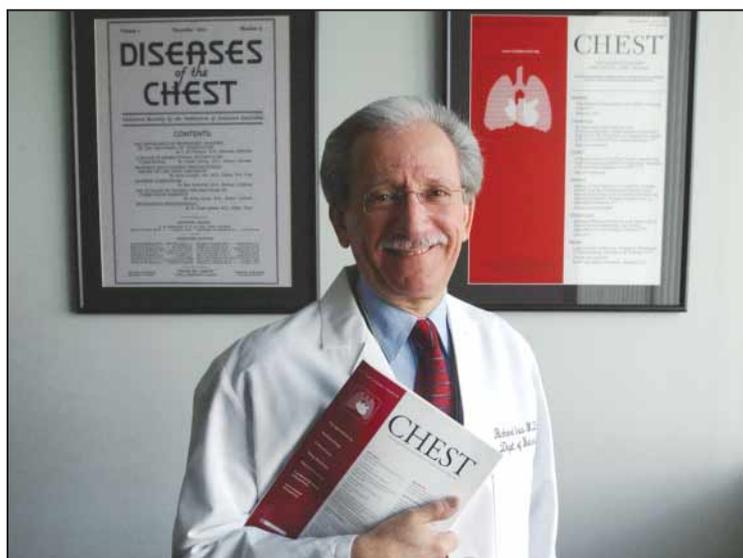




CHEST *Physician*

THE OFFICIAL NEWS PUBLICATION OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS



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Using the guidelines, physicians should be able to diagnose and treat cough better than 90% of the time, Dr. Richard S. Irwin said.

'Robust' New Guidelines Reshape Cough Care

BY CHRISTINE KILGORE
Elsevier Global Medical News

The American College of Chest Physicians' new evidence-based practice guidelines on cough made national headlines last month for the conclusion that most over-the-counter cough suppressants are ineffective for common coughs.

But Dr. Richard S. Irwin, FCCP, who chaired the guidelines-writing panel, envisions a more empowering headline: "Cough Treated According to ACCP Guidelines Should Improve."

That's because physicians who follow the guidelines, Dr. Irwin said, should be able to diagnose the cause of cough and effectively treat it "better than 90% of the time."

With a "robust" and practical focus on diagnosis and treatment of cough as a symptom, the updated guidelines significantly expand and improve upon the college's original cough consensus statement published in 1998, said Dr. Irwin, of the University of Massachusetts.

Most significantly, he said, the guidelines encourage taking an initial empiric diagnostic approach for managing adult patients with cough.

The document, "Diagnosis and Management of Cough," contains algorithms for managing acute, subacute, and chronic cough—as well as algorithms for evaluating chronic cough in children—and pays significant attention to

See **Cough** • page 2

Hypertonic Saline Cut Exacerbations In Cystic Fibrosis

Impact on lung function was 'moderate.'

BY MARY ANN MOON
Elsevier Global Medical News

Hypertonic saline inhalation using a nebulizer reduced pulmonary exacerbations in patients with cystic fibrosis and decreased their absenteeism from school, work, and their usual activities, researchers found in two separate randomized clinical trials.

The trials provided the first evidence of the long-term efficacy of this safe and relatively inexpensive treatment. Although the therapy's exact mechanism of action is not yet clear, it appears to restore the volume of liquid on the airway surfaces, which is depleted in cystic fibrosis (CF) because of excessive absorption of salt from the airway lumen. This rehydration seems to produce a sustained acceleration of mucus clearance, both groups of investigators theorized.

In the first study, 164 adults and children with stable CF were randomly assigned to

inhale 4 mL of either hypertonic (7%) saline plus a taste-masking agent or a control solution (isotonic saline) plus a taste-masking agent via nebulizer twice a day for 48 weeks. A bronchodilator was administered before each treatment to prevent or minimize narrowing of CF patients' hyperresponsive airways during nebulizer therapy, reported Dr. Mark R. Elkins, of Royal Prince Alfred Hospital, Sydney, Australia, and the University of Sydney, and his associates.

The treatment had only a moderate effect on lung function as measured by forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV₁), and no apparent effect on the typical decline in lung function over the course of the year-long study. However, it had "dramatic" effects on several clinical factors, they noted (*N. Engl. J. Med.* 2006;354:229-40).

In the treatment group, the

See **Saline** • page 5

Obesity Can Confound PAH Diagnosis

BY BRUCE K. DIXON
Elsevier Global Medical News

MONTREAL — Obese patients often have a constellation of physiological problems that together can lead to a mistaken diagnosis of pulmonary artery hypertension, according to researchers at Duke University Medical Center in Durham, N.C.

The presence of exertional dyspnea in these patients often leads to an echocardiogram and a finding of elevated right ventricular systolic pressure. "Often the pressure is just mildly elevated, and these patients don't really have pulmonary arterial hypertension but are referred for evaluation anyway," Dr. Terry A. Fortin said at CHEST 2005, the annual meeting of the American College of Chest Physicians.

To assess diagnostic strategies

for pulmonary arterial hypertension (PAH) in this often very symptomatic population, Dr. Fortin and her colleagues at Duke University retrospectively assessed consecutive cardiac catheterization data on patients referred for suspected PAH.

Suspected PAH was defined as mean pulmonary arterial pressure (mPAP) greater than 25 mm/Hg, pulmonary capillary wedge pressure (PCWP)

less than 15 mm/Hg, and pulmonary vascular resistance (PVR) greater than 3 Wood units. Patients with left ventricular systolic dysfunction, PAH clearly associated with a known syndrome, or significant valve or lung disease of sufficient severity to explain PH were excluded. That left 78 obese patients with mild pulmonary

See **Confound** • page 3

INSIDE

Pulmonary Medicine Tailoring CAP Treatment

A procalcitonin-guided protocol helped cut duration of antibiotic use by 50% in community-acquired pneumonia. • 3

Cardiothoracic Surgery GERD and Lung Transplantation

Could GERD surgery prevent chronic rejection in many lung transplant recipients? • 6



Critical Care Medicine Angle of Repose

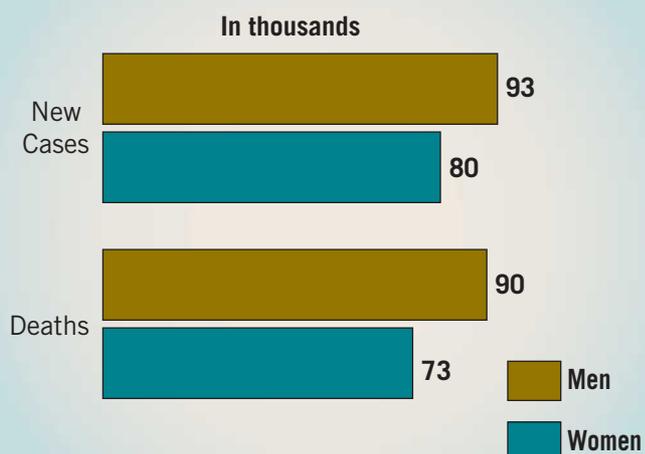
A simple solution keeps ICU beds properly elevated. • 8

Pulmonary Perspectives Rethinking CTPH

New data may challenge old assumptions about chronic thromboembolic pulmonary hypertension. • 15

VITAL SIGNS

U.S. Lung Cancer Projections for 2005



KEVIN FOLEY, RESEARCH

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IN THIS ISSUE

News From the College • 9

Critical Care Commentary

Liberation from mechanical ventilation and from the ET tube can be streamlined and enhanced by an interdisciplinary team. • 11

NEWS • 2

PULMONARY MEDICINE • 3

The Centers for Disease Control and Prevention closed out 2005 by updating its 1994 guidelines for preventing *Mycobacterium tuberculosis* in health care settings. • 4

CARDIOTHORACIC SURGERY • 6

PEDIATRIC CHEST MEDICINE • 7

CRITICAL CARE MEDICINE • 8

PALLIATIVE & END-OF-LIFE CARE • 16

The number of palliative care programs in U.S. hospitals grew from 632 in 2000 to 1,027 in 2003, an increase of 63%, according to results from a large study.

SLEEP MEDICINE • 17

CARDIOVASCULAR DISEASE • 18

PRACTICE TRENDS • 19

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'Rigorous' Review Spurs Changes

Cough • from page 1

common causes of cough such as chronic cough due to gastroesophageal reflux disease, he said.

Published as a supplement to the January issue of CHEST, the guidelines also contain a strong recommendation from the 26-member expert panel that adults up to age 65 be regularly immunized against pertussis infection with a recently approved, safe vaccine.

"This is very important," Dr. Irwin said. "Twenty-eight percent of whooping cough in the U.S. is in adults." Regular vaccination with the new dTAP series should be administered routinely to adults as well as children and adolescents, according to CDC recommendations.

The advice is based on a much more "rigorous" evidence-based review than was possible for the ACCP's 1998 report, "Managing Cough as a Defense Mechanism and as a Symptom," Dr. Irwin explained.

Each recommendation is rated for its strength, based on both the quality of evidence and the net benefit to the relevant patient population.

The rigor behind the ACCP panel's approach makes the recommendations about over-the-counter cough medications significant.

"It's a \$3.6 billion industry," Dr. Irwin said. And yet, "when we looked at the best evidence and studies, it's clear that relatively few [cough medications] have been shown to be effective for cough due to the common cold."

Most over-the-counter cough suppressants and expectorants, and newer-generation non-sedating antihistamines, have little efficacy in patients with acute cough or upper airway cough syndrome (post-nasal drip syndrome) due to the common cold and should not be used. Preparations containing zinc also are ineffective, according to the guidelines.

Instead, for cough associated with the common cold, physicians should recommend an older, first-generation antihista-

mine/decongestant preparation (brompheniramine and sustained-release pseudoephedrine).

Naproxen may also be helpful in decreasing cough in these patients.

Physicians should also strongly discourage the use of cough suppressants and other over-the-counter cough medicines in children, according to the guidelines.

The term "upper airway cough syndrome" (UACS) is one of several new diagnostic terms introduced in the guidelines to replace older terms that the expert panel concluded "may represent misnomers."

UACS should be used instead of "post-nasal drip syndrome" because it is unclear whether the mechanism of cough associated with upper airway conditions is postnasal drip, direct irritation, or inflammation of the cough receptors in the upper airway.

Another new term, "unexplained cough," should be used instead of "idiopathic cough," because the term "idiopathic" implies that one is dealing with only one disease. "It is likely that more than one unknown cause of chronic cough will be discovered," according to the document.

The guidelines also discourage use of the term "acid reflux disease" in patients with chronic cough due to gastroesophageal reflux disease "unless it can definitely be shown to apply."

The more general term "reflux disease" is more appropriate, because it does not convey the message, like acid reflux disease does, that all coughs due to GERD will improve with acid-suppression therapy, the guidelines say.

The new report, which minimizes the discussion of cough as a defense mechanism, contains numerous new sections covering topics that were not covered in 1998.

These new sections include nonasthmatic eosinophilic bronchitis, acute bronchitis, nonbronchiectatic suppurative airway diseases, environmental occupa-

CHEST PHYSICIAN Adds Experts' Insights

Beginning with this issue of CHEST PHYSICIAN, look for concise perspectives from our editorial advisory board members at the end of significant clinical articles.

tional causes of cough, tuberculosis and other infections, uncommon causes of cough, unexplained cough; and potential future therapies. ■

Dr. Susan M. Harding, FCCP, comments: These ACCP-developed, evidence-based guidelines provide up-to-date information and algorithms so that the cause(s) of cough can be determined and appropriate therapy instituted. Dr. Irwin and his 26-member expert panel should be congratulated for their outstanding work. Now it is up to us to effectively implement these guidelines and provide cough relief for our patients.

Meet a CHEST PHYSICIAN Editorial Board Member

Gerard A. Silvestri, M.D., FCCP, is associate professor of medicine at the Medical University of South Carolina in Charleston.



Dr. Silvestri is a trustee of The CHEST Foundation and serves on The Foundation Development Committee. He has participated in the ACCP Thoracic Oncology and Interventional Chest/Diagnostic Procedures NetWorks and the Health and Science Policy Committee.

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Procalcitonin Can Guide Antibiotic Use in CAP Cases

BY KERRI WACHTER
Elsevier Global Medical News

WASHINGTON — A procalcitonin-guided protocol can cut the duration of antibiotic use in patients with community-acquired pneumonia by roughly 50%, according to data presented at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

“Procalcitonin seems to be a more reliable parameter for the individual tailoring and discontinuation of antibiotics as compared with commonly and routinely used clinical and laboratory parameters,” said Dr. Mirjam Christ-Crain, an endocrinologist at the University Hospital Basel (Switzerland).

She and her colleagues proposed using procalcitonin as a biomarker to guide antibiotic treatment because the propeptide of calcitonin is increased with increasing severity of bacterial infection.

For this study, patients with community-acquired pneumonia (CAP) were randomized to receive therapy of standard duration (151 patients) or therapy whose duration was guided by procalcitonin (151 patients). Patients in both groups averaged age 70 years. Only 20% had

antibiotic pretreatment. Most patients in both groups had comorbidities. More than two-thirds of patients had severe or very severe pneumonia.

Among those in the procalcitonin group, patients with levels greater than 0.25 mcg/L were started on antibiotic therapy. Those with levels of 0.25 mcg/L or less were not given antibiotics.

