VOL. 5 • NO. 6 • JUNE 2010

CHEST Physician

THE NEWSPAPER OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS

BRUCE JANCIN/ELSEVIER GLOBAL MEDICAL NEWS

No one antimicrobial for community-acquired pneumonia showed increased risk for *C. difficile* emergence, Dr. Anke H. Bruns said.

Nosocomial *C. difficile* Was Common in CAP

BY BRUCE JANCIN
Elsevier Global Medical News

VIENNA — The three major guideline-recommended, empiric antibiotic strategies for community-acquired pneumonia are associated with similar rates of nosocomial acquisition of *Clostridium difficile*, according to a prospective, observational study.

The nosocomial *C. difficile* acquisition rates documented in the Dutch study—11.2% overall and 7.2% for the more worrisome toxigenic strains—are far from inconsequential. In the United States, with an estimated 1 million hospital admissions annually for community-acquired pneumonia (CAP), the toxigenic-strain acquisition rate extrapolates to 72,000 new carriers of toxigenic *C. difficile* per year, Dr. Anke H. Bruns pointed out at the annual European Congress of Clinical Microbiology and Infectious Diseases.

"This is a large contributor to the spread of *C. difficile*," observed Dr. Bruns of University Medical Center Utrecht, the Netherlands.

She reported on 107 Dutch patients hospitalized with severe CAP, for which 41% were treated with moxifloxacin, 44% with beta-lactam monotherapy, and the rest with beta-lactam/macrolide combination therapy. Participants were followed for 30 days, with stool samples collected on admission, 5 days later, 3 days after completion of antibiotic therapy, and on day 30.

Infectious Diseases Society of America guidelines recommend either of two antibiotic regimens as first-line treatment for CAP patients on general medical wards who are thought not to have *Legionella* pneumonia: monotherapy with a respiratory fluoroquinolone or combination therapy of beta-lactam and macrolide. Dutch guidelines recommend monotherapy with either a fluoroquinolone or beta-lactam or therapy combining a beta-lactam with either a macrolide or fluoroquinolone.

Regarding those regimens as equally effective for CAP, Dr.

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Beta-Blockers May Boost COPD Survival Rates

Study challenges traditional dogma.

BY MARY ANN MOON
Elsevier Global Medical News

Beta-blockers appeared to improve survival in chronic obstructive pulmonary disease and decreased the risk of exacerbations by nearly 30%, according to a report in Archives of Internal Medicine.

Beta-blockers are known to improve survival in patients with a wide spectrum of cardiovascular diseases. But the benefits shown in an observational cohort study were surprising, the study investigators noted, because the drugs often are withheld in COPD patients because of fear they will promote bronchospasm and induce respiratory failure.

Even more surprising was the finding that beta-blockers benefited COPD patients who had no known cardiovascular disease, said Dr. Frans H. Rutten of the University Medical Center Utrecht, the Netherlands, and his associates.

"The traditional dogma … states that beta-blockers are contraindicated in COPD because of their presumed bronchoconstrictive properties and 'competition' with beta-2 agonists," the researchers said. In theory, however, those drugs could benefit COPD patients "by tempering the sympathetic nervous system or by reducing the ischemic burden," they added (Arch. Intern. Med. 2010;170:880-7).

The researchers assessed 2,230 patients aged 45 years and older (mean age 65 years) who attended 23 general practices in the vicinity of Utrecht from 1995 through 2005. Those patients either had COPD at the start of the study period (560 patients) or developed the disorder during the study (1,670 patients).

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INSIDE

Despite Panel Vote, FDA Okays Erlotinib

BY ELIZABETH MECHCATIE
Elsevier Global Medical News

Why did the Food and Drug Administration go against the advice of its own advisory panel to approve erlotinib tablets as a maintenance therapy for patients with locally advanced or metastatic non–small cell lung cancer?

Regulatory precedents, trial design, and lack of a comparative effectiveness standard all played a part in the unusual decision, according to Dr. Robert Justice, director of the Center for Drug Evaluation's Division of Oncology Drug Products.

The Oncologic Drugs Advisory Committee (ODAC) voted 12-1 against the FDA's giving a maintenance indication to erlotinib (Tarceva) at a meeting in December 2009. Members cited concerns about the modest effect in the study that manufacturer OSI Pharmaceuticals Inc. had submitted for approval, and the fact that only one study was available to support the new indication.

"After the December meet-

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CAP Drugs and *C. difficile* Risk

CAP • *from page 1*

Bruns and her coworkers sought to learn whether the regimens are also equal in associated risks of acquiring *C. difficile* colonization. That proved to be so.

Another key study finding was that the prevalence of *C. difficile* carriage at admission was 9.4%, as determined from stool cultures. "Most of these patients were asymptomatic, and therefore they constitute an important reservoir for the spread of disease, especially because skin contamination was also involved in several cases," Dr. Bruns said.

In a multivariate analysis, the parameters strongly associated with *C. difficile* carriage were the use of intravenous antibiotics for more than 7 days (associated with a 3.9-fold risk), hospitalization within the previous 3 months (4.1-fold risk), and tube feeding (4.4-fold risk).

The study has several major clinical implications, Dr. Bruns noted. One stems from the finding that no one antimicrobial proved to be associated with increased risk for emergence of *C. difficile*. That argues against banning any specific agent, such as fluoroquinolones or cephalosporins, for the treatment of CAP, as has been advocated.

Instead, according to Dr. Bruns, it makes more sense to implement strategies aimed at reducing overall antibiotic use in CAP patients, such as shorter treatment courses or an earlier switch from intravenous to oral agents. That approach has great potential, given that treatment of respiratory tract infections accounts for two-thirds of all antibiotic use worldwide, she continued.

The other take-away point is that patients hospitalized for treatment of CAP have a roughly 1-in-10 baseline prevalence of *C. difficile* carriage. Routine screening of CAP patients and institution of appropriate hygiene measures are worth considering, Dr. Bruns said.

Dr. Bruns disclosed having no financial conflicts regarding the CAP study. ■

COMMENTARY

Dr. Jeana O'Brien, FCCP, comments: *Clostridium difficile* colitis is a problem of increasing frequency and potential mortality occurring as a consequence of antibiotic therapy. Because community-acquired pneumonia is one of the most common indications for antibiotic therapy, appreciation for the factors that influence *C. difficile* colonization is important. This study found a baseline carriage rate for *C. difficile* of 9.4%. This has significance for developing screening programs to lessen the spread of this organism from asymptomatic hospitalized patients.

FDA Explains Erlotinib Decision

Erlotinib • *from page 1*

ing, there were extensive discussions within FDA regarding the application, and the ODAC's recommendation was carefully considered," Dr. Justice responded to an inquiry by this news organization after the approval announcement April 19.

One issue was regulatory precedent, he said. The agency had approved bevacizumab (Avastin) in a regimen for nonsquamous non–small cell lung cancer (NSCLC) based on a 20% reduction in the risk of death, compared with chemotherapy alone. It had also accepted pemetrexed (Alimta) as a maintenance treatment for nonsquamous NSCLC "based on a 30% reduction in the risk of death compared to no maintenance therapy and a 21% reduction in the risk of death in patients with all types of NSCLC," noted Dr. Justice.

"The reduction in the risk of death with erlotinib maintenance treatment compared to no maintenance therapy was similar at 19%," he said.

The double-blind, international SATURN (Sequential Tarceva in Unresectable NSCLC) trial that formed the basis of the erlotinib application had randomized almost 900 patients with locally advanced or metastatic NSCLC that did not progress during first-line, platinum-based chemotherapy.

Median progression-free survival was 2.8 months in patients who were given erlotinib as maintenance therapy vs. 2.6 months in a placebo arm—a statistically significant difference that represented a 29% reduction in risk of progression. Overall survival, a secondary end point, reached a median of 12 months with erlotinib and 11 months with placebo—again, a statistically significant difference.

A second issue was trial design, Dr. Justice said. He cited general agreement "that the optimal trial design would have been erlotinib maintenance vs. erlotinib at progression of disease." Although OSI has agreed to do such a study as part of its postmarketing commitment, he suggested that "this may not reflect what will actually happen in practice."

In the SATURN trial, he noted, 259 patients (57%) of the placebo group received second-line treatments for NSCLC vs. 47% of the erlotinib group. Among those who received second-line treatments in the placebo group, 59% received an FDA-approved therapy: erlotinib or gefitinib (Iressa) at first progression in 14%, docetaxel (Taxotere) in 31%, and pemetrexed in 14%.

The new indication endorses erlotinib tablets for maintenance treatment of patients with locally advanced or metastatic NSCLC that has not progressed after four cycles of platinum-based, first-line chemotherapy. Erlotinib is also approved as a second-line treatment for locally advanced or metastatic NSCLC and, in combination with gemcitabine (Gemzar), as a first-line treatment of locally advanced, unresectable, or metastatic pancreatic cancer. ■

Jane Salodof MacNeil contributed to this report.

COMMENTARY

Dr. W. Michael Alberts, FCCP, comments: The FDA decision is interesting to say the least. A 0.2-month (i.e., 6 days) improvement in progression-free survival, although statistically significant, is probably not clinically significant.

IN THIS ISSUE

CHEST PHYSICIAN

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

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

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

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Azithromycin Fizzled in CF Without *P. aeruginosa*

BY MARY ANN MOON
Elsevier Global Medical News

A 6-month course of azithromycin did not improve lung function in children and adolescents who had mild cystic fibrosis without *Pseudomonas aeruginosa* infection, according to a report in JAMA.

The antibiotic failed to achieve the primary end point of improvement in forced expiratory volume in 1 second (FEV_1) in a randomized controlled trial of 263 CF patients with mild disease, and it also did not decrease the need for intravenous or inhaled antibiotics or for hospitalization.

However, azithromycin achieved the exploratory end points of reducing pulmonary exacerbations, preventing initiation of other oral antibiotics, and increasing thin patients' weight and body mass index.

"Further studies of azithromycin are warranted to further investigate its potential use in this population," said Dr. Lisa Saiman of the pediatrics department at Columbia University, New York, and her associates (JAMA 2010;303:1707-15).

Azithromycin has both antimicrobial and anti-inflammatory activity, although its exact mechanism of action in CF is not yet known. It is recommended as chronic therapy for CF patients infected with *P. aeruginosa*, but its use in children who do not have *P. aeruginosa* has not been well studied.

Dr. Saiman and her colleagues assessed the drug in relatively healthy CF patients aged 6-18 years who had an FEV_1 of at least 50% predicted and had negative cultures for *P. aeruginosa*. The study subjects were treated between 2007 and 2009 at 40 centers accredited for CF care throughout the United States and Canada.

The patients were randomly assigned to receive 2-3 daily azithromycin tablets (131 patients) or a matching placebo (132 patients) for 168 days, and were closely followed for 196 days. Adherence in the treatment and placebo groups was 90% and 91%, respectively, and only eight participants (five on active treatment and three on placebo) withdrew from the study.

Azithromycin did not improve FEV_1, compared with placebo. Mean FEV_1 was 2.13 at baseline and 2.22 at 6 months with the active drug, compared with 2.12 at baseline and 2.20 at 6 months with placebo.

