, P mirabilis, P aeruginosa, or A baumannii.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of DORIBAX™ and other antibacterial drugs, DORIBAX™ should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting and modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

**Important Safety Information**

DORIBAX™ is contraindicated in patients with known serious hypersensitivity to doripenem or other carbapenems, or in patients who have demonstrated anaphylactic reactions to beta lactams.

Serious and occasionally fatal hypersensitivity (anaphylactic) and serious skin reactions have been reported in patients receiving beta-lactam antibiotics. These reactions are more likely to occur in individuals with a history of sensitivity to multiple allergens. If an allergic reaction to DORIBAX™ occurs, discontinue the drug.

Serious acute anaphylactic reactions require emergency treatment with epinephrine and other emergency measures, including oxygen, IV fluids, IV antihistamines, corticosteroids, pressor amines and airway management, as clinically indicated. Carbapenems may reduce serum valproic acid concentrations to subtherapeutic levels, resulting in loss of seizure control. Serum valproic acid concentrations should be monitored frequently after initiating carbapenem therapy. Alternative antibacterial or anticonvulsant therapy should be considered if serum valproic acid concentrations cannot be maintained in the therapeutic range or seizures occur.

Clostridium difficile-associated diarrhea (CDAD) has been reported with nearly all antibacterial agents and may range in severity from mild diarrhea to fatal colitis. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over 2 months after administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C difficile may need to be discontinued.

When doripenem has been used investigationally via inhalation, pneumonitis has occurred. DORIBAX™ should not be administered by this route.

Safety and effectiveness in pediatric patients have not been established.

The most common adverse reactions (≥5%) observed in clinical trials were headache, nausea, diarrhea, rash, and phlebitis.


For more information, visit us at www.doribax.com