Procalcitonin measurements were performed on all patients on days 0, 2, 4, 6, and 8, though the results were available only for those in the procalcitonin group. The decision to continue or discontinue antibiotic therapy in the procalcitonin group was based on the cutoff levels described above. Follow-up, including a chest x-ray, was performed at 4-6 weeks. In patients with clinical uncertainty, there was follow-up remeasurement of procalcitonin in 6 hours.

Patients in the standard therapy group received antibiotics initially, and almost all of them were on antibiotics for more than 8 days. In comparison, only 85% of those in the procalcitonin group initially received antibiotics. In this group, “only about 50% had antibiotics for more than 4 days and about 30% for more than 6 days,” said Dr. Christ-Crain.

Patients in the procalcitonin group received antibiotics for an average of 6 days, compared with 13 days for the standard therapy group. “This is a highly significant reduction of antibiotic use and antibiotic duration,” said Dr. Christ-Crain, at the meeting sponsored by the American Society for Microbiology.

Clinical outcomes—as assessed by a visual analog scale and clinical parameters such as temperature, oxygen saturation, and pulse rate—were similar in both groups. Laboratory outcomes—C-reactive protein and procalcitonin levels in the normal reference ranges—assessed at 4-6 weeks were also similar.

Most experts recommend a 10-14-day course of antibiotic therapy to treat CAP, but the optimal duration is unknown. “In our opinion, the correct duration of antibiotics varies from patient to patient,” said Dr. Christ-Crain.

New tests for the determination of procalcitonin levels have improved sensitivity, enabling physicians to distinguish clinically relevant bacterial infections from other infections, as Dr. Christ-Crain and her colleagues demonstrated in a recent study involving lower respiratory tract infections (*Lancet* 2004;363:600-7). ■

Disorders Can Confuse

Confound • from page 1

hypertension (PH) with mPAP greater than 25 mm/Hg and PVR less than 5 Wood units, said Dr. Fortin of Duke University Medical Center.

Of those 78 patients, 40 had baseline syndromes or conditions that the investigators believed adequately explained the patients' PH after workup. Those conditions included connective tissue disease, congenital heart disease, chronic thromboembolic disease, portopulmonary disease, severe lung disease, high-output arteriovenous shunts, and left-sided valve disease.

Eliminating these patients left 38 patients with elevated mPAP associated with a constellation of factors that together resulted in PH, although maybe not PAH, Dr. Fortin said. Most were women with a mean age of 60 years. All were hypertensive, and virtually all had a body mass index greater than 30; half had a body mass index (BMI) greater than 40. Nearly two-thirds had diabetes and/or a sleep disorder.

“The precatheterization diagnostic tests often showed elevated right ventricular systolic pressures on referral cardiac echo, and that was typically the reason that the patients were sent to us,” Dr. Fortin explained. Many of the patients did have increased artery sizes, and their right atrium size or decreased contractility in the right ventricle was of concern. About half the patients were hypoxicemic,

and some were hypercarbic, “which is not necessarily what we would expect in pulmonary hypertension,” she added.

Low lung volume was common, and many patients had reduced diffusion capacity of carbon monoxide (DLCO). Two patients had only increased right ventricular systolic pressures.

“Looking at the cardiac cath data, PVRs were not quite 3 [Wood units] in most patients, and if you break them down into those with enlarged and normal right ventricles, they're slightly different, but not statistically so,” Dr. Fortin said. The investigators also found a slight but statistically nonsignificant difference in mean pulmonary pressures, with a predominance of elevated pressures—as expected in bigger right ventricles. Overall, the patients had normal cardiac indices and were not very sick.

Only one patient had pulmonary arterial hypertension based upon a PCWP less than 15 mm/Hg and a PVR greater than 3 Wood units, Dr. Fortin said. Hypoxemia, hypercarbia, low total lung capacity, and DLCO were all related to obesity hypoventilation and sleep disorders.

“Lest you think that obese people do not ever have pulmonary hypertension, I was quickly able to glean 13 patients ... who were morbidly obese with BMIs greater than 40 who

were seen in our clinic,” Dr. Fortin said. “All had mPAPs greater than 25 with elevated pulmonary vascular resistances. In fact, their average pulmonary artery pressure was 60, and their PVR was 12, while their cardiac indices were very low; these were very sick patients.”

The study's researchers concluded that a number of factors can contribute to a mistaken diagnosis of PAH, including systemic hypertension, obesity, sleep-disordered breathing and hypoventilation, and elevated pulmonary capillary wedge pressure.

“It should not be assumed that patients with an elevated right ventricular systolic pressure by echo have pulmonary arterial hypertension,” Dr. Fortin cautioned. “Pulmonary capillary wedge pressure and diastolic dysfunction may be causative.”

Aggressive management of weight, sleep disorders, hypertension, hypoxemia, and diabetes may limit the development of diastolic dysfunction and secondary pulmonary hypertension, though that's easier said than done, she added.

“Patients with this complex of disorders often have findings similar to those in full-blown PAH, and thus cardiac catheterization is necessary to help sort this out,” Dr. Fortin said. “I think that diagnostic testing also should definitely include sleep studies, as 70% of these patients had sleep disorders that were not necessarily diagnosed at the time of presentation.”

It's not necessary to go right to a diagnostic test, Dr. Fortin said, “as long as you're following the patient carefully; try to fix these other factors first before going to cardiac catheterization.” ■

Pneumonia Hospitalizations Increase in Older Adults

The burden of pneumonia among U.S. patients aged 65 and older is large and increasing, according to Dr. Alicia M. Fry and her colleagues at the Centers for Disease Control and Prevention, Atlanta.

National hospital discharge data show that among the 173 million people aged over 64 years who were hospitalized from 1988 through 2002, about 9% had pneumonia as a discharge code, and 6% had pneumonia as a first-listed discharge code. From 2000 to 2002, compared with 1988-1990, there was a 20%-25% increase in pneumonia hospitalizations among those aged 65-74 years and 75-84 years (*JAMA* 2005; 294:2712-9).

The hospitalization rate for those aged over 84 years held steady, but was twofold higher overall than the rate among younger patients (51 vs. 12-26 per

1,000 population for a first-listed pneumonia discharge code).

Of 9 million deaths among hospitalized patients, 22% were among those with a pneumonia-related hospitalization; the risk of death in these patients was 1.5 times greater than the risk in patients with any of the 10 other most common causes of hospitalization. Additionally, the proportion of comorbid conditions, including chronic cardiac or pulmonary disease and diabetes, increased from 66% during 1988-1990 to 80% during 2000-2002.

An increase in chronic underlying conditions appears to be a contributing factor in pneumonia hospitalizations in older adults; preventing pneumonia in this population should focus on reducing comorbidity and improving vaccine programs and effectiveness, the investigators concluded.

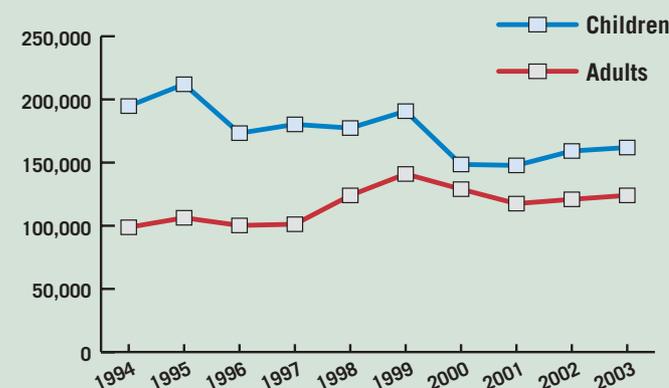
—Sharon Worcester



Several factors can contribute to a mistaken diagnosis of pulmonary arterial hypertension.
DR. FORTIN

DATA WATCH

Hospital Discharges for Simple Pneumonia and Pleurisy



Note: Based on weighted national estimates from the Healthcare Cost and Utilization Project's Nationwide Inpatient Sample.
Source: U.S. Agency for Healthcare Research and Quality

CDC Issues Updated Guidelines For Preventing Tuberculosis

BY DOUG BRUNK
Elsevier Global Medical News

The Centers for Disease Control and Prevention closed out 2005 by updating its 1994 guidelines for preventing *Mycobacterium tuberculosis* in health care settings.

The exhaustive guidelines were updated in an effort to respond to “shifts in the epidemiology of TB, advances in scientific understanding, and changes in health care practice that have occurred in the United States during the previous decade,” wrote the authors, led by Paul A. Jensen, Ph.D., in the division of tuberculosis elimination at the CDC’s National Center for HIV, STD, and TB Prevention (MMWR 2005;54 (RR-17): 1-121).

The authors noted that although TB rates have declined in recent years, the U.S. incidence rate remains higher than the national goal.

“Despite the progress in the United States, the 2004 rate of 4.9 per 100,000 remained higher than the 2000 goal of 3.5. This goal was established as part of the national strategic plan for TB elimination; the final goal is less than 1 case per 1,000,000 population by 2010,” they wrote.

Also, health care workers (HCWs) in different areas of the country face different risks. For example, in 2004 the risk of TB per 100,000 population was 1.0 in Wyoming, 7.1 in New York, 8.3 in California, and 14.6 in the District of Columbia.

One key change that makes these updated guidelines different is the use of the term “tuberculin skin tests” (TSTs) instead of purified protein derivative.

Also, the guidelines state that the QuantiFERON-TB Gold test can be used instead of tuberculin skin tests in TB screening programs for health care workers. This one-step blood assay for *M. tuberculosis* (BAMT) has been approved by the Food and Drug Administration.

The revised guidelines also include these changes:

► **Expansion of settings.** The guidelines have site-specific recommendations for more types of inpatient and outpatient settings, including surgical suites, laboratories, bronchoscopy suites, autopsy suites, dialysis units, and dental care settings.

► **More concise criteria to help determine who needs serial testing for TB infection.** Recommendations vary depending on the type of health care setting. In some settings, the frequency of TB screening for HCWs has been decreased. Screening guidelines are also included for workers who transfer to other health care settings.

► **New airborne terms.** The term “airborne isolation” replaces “respiratory isolation” while the term “airborne infection isolation room” (AII room) is defined as “a special negative-pressure room for the specific purpose of isolating persons who might have suspected or confirmed infectious TB disease from other parts of the [health care] setting.”

► **Instructions on proper respirator use.** This includes criteria for selecting respirators and recommendations for annual training and fit testing.

► **A nine-page “frequently asked questions” section.** One of the questions posed is: “Do health care settings or areas in the United States exist for which baseline two-step skin TST for newly hired HCWs is not needed?”

The reply reads: “Ideally, all newly hired HCWs who might share air space with patients should receive baseline two-step TST (or one-step BAMT) before starting duties. In certain settings, a choice might be offered not to perform baseline TST on HCWs who will never be in contact with or share air space with patients who have TB disease, or will never be in contact with clinical specimens (e.g., telephone operators in a separate building from patients).”

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THE UPDATE REFLECTS ‘SHIFTS IN THE EPIDEMIOLOGY OF TB, ADVANCES IN SCIENTIFIC UNDERSTANDING, AND CHANGES IN HEALTH CARE PRACTICE.’

Ralstonia Prompts Recall Of Vapotherm Devices

BY MARY ANN MOON
Elsevier Global Medical News

Vapotherm respiratory gas administration devices are being voluntarily recalled, following federal government reports that twenty-nine hospitals in 16 states found *Ralstonia* organisms colonizing the devices, and cultures from approximately 40 pediatric patients also yielded the bacteria.

The Centers for Disease Control and Prevention and the Food and Drug Administration late last year had advised clinicians to use alternative devices to provide humidified oxygen therapy until the source of contamination has been identified and removed. They also recommended that any patients who have been exposed to the Vapotherm system be monitored for signs and symptoms suggesting infection, including fever, poor feeding, irritability, and changes in hematologic indices.

In addition, “clinicians may want to consider *Ralstonia* species infection in the differential diagnosis of symptomatic patients even if the organism has not been isolated,” the FDA said in a public health notification (www.fda.gov/cdrh/safety/122005-vapotherm.html).

In response, the device manufacturer, Vapotherm, announced last month that it would recall and disinfect Vapotherm 2000i and 2000h devices. Units will then be returned to the owners with updated disinfection and usage recommendations.

Contamination of the Vapotherm system was first reported by the CDC and the FDA in October 2005, after a Pennsylvania hospital isolated *Ralstonia* in several patients who

had used the device. The Vapotherm system is used “to add moisture to and to warm breathing gases for administration to patients,” according to its manufacturer.

Since the October reports, the CDC and FDA have found additional cases of *Ralstonia* contamination. Cultures of unused Vapotherm cartridges at two hospitals yielded *Ralstonia*, but cultures of other unused cartridges from the same lot did not grow the organism.

After the procedures for disinfecting the device that were listed in its original instructions were found to be inadequate, the manufacturer issued new instructions for chloride dioxide disinfection. However this method also “may not achieve sustained bacterial control,” according to the FDA.

Several alternative devices are listed on the FDA Web site cited above.

Ralstonia, gram-negative bacteria usually found in water and soil and on plants, formerly were included in *Pseudomonas* or *Burkholderia* species and still can be misidentified as such.