Similarly, azithromycin failed to improve other indicators of pulmonary function, such as forced vital capacity and forced midexpiratory flow rate. There were no differences between the treatment and placebo groups in the number of hospitalizations or the need for intravenous or inhaled antibiotics, the investigators said.

However, azithromycin decreased the number of pulmonary exacerbations by nearly half and the need for new oral antibiotics by 27%, compared with placebo. It was also associated with a significant weight gain (0.58 kg) and a significant increase in body mass index (0.34 units).

The drug was well tolerated, producing no increase in the rates of nausea, diarrhea, wheezing, and serious or nonserious adverse events, compared with placebo.

The only significant differences between the two groups in treatment-emergent pathogens were found with macrolide-resistant *S. aureus* and *Haemophilus influenzae*, Dr. Saiman and her associates said. Azithromycin users had 27% and 7% more emergence of those organisms, respectively, than did placebo participants.

CF Foundation Therapeutics Inc. funded the study, and Pfizer Inc. supplied the azithromycin and the placebo. Dr. Saiman reported ties to Pfizer Inc., maker of azithromycin, and Aridis Pharmaceuticals LLC, Bayer, CF Foundation Therapeutics Inc., Chiesi Pharmaceuticals Inc., Gilead Sciences Inc., Johnson & Johnson, Mpex Pharmaceuticals Inc., Novartis, SmithKline Beecham Inc., and Transave Inc. ■

COMMENTARY

Dr. Philip Marcus, MPH, FCCP, comments: It is difficult to make any additional conclusions from this study, other than to keep looking for agents that may improve lung function in these patients. The rates of resistant organisms in the azithromycin group are not surprising, and the ability of azithromycin to reduce infectious exacerbations was impressive.

Smoking Abstinence Inspired by Ban In Minnesota

BY HILLEL KUTTLER
Elsevier Global Medical News

BALTIMORE — Minnesota's passage of a statewide ban on smoking in bars and restaurants made smokers 4.1% more likely to quit, compared with pre-ban smokers.

The state's 2007 enactment of the Freedom to Breathe Act had a significant effect on abstinence, although it was not as strong a factor as a smoker having a high level of confidence in quitting (12.3%), degree of utilization of cessation programs (7.8%-18.4%), and use of nicotine replacement therapy (7.5%) and other medications, according to a poster presented at the annual meeting of the Society for Research on Nicotine and Tobacco.

The cross-sectional study surveyed 2,917 people who were enrolled in four tobacco cessation programs conducted by ClearWay Minnesota, a nonprofit smoking cessation research and public outreach group that was established following the landmark national tobacco settlement.

The study data reflect the period 2 years prior to the 2007 enactment and 1 year afterward. Data were collected at each participant's time of enrollment in the cessation program, and then each individual was surveyed 7 months later.

Prior to the legislation, 15 jurisdictions in the state had ordinances in place that prohibited smoking in indoor work sites; however, some jurisdictions exempted bars and restaurants.

The study, conducted by Professional Data Analysts (PDA), a Minneapolis firm, found that the statewide ban's influence was "diluted" in areas that already had a ban—for each year of living in such areas, smokers were 2.5% less likely to have the ban affect their decision to remain abstinent.

Julie Rainey, PDA's vice president, surmised that smokers who had already been living under a local ban had by then adapted their behaviors by stepping outside to smoke or by not smoking at all.

The statewide ban further affected social norms, because "smoking was more stigmatized," she said.

"People who were thinking of quitting and who couldn't go out to eat and smoke after work—maybe they thought, 'Now, I need to quit.' High confidence is a good motivator. … The triggers for relapse—sitting in a bar [and smoking]—aren't there, so it sustains their ability to quit," Ms. Rainey added.

Ms. Rainey reported having no conflicts of interest. ■

COPD Exacerbations Reduced

Beta-Blockers • *from page 1*

A total of 665 patients used beta-blockers, while 1,565 did not.

Overall, 686 patients in the study died. The all-cause mortality rate was 27% among those who used beta-blockers, a significantly smaller proportion than the 32% among subjects who did not use the drugs.

Similarly, 1,055 of the study's patients had at least one COPD exacerbation during follow-up. That included 43% of those who used beta-blockers, a significantly smaller proportion than the 49% rate in patients who did not use the drugs.

"To our knowledge, this is the first observational study that shows that long-term treatment with beta-blockers may improve survival and reduce the risk of an exacerbation of COPD in the broad spectrum of patients with a diagnosis of COPD," Dr. Rutten and his colleagues said.

"Cardioselective beta-blockers had larger beneficial effects on mortality than nonselective ones, but similar effects on risk of exacerbation of COPD," they added.

"Interestingly, the association of beta-blocker use with all-cause mortality and risk of exacerbation of COPD also remained in patients who were taking two or more pulmonary drugs or who were using inhaled beta-2 sympathicomimetics or anticholinergic agents," the investigators noted. "Therefore, inhaled pulmonary medication seems not to interfere with the results of beta-blocker use."

A recent meta-analysis of randomized trials has already shown that beta-blockers are well tolerated by COPD patients.

Adding the results of the observational study to those findings, it seems clear that "the time has come to confirm these results in a randomized controlled trial," according to Dr. Rutten and his associates.

The study findings "provide a rationale for the practicing clinicians to use beta-blockers (even noncardioselective ones such as carvedilol) cautiously in their patients with COPD who also have a coexisting cardiovascular condition for which a beta-blocker is required," noted Dr. Don D. Sin, FCCP, and Dr. S. F. Paul Man, FCCP, both of the University of British Columbia and Providence Heart and Lung Institute, Vancouver, in an editorial comment accompanying the report (Arch. Intern. Med. 2010;170:849-50).

"These data may be of great clinical relevance in COPD because cardiovascular diseases (and not respiratory failure) are the leading causes of hospitalization," Dr. Sin and Dr. Man noted. Cardiovascular diseases account for almost 50% of all hospital admissions, "as well as being the second-leading cause of mortality, responsible for 25% of all deaths, in patients with mild to moderate COPD," they wrote.

"By encouraging more liberal use of beta-blockers, we may be able to reduce the overall burden of disease and improve health outcomes in patients with COPD," they said.

Although Dr. Sin and Dr. Man agreed that a large randomized controlled trial is needed to confirm the results, they noted that the study "has turned the story of beta-blockers in COPD into a curious case of a foe becoming a potential friend to millions of patients with COPD worldwide."

No financial conflicts of interest were reported. ■

Neuraminidase Inhibitors Blunted Flu Complications

BY BRUCE JANCIN
Elsevier Global Medical News

VIENNA — It's well established that timely prescription of the neuraminidase inhibitors can reduce the duration of seasonal influenza symptoms; now there's good evidence that the drugs are effective in reducing influenza-related complications, too.

A meta-analysis of 11 placebo-controlled randomized trials—10 of them double blind—demonstrated that treatment with oseltamivir (Tamiflu) or zanamivir (Relenza) reduced the overall rate of flu-related complications by 26% in otherwise healthy patients with confirmed seasonal influenza, Dr. Matthew Falagas reported at the annual European Congress of Clinical Microbiology and Infectious Diseases.

The magnitude of benefit was substantially greater in high-risk patients than in those who were previously healthy. In the four trials totaling 475 high-risk patients, the rate of flu-related pneumonia, bronchitis, sinusitis, pharyngitis, and other complications was 8% in neuraminidase inhibitor–treated patients compared with 25% with placebo—for a 63% relative risk reduction, said Dr. Falagas, director of the Alfa Institute of Biomedical Sciences, Athens.

In the six trials totaling nearly 2,000 subjects in which administration of antibiotics was an end point, treatment with a neuraminidase inhibitor conferred a 23% reduction in the use of antibiotic therapy, he continued.

The overall reduction in flu-related complications in the group receiving antivirals was driven by a highly significant 50% decrease in the rate of acute otitis media. Indeed, the number of patients who needed to be treated (NNT) with a neuraminidase inhibitor to prevent one additional case of acute otitis media was 18.

There were consistent albeit weaker trends for lower rates of pneumonia, sinusitis, and the other flu-related complications in neuraminidase inhibitor–treated patients, none of which achieved significance. For example, the incidence of pneumonia in the placebo group was just 2%, and it was estimated that roughly 330 patients would need to be treated with a neuraminidase inhibitor to prevent one additional case of pneumonia.

Only four trials included mortality as a study end point. There were no deaths.

The 11-trial meta-analysis involved 5,315 randomized patients. Three of the trials were done in children; the rest were done in adults and adolescents. The magnitude of risk reduction with neuraminidase inhibitor therapy was similar in children and adults, and with oseltamivir compared with zanamivir.

Whether these meta-analysis results apply to 2009 H1N1 influenza–related complications as well is anybody's guess, in Dr. Falagas's view, because there are as yet no good randomized controlled trials of neuraminidase inhibitors in patients infected with H1N1 flu.

THE BENEFIT WAS SUBSTANTIALLY GREATER IN HIGH-RISK PATIENTS THAN IN PREVIOUSLY HEALTHY PATIENTS.

He deemed the safety profile of the drugs to be acceptable. There were no significant differences between the neuraminidase inhibitors and placebo in the rates or severity of any adverse events. Although the rate of nausea/vomiting was 13% in the neuraminidase inhibitor–treated patients compared with 6.4% with placebo, this trend fell shy of statistical significance. There was a 30% reduction in diarrhea with the neuraminidase inhibitors, but again this failed to reach significance. Of note, none of the trials recorded neuropsychiatric adverse events.

One audience member observed that in February the World Health Organization recommended that the neuraminidase inhibitors generally be reserved for high-risk patients in the setting of H1N1 flu. Does this new meta-analysis argue for using the drugs in otherwise healthy patients as well? he asked.

Not really, Dr. Falagas replied. The observed overall significant reduction in flu-related complications occurred as a result of the sharp drop in acute otitis media, which "is not a killer disease," he said. There was no significant reduction in the far more serious complication of pneumonia and no apparent treatment impact upon mortality. It is thus quite reasonable in Dr. Falagas's view to save these fairly costly drugs for high-risk patients, thereby minimizing problems with the development of antiviral resistance.

"Our data are not in disagreement with the WHO recommendation that neuraminidase inhibitors are best for high-risk patients," he stressed.

The meta-analysis was supported by the nonprofit Alfa Institute of Biomedical Sciences. Dr. Falagas reported having no financial conflicts. ■

Report: H1N1 Accounts for 99% of Influenza A in U.S.

BY KATE JOHNSON
Elsevier Global Medical News

The H1N1 virus has been virtually the only influenza virus circulating in the United States since it was first identified in April 2009, according to a report from Quest Diagnostics.

In an analysis of 195,000 lab tests performed at five of the company's laboratories, 99% of samples testing positive for influenza A were identified as H1N1, according to the report, titled "H1N1 Testing in America: H1N1 the Dominant Flu of 2009-2010."

"Our laboratory testing data also show an absence of influenza B viruses," the report noted. "These findings suggest the H1N1 virus has 'crowded out' other flu viruses."

The data confirm that two waves of H1N1 infection have occurred, with no evidence of a third wave, the report's authors explained.

The first wave, beginning in April or May of 2009, ended in mid-August 2009. The second wave started in late August/early September 2009, and peaked in late October 2009. "Our data suggest that the return of children to school in the fall was likely the trigger for a second wave of H1N1 infection," the report's authors wrote.

"This trend—where children are the first to suffer from a new influenza virus that then spreads to other age groups—is consistent with the behavior of prior flu viruses."

The report showed that H1N1 positivity was highest among children aged 10-14 years during both waves. Among that age group, the rate of H1N1-positive tests was 83% and 82% in the first and second waves, respectively. That compares with rates of 76% and 78%, respectively, in the 5- to 9-year age group. Among adults aged 25-49 years, the rates were 46% and 50%, respectively.

Since the end of the second wave, older children continue to have the highest positivity rates, compared with the other age groups, according to the report. In the 4 weeks ending April 15, 2010, 26% of tests were positive in the 10- to 14-year age group, compared with 18% among younger children and 13% among adults.

When analyzed by geographical region, positivity rates during the same 4-week period were highest (26%) in the southeastern United States (Alabama, Florida, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, and Tennessee). In the central-southern states (Arkansas, Louisiana, New Mexico, Oklahoma, and Texas), the rate was 22%. Those rates are in contrast to a combined 6% rate in the rest of the country.

The full report is available at www.QuestDiagnostics.com/HealthTrends. ■

Early Antibiotics Helped Stem COPD Exacerbations

Prompt administration reduced need for mechanical ventilation and decreased inpatient mortality.

BY MARY ANN MOON
Elsevier Global Medical News

Early use of antibiotics in patients hospitalized for acute exacerbations of chronic obstructive pulmonary disease improved the rate of treatment success, according to a report in the May 26 issue of JAMA.

In a large retrospective cohort study, prompt administration of antibiotics also reduced the need for mechanical ventilation and decreased inpatient mortality, said Dr. Michael B. Rothberg of the Center for Quality of Care Research at Baystate Medical Center, Springfield, Mass., and his associates (JAMA 2010;303:2035-42).

The findings suggest that routine use of antibiotics might be appropriate in this patient population, and should not be reserved only for those who have purulent sputum and increased sputum production or dyspnea, as is recommended in treatment guidelines, the investigators noted.

The evidence supporting those guidelines derives from "11 small randomized trials"—a "surprisingly limited" source for such a common condition. "Only 917 patients have been enrolled in randomized trials, and all but one of these studies were conducted before 1992," Dr. Rothberg and his colleagues said.

They studied antibiotic use for COPD exacerbations using data from 413 acute care facilities across the United States that participate in a program monitoring health care quality. The medical centers are primarily small- to medium-size nonteaching hospitals in urban areas.

The study sample comprised 84,621 patients. The median patient age was 69 years.

A total of 79% of patients received at least 2 consecutive days of antibiotic treatment beginning within 1 day of admission. The most commonly used drugs were quinolones (60% of patients); macrolides (38%) and cephalosporins (37%) also were administered frequently.

Compared with patients who were not given antibiotics, those who were given the drugs had a 13% lower rate of treatment failure (9.8% vs. 11.8%), a significant difference. Patients who received antibiotics also were significantly less likely to require mechanical ventilation (1.1%) than those who did not receive antibiotics (1.8%).

Patients who were given antibiotics also had significantly lower inpatient mortality (1.0%) and significantly lower rates of readmission within 30 days for COPD (7.9%) than did those who weren't given antibiotics (1.6% and 8.8%, respectively).

Patients given antibiotics had a significant 13% lower rate of treatment failure than those not given the drugs.

DR. ROTHBERG

"We found little evidence of harm associated with antibiotic prescribing—we noted no increase in allergic reactions and only a slight increase in readmissions with [*Clostridium*] *difficile* diarrhea," Dr. Rothberg and his associates said.

Moreover, the benefits of antibiotic therapy were consistent across all subgroups of patients.

"These two findings, that all patient groups seemed to benefit from therapy and that harms were minimal, support the notion that all patients hospitalized with acute exacerbations of COPD should be prescribed antibiotics," they said.

No financial conflicts of interest were reported. ■

Smoking Quit Rate Rose With Longer Therapy

BY SHERRY BOSCHERT
Elsevier Global Medical News

SAN FRANCISCO — An intensive smoking-cessation program helped 33% of 202 patients in drug treatment quit smoking, an intent-to-treat analysis found.

A high proportion of patients in treatment for substance use also smoke cigarettes and generally have a hard time quitting, with previous studies suggesting quit rates of 5%-12%, Dr. Milan Khara said at the annual meeting of the American Society of Addiction Medicine.

The study enrolled 252 patients who were in drug treatment programs in 8 weeks of group therapy for smoking cessation plus free pharmacotherapy for smoking cessation during the group therapy and for up to an additional 18 weeks, for a total program length of 26 weeks. Fifty patients who participated for 2 weeks or less were dropped from the analysis, said Dr. Khara of the University of British Columbia, Vancouver.

The overall quit-smoking rate of 33% in the intent-to-treat analysis was exceeded by a quit rate of 43% among 152 patients who completed the program, meaning they had at least 6 weeks of contact with smoking-cessation group counseling, individual counselors, or health care professionals in the program.

Among these completers, the quit rate was 51% in those who attended the 8 weeks of smoking-cessation group therapy and participated in after-care, compared with 18% of completers who only attended the 8 weeks of group therapy, reported Chizimuzo T.C. Okoli, Ph.D., also of the university, who conducted the study with Dr. Khara.

About 80% of people in drug treatment programs smoke tobacco. "We often believe that these patients don't want to quit smoking," Dr. Khara said. But other studies have shown that 44%-80% of patients in drug treatment express interest in quitting.

Previous results for smoking-cessation programs during drug treatment range from quit rates of 23% at 1-week follow-up to 5% at 6-month follow-up, or 12% in a meta-analysis of 18 studies, he noted. "It may be that we need a more intensive approach than an 8- or 10-week program," Dr. Khara said.

The current study enrolled patients at three sites who were aged 19 years or older, who had a history of a substance use disorder and/or mental illness, and who were financially disadvantaged. A 1-hour intake assessment included measurement of the carbon monoxide content in expiration.

After each of the structured, syllabus-based group therapy sessions, patients had one-on-one assessments with a physician or nurse and received smoking-cessation medication if needed, using one or more of the six first-line medications available in Canada. Clinicians were allowed to consider off-label prescribing, including higher doses, drug combinations, and extended durations of use. In all, 82% of patients received nicotine replacement therapy alone, 6% received oral medication alone, and 12% received both.

Most patients (89%) had a primary substance use disorder, primarily involving alcohol (33%) or cocaine (27%), with 12% dependent on heroin or other opiates, 11% dependent on marijuana, and 6% dependent on methamphetamine or related drugs. Primary mental health disorders in 65% of patients included mood disorders in 45%, anxiety disorder in 14%, and psychotic disorder in 6%.

The 11% of patients diagnosed with mental illness but not substance dependence were less likely to quit smoking than were patients with both disorders or with substance dependence alone. Those patients with lower expiratory carbon monoxide levels at baseline were more likely to complete the program and to quit smoking. Using both nicotine replacement therapy and an oral medication increased the likelihood of completing the program, and attending more of the program sessions increased the odds of quitting.

The study defined smoking cessation as patients reporting having not smoked tobacco in the previous 7 days, confirmed by a carbon monoxide level of less than eight parts per million in expired air.

Patients averaged age 48 years and said they had started smoking at a mean age of 14 years. They smoked an average of 22 cigarettes per day at baseline, with a mean expiration carbon monoxide level of 23 parts per million.

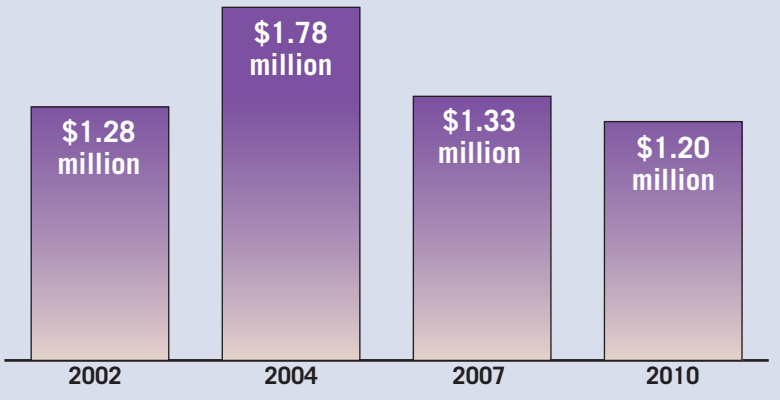
Dr. Khara has received funding from or been a consultant for Pfizer and Johnson & Johnson, which make smoking-cessation medications. Johnson & Johnson and divisions of the Canadian government funded provision of the medications in the study. ■

COMMENTARY

Dr. Philip Marcus, MPH, FCCP, comments: This study shows that even "hardcore" smokers can stop smoking. However, it remains to be seen if the results at 7 days can persist for a longer period of time consistent with sustained abstinence and a better marker of success. This study also reinforces the relationship between substance abuse, mental illness, and cigarette smoking.

DATA WATCH

Annual Hospital Revenue Generated per Pulmonologist Down Nearly 10% Since 2007



Note: Based on survey responses from 114 U.S. hospitals. Includes hospital-employed physicians and those in independent practice.
Source: Merritt Hawkins 2010 Physician Inpatient/Outpatient Revenue Survey

ELSEVIER GLOBAL MEDICAL NEWS

Prophylactic Antibiotic Decontamination Cut ICU Mortality

BY BRUCE JANCIN
Elsevier Global Medical News

VIENNA — Selective decontamination of the oropharynx and digestive tract are prophylactic antibiotic regimens that proved similarly effective at reducing mortality in ICU patients in a large randomized trial.

Both strategies decreased the rate of ventilator-associated pneumonia and other respiratory tract infections in the ICU setting, thereby reducing mortality.

Among the 5,939 patients with an anticipated mechanical ventilation duration of more than 48 hours at 13 Dutch ICUs participating in the study, the 28-day mortality rate of 27.5% in controls assigned to standard therapy was reduced by an adjusted absolute 3.5% in the selective digestive tract decontamination group and similarly by an absolute 2.9% with selective oropharyngeal decontamination, Dr. Anne Marie de Smet reported at the annual European Congress of Clinical Microbiology and Infectious Diseases.

Selective oropharyngeal decontamination may be the more attractive of the two strategies. This approach employs a smaller volume of topical antibiotics and doesn't include prophylaxis with intravenous cephalosporins, which could pose more risk of promoting antibiotic resistance in the long term.

Moreover, the cost of the components for selective oropharyngeal decontamination was $1 per day. The more comprehensive selective decontamination of the digestive tract costs $12 per day, added Dr. de Smet, an intensivist at University Medical Center Utrecht, the Netherlands.

The selective digestive tract decontamination regimen entailed 4 days of intravenous cefotaxime along with a topical paste of tobramycin, colistin, and amphotericin B in the oropharynx and stomach. Selective oropharyngeal decontamination consisted of topical application of the same antibiotic paste to the oropharynx.

Routine use of these prophylactic antibiotic strategies in ICUs has been controversial. These strategies are not recommended in any major practice guidelines due to a lack of strong supporting evidence in the form of large, multicenter, randomized trials. Dr. de Smet and her colleagues sought to rectify this shortcoming.