For more information about the recall, visit www.vtherm.com/recall. Cases of colonization or infection with *Ralstonia* or related bacteria (gram-negative rods) in patients exposed to Vapotherm should be reported to the manufacturer, to local or state health departments, and to the CDC at 800-893-0485.

Adverse events associated with medical devices should be reported to the FDA’s MedWatch program at www.fda.gov/Medwatch or by calling 800-332-1088 or faxing 800-332-0178.

Flu Virus Shedding Found to Last Longer Than 5 Days

BY AMY PFEIFFER
Elsevier Global Medical News

WASHINGTON — Influenza A virus shedding has been found to last for longer than 5 days, Dr. Surbhi Leekha reported at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

“In general, adults are considered to be infectious from a day or two before to approximately 5 days after the onset of symptoms,” said Dr. Leekha, an internal medicine resident at the Mayo Clinic.

The Centers for Disease Control and Prevention recommends providing standard precaution and droplet isolation for 5 days after symptom onset in hospitalized patients who are suspected or confirmed to have influenza. It is also recommended that infected health care workers not provide patient care for 5 days after the onset of flu symptoms, and that sick people not visit hospitalized patients for 5 days after

their symptom onset, Dr. Leekha said at the meeting sponsored by the American Society for Microbiology.

But based on the new findings, prolonged infection control should be considered for patients with influenza A, as well as vaccination for all health care workers who care for patients, she said.

Of 50 patients hospitalized at the Mayo Clinic, Rochester, Minn., from December 2004 to March 2005, 22 (44%) were found to have influenza virus shedding on day 7 after symptom onset, she said.

Patients were considered for study inclusion if they were older than 18 years and were hospitalized with lab-confirmed influenza A. The 50 patients enrolled in the study ranged in age from 21 to 91 years (mean age 76), and 62% were male, Dr. Leekha said. She and her associates excluded patients from whom written consent could not be obtained.

Almost all study participants had one or

more underlying chronic medical conditions. Of the 50 patients, 81% had received an influenza vaccination; 54% were undergoing antiviral therapy.

Throat swabs were taken at symptom initiation, and then again at days 2, 3, 5, and 7 and then tested by culture and polymerase chain reaction (PCR) if the patient was still hospitalized, Dr. Leekha said.

“Positivity falls with increasing duration from symptom onset. But even beyond day 5, several samples continue to be positive,” she said.

At day 7, 22 patients were still shedding the influenza virus as detected by PCR, and 12 patients were shedding as detected by cultures. Of the 22 positive patients, the median age was 76 years, 64% were male, 71% had received a flu vaccination, 50% were receiving antiviral therapy, 4 had an identifiable cause of immunosuppression, and their median hospital stay was 6 days, Dr. Leekha said.

The longest duration of shedding lasted for 14 days as detected by all three methods.

A greater than expected proportion of hospitalized patients with influenza A continued to shed detectable virus beyond 7 days after symptom onset in the study, Dr. Leekha said.

“Such prolonged shedding of influenza A virus has previously been shown in immunocompromised adults, also in children, and has been associated with drug-resistant strains in both these populations in previous studies. However, there are no studies of viral shedding in adults with other chronic illnesses,” she said.

Influenza immunity declines with age and is multifactorial, so “it is possible that adult patients who are hospitalized with influenza represent an older and sicker cohort of patients who may possibly be infected for longer than the traditional period of infectivity,” Dr. Leekha said.

Therapy Trimmed Antibiotic Use

Saline • from page 1

mean number of symptom exacerbations was 1.32 per person, compared with 2.74 per control subject. The mean duration of exacerbations was 22 days in the treatment group, compared with 69 days in the control group. And the length of time spent free of exacerbations, expressed as “48-week exacerbation-free survival rate,” was 41% in the treatment group, compared with 16% in the controls. All of these differences were highly statistically significant.

Similarly, antibiotic use during exacerbations was much lower for the active treatment group, with a median of 11 days of antibiotic use (range, 0-49 days), than for the control group, which had a median of 50 days of antibiotic use (range, 6-144 days).

Patients in the active treatment group reported a mean of 7 days (range, 0-21) when they were unable to participate in

found that the treatment did indeed hasten the rate of mucus clearance from the lungs and “produced a larger and more sustained increase in the volume of airway surface liquid” in CF patients than in healthy controls. These findings support their theory about the treatment’s mechanism of action, Dr. Donaldson, Dr. Bennett, and associates said (N. Engl. J. Med. 2006;354:241-50).

The findings “suggest that inhaled hypertonic saline may indeed be a therapeutic option” for CF patients, Dr. Felix

Ratjen of the University of Toronto said in an editorial comment accompanying the publication of both reports.

Previous small studies had shown that hypertonic saline inhalation increased mucociliary transport in CF patients—but the effect was presumed to be short-lived because sodium deposited on epithelial surfaces would be taken up rapidly. The new research demonstrates “that this assumption is probably incorrect,” since the treatment “not only had a prolonged effect on the amount of airway surface liquid in epithelial cells ... but also resulted in a sustained improvement of mucociliary transport,” Dr. Ratjen

said (N. Engl. J. Med. 2006;354:291-3).

Dr. Ratjen noted that the treatment has an unpleasant taste, induces coughing, and “would add at least 30 minutes of time to the patient’s already burdensome daily treatment schedule,” all of which may limit compliance. Faster and more effective inhalation devices that are already in development may address these issues.

Perhaps a more important limitation of the therapy is that the medication may not reach the small airways, where it is also needed. Similarly, the medication cannot penetrate to areas obstructed by mucus, which are the areas most in need of treatment, he said. ■

ANTIBIOTIC USE DURING EXACERBATIONS WAS MUCH LOWER FOR THE ACTIVE TREATMENT GROUP, WITH A MEDIAN OF 11 DAYS OF USE.

school, work, or usual activities, compared with a mean of 24 days (range, 12-48) for the controls. The treatment group also scored significantly higher on quality of life measures.

The treatment did not alter the levels of *Pseudomonas aeruginosa* or *Staphylococcus aureus* in the sputum, nor did it affect the rate of acquisition of these organisms: *Burkholderia cepacia*, *Stenotrophomonas maltophilia*, *Candida albicans*, aspergillus species, or *Hemophilus influenzae*. This finding was “reassuring,” given that some researchers have speculated that hypertonic saline might inactivate endogenous antimicrobial compounds in CF patients, which would enhance bacterial growth.

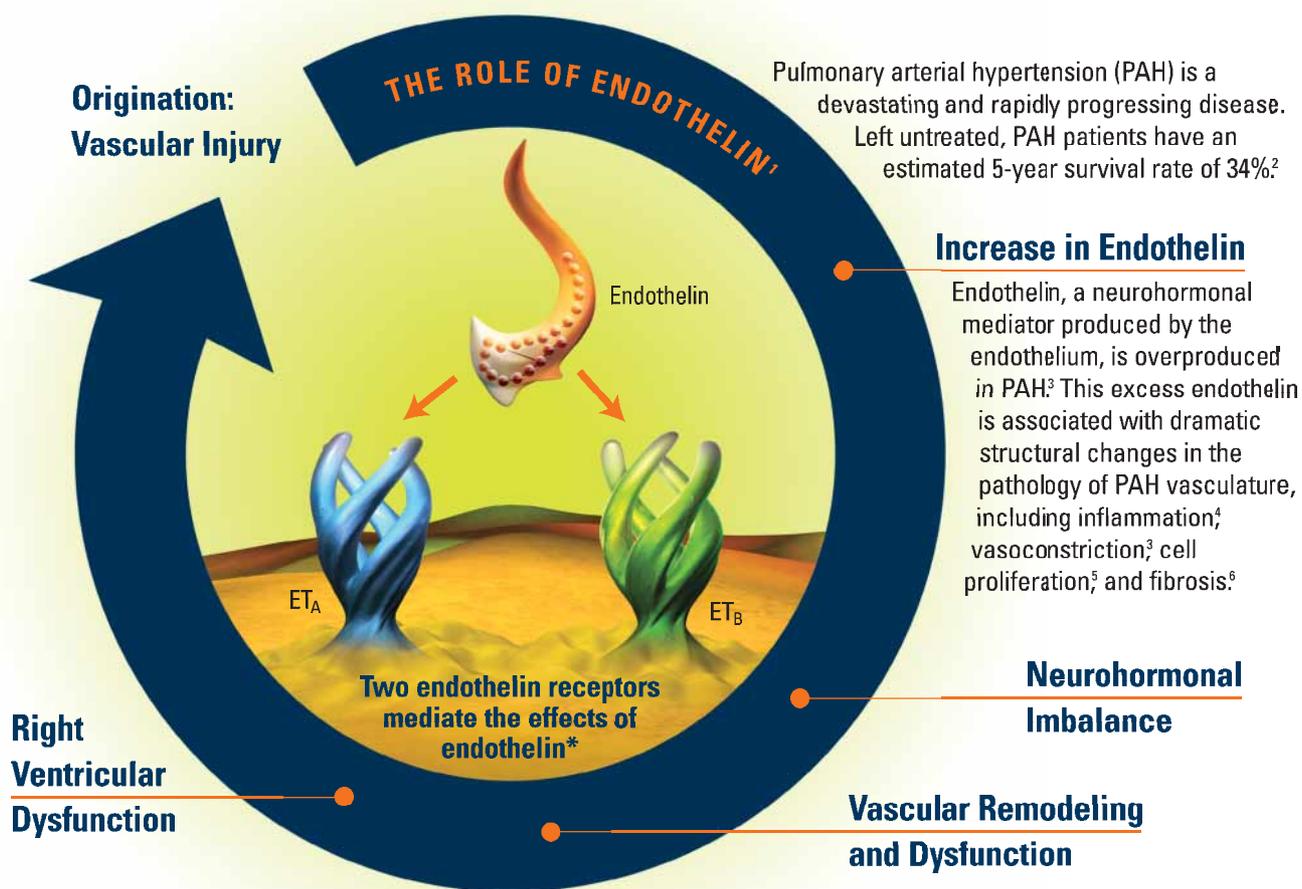
In the other clinical trial, investigators reasoned that slowing the absorption of nebulized hypertonic saline by premedicating CF patients with amiloride, a sodium channel blocker, would enhance patient response by extending the duration of airway rehydration.

Twenty-four CF patients aged 14 years and older were randomly assigned to receive pretreatment with either amiloride or a taste-masked placebo, followed by hypertonic saline via nebulizer four times daily for 14 days. As with the study by Elkins et al., all the subjects received a bronchodilator via inhaler 30-60 minutes before the nebulizer treatment, to prevent or minimize nebulizer-induced narrowing of their hyperresponsive airways.

Although the pretreatment with amiloride did not improve the response to hypertonic saline as anticipated, the study did confirm that hypertonic saline significantly improved CF symptoms, lung function, and quality of life, reported Dr. Scott H. Donaldson and Dr. William D. Bennett of the University of North Carolina at Chapel Hill Cystic Fibrosis Research and Treatment Center and their associates.

Perhaps as important, the researchers

Endothelin’s Role in the Rapid Progression of Pulmonary Arterial Hypertension



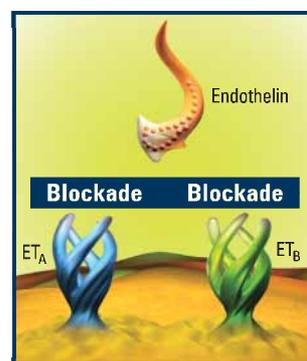
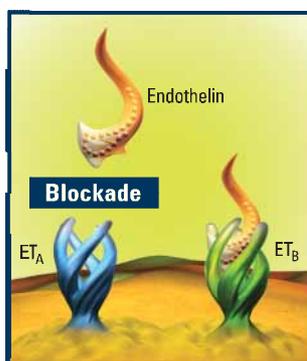
Blockade of Both ET_A and ET_B Receptors Is Critical

ET_A Activity in PAH*

Cell proliferation⁵
Vasoconstriction³
Inflammation⁴

ET_B Activity in PAH*

Cell proliferation⁵
Vasoconstriction³
Inflammation⁴
Fibrosis⁶
Hypertrophy⁶



To learn more about the effects of endothelin in pulmonary arterial hypertension, please visit www.endothelinscience.com

*Statements are based on observations reported from in vitro or animal trials.

1. Gaine SP, Rubin LJ. Primary pulmonary hypertension. *Lancet*. 1998;352:719-725. 2. D'Alonzo GE, Barst RJ, Ayres SM, et al. Survival in patients with primary pulmonary hypertension. Results from a national prospective registry. *Ann Intern Med*. 1991;115:343-349. 3. Miyauchi T, Masaki T. Pathophysiology of endothelin in the cardiovascular system. *Annu Rev Physiol*. 1999;61:391-415. 4. Muller DN, Mervaala EM, Schmidt F, et al. Effect of bosentan on NF-kappaB, inflammation, and tissue factor in angiotensin II-induced end-organ damage. *Hypertension*. 2000;36:282-290. 5. Davie N, Haleen SJ, Upton PD, et al. ET(A) and ET(B) receptors modulate the proliferation of human pulmonary artery smooth muscle cells. *Am J Respir Crit Care Med*. 2002;165:398-405. 6. Gaiad A, Yanagisawa M, Langleben D, et al. Expression of endothelin-1 in the lungs of patients with pulmonary hypertension. *N Engl J Med*. 1993;328:1732-1739.