In a multivariate logistic regression analysis with adjustment for Acute Physiology and Chronic Health Evaluation (APACHE II) scores, age, gender, and other potential confounders, selective digestive tract decontamination was found to provide a 13% relative risk reduction in 28-day mortality compared with standard ICU care, while selective oropharyngeal decontamination offered a similar 11% reduction. The number needed to treat with selective oropharyngeal decontamination instead of standard care in order to prevent one additional death by day 28 was 34. The number needed to treat with selective digestive tract decontamination was 29, she said.

SELECTIVE DIGESTIVE TRACT DECONTAMINATION YIELDED A 13% RELATIVE RISK REDUCTION IN 28-DAY MORTALITY VS. STANDARD ICU CARE.

During roughly 20,000 patient-days of follow-up for each of the three treatment groups, periodic surveillance cultures demonstrated that both methods of selective decontamination were associated with lower prevalence of antibiotic-resistant bacteria in the respiratory tract, compared with standard therapy. The number needed to treat with selective digestive tract decontamination rather than standard care in order to prevent one additional patient from acquired respiratory tract colonization with a highly resistant microorganism was 18. For selective oropharyngeal decontamination, it was 22. Neither antibiotic prophylaxis group had an increased risk of acquired respiratory tract colonization with tobramycin-resistant Gram-negative rods.

The selective digestive tract decontamination group had a 59% reduction in the rate of acquired bacteremia with a highly resistant microorganism compared with controls, and a 67% reduction in candidemia. Rates in the selective oropharyngeal decontamination group and controls weren't significantly different.

Selective digestive tract decontamination was associated with a lower prevalence of antibiotic-resistant bacteria in rectal swabs. The total use of systemic antibiotics was 12% less for the selective digestive tract decontamination group compared with controls, and 10% less in the selective oropharyngeal decontamination group.

Dr. de Smet disclosed having no financial conflicts regarding the multicenter study, which was sponsored by a Dutch trialists' organization. ■

Preemptive Azithromycin Paid Off in Lung Transplants

BY SHARON WORCESTER
Elsevier Global Medical News

CHICAGO — Azithromycin is safe and appears to be very effective for preventing bronchiolitis obliterans syndrome when given preemptively following lung transplantation, according to a prospective, double-blind, randomized Belgian study of 83 patients.

Treatment with azithromycin was associated with a 70% reduction in the prevalence of BOS compared with placebo, Dr. Robin Vos reported at the annual meeting of the International Society for Heart and Lung Transplantation.

Azithromycin was being evaluated for use in improving pulmonary function in chronic rejection, since its efficacy in attenuating the rate of progression of BOS has been suggested in several case series.

The current findings, derived from an off-label use of the medication, suggest it has value as a preventive measure, Dr. Vos of University Hospitals Leuven, Belgium, reported via WebEx.

Subjects in the study included all lung and heart/lung transplant patients treated at a single center between July 2005 and December 2007 who met inclusion criteria. All patients were treated with the standard of care plus azithromycin or placebo post transplant. Azithromycin was dosed at 250 mg daily for 5 days, followed by 250 mg every other day until the end of the study period.

Analysis showed that the treatment and placebo groups had similar mortality, probably because all patients who developed BOS during the study were switched to open-label azithromycin treatment based on previous trials indicating that this intervention delays BOS progression, Dr. Vos noted.

"If we take a look at the primary outcome measures [BOS stage I or higher and mortality], we can see there was significantly better BOS-free survival in the azithromycin patients than in placebo patients. In fact, the prevalence of BOS at 2 years was reduced from 44% to 12%," he said.

Clinical characteristics of the patients were similar in the treatment and placebo groups, and no significant differences were seen in secondary outcome measures, including acute rejection, severe acute rejection, and infections, according to Dr. Vos.

BOS was detected primarily by deterioration of forced expiratory volume in 1 second (FEV_1) over time after the transplant procedure.

The evolution of FEV_1 over time was significantly better in the treatment group than in the placebo group. In more than half of the 5 azithromycin patients and 18 placebo patients who developed BOS and were switched to open-label azithromycin, FEV_1 improved at least 10%, primarily in the placebo patients.

Two of the five patients who were given azithromycin experienced improvement during the open-label phase of the study, but later admitted that they had not complied with the treatment protocol during the double-blind phase.

"The results of this study may perhaps lead us to use azithromycin as a standard of care for the prevention of BOS in heart and lung transplantation," Dr. Vos concluded.

He noted that the investigation had no commercial sponsor, and that there were no relevant financial or other relationships to disclose with regard to his presentation. ■

COMMENTARY

Dr. Joseph Barney, FCCP, comments: Azithromycin seems to have significant potential in the treatment of bronchilitis obliterans syndrome in lung transplant patients outside of its antibiotic mechanism of action. Significant research efforts are underway to understand the anti-inflammatory properties of azithromycin in many pulmonary disorders, including BOS. Although larger multicenter trials are needed to clearly demonstrate clinical efficacy against BOS, there seems to be a durable effect that is recapitulated in different patients when it comes to preventing the onset of airflow obstruction in lung transplant patients.

Gender Predicted Stroke Risk in Sleep Apnea

In men, there was a strong association between stroke and apnea-hypopnea index.

BY KERRI WACHTER
Elsevier Global Medical News

An obstructive apnea-hypopnea index associated with more than 15 events per hour increased the risk of ischemic stroke by 30% in men in the Sleep Heart Health Study of nearly 5,500 adults.

Risk began to increase at rates above 5 events per hour, and each unit of increase in the obstructive apnea-hypopnea index was estimated to increase the hazard ratio by 6%. The index was defined as the average number of obstructive apneas plus hypopneas per hour of sleep.

The apnea-hypopnea index was not associated with stroke risk in women after adjustment for other risk factors such as age, diabetes, hypertension, and smoking history.

Further, the researchers found that a higher sleep arousal index was associated with a reduced incidence of stroke in women, such that women who had an arousal index of greater than 12, had a 40%-60% decreased hazard ratio for ischemic stroke, compared with women with a lower arousal index.

The authors suggested several possible explanations for the gender differences, including statistical power for events in women.

The study addresses some of the shortcomings of previous studies in which the "temporal associations between stroke and OSA [obstructive sleep apnea] could not be determined," wrote Dr. Susan Redline and her coinvestigators (Am. J. Respir. Crit. Care Med. 2010 [doi:10.1164/rccm.200911-1746OC]).

The Sleep Heart Health Study (SHHS) is a community-based, prospective cohort study of the cardiovascular consequences of OSA. Quality data were analyzed on 5,422 men and women at least 40 years of age. At the baseline SHHS examination, participants filled out questionnaires for sleep habits, general health, and medication use. At the same time, researchers measured height, weight, and blood pressure and obtained overnight unattended polysomnography. At intervals of 3-5 years after the baseline polysomnogram, a survey regarding diagnosis of and treatment for OSA was performed. Subjects were followed for an average of 8.7 years.

Participants were followed until a first stroke occurred between the date of the polysomnogram and the final censoring date. Those who did not develop a stroke were censored at the date of death or last contact. Participants who developed strokes were censored at the time of the stroke occurrence.

IN WOMEN, THE APNEA-HYPOPNEA INDEX WAS NOT ASSOCIATED WITH STROKE RISK AFTER ADJUSTMENT FOR OTHER RISK FACTORS.

The cohort consisted of 2,462 men and 2,960 women without a history of stroke, and who were untreated for OSA with pressure therapy at the baseline exam. During follow-up, a total of 193 ischemic strokes were observed (85 in men; 108 in women). The estimated incidence rates were 4.4 ischemic strokes per 1,000 person-years in men and 4.5 in women.

Incident stroke was associated with increasing age and systolic blood pressure, use of antihypertensives, and atrial fibrillation. In women, stroke was higher in blacks and lower in Native Americans, and was marginally associated with diabetes. However, stroke was not associated with body mass index, smoking status, or alcohol use in men or women.

In men, the unadjusted increased odds of incident stroke for an individual with OSA, compared with someone without OSA, was 2.26, which is approximately equivalent to the increased risk associated with a 10-year increase in age (odds ratio 2.37), noted Dr. Redline, who is the academic program director of the Center for Clinical Investigation at Case Western Reserve University, Cleveland.

A lower odds ratio for stroke was observed in women (1.65), which is roughly equivalent to the risk of stroke associated with diabetes in this cohort (1.79).

The National Heart, Lung, and Blood Institute funded the study. One author reported that he is a coinventor of the BiPAP device, manufactured by Philips Respironics Inc., and is a scientific consultant to the company. Another author reported receiving honoraria from Respironics. ■

UARS: A Kind of Sleep-Disordered Breathing

BY M. ALEXANDER OTTO
Elsevier Global Medical News

SEATTLE — Even without apnea, snoring, or other obvious signs of sleeping problems, sleep can be disturbed enough in children to cause attention-deficit/hyperactivity disorder–like symptoms during the day, said Dr. Maida Chen of the pediatric sleep center at Seattle Children's Hospital.

Sleep specialists have carved out a diagnostic niche called upper airways resistance syndrome (UARS) for children (and adults) who don't have overt sleep apnea and may not even snore but still cannot get a good night's sleep.

UARS IS DEFINED BY SLEEP FRAGMENTATION WITHOUT EPISODES OF APNEA, EITHER WITH OR WITHOUT MILD GAS-EXCHANGE ABNORMALITIES.

The term captures the middle ground between obstructive sleep apnea and primary snoring, Dr. Chen said at a conference sponsored by the North Pacific Pediatric Society.

Sleep experts coined the term about 20 years ago when they realized they were missing a group of patients who suffered from disturbed sleep. "A normal apnea-hypopnea index [during sleep studies] did not always correlate with doing okay during the day," she said. "But people are not as aware of UARS, because it is not as well quantified by research" as obstructive sleep apnea is.

Sleep apnea, snoring, and UARS are all different manifestations of what Dr. Chen referred to as sleep-disordered breathing. The conditions have one characteristic in common: a narrowing of the upper airways during sleep that can be caused by enlarged adenoids and tonsils, airway inflammation, obesity, and other problems. Whatever the disorder's cause, fragmented sleep in children, as in adults, can cause daytime dysfunction.

It's important during any office visit that a health care practitioner assess how children are functioning during the day and sleeping at night. "Less-than-optimal academic performance or behavior" is the reason that most children are referred to the sleep clinic at Children's Hospital, Dr. Chen said.

Hyperactivity and inattention are early signs of sleep trouble in younger children. Fatigue is typically a later finding, although it can be the primary symptom of sleep apnea in older, obese children. Obstructive sleep apnea also has been associated with hypertension, impaired growth, and other significant problems.

Abnormal overnight pulse oximetry has high predictive value for sleep apnea, but normal readings do not rule out sleep-disordered breathing, Dr. Chen said. There is less information regarding the effects of snoring and UARS, because these conditions have not been studied as intensely as sleep apnea.

UARS is defined by sleep fragmentation without episodes of apnea, either with or without mild gas-exchange abnormalities. Most children with UARS snore, but not all of them do; they may just breathe loudly or through their mouths. Nasal airflow tends to be abnormal, as well.

But UARS is still being defined. "We need more research," Dr. Chen said.

"Snoring is abnormal in every circumstance," and it signals upper airway resistance at some level, Dr. Chen said. Snoring falls within the spectrum of sleep-disordered breathing if it is present more than 3 nights a week for more than a month.

An overnight polysomnogram is the preferred method for diagnosing sleep issues, Dr. Chen said. Brain waves, airflow, breathing effort measures, number of apneic episodes per hour, and movement are among the things monitored during the night.

Treatment depends on cause. In most children, adenotonsillectomy resolves obstructive sleep apnea and, presumably, UARS and snoring in children, she said. Treating underlying airway inflammation can help, too.

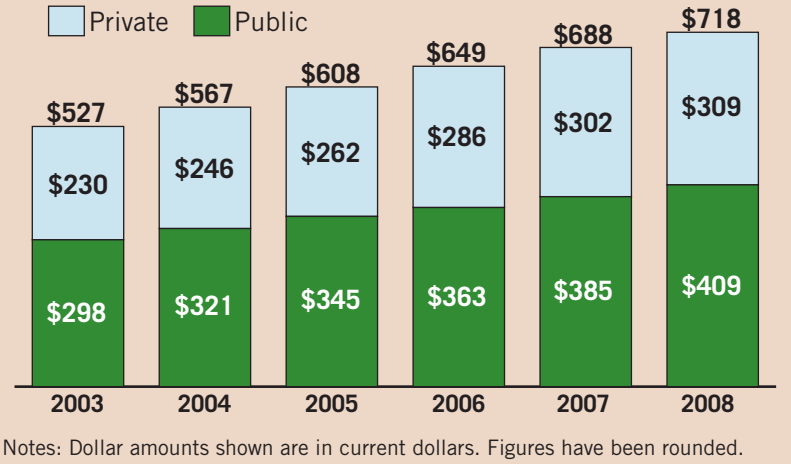
Sleeping inclined or on the side can help in mild cases. A tennis ball can even be taped to the back of a child's pajama top to keep the child from sleeping on his or her back. Positive airway pressure is another option. It is most commonly used—along with inclined sleeping—in obese children and children with underlying medical conditions.

Sometimes children will grow out of the problem; as they grow, so do their upper airways.

Dr. Chen reported no conflicts of interest. ■

DATA WATCH

Hospital Care Expenditures Topped $700 Billion in 2008



Notes: Dollar amounts shown are in current dollars. Figures have been rounded.
Source: Centers for Medicare and Medicaid Services

ELSEVIER GLOBAL MEDICAL NEWS

BY PAUL A. MARKOWSKI, CAE

FROM THE CEO

Responding ...

In my April message, I informed you that we would be proceeding with a member survey as one piece of data needed to effectively do our strategic planning and budgeting. An overwhelming number of you took the time to provide us with a solid baseline of information—information we had not collected in many years. I want to thank those of you who responded. As you are well aware, health care today is data-driven, and data comprise the basis for making sound decisions.

When the Board of Regents met in April for strategic planning, members were presented with the results of the member survey, along with an environmental snapshot disclosing forecasts for ACCP 2010 from each of the functional units of the College.

AS YOU READ THIS IN THE JUNE ISSUE OF *CHEST PHYSICIAN*, WE ARE WELL ON OUR WAY, AS A STAFF, TO REALIGNING OURSELVES FUNCTIONALLY.

These two pieces of information generated a very robust and interactive discussion by members of the Board, which led to an executive summary of the discussion and findings that was given Board approval to move forward. Our staff is now applying key tactics and metrics to the strategic plan in parallel with an aligned budget. The final product will be in front of the Board of Regents for approval at the June 2010 meeting. The strategic plan and budget will set the next course for the ACCP beginning July 1, 2010.

One of the most important things for the ACCP, and for other professional associations today, is to maintain alignment with our strategic plan in a constantly shifting environment. An associated key point is to make sure that our "team," our staff, is able to maximize its skills and remain an integral part in providing you with the best service and educational products.

As you read this in the June issue of *CHEST Physician*, we are well on our way, as a staff, to realigning ourselves functionally. Some of the functional areas have been combined in order to provide more resources to those strategic areas that you pointed out were the heart and soul of the ACCP. As you can imagine, aligning our staff and preparing the strategic tactics, metrics, and budget, all within a 6-week period, has been a daunting task.

I can't tell you how much I appreciate the support of the leadership and Board of Regents.

But most of all, I am so appreciative of our staff members for their support and long hard hours spent in preparation for the June Board of Regents meeting. They did it all, while keeping the business of the ACCP going and on-target.

The next time you speak to one of them, share an e-mail, or visit with them at a committee meeting, please acknowledge and thank them for their efforts. It is our staff that is your greatest asset.

While there has been a lot of change and probably more to come, the most important thing to tell you is what hasn't changed, that being the commitment of leadership and staff to ensure that you continue being proud of your ACCP.

One other thing that hasn't changed is the conflicting weather during my travels. High winds and storms prevailed during the entire April Spring Board of Regents meeting in Ft. Lauderdale, Florida. Can you believe it? You probably can! ■

MR. MARKOWSKI *is Executive Vice President and Chief Executive Officer of the American College of Chest Physicians.*

Critical Care Commentary

Early Mobilization in the ICU: Improving Patient Outcomes

Patients in the ICU are frequently exposed to deep sedation and prolonged immobility, with limited access to rehabilitation services (Needham. *JAMA*. 2008;300[14]:1685). This patient care paradigm was developed out of concern for physiologic instability, potential dislodgement of medical equipment, and patient discomfort.

However, the detrimental effects of bed rest are well-described, including insulin resistance, thromboembolic disease, disuse atrophy of muscles, and joint contractures (Brower. *Crit Care Med*. 2009;37[suppl 1]:S422). Survivors of critical illness may experience severe and prolonged muscle weakness and impairment in physical function (Herridge et al. *N Engl J Med*. 2003;348[8]:683). As ICU mortality rates continue to decline, the paradigm for ICU care must shift to reducing survivors' long-term morbidities.

Early mobilization in the ICU seeks to reduce post-ICU physical morbidities through focused interventions that begin as soon as hemodynamic and respiratory problems have stabilized, frequently within the first 48 h after ICU admission. Growing numbers of studies demonstrate that early mobilization in the ICU is safe, feasible, and beneficial in improving patients' short-term physical function (Schweickert et al. *Lancet* 2009;373[9678]:1874; Korupolu et al. *Contemp Crit Care*. 2009;[9]:1). Consequently, many ICUs are becoming interested in adopting early mobility programs and changing the culture of their ICU to include a model of care focused on improving patients' long-term outcomes after ICU discharge.

Establishing a Multidisciplinary Team

Development of a successful ICU early mobility program requires a strong multidisciplinary team with a shared vision and common goals. While the ICU typically functions as a multidisciplinary environment, the ICU team must expand to include rehabilitation clinicians. This extended group includes physical and occupational therapists, sleep language pathologists, and physical medicine and rehabilitation physicians.

Learning to effectively work together requires designation of team representatives for each of the involved specialties, followed by interdisciplinary education and training, understanding each other's roles, and clarification of the appropriate indications for early mobilization in the ICU. Regular communication and team meetings are key to understanding and addressing barriers to early mobilization of patients in the ICU.

Finally, we recommend developing a screening algorithm for early mobilization (Fig 1) to assist ICU staff in identifying eligible patients and highlighting safety issues.

Equipment and Devices

Specific equipment and devices help ensure the safety and efficiency of early mobility activities, especially for patients supported by mechanical ventilation.

At minimum, a portable cardiac monitor and pulse oximeter, wheeled IV pole, walker, and wheelchair are necessary (Fig 2). Mechanical ventilation can be provided through a number of methods, including the use of (1) the patient's own ventilator under battery power; (2) a portable ventilator commonly used for intrahospital patient transport; or (3) a bag-valve mask with supplemental oxygen. Custom-designed biomedical devices have been created to easily and safely carry all required equipment and devices on a single wheeled pole and decrease the number of personnel required to provide mobility for a patient (Needham. *Crit Care Med*. 2009;37[10 suppD]:S436). Videos demonstrating one such device, along with early mobilization of mechanically ventilated patients and patient interviews, can be found at www.hopkinsmedicine.org/OACIS.

Additional rehabilitation-specific equipment and technology may play an important role for patients in the ICU. Neuromuscular electrical stimulation (NMES) therapy causes repeated muscle contractions and can be used even when patients are deeply sedated or comatose. NMES may help reduce muscle atrophy and improve weakness and physical function (Zanotti et al. *Chest*. 2003;124[1];292).

In addition, specialized bedside cycle ergometers (with or without NMES) allow passive leg movement in sedated or comatose patients and active muscle training in awake patients while lying supine in bed. This cycling technology can serve as an adjunct to physical therapy and improve physical function by hospital discharge (Burtin et al. *Crit Care Med*. 2009;37[9]:2499). Interactive participation with video game systems may also allow progression of activity from a seated position to a standing position, where dynamic balance, coordination, and weight-bearing activities can be initiated.

Challenges

Despite the many benefits of early mobility, challenges both within and outside the ICU must be overcome to create a successful program. First, ICU culture must change to promote patients being awake and moving. Second, an adequate, dedicated rehabilitation staff is required, which frequently requires negotiations with hospital leaders and administrators, including a cost-benefit analysis (eg, cost of early mobilization program vs savings achieved in decreasing hospital length of stay) (Korupolu et al. *Contemp Crit Care*. 2009;6[9]:1). Third,