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Clinical Need, Likely Survival to Govern Lung Allocation

The UNOS system could speed selection of transplant recipients.

BY MARY ELLEN SCHNEIDER

Elsevier Global Medical News

NEW YORK — The new need-based lung allocation system that went into effect last May has the potential to reduce the number of deaths of patients on the waiting list for a transplant, Dr. Joshua R. Sonett said at a conference on pulmonary and critical care medicine sponsored by Columbia University.

The new system allocates

lungs on the basis of clinical need and likely survival after transplant rather than on the sole basis of time spent on the waiting list. The United Network for Organ Sharing gives each patient a score from 0 to 100 based on an algorithm that includes the patient's diagnosis and other factors that affect survival both on the waiting list and post transplant.

The new design could help patients in later stages of disease who, under the old system, might not have survived the 1-3

years on the waiting list, said Dr. Sonett, surgical director of the Columbia University lung transplantation program.

The old system also wasted time when a lung became available because physicians had to sort through hundreds of patients who were high on the waiting list but weren't ready for a transplant. Under the new system, patients move up or down the list on the basis of clinical changes, so they should be given a high score only when they are ready for a transplant, he said.

But the system has potential drawbacks, Dr. Sonett said. For starters, the new design is complex

and has not been prospectively evaluated.

In addition, because patients no longer spend years accruing time on the waiting list, they may be less physically and psychologically prepared for their transplant.

A lung transplant is complex, and patients' conditioning is critical to their 5- and 10-year survival, Dr. Sonett said. It's key for physicians to make early referrals to a transplant team so patients can begin to prepare for a transplant, he said.

Officials at the Department of Health and Human Services published a final rule in 1999

that required the United Network for Organ Sharing to amend organ distribution algorithms to direct organs to those most in need—those most at risk of death without a transplant. This was to be balanced with utility to avoid futile transplants.

The problem under the old system was that too many patients on the list were dying as they waited for a transplant. But the challenge in revising the system to reflect a need-based approach is that pulmonary diseases are so different from most other diseases that it's difficult to figure out which patients are sicker, Dr. Sonett said. ■

Inhaled Cyclosporine Extended Survival After Lung Transplant

BY MARY ANN MOON

Elsevier Global Medical News

Inhaled cyclosporine substantially improved survival in lung transplant recipients and extended the interval in which they were free from chronic allograft rejection, reported Dr. Aldo T. Iacono of the University of Pittsburgh Medical Center and his associates.

The treatment, however, did not reduce the rate of acute allograft rejection as the researchers in this small, single-center study had hoped. Further investigation is needed to confirm that this therapy will at least address chronic rejection, which remains the leading cause of death following lung transplantation, they said (*N. Engl. J. Med.* 2006;354:141-50).

The subjects were enrolled from 1998 to 2001. Follow-up ranged from 24 to 56 months.

A total of 56 patients (46%) completed

the study. Of these, 26 had been randomly assigned to thrice-weekly self-administered nebulizer treatments with inhaled cyclosporine and 30 to placebo aerosol for a mean of 400 days.

Both groups also received conventional immunosuppression, including tacrolimus, azathioprine, and prednisone, as well as enhanced immunosuppression with pulsed corticosteroids or intravenous ganciclovir if rejection developed.

Cyclosporine conferred a substantial survival advantage, with 3 deaths (11%) in the treatment group and 14 deaths (47%) in the placebo group. Multivariate regression analysis indicated that the risk of death was 5 times higher for placebo

than for cyclosporine recipients.

Chronic-rejection-free survival also improved with cyclosporine. There were 10 cases of bronchiolitis obliterans syndrome in the treatment group, compared with 20 in the placebo group.

The number of acute rejection episodes did not differ significantly, however, with 0.44 per patient per year after administration of cyclosporine and 0.46 per patient per year after placebo.

Both aerosols caused local irritation, with 52% of the subjects reporting cough, sore throat, or dyspnea.

These symptoms of irritation typically were mild or moderate and transient, resolving within a period of 30-45 minutes after nebulizer treatment.

THE RISK OF DEATH WAS 5 TIMES HIGHER FOR PLACEBO THAN FOR CYCLOSPORINE RECIPIENTS, AS INDICATED BY MULTIVARIATE REGRESSION ANALYSIS.

"Many patients who had some initial minor respiratory symptoms developed a tolerance for the medication after a few treatments," the researchers said.

In an editorial comment that accompanied this report, Dr. Malcolm M. DeCamp Jr., of Beth Israel Deaconess Medical Center, Boston, said that physicians and surgeons should receive these findings "enthusiastically," even though they have yet to be confirmed in a larger multicenter trial. Large trials are "woefully lacking" in the field of lung transplantation because a majority of medical centers perform very few of the procedures each year.

In this study, the researchers aimed to enroll 136 patients but fell short of that goal, Dr. DeCamp said.

Moreover, fewer than half of those enrolled complied with treatment and completed the study, he noted (*N. Engl. J. Med.* 2006;354:191-3). ■

GERD Surgery May Help Prevent Chronic Rejection in Lung Transplants

BY MARY ELLEN SCHNEIDER

Elsevier Global Medical News

NEW YORK — Surgeons at Columbia University in New York are performing laparoscopic Nissen fundoplication in many lung transplant recipients who show evidence of significant gastroesophageal reflux and chronic rejection, Dr. Joshua R. Sonett said at a conference on pulmonary and critical care medicine sponsored by Columbia University.

The theory behind the surgery is that gastroesophageal reflux disease (GERD) contributes to lung injury and the development of bronchiolitis obliterans syndrome (BOS), an Achilles heel for long-term survival of lung transplant patients. Hence, preventing GERD will improve lung function and prevent chronic

rejection after transplant, said Dr. Sonett, surgical director of the Columbia University lung transplant program.

In a study published in 2003, researchers from Duke University, Durham, N.C., found that performing fundoplication in lung transplant recipients with GERD improved lung function (*J. Thorac. Cardiovasc. Surg.* 2003;125:533-42).

In that study, researchers used an esophageal pH probe to assess reflux, and found abnormal pH values in 93 of 128 patients (73%) who had undergone a lung transplant. Patients who underwent fundoplication had improved bronchiolitis obliterans syndrome scores, and some no longer met the criteria for BOS. Researchers at the University of Toronto obtained similar results, said Dr. Sonett.

The improvement in scores

exhibited by those who received fundoplication is key, because for most lung transplant recipients who begin to have bronchiolitis obliterans syndrome, there is no turning back, Dr. Sonett said.

In addition to contributing to BOS, reflux disease may cause bronchospasm and aspiration, and exacerbate asthma, he added.

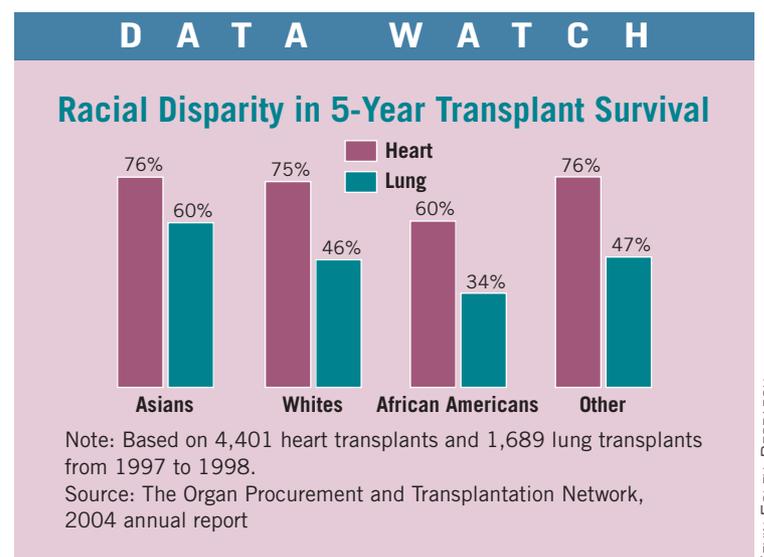
Thus far, there have been virtually no effective therapies to stop chronic rejection, he said.

"It's not the whole story, but there's certainly a population of patients post transplant who have reflux that go on to chronic rejection, and if you stop that reflux, they will stop having chronic rejection," Dr. Sonett said.

Researchers also have begun to consider the role that reflux disease plays in patients with interstitial lung disease and other lung diseases preoperatively. Clearly, physicians should not

perform reflux procedures in patients just because they have GERD and interstitial lung disease, he said, but researchers need to continue to look at what subset of patients could benefit from antireflux procedures. ■

Dr. Susan M. Harding, FCCP, comments: Dr. Sonett provides interesting data; however, the jury is still out concerning whether reflux is a potential causative mechanism for BOS development.



FluMist Bested Injectable Vaccine in Younger Children

BY HEIDI SPLETE
Elsevier Global Medical News

WASHINGTON — A new refrigerator-stable version of the live, attenuated intranasal influenza vaccine is significantly more effective than the standard injectable vaccine in preventing the flu in children aged 6-59 months, according to data from a phase III trial released by MedImmune Inc.

The vaccine, known as CAIV-T (cold-adapted influenza vaccine, trivalent), represents the next generation of FluMist, the currently approved frozen intranasal vaccine. FluMist was first licensed in 2003 for healthy people aged 5-49 years.

"There has been intense interest in expanding the age group downward, because the data from clinical trials have suggested that these vaccines would be highly effective in very young children, who are particularly susceptible to infection and who have the strongest immune response," Dr. John J. Treanor said at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

"I think this would be a useful product for very young children," said Dr. Treanor, professor of medicine and a member of the Infectious Disease Unit at the

University of Rochester (New York). He has been an investigator in some FluMist clinical trials.

Children younger than 5 years would begin with a two-dose schedule and receive a single dose in subsequent years, he said.

During the 2004-2005 flu season, 8,492 children participated in a randomized, double-blind study at 249 sites in 16 countries. In a head-to-head comparison, the children received either CAIV-T or the injectable vaccine, along with either a placebo nasal spray or placebo injection to preserve the blinded study design.

Overall, CAIV-T demonstrated a 55% greater reduction in the number of confirmed influenza-like illnesses caused by any strain, compared with the injectable vaccine.

The attack rate was significantly lower in the CAIV-T group, compared with the standard vaccine group, for both matched strains (1.4% vs. 2.4%) and unmatched strains (2.6% vs. 6.2%).

The incidence of serious adverse events was similar in both groups, according to MedImmune's statement. Predictably, run-

ny and stuffy noses were more common among children in the CAIV-T group, and injection site events were more common among those in the standard vaccine group.

Although there are some concerns about the use of CAIV-T in children with asthma, there were no significant differences in wheezing between the CAIV-T and placebo groups.

This pivotal trial is the third phase III study to demonstrate significant reductions in influenza with CAIV-T, compared with the standard vaccine, against both matched and mismatched strains. MedImmune plans to submit the data to the Food and Drug Administration later this year with a request for priority review. The vaccine may be available for the 2007 flu season, according to a company statement.

Although the two licensed and available vaccines—the inactivated vaccine shot and the live intranasal FluMist—have demonstrated safety and effectiveness, there is room for improvement, Dr. Treanor noted at the meeting sponsored by the American Society for Microbiology.



The attack rate was significantly lower in the CAIV-T group than in the standard vaccine group.

DR. TREANOR

Childhood Asthma May Lead To Permanent Lung Deficits

BY MARY ANN MOON
Elsevier Global Medical News

Many young adults who had moderate to severe asthma as children show permanent lung function deficits that are resistant to albuterol and high-dose prednisone, reported Dr. Susan L. Limb and her associates at Johns Hopkins University, Baltimore.

This finding suggests that early impairment is followed by ongoing disease progression in a large subset of asthma patients, the researchers said.

They recalled subjects who had participated in the Childhood Asthma Study (1984-1994), a randomized clinical trial of immunotherapy as an adjunct treatment of allergic asthma. The 121 original subjects were aged 5-12 years at enrollment and had moderate to severe asthma requiring daily medication. (The CAS found no differences in asthma symptoms between patients who received active immunotherapy and those who received placebo.)

In this follow-up study, Dr. Limb and her associates aimed to evaluate all 121 of the original subjects, but were able to recruit only 84 of them. These subjects were evaluated between 2001 and 2003 at a mean age of 24 years.

They underwent spirometry testing 20 minutes after inhaling two puffs from an albuterol inhaler, and nearly half (40 of the 84, or 48%) showed abnormal results. Deficits in forced expiratory volume in 1 second (FEV₁) and

the FEV₁/FVC (forced vital capacity) ratio were predominant, "which is consistent with pulmonary obstruction," the investigators said (J. Allergy Clin. Immunol. 2005;116:1213-9).

Even after inhaling albuterol, 16 subjects had an FEV₁ less than or equal to the fifth percentile, and another 9 had an FEV₁ between the fifth and tenth percentiles.

Of the 40 subjects with abnormal initial spirometry results, 28 received 7 days of high-dose (1 mg/kg) oral prednisone and returned for repeat spirometry. A total of 21 of the 28 (75%) showed no significant improvement. Even the seven who did respond to corticosteroid therapy showed "modest and incomplete" improvement. This apparent steroid resistance "suggests the presence of postinflammatory structural alterations," the researchers noted.