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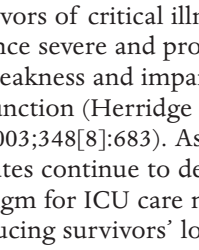
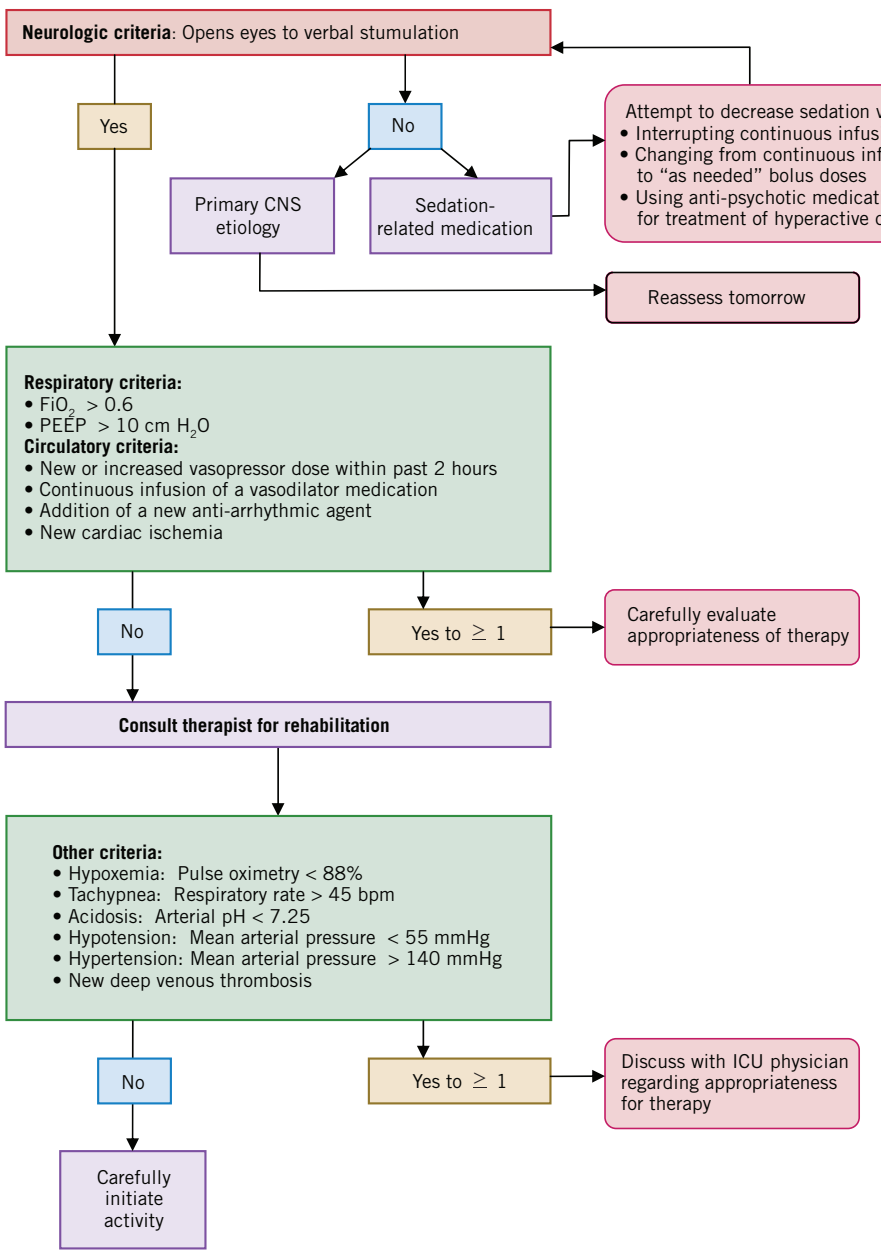


DR. NEIL HALPERN, FCCP
Section Editor,
Critical Care Commentary

Figure 1. A screening algorithm for patient mobilization in the ICU.



Abbreviations: FiO_2=fraction of inspired oxygen; PEEP = positive end-expiratory pressure.
From Korupolu R, Gifford JM, Needham DM. Early mobilization of critically ill patients: reducing neuromuscular complications after intensive care. *Contemp Crit Care*. 2009;6(9):1. Reproduced with the permission of Lippincott Williams & Wilkins.

Gulf Thoracic 2010: Promoting Pulmonology Partnerships Around the Globe

BY DR. SUHAIL RAOOF, FCCP; DR. DAVID GUTTERMAN, FCCP; AND DR. KALPALATHA K. GUNTUPALLI, FCCP

The ACCP recognizes the importance of global medical education and collaboration. This is especially important in light of people migrating to different countries, infectious diseases crossing regional boundaries, and the importance of sharing clinical practice patterns and research globally.

Several months ago, the ACCP received a proposal from the Gulf Thoracic Society to partner with them in the first ACCP/Gulf Thoracic conference. It was agreed that such a conference would be mutually beneficial to both societies. It would allow collaboration between the ACCP and an important partner in the Middle East; help identify pulmonologists and intensivists from the Middle East region interested in working closely with the College; and promote partnership with industry from that region.

Five ACCP members participated in the First Annual Gulf Thoracic Society Meeting, held March 17-20, 2010. These physicians included Dr. Kalpalatha K. Guntupalli, FCCP, President; Dr. David Gutterman, FCCP, President-Elect; Dr. Suhail Raoof, FCCP, President-Designate; Dr. David Naidich, FCCP; and Dr. Nick Hanania, FCCP.

The educational content of the conference was excellent. There were outstanding workshops on pulmonary function testing interpretation, chest imaging, and interventional pulmonology. Sessions were organized under several tracks, including COPD, pleural disorders, pediatric lung diseases, interstitial lung disorders, and lung cancers. Many faculty members were invited to present "Meet the Professor Sessions." Several local speakers did an outstanding job in presenting information on diseases more widely prevalent and pertinent to the Gulf area. Many other internationally renowned speakers contributed to the success of the conference. ACCP participants were given a very prominent place in the conference.

Courtesy ACCP and Gulf Thoracic Leadership

ACCP and Gulf Thoracic leadership took part in the First Annual Gulf Thoracic Society Meeting, held March 17-20, 2010.

The conference served several important purposes. It brought the ACCP group close to the Gulf Thoracic Society leadership; it identified active people who were joint members of the Gulf Thoracic Society and the ACCP; and it provided a venue for regional physicians to learn more about ACCP activities and education programs. Proposals for further collaborative work and joint conferences were discussed, and meetings were held with industry to explore venues of common interest, support of educational activities, and enhanced attendance at ACCP annual meetings.

The meeting was very well attended, with more than 1,000 participants from all over the world. The atmosphere was extremely congenial and conducive to major collaborative work.

The experiences gained from this conference put into perspective the needs of international physicians from that region, as well as the difficulties they encounter in attending our annual meetings. Utilizing this model, similar efforts are being pursed in other regions of the world identified as strategic areas for the College.

The ACCP booth was busy, secured many new members, and showcased our upcoming CHEST 2010 meeting and many of our educational products. Also representing the ACCP, Executive Vice President and CEO, Mr. Paul Markowski, and Ms. Marisa McCarren greeted meeting attendees and fostered lasting relationships with physicians from the region.

Finally, the College would like to extend its warmest appreciation to the local sponsors: Dr. Al-Hajjaj, Dr. Al Ameri, Dr. Dalaan, Dr. Mahboub, Mr. Alorainy, Dr. Atul Mehta, and others for their enthusiasm for future collaborative programs. The ACCP is grateful for their hospitality, collegiality, and friendship. ■

Continued from previous page

during daily ICU functioning, team leaders must regularly communicate to identify suitable patients for mobilization, and to coordinate, schedule and prioritize rehabilitation in conjunction with other ICU activities. Moreover, the complexity of patient problems in the ICU, including physiologic instability, delirium, and the presence of multiple medical devices, requires appropriate training, skills, and collaboration of a full multidisciplinary ICU and rehabilitation team.

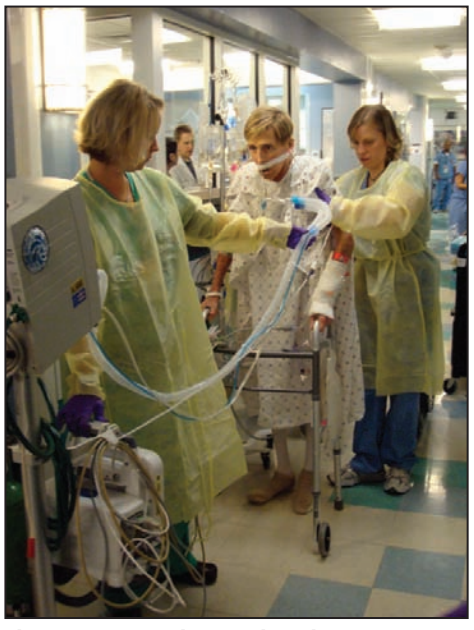


Figure 2. Therapists assist with early mobilization of a mechanically ventilated COPD patient in the Johns Hopkins Hospital MICU. (JAMA. 2008;300[14]:1685-1690. Copyright (2008) American Medical Association. All rights reserved.)

Conclusion

ICU survivors frequently experience weakness and impairment in physical function, which can be severe and long-lasting after hospital discharge. Immobility is an important contributing factor to these morbidities.

Early mobilization in the ICU plays a crucial role in helping improve patients' physical health after critical illness. Expanding the ICU multidisciplinary team to include physical medicine and rehabilitation clinicians, and changing ICU culture and teamwork to embrace early mobilization can make important contributions to patients' recovery after critical illness. ■

Jennifer M. Zanni, PT, MSPT; Dr. Radha Korupolu; and Dr. Dale M. Needham, PhD. From the Department of Physical Medicine and Rehabilitation (JMZ) and Critical Care Physical Medicine and Rehabilitation Program (JMZ, RK, DMN), Johns Hopkins Hospital; OACIS Group, Division of Pulmonary and Critical Care Medicine, Johns Hopkins University (RK, DMN); and Department of Physical Medicine and Rehabilitation (JMZ, DMN), Johns Hopkins University, Baltimore, MD.

ACCP Product of the Month

A Physician's Perspective®

A Physician's Perspective is an online video forum providing free, periodic postings, expert reviews, opinions, and highlights on clinical information that is relevant to the chest professional health-care community.

Captured during CHEST annual meetings, these video interviews pertain to the issues observed and practiced by chest physicians and health-care professionals every day.

To access the Physician's Perspective page, please visit www.chestnet.org/accp/physicians-perspective.

PCCU Becomes PCCSU: New Name Reflects All Three Specialties

May

▶ **Management of Acute Liver Failure in the ICU.** *By Dr. Mark D. Siegel, FCCP; and Dr. Shyoko Honiden*

▶ **Treatments To Alter the Natural History of COPD.** *By Dr. Bartolome R. Celli, FCCP; Dr. Miguel J. Divo; and Dr. Victor M. Pinto-Plata, FCCP*

June

▶ **Outcomes Obtained With Pulmonary Rehabilitation.** *By Suzanne Lareau, RN, MS; and Dr. Linda Nici*

▶ **Invasive Procedures for Emphysema.** *By Dr. Armin Ernst, FCCP; and Dr. Devanand Anantham, FCCP*

PCCSU
PULMONARY, CRITICAL CARE, SLEEP UPDATE

www.chestnet.org/accp/pccsu

A Personal Recommendation: Top Five Places To Visit in Vancouver

DR. ROBERT D. LEVY, FCCP

When visiting a city and looking for ideas on what to see or do, there's nothing quite like advice from a local resident. Meet Dr. Robert D. Levy, FCCP. In addition to serving as Co-Chair for the CHEST 2010 Scientific Program Committee, Dr. Levy is Professor of Medicine, Respiratory Division, University of British Columbia. He calls Vancouver his adopted home and says, "What a great choice!" Check out his top picks and personal commentary about places you should visit while in Vancouver for CHEST 2010.

1. Granville Island: "A fun market with lots of places to eat—worth visiting for the buskers alone. Add to the fun and arrive by Aquabus!" *www.granvilleisland.com*

2. Vancouver Art Gallery: "A great central location—only a 10-minute walk from the convention center. It's worth the visit to see Emily Carr's great collection." *www.vanartgallery.bc.ca/index.html*

3. Stanley Park: "Stanley Park offers a spectacular bike ride, run, or walk and is mere steps from the convention center." *vancouver.ca/parks/parks/stanley*

4. Museum of Anthropology: "This isn't just any old museum. In 1976, architect Arthur Erickson created a classic native post-and-beam-style structure out of poured concrete and glass to house one of the world's finest collections of West Coast native art. It's a 15-minute taxi ride from the convention center and also a great chance to visit the spectacular University of British Columbia campus." *www.moa.ubc.ca*

5. Grouse Mountain: "Take a trip up the tram for a stunning view overlooking the city, English Bay, and the Gulf Islands. There are lots of hiking paths and good spots for a meal or libation." *www.grousemountain.com/Winter*

Dr. Levy has even more recommendations for the Vancouver area. "If the weather is nice, head to Cypress Provincial Park on the North Shore and take a hike. If you're really looking for adventure and we have early snow, it's a great place to downhill or cross country ski and snow shoe. Stop in the Hollyburn Lodge and have lunch. Or, visit Whistler Mountain—great in the fall for mountain biking, early skiing, or zip line riding—Victoria (by ferry), and Butchart Gardens."