Adult lung function values correlated closely with childhood values across the entire cohort, "suggesting that lung impairment begins early in life and that individuals at risk might be identifiable at a young age," they said.

The entire cohort also showed significant declines over time in FEV₁ (from 96% in childhood to 84% in adulthood) and in FEV₁/FVC ratio (92% to 82%).

"Our results extend observations that airway hyperresponsiveness in childhood" not only might indicate current asthma severity but also might predict future lung deficits, Dr. Limb and her associates said. ■

Corticosteroid Topped Leukotriene In Mild, Moderate Asthma Cases

Asthma control in children with mild to moderate disease improved consistently and significantly more with an inhaled corticosteroid than with a leukotriene receptor antagonist in a recent multicenter crossover trial.

The findings provide pediatric-based support for existing recommendations favoring inhaled corticosteroids as the first-line controller therapy in patients with mild to moderate persistent asthma. Those recommendations were based on evidence from adult trials, Dr. Robert S. Zeiger of the University of California, San Diego, and his colleagues reported.

A total of 140 children aged 6-17 years with mild to moderate persistent disease using only as-needed bronchodilators were enrolled in the present double-masked, two-sequence, 16-week study in which an inhaled corticosteroid (fluticasone propionate given as a 100-mcg inhalation twice daily) and a leukotriene receptor antagonist (montelukast given as a 5- to 10-mg tablet, depending on age, once at night) were compared head to head in each patient.

Fluticasone was superior in its effects on asthma control, pulmonary function, and inflammatory biomarkers. For example, asthma control days increased significantly more with fluticasone (by 2.8 days/week, vs. 2.1 days/week with

montelukast). Similarly, Asthma Control Questionnaire scores improved significantly with both drugs (from a mean of 0.96 at baseline to 0.59 with fluticasone and 0.76 with montelukast), but indicated significantly better control with fluticasone (J. Allergy Clin. Immunol. 2006;117:45-52).

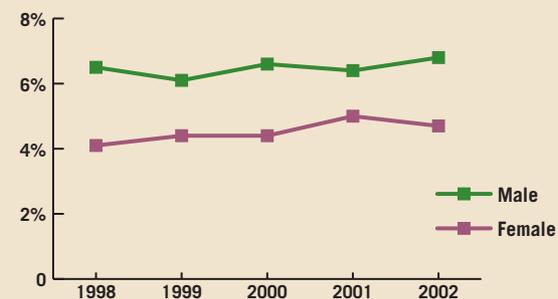
Also, fluticasone use led to significantly greater improvements than did montelukast in prebronchodilator FEV₁/forced vital capacity, peak expiratory volume variability, morning peak expiratory volume, resistance of the respiratory system at 5 Hz, and area of reactance.

Exhaled nitric oxide was shown in this study to be both a predictor of asthma control days and a response indicator, and could prove useful as a marker for identifying children only on as-needed bronchodilators who would achieve better outcomes with an inhaled corticosteroid than with a leukotriene receptor antagonist.

—Sharon Worcester

DATA WATCH

Percentage of Children Aged 0-17 Years With Asthma



Source: Child Trends analysis of National Health Interview Survey data

Device May Decrease Ventilator-Associated Pneumonia

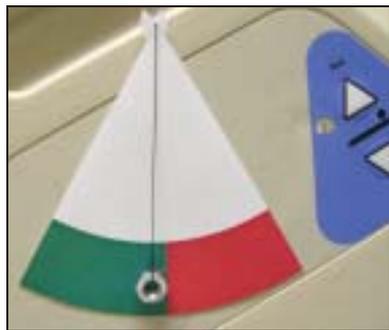
BY ROBERT FINN

Elsevier Global Medical News

SAN FRANCISCO — A simple, easy-to-build device significantly increases compliance with recommended guidelines on elevating the head of the bed in the intensive care unit, Dr. Zev Williams reported at the annual congress of the Society of Critical Care Medicine.

Previous studies have shown that elevating the head of the bed 30-45 degrees in intubated patients can greatly decrease aspiration, which is one of the main causes of ventilator-associated pneumonia (VAP). VAP afflicts 9%-40% of all patients in the ICU, resulting in significant increases in ICU stays, financial costs, and mortality.

The Centers for Disease Control and Prevention has stated that unless there's a contraindication, the head of the bed should be elevated in all patients at high risk of developing aspiration pneumonia. Although many hospitals have incorporated this recommendation as part of their official policy, and although elevating the head of the bed is both simple and costless, observational studies show the mean elevation of intubated patients to be between 16 and 22 degrees—and the majority of patients, up to 86%, remain in the supine position.



When the head of the ICU bed is elevated to precisely 30 degrees, the indicator rests on the border between the red and green bands.

There are several reasons for this poor compliance, said Dr. Williams, of Brigham and Women's Hospital and Massachusetts General Hospital, Boston. For one thing, it's surprisingly difficult to estimate angles accurately, and staff tends to overestimate angles. While some hospital beds now come with angle indicators, the gauges are often under the bed and difficult to read. And these indicators can provide inaccurate readings, especially when the patient is placed in the Trendelenburg position.

Furthermore, in Dr. Williams' view, most of these angle indicators provide too much information. They often measure angles in 5 degree increments from 0 to 60 degrees or higher, when all that's

really important is whether the angle is more or less than 30 degrees.

His solution: Cut a piece of paper into a pie-shaped wedge, and mark two bands of red and green at the bottom. Affix a string to the wedge vertex and hang a small weight—a hexagonal nut from a bolt.

This device, for which a patent is pending at Massachusetts General Hospital, is fastened to a hospital bed and calibrated. When the head of the bed is elevated to precisely 30 degrees, the indicator rests on the border between the red and green bands. At lower angles, the indicator is fully in the red; at higher angles, it's fully in the green.

Dr. Williams and his colleagues conducted a study to investigate whether this

simple device could improve compliance with the recommendations.

For 2 weeks before attaching the devices, the investigators took daily measurements of the beds of all ICU patients, except those for whom head elevation was contraindicated. Elevations of 28 degrees or higher were counted as compliant. Out of 166 measurements, only 23% were in compliance, and the average elevation angle was just 22 degrees.

Similar measurements were made for 2 weeks after attaching the devices. Of 102 measurements, 72% were in compliance, and the average angle was 31 degrees. Both differences were statistically significant.

A survey of nursing staff revealed that 72% regarded the device as an improvement. Further studies will be required to determine whether the device results in measurable improvements in the incidence of VAP, Dr. Williams said. ■

Dr. Michael H. Baumann, FCCP, comments: Dr. Williams should be commended for introducing simplicity into an ever more complex intensive care environment. His concept for indicating appropriate elevation of the head of the bed has the potential for tremendous patient care improvement.

AMERICAN COLLEGE OF CHEST PHYSICIANS

2006

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Celebration of Pediatric Pulmonology 2006
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April 6-9

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August 25-27

ACCP Clinical Grand Rounds on Cardiothoracic Surgery and Critical Care
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ACCP Sleep Board Review Course 2006
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August 25-29

ACCP Critical Care Board Review Course 2006
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NEWS FROM THE COLLEGE



PRESIDENT'S REPORT

Cough Guidelines: Better Outcomes Are the True Goal

As I sit to compose this month's President's Report, the College is all over the news (and fortunately, all good). The release of the "Cough Guidelines" in *CHEST* has certainly created a "lot of buzz." For example, I saw Dr. Richard Irwin, Chair of the "Diagnosis and Management of Cough: Evidence-Based Clinical Practice Guidelines" last night on the "ABC Nightly News," and Dr. Peter Dicipinigitis this morning on "Good Morning America." I was interviewed yesterday by



BY W. MICHAEL ALBERTS, MD, FCCP

numerous newspapers, several radio stations, and just now Irish Public Radio. (I plan to "google" myself later today just to see if they printed what I thought I said.) The Wall Street Journal and USA Today, among many other (if not most) newspapers, carried prominent articles today, and the television exposure has been impressive.

While this sort of publicity is great, it is not the primary goal of the guideline development effort. Led by the Health and Science Policy Committee,

the College has produced a number of extremely valuable documents that aim to assist clinicians in delivering the most appropriate care, so that they may achieve the best possible outcomes given the current state of medical care.

As one might imagine (and those who have been on the development and writing committees can attest), production of true evidence-based clinical practice guidelines is not easy (or cheap, if you do it right). To excerpt a long and arduous process, the entire relevant literature must be systematically reviewed, and those studies judged appropriate are graded. Based on the collected information, recommendations are then formulated. Your College has invested a lot of time, effort, and resources in developing these guideline documents, but as this is a natural extension of our core competence, namely education, the final result is well worth the effort.

After development of guidelines, the

next logical step is to use them. For some inexplicable reason, this has proven to be problematic. Even though the guideline recommendations are based on the best available information, study after study has shown that physicians do not always, or quickly, incorporate the recommendations into their daily practice. There are many postulated reasons for this phenomenon (patient choice, comorbid conditions, and economic limitations, among others), but much more study is needed. The College is on top of that also, as evidenced by the establishment of a new committee, namely the Quality Improvement Committee, but more about that initiative in a future column.

So let me close by again thanking the chair and members of the cough guideline committee, the authors of the document, and the College staff for a job well done and congratulate them on generating some well-deserved publicity for the ACCP and its "patient-focused" efforts. ■

First Joint APSR/ACCP Meeting Kicks Off With Great Success

BY STEVE WELCH

ACCP Vice President of Publications & Executive Editor, *CHEST*

The First Joint Congress of APSR/ACCP (10th Congress of the APSR) was held November 11-14, 2005, in Guangzhou, China.

The congress program, overseen by NanShan Zhong, MD, FCCP, touted speakers from many countries, including more than 20 members of ACCP leadership who agreed to participate at the request of ACCP Immediate Past President and APSR/ACCP Congress joint-chair Paul Kvale, MD, FCCP. ACCP President Dr. W. Michael Alberts and President-Elect Dr. Mark Rosen attended on behalf of the ACCP Executive Committee. A full list of faculty is available at the congress Web site, www.apsr2005.com. More than 2,500 attendees enjoyed the conference, a substantial increase over the 1,800 estimated to attend, making it the highest attended APSR meeting in the society's history. APSR and ACCP hope that these joint congresses will continue to provide educational excellence in the Asia-Pacific region.

APSR and ACCP have agreed to

follow up on the success of the first joint congress by holding the second joint congress in 2007 on Australia's Gold Coast. In addition, ACCP and APSR leaders met to discuss future collaboration, including participation in guideline development projects, more joint educational programs during each society's meetings. ACCP thanks APSR for the opportunity to participate in the first joint congress.

During the Guangzhou congress, the ACCP had a highly trafficked booth situated adjacent to a booth for the *CHEST* China Edition, which was staffed by Wendy Wu and the staff of Everwell Publishing of Shanghai, the translation partners for the *CHEST* China Edition. Immediately following the congress, Everwell Publishing and *CHEST* China held the *CHEST* China First International Key Journal Manuscript Submission Training Program seminar. Faculty included Richard S. Irwin, MD, FCCP (Editor in Chief of *CHEST*), Stephen J. Welch (Executive Editor of *CHEST*), Prof. J. Patrick Barron (Tokyo Medical University) and Raoul Breugelmans (Tokyo Medical University). The seminar was chaired by NanShan Zhong, MD, FCCP (ACCP Regent for China). ■



Presidential symposium participants (L-R): W. Michael Alberts, MD, FCCP (ACCP President); Yoshinosuke Fukuchi, MD, FCCP (APSR); Giovanni Viegli, MD (ERS); NanShan Zhong, MD, FCCP (ACCP Regent for China, president of CMA); and Paul Kvale, MD, FCCP (ACCP Immediate Past President). Not pictured: Peter Wagner (ATS)

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THE CHEST FOUNDATION Announcing 2006 Award Opportunities

2006 Award Opportunities

Each year, through its extensive awards program, The CHEST Foundation confers awards to ACCP members in clinical research in chest and critical care medicine and for humanitarian service. In 2005, The CHEST Foundation proudly awarded over \$600,000 for research, leadership in end-of-life care, and pro bono service. In 2006, it will continue the tradition of recognizing and rewarding health-care professionals who are making a difference in the lives of patients and their families.

Applications are being accepted for:

The Alpha-1 Foundation/CHEST Foundation Clinical Research Award in Alpha-1 Antitrypsin (AAT) Deficiency

▶ Deadline of April 28, 2006

▶ Who should apply? ACCP members involved in AAT deficiency research

▶ 1-year research grant of \$25,000

The American Society of Transplantation (AST)/CHEST Foundation Clinical Research Award in Lung Transplantation

▶ Deadline of April 28, 2006

▶ Who should apply? AST or ACCP members involved in lung transplantation

▶ 1-year research grant of \$40,000

The Association of Specialty Professors/CHEST Foundation of the American College of Chest Physicians Geriatric Development Research Award

▶ Deadline of March 31, 2006

▶ Who should apply? ACCP members

who are within their first 3 years of faculty appointment involved in chest medicine that relates to geriatrics

▶ 2-year research grant of \$50,000 each year

The CHEST Foundation Humanitarian Awards

Humanitarian Recognition Awards

▶ Deadline of May 15, 2006

▶ Who should apply? ACCP members involved in pro bono service

▶ Award of \$5,000 toward winning project/service



Dr. Subhakar Kandi, a 2005 Humanitarian Recognition Award winner, examines a child at his project in India.

Humanitarian Project Development Grants

▶ Deadline of June 15, 2006

▶ Who should apply? ACCP members involved in pro bono service

▶ Award of \$25,000 toward winning project/service

The CHEST Foundation/LUNGEvity Foundation Clinical Research Award in Lung Cancer

▶ Deadline of April 28, 2006

▶ Who should apply? ACCP members involved in lung cancer research

▶ 2-year research grant of \$37,500 each year

Clinical Research Trainee Awards in Asthma, COPD, and Pulmonary Fibrosis

[financial support from GlaxoSmithKline (asthma), ALTANA Pharma US (COPD), and Pulmonary Fibrosis Foundation (pulmonary fibrosis)]

▶ Deadline of May 1, 2006

▶ Who should apply?

ACCP affiliate members involved in a subspecialty program that relates to asthma, COPD, or pulmonary fibrosis

▶ Two 1-year research grants of \$10,000 each in asthma, COPD, and pulmonary fibrosis

▶ The CHEST Foundation Clinical Research Award in Women's Health

▶ Deadline of May 15, 2006

▶ Who should apply? ACCP members (all career levels) who are involved in research focused on women's health care

▶ 1-year research grant of \$10,000

Roger C. Bone Advances in End-of-Life Care Award

▶ Deadline of April 15, 2006

▶ Who should apply? ACCP members who demonstrate outstanding leadership in end-of-life care, with a focus on improved communication, compassion, and effective listening between physician, patient, and family

▶ 1-year award of \$10,000 toward project/service

Scientific Abstract-Related Awards

▶ Deadline of May 24, 2006

▶ Who should apply? Authors of original investigative work who successfully present their scientific abstract at CHEST 2006

▶ Various grants from \$500 to \$2,275 in the categories of Best Posters, Alfred Soffer Research Awards, and Young Investigator Awards

Access more details about these award opportunities at www.chestfoundation.org. Don't delay! Note that many of the awards have an early spring application deadline.



Wristband Sales Are Thriving

ACCP members are getting involved in the antismoking efforts of

The CHEST Foundation by purchasing the "Love Your Lungs™" wristbands at www.chestfoundation.org.

Individual youth- and adult-size wristbands are \$2 each and \$75 for 50. These make wonderful gifts for patients, elementary school children, high school teens, and family members. They serve as powerful reminders to keep your lungs healthy.

The CHEST Foundation's Ambassadors Group created the wristbands to raise funds to support The CHEST Foundation's lung health education programs.

Through the generous financial support of Boehringer Ingelheim Pharmaceuticals, Inc., the "FIGHT COPD" wristbands were made to create awareness about COPD, a life-threatening disease. COPD includes the diseases of chronic bronchitis and emphysema. Both ACCP and Boehringer Ingelheim Pharmaceuticals are committed to finding a cure for COPD.

Adult- and youth-size wristbands are available for purchase from the ACCP Product Catalog at the ACCP Store at www.chestnet.org. The cost is \$2 for individual wristbands and \$75 for 50. Funds collected from the sales of these wristbands support COPD awareness and clinical research activities.

Don't delay! Order your wristbands today! ■

EDUCATIONAL RESOURCES

Health and Science Policy: What's Here, What's New, What's Coming

BY CARLA HERRERIAS
ACCP Clinical Research Analyst

The ACCP, through its Health and Science Policy Committee, is the leading resource in development of evidence-based guidelines in the field of chest medicine. Health and Science Policy has been very busy in its efforts to develop evidence-based clinical practice guidelines, promote evidence-based medicine, and optimize patient care by integrating the guidelines into clinical practice. In 2005, two

new practice guidelines were published on aerosolized medications and atrial fibrillation following cardiac surgery.

This year will bring the release of the aerosol *Clinical Resource*, which will include the physician quick reference guide, patient education materials, a slide set, as well as other useful resources for the clinician. In addition, the comprehensive guidelines on managing cough will be published in *CHEST*, along with an accompanying *Clinical Resource*. The guidelines define acute, subacute, and

chronic cough and provide evidence-based recommendations and algorithms for diagnosing and treating chronic cough due to a variety of causes, from the most common to very infrequent. Finally, the revised guidelines on pulmonary rehabilitation will be published and provide new evidence, new recommendations, and changes from the previous guidelines.

Guideline projects currently in development include the Diagnosis and Management of Lung Cancer (second edition). This will be a comprehensive

update of the previous lung cancer guidelines, with systematic reviews of the available treatments at all stages of the disease. Writing is underway for new guidelines on occupational asthma. Finally, the treatment section of the pulmonary arterial hypertension guidelines is being updated due to the recent approval of new therapeutics.

Several new projects are just beginning. Two new evidence-based guidelines are being developed on monitoring of immunosuppressive drugs used in lung disease and management

of dyspnea in advanced lung disease and congestive heart failure. In addition, the ACCP has begun a project to develop evidence-based guidelines on a nonclinical topic. We are working with the Agency for Healthcare Research and Quality to put together an evidence report on the effectiveness of continuing education. The report will be used to develop guidelines.

For further information on all Health and Science Policy activities, please visit the HSP Web site at www.chestnet.org/education/guidelines/. ■

NEWS FROM THE COLLEGE



CRITICAL CARE COMMENTARY

Interdisciplinary Liberation: The Modern Weaning Team

Successful separation of the patient from mechanical ventilatory support has evolved in recent years from a physician-dictated process of gradual reduction in the level of ventilatory support, *ie*, traditional weaning, to one of identifying a state of high likelihood that the patient will be able to breathe independently, achieved through coordinated interdisciplinary testing (MacIntyre et al. *Chest* 2001; 120:375S). In order to achieve successful independent breathing and removal of the endotracheal (ET) tube, the patient should have demonstrated improvement in the underlying indication for mechanical ventilation; good medical stability; sufficient drive to breathe; adequate thoracic mechanics and gas exchange to meet ventilation and oxygenation targets; endurance to maintain unsupported ventilation; ability to maintain a patent upper airway of sufficient caliber; intact protective airway reflexes; and adequate cough for secretion clearance (Ramachandran et al. *Crit Care* 2005; 9:138).

A structured assessment of these factors, performed by on-site nurses and respiratory therapists in a rapid, step-wise fashion, can streamline the process and reduce time with the ventilator while preserving accuracy. Benefit of these protocols has been demonstrated in many (Ely et al. *N Engl J Med* 1996; 335:1864; Kollef et al. *Crit Care Med* 1997; 25:567; Marelich et al. *Chest* 2000; 118:459; Grap et al. *Am J Crit Care* 2003; 12:454; Tonnelier et al. *Crit Care* 2005; 9:R83), but not all (Krishnan et al. *Am J Respir Crit Care Med* 2004; 169:673), prospective clinical trials.

The structure of most protocols consists of a set of screening criteria that address many factors, followed by a test of ventilatory endurance—the spontaneous breathing trial (SBT). Some approaches add a test intended to detect impending postextubation stridor prior to extubation. If all components are successfully

passed, the patient is extubated. Goals of the screening criteria include establishing that the SBT will be safe and will have a reasonable likelihood of success and assessing factors other than those related to ventilation and endurance. It is important to consider, however, that overly conservative criterion might unnecessarily impede progressing to the SBT and, inadvertently, delay extubation.

The screening evaluation generally includes some assessment of the *medical stability*, because medical factors influence the likelihood of reintubation following planned or unplanned extubation (Epstein. *Intensive Care Med* 2002; 28:535; Listello and Sessler. *Chest* 1994; 105:1496). Often, the absence of ongoing vasopressor therapy for shock is used as a surrogate for medical stability. Among the nonventilation criteria, mental status is perhaps most tightly linked to weaning success (Salam et al. *Intensive Care Med* 2004; 30:1334). A patient who is not alert may have a suboptimal drive to breathe, have an inability to maintain a patent upper airway, be predisposed to aspiration, and/or have trouble clearing secretions. Further, level of consciousness is determined largely by the amount of sedative and analgesic medications administered. Strategies to reduce continuous infusion sedation using a treatment protocol (Brook et al. *Crit Care Med* 1999; 27:2609; Tonnelier et al. *Crit Care* 2005; 9:R83), to use analgesia (rather than sedative-based therapy) (Breen et al. *Crit Care* 2005; 9:R200), and to employ daily cessation of sedative therapy (Kress. *N Engl J Med* 2000; 342:1471) have been associated with earlier weaning and, thus, shorter duration of mechanical ventilation in randomized, controlled trials. Daily cessation of sedatives likely presents additional opportunities for weaning assessment

during the awake periods (Sessler. *Crit Care Med* 2004; 32:1413). Adequate alertness to proceed to the SBT is inferred in some screening protocols by absence of continuous infusion sedation, whereas direct evaluation of mental status using a sedation scale is utilized in others.

Reintubation, or extubation failure, is commonly caused by progressive hypoxemia and/or hypercapnia. Thus, identifying patients who are at high risk for these gas-exchange problems is important. Acceptable oxygenation while mechanically ventilated is a component of virtually all screening tests. The criteria include tolerance of reduction in fraction of inspired oxygen (F_{iO_2}) and positive end-expiratory pressure to acceptable levels (usually 0.5 and 5 to 8 cm H_2O , respectively) and/or measurement of $PaO_2:F_{iO_2}$, with thresholds of 200, 150, or 120 mm Hg, described in different protocols. A more liberal approach to oxygenation may be preferred, because conservative oxygenation criteria ($PaO_2:F_{iO_2}$ 200 mm Hg) was the most common reason for screening failure among patients who were eventually and successfully extubated, despite never passing a daily screen in one large case series (Walsh et al. *Br J Anaesth* 2004; 92:793).

Adequate ventilation, including ventilatory reserve, is crucial for successful extubation, and, over the years, tests of gas exchange, respiratory muscle strength, ventilatory volume, and endurance have been utilized. Some estimate of lung mechanics and muscle strength can be gleaned from a rapid, shallow breathing index, in which the respiratory rate is divided by the average tidal volume during 1 min of unsupported breathing. The rapid, shallow breathing index is utilized in some screening protocols, with a threshold of 105 to proceed, although some protocols use a more liberal (125) threshold or omit it altogether.

The SBT tests the patient's ability to breathe independently (or nearly so) for an extended time period prior to extubation. To perform the SBT, mechanical ventilatory support of a magnitude estimated to be just enough to overcome the work of breathing through the ET tube is applied, using continuous positive airway pressure, pressure support ventilation, or automatic tube compensation. While the SBT is being conducted for 30 to 120 min (depending upon the protocol), the patient is closely observed for evidence of intolerance of the reduced level of ventilatory support, as indicated by significant deterioration in vital signs, sustained hypoxemia, respiratory fatigue, respiratory distress, or other clinical deterioration. If the SBT is passed, the patient is extubated; if SBT intolerance occurs, ventilatory support is reinstated. While the SBT is

considered the pivotal test for independent breathing, it is noteworthy that many approaches are utilized with varying durations of testing, means of providing low-level mechanical ventilatory support, levels of support, and criteria for SBT failure.

Clinicians have often noted that patients who fail extubation have other common clinical characteristics, such as inability to clear secretions or waxing and waning mental status, each difficult to quantify and, thus, may not be effectively examined in screening criteria. Indeed, in a recent prospective series, all patients who had passed an SBT but had marginal mental status, poor cough (cough peak flow 60 L/min), and large sputum volume failed extubation (Salam et al. *Intensive Care Med* 2004; 30:1334). Future weaning and extubation protocols should incorporate these parameters.

Prior to extubation, many clinicians perform an informal or, less frequently, a quantitative test of air movement around the ET tube and through the vocal cords, with the ET tube cuff deflated. Postextubation stridor is estimated to occur in 2 to 16% of ICU patients (Jaber et al. *Intensive Care Med* 2003; 29:69), and the intent of the "cuff-leak" test is to help identify the high-risk patient prior to extubation. Several investigators have demonstrated that a leak of 11 to 12% or 110 to 130 mL has good sensitivity and specificity for predicting stridor, particularly for patients with longer duration of intubation (Jaber et al. *Intensive Care Med* 2003; 29:69; Miller and Cole. *Chest* 1996; 110:1035; Sandhu et al. *J Am Coll Surg* 2000; 190:682). However, this approach was not effective for predicting stridor after brief intubation for cardiac surgery (Engoren. *Chest* 1999; 116:1029).

In summary, liberation from mechanical ventilation and from the ET tube is a process that can be streamlined and enhanced by using a comprehensive approach conducted by an interdisciplinary team of physicians, nurses, and respiratory therapists. Many clinical factors can influence the success, and a structured strategy implemented by on-site clinicians ensures that this can be performed in a timely fashion. Can the weaning team be improved upon? Investigators are piloting computer-driven, closed-loop, ventilator management and weaning systems that may be faster than intensivists (Bouadma et al. *Intensive Care Med* 2005; 31:1446), so stay tuned. ■

Curtis N. Sessler, MD, FCCP
Orhan Muren Professor of Medicine
Virginia Commonwealth University Health System
Medical Director of Critical Care
Medical College of Virginia Hospitals
Richmond, VA
Section Editor—Critical Care Commentary



ACCP To Climb the 'Hill' Once Again

Now a respected tradition of the ACCP, the 13th Annual ACCP Capitol Hill Caucus will be held this year on March 6 and 7.