Don't miss CHEST 2010, October 30 – November 4, in Vancouver. Recognized around the world as the authority in clinical chest medicine, CHEST 2010 will feature an essential learning program in pulmonary, critical care, and sleep medicine. Learn more at www.chestnet.org/CHEST. ■

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Editor in Chief, CHEST

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▶ **Characterization of Pulmonary Arterial Hypertension Patients Walking More Than 450 m in 6 Min at Diagnosis.** *By Dr. B. Degano, et al.*

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NETWORKS

Chronic Care of COPD, AH! Program for Asthma

Airways Disorders

COPD as a Multisystem Disease

The Airways Disorders NetWork has created regional meetings to teach primary care physicians a comprehensive approach to caring for patients with COPD. Traditional management of COPD is focused on treating acute pulmonary symptoms, rather than preventing complications. Therefore, a shift of focus from an acute to a chronic care model is needed.

Providing high quality, long-term care is a process requiring good communication skills and active partnerships with the patient, family, health-care team, and the community.

The key components involved in a comprehensive chronic care model include: (1) self-management support (ie, a well-informed patient actively participates in the care plan through self-management); (2) delivery system design (ie, medical practice-structured to facilitate preventive care); (3) decision support; and (4) clinical information systems (ie, integrating computerized registries for planning patient care).

A systematic review demonstrated that patients with COPD who received interventions with two or more of these components had lower rates of hospitalizations, fewer emergency/unscheduled visits, and shorter length of stay compared with control groups.

It is important to recognize that over half of the cost, health-care utilization, and death associated with COPD is attributable to comorbid conditions. In fact, for every smoker who dies of COPD, three others die of smoking-related cardiovascular disease, cancer, and other nonrespiratory-related conditions.

The presence of airway obstruction imposes additional risk of death from cardiovascular disease and cancer, possibly due to chronic systemic and pulmonary inflammation.

Another comorbidity associated with poor outcomes in patients with COPD is osteoporosis. The proportion of patients with osteoporosis increases with the severity of the obstruction. In addition, many patients with COPD have muscle wasting, which is associated with poor prognosis, reduced exercise tolerance, and worse quality of life.

Psychiatric effects, such as anxiety, sleep disturbances, and depression, are surprisingly common and amplify the morbidity associated with COPD. The rates of depression and/or anxiety among patients with COPD vary from 20% to 65% and increase as the severity of obstruction increases. Unfortunately, depression and anxiety are undetected and untreated in the majority of patients with COPD.

To improve outcomes in COPD, attention should be focused on preventing complications and appropriately diagnosing and managing comorbidities in these patients.

Dr. Sandra G. Adams, FCCP
Steering Committee Member

Allied Health

AH! Asthma Health at Maine Medical Center

Improvement of daily symptoms and decreased exacerbations are associated with appropriate classifications and treatment of asthma using the NHLBI guidelines and comprehensive educational programs. The AH! Program is a comprehensive education program that mutually engages parents, patients, and providers in the guideline-based care of asthma.

Implemented initially in the pediatric clinic and pediatric inpatient environments with direct patient contact, the program at Maine Medical Center has matured into a three-armed, comprehensive, community-based approach to asthma education. The program targets patients and families directly, supports hospital and other providers' office staffs with resource-sharing educational sessions, and provides support for community-based providers, such as school clinics.

Patients are invited to participate in the "AH!" program through self-referral or by referral from a primary care provider, ED, or hospitalist. The hour-long, one-on-one session with a certified asthma educator is intended to prepare patients to become active partners and advocates, emphasizing the family's role in supporting the patient's well-being and helping with care during illness. The educator delivers consistent, focused messages about healthy lifestyles and assesses patients for readiness to change and self-efficacy.

Enhanced integration with the hospital-based asthma care community now provides automatic referrals to the asthma educator for patients presenting to the ED. The educator also provides ongoing support and reinforces best-practice guidelines for hospital staff and respiratory therapists.

Over the lifetime of the AH! Program, a consistent reduction in reported ED visits, hospitalizations, and missed school/workdays was noted across all age groups after participation in the program. Collected data from 1999 to 2008 investigated the effect of the program on asthma control. After participation in the program, ED visits were reduced by about 25%, and hospitalization rates decreased an average of 29%.

Christopher Hirsch, MPH, RRT
Allied Health NetWork
Steering Committee Member
Dr. Barbara A. Chilmonczyk
Pediatric Allergy and Asthma Specialist
Rhonda Vosmus, RRT
Asthma Education Specialist

Pulmonary Perspectives

Limited Resection for Non-small Cell Lung Cancer

The standard treatment for stage I non-small cell lung cancer (NSCLC) is lobectomy with mediastinal lymph node sampling or dissection. This standard of care was effectively established by the landmark publication from the Lung Cancer Study Group in 1995 demonstrating decreased local recurrence rates and a trend toward improved survival after lobectomy compared with sublobar resections, including anatomic segmentectomies requiring individual pulmonary arterial and bronchial division, as well as nonanatomic pulmonary wedge resections (Ginsberg and Rubinstein. *Ann Thorac Surg.* 1995;60[3]:615).

Limited or sublobar resections have been restricted in North America and Europe to patients with diminished pulmonary reserve. Renewed enthusiasm for limited resection for NSCLC has been driven by the growing number of smaller tumors detected from the recent widespread use of CT scanning. In addition, recent retrospective observational data from the Western and Japanese literature, comparing limited resection to lobectomy, have questioned the lobectomy standard, especially for patients with peripheral tumors less than 2 cm in size (T1a in Edge et al, eds. *AJCC Cancer Staging Manual.* Philadelphia, PA: Springer; 2010 [AJCC 7th Edition]). In addition, clinicians are increasingly confronted with an aging population with significant comorbidities who might benefit from lesser resections (Table 1). In this review, we will examine the literature supporting the use of limited resection for stage I non-small cell lung cancer and focus on what groups of patients should be considered for such resections.

Limited Resection Studies

North American and European studies of sublobar resection are mainly limited to analysis of patients with impaired pulmonary function. Warren and Faber compared local recurrence and survival in 68 patients who underwent segmentectomy to 105 patients who underwent lobectomy for stage I NSCLC (T1N0, T2N) (AJCC 6th Edition). Wedge resection or segmentectomy was performed at the discretion of the surgeon. A segmentectomy was performed in those patients with small peripheral lesions who would have otherwise tolerated a lobectomy. In this analysis, the rate of local recurrence was higher for the segmentectomy group than for the lobectomy group (22.7% vs 4.9%, respectively). Although there was a survival benefit for patients undergoing lobectomy for tumors greater than 3 cm, no significant survival difference was seen in patients with tumors less than 3 cm (Warren and Faber. *J Thorac Cardiovasc Surg.* 1994;107[4]:1087). Similarly, in an analysis of 219 patients with stage I NSCLC who underwent wedge resection or lobectomy, Landreneau and colleagues demonstrated no statistical difference in 5-year survival between the wedge (both open and thoracoscopic) and lobectomy groups (5-year survival: 58% open wedge, 65% thoracoscopic wedge, and 70% lobectomy, *P*=.056). In this study, the patients undergoing wedge resections had significantly worse pulmonary function (Landreneau et al. J *Thorac Cardiovasc Surg* 1997;113[4]:691). To control for this and other potential confounding factors, a Cox proportional hazards model was created that, in turn, demonstrated lobectomy to be associated with superior survival compared with wedge (hazard ratio 0.80, *P*=.042). In a comparison of 784 patients with stage I NSCLC, 207 patients treated by sublobar resection and the remaining 577 patients by lobectomy, El-Sherif and colleagues demonstrated in 2006 identical, disease-free survival of 65% at 7 years (*P*=.308) for patients with stage IA disease (*Ann Thorac Surg.* 2006; 82[2]:408).

Whereas the aforementioned Western studies describe the use of limited resection in patients with compromised pulmonary function, the Japanese literature reflects a longer standing tradition of sublobar resection in medically fit patients with early lung cancer, who would otherwise tolerate a lobectomy. In an analysis by Okada and colleagues of 139 patients with cT1N0 NSCLC, 2 cm or less in size, 70 patients underwent "extended" segmentectomy (segmentectomy with parenchymal division slightly outside segmental boundary) if they had no intraoperative evidence of nodal disease. There was no difference in 5-year survival between the two groups (87.1% in the extended segmentectomy group vs 87.7% in the lobectomy group (*P*=.8)) (Okada et al. *Ann Thorac Surg.* 2001;71[3]: 956). A similar survival was reported by Yoshikawa and coworkers in a multi-institutional Japanese trial of 55 patients with peripheral NSCLC lesions, 2 cm or less, who underwent extended segmentectomy (81.8% 5-year overall survival) (Yoshikawa et al. *Ann Thorac Surg.* 2002;73[4]:1055). In another analysis of 233 patients with peripheral T1N0 NSCLC, 2 cm or less (60 segmentectomies, 14 wedge, 159 lobectomies), overall 5-year survival was no different between the limited resection and lobectomy groups (89.1% vs 90.1%, respectively) (Koike et al. *J Thorac Cardiovasc Surg.* 2003;125[4]:924). Similarly, Watanabe and colleagues reported a study of 91 patients with stage I NSCLC with lesions less than 2 cm, who underwent either a limited resection or lobectomy (57 lobectomy, 14 wedge, 20 extended segmentectomy). There was no survival difference at 5 years between the two groups. Those who underwent an extended segmentectomy had a 5-year survival of 93%, while the lobectomy group had a 5-year survival of 84% (Watanabe et al. *Jpn J Thorac Cardiovasc Surg.* 2005;53[1]:29-35).

Special Populations

Small Tumors

Tumor size has been established by several studies as a prognostic factor for survival. The 7th edition of the AJCC staging system recognizes this and has further subdivided T1 tumors into T1a (= 2 cm), T1b (2-3 cm), and has placed the largest lesions more than 7 cm) into a T3 designation. In a review of 244 patients with stage IA NSCLC, we previously reported that the overall 5- year survival for patients with tumors = 2 cm to be superior to those with tumors more than 2 cm (77.2% vs 60.3%, *P*=.03, respectively) (Port et al. *Chest.* 2003;124[5]:1828). Similarly, in a study of 83 patients with subcentimeter tumors by Lee and colleagues, 5-year survival was 94%, with a disease-specific survival of 100% (Lee et al. *J Thorac Cardiovasc Surg.* 2006;132[6]:1382). These findings are most likely related to the link between nodal metastases and increasing tumor size (Lee et al. *Ann Thorac Surg* 2007;84[1]:177). Because nodal disease would preclude a limited resection for curative intent, it would be reasonable to suggest that a limited resection be considered for T1a tumors (= 2 cm) that would be associated with a 4.8% rate of occult mediastinal nodal disease.