Previous Caucus events have hosted an array of important speakers, including Senator Bill Frist, MD, FCCP; Senator Richard Durbin (D-IL);

State Attorney General, J. Joseph Curran, Jr., of Maryland; noted author, Christopher Buckley; and the tobacco "insider," Jeffrey Wigand.

The annual Caucus gives ACCP participants an opportunity to meet with

members of Congress to educate them about issues impacting chest and critical care medicine. Likewise, ACCP members can hear updates from Congressional leaders on policies affecting the pulmonary/critical care workforce shortage, Medicare reimbursement, pay for performance, and more.

ACCP Governors are being invited to the Caucus this year with the hope of representation of all US states.

Watch for a late spring issue of CHEST PHYSICIAN for a report on Caucus outcomes. ■



Inside NetWorks: Web Page Templates, Home Ventilation Resources

Disaster Response NetWork

This is one of the newest ACCP NetWorks and is showing its extreme versatility and flexibility with the rapidly evolving field of disaster medicine. The NetWork has assisted The CHEST Foundation with its response to both the tsunami and the recent hurricanes. Members have created and distributed the course, "Disaster Medicine: Beyond the First Response," for hospital physicians and providers. This course is available on CD and is currently being evaluated for presentation in Thailand. Additional NetWork endeavors include creating a national response database of potential volunteers, facilitating volunteer opportunities with other relief organizations for our membership, creating a Web-based education module, and championing disaster medicine education in medical schools. The NetWork comprises a broad representation of clinicians with military and civilian expertise in disaster preparedness, response, and management. The Disaster Response NetWork welcomes all interested ACCP members to join the NetWork via the ACCP Web site (www.chestnet.org). Experience in disaster medicine not necessary for membership.

e-Advisory NetWork

The e-Advisory NetWork's mission is to promote and facilitate pulmonary and critical care medicine education using information technologies and telecommunications. Current projects include the evaluation of other organizations' Web sites, developing Web site standards, and working with the ACCP to develop new Web site standards, with an initial focus on assisting the ACCP's 26 NetWorks in the development of standard Web page format and guidelines for posting content.

At our NetWork meetings during CHEST 2005, and in a recent teleconference, the e-Advisory Steering Committee discussed the need for greater utilization of the ACCP Web site to improve the delivery of information and to improve communication between members. In these discussions, the development of a standard template

design for NetWork Web pages and user-friendly interfaces were recommended. The Council of NetWorks has asked the e-Advisory NetWork to spearhead the development of this standard Web page format for all the NetWorks and create guidelines for posting content. In addition, the NetWork will make recommendations regarding the development and adoption of more sophisticated Web communication tools. Emerging technologies can be utilized to meet the needs of the ACCP and NetWorks; these include template designs, password-protected threaded conversations, and podcasting.

The e-Advisory NetWork would like to hear your suggestions on how the ACCP Web site and, specifically, Web pages, can enhance ACCP membership, increase involvement, and meet your needs. Suggestions can be e-mailed to networks@chestnet.org.

Home Care NetWork

The Home Care NetWork continues to contribute significantly toward the overarching mission of the ACCP through its active involvement. The NetWork continues to pursue endeavors in the three goal areas established at the NetWork's inception (see our Web page at www.chestnet.org/networks/home_care/index.php). The goals include providing NetWork members access to information and research, enhancing members' understanding about the clinical aspects of home care, and serving the ACCP as the resource for state-of-the-art home care.

We have recently received approval from the ACCP Council of Committees for a project to develop a Home Ventilation Resource Center that will serve as an information repository on many aspects of home ventilation for both national and international use. This project will be a major focus of the steering committee in the coming year.

On a sad note, the Home Care NetWork recently lost one of its stalwart and founding members, Edward "Tony" A. Oppenheimer, MD, FCCP, to complications of multiple myeloma. Tony was inexhaustible in his efforts to help those with neuromuscular disease

and respiratory issues achieve a better quality of life. He worked on all levels to achieve this goal. He will be sorely missed but not forgotten by all of us in the home care community.

Interstitial and Diffuse Lung Disease NetWork

There was clearly a great deal of interest in interstitial lung disease at CHEST 2005. The Interstitial and Diffuse Lung Disease (IDLD) NetWork Open Meeting was very well attended, and Michael P. Keane, MD, FCCP, gave an excellent update on our current knowledge of interstitial pulmonary fibrosis (IPF) pathogenesis and potential therapies. Other IDLD NetWork presentations included clinical trial results for infliximab for sarcoidosis and etanercept for IPF. The IDLD Web page now provides a patient brochure on IPF, a questionnaire for patients undergoing evaluation for suspected ILD, and a directory of ACCP Fellows with interest and expertise in IPF or sarcoidosis. An ongoing project on early diagnosis of ILD is underway, and proposals for new projects are welcome. The 2006 CHEST IDLD track promises to provide interesting and controversial sessions. Highlight sessions on sarcoidosis, IPF, and vasculitis will be presented, and the newly organized, NIH-sponsored Clinical Trial Network's agenda for treatment of IPF will be presented.

Interventional Chest/Diagnostic Procedures NetWork

The Interventional Chest/Diagnostic Procedures NetWork has a particular interest in all aspects of invasive airway interventions. The steering committee comprises thoracic surgeons and interventional pulmonologists. The NetWork has focused, not only on the conduct of interventional procedures, but also on the education and training issues unique to advanced pulmonary procedures.

Accomplishments include the publication of guidelines for procedure standards (*Chest* 2003; 123:1693); a bronchoscopy infection control paper (*Chest* 2005; 128:1742); and two papers about perceived adequacy of training in interventional procedures (*Chest* 2005;

127:1614; *J Bronchol* 2005; 12:88).

Current projects include the creation of a consensus document about the ideal bronchoscopy suite design; validation of procedure performance metrics processes; and development, implementation, and validation of an evaluation tool for fellowship bronchoscopy training. For more information, e-mail networks@chestnet.org.

Occupational and Environmental Health NetWork

The Occupational and Environmental Health (OEH) NetWork is dedicated to increasing the understanding of the lung and cardiac manifestations of disease caused by exposures in the home, work, and recreational environment. The NetWork has several ongoing projects and invites ACCP members to become active in these projects, propose new projects, and come to the NetWork open meeting held at each annual CHEST meeting.

Our current projects include:

- ▶ Working on the Supplemental Aviation Oxygen Awareness Project, which will have professional and patient education components, led by Clayton T. Cowl, MD, FCCP.
- ▶ Working with the Health and Science Policy Committee to develop evidence-based guidelines on occupational asthma, under the leadership of Susan M. Tarlo, MBBS, FCCP.
- ▶ Developing the OEH NetWork Web page, under the leadership of Ware G. Kuschner, MD, FCCP, NetWork Vice-Chair.
- ▶ Continuing the Delphi Project on Asbestos-Related Lung Disease, which is in its final phase before publication, under the leadership of Daniel E. Banks, MD, FCCP.

We are looking for participation by clinicians in practice and academics for suggestions on how we can help you care for patients with occupational and environmental disease. Please visit our Web page at www.chestnet.org/networks/oeh/index.php. To contact us regarding OEH NetWork activities and projects, write to the NetWork Chair, Feroza M. Daroowalla, MD, FCCP, at feroza.daroowalla@stonybrook.edu. ■

ACCP, The CHEST Foundation Recognize 'Friends of the College'

The ACCP and The CHEST Foundation are proud to recognize the following Friends of the College for their financial support of College activities during 2005:

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NEWS FROM THE COLLEGE



Shelter Medicine: Beyond the First and Second Response

BY ASHA DEVEREAUX,
MD, MPH, FCCP

Chair—ACCP Disaster Response NetWork
Lead Physician, San Diego Medical
Reserve Corps

I was one of 30,000 eager medical volunteers who responded to the call by the US Department of Health and Human Services (HHS) to assist the Gulf area following Hurricane Katrina. I was nominated for deployment by our local Medical Reserve Corps (a volunteer medical service group under the umbrella of the HHS). As an alumnus of Tulane University's School of Medicine, I felt a gravitational pull to give back to the community that educated me. As a pulmonary/critical care physician with 11 years in the US Navy, I felt that I could be ready for whatever I faced.

Leaving 1 month following Katrina's landfall, I envisioned providing pulmonary/critical care coverage for weary physicians at local hospitals, wrongly assuming that most ill patients would have been placed in facilities by now. However, following my arrival to FEMA's tent city in Baton Rouge, Louisiana, along with volunteers from across the United States, I discovered that there were still many in shelters. I volunteered to assist at a special needs shelter in Alexandria, Louisiana, while others offered to work in mobile immunizations units or at other area shelters. The Alexandria shelter primarily housed people who required medical support devices, home health care, or dialysis on a routine basis. There is very little literature regarding "shelter medicine," but special needs shelters are a routine part of the public health system operations in hurricane-prone areas. These shelters typically house patients for 1 to 2 days until roads, power, and utilities are reestablished following hurricane evacuations. The magnitude of devastation following Katrina resulted in a prolonged stay for most evacuees who required multiple medications, dressings, and supplies (Needs assessment of the displaced population following the August 1999 earthquake in Turkey. *Disasters* 2001; 25:67-75).



We set up a pharmacy in a small 'coatroom' next to the shelter, with phones, walkie-talkies, and a copy/fax machine.



This was our 'stockroom.' It was exposed on the stage due to convenience and a lack of storage rooms.

The special needs shelter in Alexandria was located in a former YMCA gymnasium. Aside from two EMS ambulances and an Air Force guard, there was no indication that over 100 evacuees were living in the gym, with an additional 100 higher acuity evacuees in a building a block away. Approximately half of our evacuees were from the New Orleans area and the other half from Lake Charles. Hurricanes Katrina and Rita placed a double burden on the Alexandria shelter as it met the needs of both victims. No one could return home until guarantee of running water, electricity, transportation, and a safe home was assured.

Restrooms were shared with the evacuees, showers were outdoors with some lukewarm water piped in, and everyone slept on folding cots. Our cell-phones became our beepers.

A pulmonologist was a welcome addition to the 20 medical staff at the shelter, so I was assigned to review all patients receiving oxygen and to anticipate additional oxygen requirements for new arrivals.

There were only two concentrators (since many were 'discharged' with patients upon transfer), so H and E cylinders were providing continuous oxygen with two respiratory therapists performing all tank changes. The tanks were being re-supplied by a

local hospital that had received a FEMA grant to support the shelter. Electrical extension cords and outlets were also early limitations to the use of concentrator units.

The respiratory therapists and I formed a "pulmonary team" that then connected with area oxygen vendors, distributed concentrators to those patients who needed continuous oxygen (reducing the middle of the night pages), and modified patient medications to decrease the frequency and need for nebulizer treatments. A previous volunteer physician had brought levalbuterol inhalation solution and tiotropium inhalation devices (not on the Strategic National Stockpile formula), so this helped with the change.

Unfortunately, smoking was a form of comfort and socialization for the evacuees, despite many who had formerly quit. One of our best contributions was to eliminate the presence of oxygen tanks in the smoking areas, since we had witnessed one of the more severe COPD patients smoking while using oxygen. Although this safety hazard seems so obvious now, the chaos associated with providing meals and medical care to a displaced population in the setting of impaired communication, supply limitations, and staff turnover makes the easiest tasks seem Herculean.

COPD exacerbations and aspiration pneumonia were some of the pulmonary conditions requiring my expertise. A variety of other medical conditions were also addressed at this shelter, including alcohol withdrawal, depression, delirium, a diarrheal outbreak, hypertension, diabetes, newly diagnosed malignancy, and bowel obstruction. An evacuee was receiving gamma interferon for IPF, while another was on a continuous infusion of milrinone via PICC. Coumadin dose monitoring was performed and a sleep study arranged for witnessed sleep apnea and severe snoring disrupting the other 50 'roommates'.

As staff turnover occurred, the corporate memory left, and reeducation was continually needed. Anything I learned about an evacuee, I shared at least three times with others, so that things didn't "fall through the cracks." Communication was vital to everything we did.

Most of us left with much less clothing than when we arrived, leaving most of our jeans, shoes, socks, and t-shirts with evacuees of similar size. They were touched. We were honored!