Elderly Population

The elderly represent a specific subset of patients in whom a limited resection may be advantageous. Not only has age been shown to be an independent predictor of mortality for patients undergoing resection, but it is also this group of patients who harbor the most significant comorbidities, with limited physiologic reserve. Whether the survival

Continued on following page

Dr. Marilyn G. Foreman, FCCP
Editor, *Pulmonary Perspectives*

Dr. Loren J. Harris, FCCP
Deputy Editor, *Pulmonary Perspectives*

Editor's Insights

This short summary of the concepts and science of limited pulmonary resection for early non-small cell lung cancer represents information from a large and complex international body of clinical work published over the last 20 to 30 years. The Lung Cancer Study Group data from 1995, despite several statistical and design flaws, is the only prospective, randomized, multicenter trial on this topic published to date and is still felt by many to be the definitive reference and opinion on this issue.

Since this study, however, there has been a large accumulation of data on patients treated with limited resections for selected tumors, as referenced here, which implies that, in the appropriately selected patient, these limited resections may, in fact, lead to comparable disease-free and long-term survival. At present, the standard treatment for a stage I non-small cell lung cancer remains formal lobectomy with mediastinal lymph node sampling or dissection. From these data, however, several issues concerning limited resection in patients who would otherwise tolerate lobectomy are suggested:

1. Limited resection may be an appropriate definitive treatment for older patients (more than 70 years), for patients with either synchronous or second primary tumors, and for patients with small bronchoalveolar cancers (BAC).

2. Limited resection procedures, at present, should only be considered for patients with tumors = 2 cm in diameter, should include tumor-free margins at least equal in length to the diameter of the tumor (ie, M/T 1), and should only be offered to patients proven to be free of lymph node metastases.

At present, there are several large prospective randomized trials underway that are designed to answer some of the key questions regarding this approach to early lung tumors, such as whether or not limited resection provides comparable survival to lobectomy and whether or not adjuvant radiation therapy can improve local recurrence rates following limited resection.

It would not be surprising to find that, like patients with breast cancer, small lung cancers can be treated with limited resections, including lymph node sampling or dissection along with intraoperative or postoperative radiation therapy and achieve similar long-term outcomes to the larger operations that are presently the standard of care.

—Dr. Loren J. Harris, FCCP
Deputy Editor,
Pulmonary Perspectives

Continued from previous page

benefit from lobectomy in early stage lung cancer persists in the elderly must be questioned, as well. Analysis of the Surveillance, Epidemiology, and End Results (SEER) database, a large multi-institutional cancer registry, by Mery and coworkers, demonstrated no survival benefit for lobectomy when compared with limited resection in patients 71 years or older (Mery et al. *Chest*. 2005;128[1]:237). Similarly, in an analysis of the SEER-Medicare database of patients 65 years or older, with stage IA NSCLC with lesions less than 2 cm, Wisnivesky and colleagues showed no survival benefit when lobectomy was compared with limited resection (Wisnivesky et al. *Ann Surg*. 2010;251[3]:550).

Second Primary Tumors

Another subset of patients where limited resection may be useful is in those patients with a second primary who have previously undergone resection. A limited resection might allow for improved postoperative function, improved pulmonary reserve, and greater likelihood that adjuvant therapies might be delivered. To support this theory, a Veteran's Administration study has shown that both morbidity and 30-day mortality for re-resectional lung surgery is higher, with the mortality increasing with the extent of resection (Linden et al. *Ann Thorac Surg*. 2007;83[2]:425).

Bronchoalveolar Carcinoma

Bronchoalveolar carcinoma (BAC) is a subtype of adenocarcinoma defined as a lung tumor without invasion. BACs often present in women and nonsmokers and can be multifocal. Therefore, multiple resections may be offered to these patients. Because these lesions are often discovered as small ground glass opacities by incidental CT scan, their characterization, diagnosis, and treatment are controversial. Many clinicians have suggested more limited resection for these favorable, slow-growing lesions.

Recent reviews of the treatment of BAC have reported excellent long-term survival for limited resection, especially for small lesions. Disease-free survival has approached 95% or greater at 5 years in highly select patients (Barlesi et al. *Eur J Cardiothorac Surg*. 2003;24[1]:159; Fukui et al. *J Thorac Oncol*. 2007;2[8]:546; Nakayama et al. *Ann Thorac Surg*. 2007; 84[5]:1675). Subset analysis of larger ongoing trials, such as the CALGB 140503 discussed below, should help clarify the role of limited resection for BACs.

Technical Considerations

The location of a tumor must also be considered when a limited resection is planned. Wedge resections are most practical for tumors that are close to the pleural surface, preferably within the outer one-third of the lung periphery. While no standard has been accepted for the size of the wedge resection, most surgeons will attempt to obtain a margin at least equivalent to size of the lesion that is resected. For more central tumors, anatomic segmentectomies are a more appropriate option, as long as the lesion is clearly contained within the anatomic boundaries of the segment.

Limited resection can be performed either via open thoracotomy or by video-assisted thoracoscopic (VATS) techniques. Traditionally, a segmentectomy was performed by open thoracotomy because of its increased technical complexity, requiring isolation of segmental pulmonary artery and bronchi.

However, recently there has been an increased interest in performing VATS segmentectomies. To date, several reports have shown the technique to be safe and, at least, equivalent to open techniques (Schuchert et al. *J Thorac Cardiovasc Surg*. 2009;138[6]:1318).

Future Directions

Brachytherapy

To address the concern for a possible increase in local recurrence rates following sublobar resection, several investigators have offered adjuvant radiation therapy. Radiation can be delivered in the form of external beam, endobronchial or intraoperative brachytherapy with iodine 125 seeds placement (d'Amato TA et al. *Chest*. 1998;114[4]:1112). In a retrospective analysis of 124 patients undergoing sublobar resection for pT1N0 disease, 60 patients had intraoperative iodine 125 seed placement (Fernando et al. *J Thorac Cardiovasc Surg* 2005;129[2]:261). In this report, the local recurrence rate decreased from 17.7% to 3.3% with seed implantation. Other single institutional results report similar findings. Confirmation of these promising results may come from the American College of Surgeons Oncology Group (Z04042) trial, which is a randomized trial of sublobar resection (segmentectomy or wedge) with and without intraoperative iodine 125.

CALGB 140503

The question of whether it is appropriate to offer medically fit patients a limited resection for small peripheral lesions is under investigation in a randomized prospective controlled study. Patients with stage IA NSCLC with lesions = 2 cm are currently being randomized to limited resection vs lobectomy in the Cancer and Leukemia Group B phase III trial (CALGB 140503). An N0 nodal status is confirmed intraoperatively prior to randomization. Disease-free survival is the primary endpoint, with overall survival and rates of local and systemic recurrences as secondary endpoints. This trial, along with a similar Japanese cooperative trial (JCOG0802), will yield a better understanding of the role of limited resection for early stage NSCLC.

Conclusions

Currently, a lobectomy remains the standard of care for patients with resectable NSCLC. Limited or sublobar resections, including wedge and segmentectomy, have been reserved, for the most part, for patients with poor pulmonary function. Recent institutional series, as well as analyses of large multi-institutional registries, suggest that lobectomy and limited resection may lead to similar disease-free and, possibly, overall survival in appropriately selected patients with early disease. It appears reasonable to offer a limited resection to medically compromised patients, the elderly, to those with multiple primary lesions, and to patients with BAC tumors. We await the results from the ongoing CALGB 140503 trial to further elucidate the role for expanding these indications to a broader patient population. ■

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Table 1. *Selected Studies of Limited Resection for Stage I NSCLC*

Study, Year	No. of Procedures	Type of Resection	Local Recurrence	5-Year Survival
Warren et al., 1994	68 105	Segmentectomy Lobectomy	23% 5%	50% 70%
Ginsberg et al., 1995	122 125	Segmentectomy (82), wedge (40) Lobectomy	17% 5%	50% 70%
Landreneu et al., 1997	42 60 117	Open Wedge VATS Wedge Lobectomy	24% (Open) 16% (VATS) 9%	58% (Open) 65% (VATS) 70%
El Sherif et al., 2006	207 577	Segmentectomy Lobectomy	29% 28%	40% 54%
Okada et al., 2001	70 139	Extended segmentectomy Lobectomy	0% N/A	87% 87%
Yoshikawa et al., 2002	55	Extended segmentectomy	1.8%	82%
Koike et al., 2003	74 159	Segmentectomy (60), wedge (14) Lobectomy	2.7% 1.3%	89% 90%
Watanabe et al., 2005	34 57	Extended segmentectomy (20), wedge (14) Lobectomy	0% N/A	93% 84%

Tobacco Dependence Treatment Tool Kit

New Online Resources Now Available—Free to ACCP Members

The American College of Chest Physicians (ACCP) Health and Science Policy Committee has developed an evidence-based, comprehensive, user-friendly online tool kit to help you help your patients to safely and comfortably stop using tobacco.

This resource includes a collection of background materials and tools designed to assist physicians and other professionals to provide successful treatment for their tobacco-using patients. Now, physicians can be reimbursed for discussing cessation treatment, so information on how to code for these services also is provided.

Tobacco dependence is a chronic medical condition, and physicians are encouraged to treat it as such, just as they would asthma, diabetes, or other chronic conditions. This means that patients should be placed onto a treatment protocol, managed, and followed to assess whether their symptoms are improving or whether the treatment protocol needs to be altered.

Similar to the treatment for asthma, the recommended approach calls for the combined use of a long-acting controller-type medication and a short-acting reliever to alleviate breakthrough withdrawal symptoms. Other modalities, such as behavioral interventions, quit lines, and support groups, are also encouraged.

This is the third edition, now online, of the previously titled *Tobacco Cessation Tool Kit*. New to this edition are treatment algorithms, updated pharmacotherapeutic guidance, many new tools, slide sets, and a video demonstrating how to successfully adopt the therapeutic approach with tobacco-dependent patients. Many of the tools can be downloaded directly to your PDA.

This edition also promotes the creation of teachable opportunities for pediatricians to work with tobacco-using parents to discuss the negative effects of second-hand smoke exposures. Social smoking or non-daily smoking, which has received little attention until now, is increasing in frequency and associated with an increased risk of coronary artery disease, cancer, lower respiratory tract infections, cataracts, compromised reproductive health, and poor bone mineral density, as well as reduced quality of life.

Information and resources for advocating on behalf of smoke-free legislation, information on tobacco treatment performance measures, and many additional resources are also contained in this new edition of the tool kit.

The ACCP Tobacco Dependence Treatment Tool Kit is now available online for free to all ACCP members.

Now through August 31, 2010, obtain your free access at http://tobaccodependence.chestnet.org/sales-page. Click on "Order Now" and follow the directions for ACCP members.

Only members who access the tool kit during this 3-month period will continue to receive **free unlimited access** to all content in this tool kit, now and in the future, throughout the duration of this edition.

Gain access at www.chestnet.org. Address questions to Sandra Zelman Lewis, PhD, slewis@chestnet.org, or Chris Harrod at charrod@chestnet.org. ■

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