Disasters will occur again, respiratory illnesses are common, and the chest physician will be welcomed in any disaster situation because of his/her ability to create order out of chaos! ■

This Month in CHEST: Editor's Picks

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

► **Applied Medical Informatics for the Chest Physician: Information You Can USE!**

William F. Bria II, MD, FCCP

► **Serum Cardiovascular Risk Factors in Obstructive Sleep Apnea**

Murat Can, MD; Serefden

Açikgöz, MD; Görkem Mungan, MD; Taner Bayraktaroglu, MD; Erdem Koçak, MD; Berrak Güven, MD; and Selda Demirtas, MD

► **Budesonide/Formoterol in a Single Inhaler for Maintenance and Relief in Mild to Moderate Asthma: A Randomized, Double-blind Trial**

Klaus F. Rabe, MD, PhD; Emilio Pizzichini, MD, PhD; Björn Ställberg, MD; Santiago Romero, MD;

Ana M. Balanzat, MD; Tito Atienza, MD; Per Arve Lier, MD; and Carin Jorup, MD

► **Translating Research to Clinical Practice: A One-Year Experience With Implementing Early Goal-Directed Therapy for Septic Shock in the Emergency Department**

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► **Randomized Controlled Trial of Emergency Department Interventions to Improve Primary Care Follow-up for Patients With Acute Asthma**

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Cydulka, MD, MS; Brian H. Rowe, MD, MSc; Sunday Clark, MPH; and Carlos A. Camargo, Jr., MD, DrPH

► **Effect of Interactions Between Lower Airway Bacterial and Rhinoviral Infection in Exacerbations of COPD**

Tom M. A. Wilkinson, MBBS; John R. Hurst, MD; Wayomi R. Perera, MD; Mark Wilks, PhD; Gavin C. Donaldson, PhD; and Jadwiga A. Wedzicha, MD

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NEWS FROM THE COLLEGE

The New Face of *CHEST* and New Instructions to Authors

BY STEVE WELCH

ACCP Vice President of Publications & Executive Editor, *CHEST*

January 2006 heralded a host of changes for the ACCP's flagship medical journal, *CHEST*. In his editorial in that issue (Irwin RS. The new "face" of *CHEST* heralds a new era. *CHEST* 2006; 129:1-3), Editor in Chief Richard S. Irwin, MD, FCCP, outlines the noteworthy changes and his rationale for the all-new *CHEST* cover, mast-head, and table of contents designs; new Associate Editors group; new editorial board; and all-new journal sections replacing the former stand-alone departments. Readers will also be happy to know that the changes will include a smaller page count (in contrast to the extra large issues we published at the end of 2005 to clear out the backlog of old manuscripts).

We encourage all our ACCP

members and *CHEST* readers to read Dr. Irwin's editorial online at www.chestjournal.org.

In addition, *CHEST* has revised its Instructions to Authors to reflect the new procedures, policies, and changes to the journal. More thorough policies on potential conflict of interest (including required statements that will be published with all manuscripts), required IRB statements, and new stricter word limits on all article types are only a few of the changes to note. The full instructions are available online at www.chestjournal.org/misc/ifora.shtml, and we urge all potential authors to thoroughly familiarize themselves with the instructions.

We encourage members and readers to give us feedback on the new changes and welcome your suggestions on how we can continue to improve our educational offerings. Thank you! ■

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Editorials	Topics in Practice Management	Chest Imaging for Clinicians
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ABSTRACT SUBMISSION DEADLINE: APRIL 21, 2006

Pulmonary Perspectives

Chronic Thromboembolic Pulmonary Hypertension: An Update

It has now been over 50 years since the first description of organized thrombus causing pulmonary hypertension and cor pulmonale (Owen et al. *N Engl J Med* 1953; 249:919) and over 35 years since Dr. Kenneth Moser suggested that a thromboendarterectomy might be a curative procedure. Despite this relatively long history, much remains unknown about this disease, and ongoing controversies have centered on its nature, etiology, and incidence. Fortunately, a recent, prospective study provides new information that may help direct future research and clinical efforts.

Pathology

Acute pulmonary emboli usually resolve within days to weeks through endogenous lytic mechanisms, with or without treatment. Some residua are common in the form of minor bands and webs, without apparent clinical sequelae. In a minority of patients, clots do not resolve but organize into fibrotic material that becomes incorporated into the vessel wall, causing major large vessel obstruction. The residua in this situation consist of any combination of intimal thickening, bands, webs, and mass-like obstructions, often with some degree of recanalization (Shure et al. *Ann Intern Med* 1985; 103:844).

In addition to vascular obstruction, pathologic changes can be seen distal to the obstruction. These changes are identical to those often seen with other causes of pulmonary hypertension (intimal thickening, medial hypertrophy, and plexiform lesions), even though the distal bed is mostly protected from the high pressure in the patent proximal bed by the obstructing material (Moser and Bloor. *Chest* 1993; 103:685). These postobstructive, arteriopathic changes have also been seen in a canine model of surgical ligation of a main pulmonary artery in the absence of pulmonary hypertension (Shure and Bloor. *Chest* 1988; 93:154S), suggesting that the changes are a form of vascular injury related to obstruction itself, rather than to the organized thrombotic material. These arteriopathic changes may play a role in post-surgical reperfusion edema, in pulmonary arterial hypertension apparently dispropor-

tionate to the degree of large vessel obstruction, and in the gradual fall in pulmonary artery pressure, seen up to a year after successful thromboendarterectomy.

Controversies

It has long been felt that chronic thromboembolic pulmonary hypertension (CTPH) results from organized thromboemboli that do not normally resolve, and the incidence has been thought to be about 0.1 to 0.5% of acute thromboembolism survivors (Fedullo et al. *N Engl J Med* 2001; 345:1465). The cause remains unknown. Some increase in prothrombotic factors, particularly antiphospholipid antibodies in 10 to 20% of patients and persistently elevated plasma factor VIII levels in up to 40%, have been found in this patient population (Bonderman et al. *Thromb Haemost* 2003; 90:372). However, no evidence has been found of inherent lytic defects that would account for lack of thrombus resolution.

Based on many unanswered questions about etiology and incidence, some have questioned the very concept of CTPH (Egermayer and Peacock. *Eur Respir J* 2000; 15:440). These authors raise several points. They question the rarity of CTPH given the high incidence (60 to 90%) of observed thrombotic sequelae at autopsy. They also question why the majority of emboli have been asymptomatic (Fedullo et al. *N Engl J Med* 2001; 345:1465) and suggest that the lack of evidence of prior embolization may not reflect a honeymoon period in symptom development, but rather that prior emboli did not occur. They further site the lack of an animal model of CTPH and the impossibility of distinguishing thrombi *in situ* from embolic thrombi. In the absence of prospective studies with long-term follow-up of a population experiencing acute thromboembolic disease, these issues have remained open to debate.

New Data

A recently published study by the Thromboembolic Pulmonary Hypertension Study Group has provided important new information that is worthy of detailed review (Pengo et al. *N Engl J Med* 2004; 350:2257). This prospective study from the University of Padua, Italy, examined the incidence of symptomatic CTPH after well-treated, acute, pulmonary embolism in a population without prior pulmonary emboli. Treatment of acute disease consisted of heparin, thrombolytics for massive pulmonary embolism, and, rarely, thrombectomy. The

minimum duration of anticoagulation was 6 months; the average was greater than 1 year. Persistent or unexplained dyspnea triggered further evaluation with echocardiography, followed by ventilation-perfusion lung scanning and angiography. The study separately examined risk factors for the development of CTPH in a combined population of those with and without prior episodes of thromboembolic disease.

The population of 223 patients without prior disease was followed for a median of 7.85 years and a maximum of 10 years. The shortest follow-up was 1 year. In this cohort population, the cumulative incidence of symptomatic CTPH was 0.0% at 3 months, 1.0% at 6 months, 3.1% at 1 year, and 3.8% at 2 years. No cases occurred after 2 years. This finding is strikingly different from the commonly held belief that the disease usually occurs years after the initial episode of thromboembolism (Fedullo et al. *N Engl J Med* 2001; 345:1465). Perhaps the impression of a great delay in the occurrence of symptoms relates to the delay in people seeking attention for an insidious process or the delay in treating physicians recognizing the nature of the problem, particularly in the setting of undiagnosed or clinically silent thromboembolic disease. Interestingly, over the 10 years of the study, the rates of recurrent acute thromboembolic disease continued to increase from 4.9% at 3 months, to 8% at 1 year, 22.1% at 5 years, and 29.1% at 10 years, despite the fact all cases of CTPH occurred within the first 2 years of follow-up.

Etiologic risk for pulmonary embolism at initial presentation was classified as transient (such as trauma), permanent (such as prothrombotic disorders), or idiopathic (no known cause). The 305 patients included in the multivariate risk analysis for CTPH included the 223 in the cohort study who had a 3.8% incidence of CTPH, 58 patients with prior deep venous thrombosis who had a 5.2% incidence of CTPH, and 24 patients with prior pulmonary embolism who had a 33.3% incidence of CTPH. The following factors were identified as independent risk factors for the development of CTPH:

- ▶ prior pulmonary embolism; odds ratio 19.00
- ▶ idiopathic presentation; odds ratio 5.70
- ▶ larger perfusion defect; odds ratio 2.22 per decile decrement in perfusion
- ▶ younger age; odds ratio 1.79 per decade.

The magnitude of the risk for prior embolization may be related, in part, to the fact that prior episodes outside of the cohort incidence study were often not treated adequately. In the cohort incidence study, only two people who developed CTPH had experienced recurrent pulmonary embolism before the development of CTPH.

Conclusion

This important study from Padua gives us new insight into some of the remaining mysteries concerning CTPH. Perhaps most importantly, we now have evidence that the condition is truly not rare, but underdiagnosed. Since the study examined only symptomatic pulmonary hypertension in a well-anticoagulated population, the incidence of 4% may represent a lower limit. Pulmonary vascular disease, including CTPH, needs to be considered strongly in the evaluation of unexplained dyspnea.

Second, this form of pulmonary hypertension does follow from acute thromboembolic disease. We are, however, still left with many puzzles regarding causation. Although prior embolization was a significant risk factor for the development of CTPH in the combined risk analysis, the incidence of recurrent pulmonary embolism in the cohort incidence study continued to increase over the 10-year study period, while the development of CTPH occurred only within the first 2 years following the initial event. This finding suggests the possibility of an as-yet unidentified predisposing factor. Simple recurrent thromboembolic disease may be a factor, but it is not the entire answer.

A basic conclusion based on these new data is that we need to closely follow patients after thromboembolic disease and aggressively evaluate symptoms. We need to continue to direct our research efforts toward an understanding of the underlying cause or causes of this fascinating disorder. Although no genetic predisposition has been found, it remains a tempting area of investigation. Something different occurs in this patient population that leads to a massive fibrotic organization of acute thrombus, rather than normal resolution. We need to identify these factors. ■

Deborah Shure, MD, Master FCCP
Editor, Pulmonary Perspectives
Miami, FL

Editor's Insight

This Perspective highlights several important issues and generates more questions about a highly complex disease process. CTPH occurs after an acute pulmonary embolism much earlier and more commonly than previously thought. It is also striking that recurrence rates for pulmonary embolism remain so high, despite modern therapies. These are timely and troubling issues, requiring further investigation to solve these persistent unknowns.

—Deputy Editor

Deborah Shure, MD, Master FCCP
Editor, Pulmonary Perspectives

Aymarrah Robles, MD, FCCP
Deputy Editor, Pulmonary Perspectives

Rapid Growth Seen in Hospital Palliative Care Programs

BY DOUG BRUNK
Elsevier Global Medical News

The number of palliative care programs in U.S. hospitals grew from 632 in 2000 to 1,027 in 2003, an increase of 63%, according to results from a large study.

The study “demonstrates the increasing recognition by hospitals in the United States and those providing primary care for patients with advanced illness of the need for palliative care services,” said Dr. R. Sean Morrison, the study’s primary author. “We have seen growth from a fraction of hospitals having hospital-based palliative care programs to where now 1 in 4 hospitals have a program.”

He and his associates obtained data from the 2001-2004 American Hospital Association annual surveys, which covered calendar years 2000-2003. The AHA’s annual survey defines a palliative care program as “an organized program providing specialized medical care, drugs, or therapies for the management of acute or chronic pain and/or the control of symptoms administered by specially trained physicians and other clinicians; and supportive care services, such as counseling on advanced directives, spiritual care, and

social services, to patients with advanced disease and their families,” said Dr. Morrison, vice chair of research in the department of geriatrics at Mount Sinai Medical Center, New York.

The researchers identified all programs that self-reported the presence of a hospital-owned palliative care program and acute medical and surgical beds, and then used multivariate logistic regression to pinpoint factors that were associated with the presence of an adult palliative care program in the 2003 survey data (*J. Palliat. Med.* 2005;8:1127-34).

They found that hospitals in the Northeast, Pacific, and Mountain areas of the country are more likely than those in other geographic regions to have programs. The greater the number of hospital beds and acute care beds, the more likely a facility has a palliative care program. Similarly, being a Veterans Affairs hospital or a not-for-profit hospital increases the likelihood.

Among the factors associated with having a palliative care program are being a member of the American Association of Medical Colleges Council of Teaching Hospitals and being a cancer hospital that is approved by the American College of Surgeons.

“The fact that the American College of Surgeons would want to incorporate access to palliative care as one of their benchmarks of good care in a cancer setting is a sign that palliative care has been very successful in legitimizing its place in the continuum of medical practice,” said Dr. Geoffrey P. Dunn, an Erie, Pa.-based surgeon who cochairs the ACS’s Surgical Palliative Care Task Force.

“People are becoming increasingly aware that palliative care is an extension of the already well-known and very successful hospice programs in this country. As this study shows, there are more occasions where they will have the opportunity for those services. I think that’s going to increasingly generate that expectation in care, whether it’s at a cancer center or elsewhere,” said Dr. Dunn.

Dr. Daniel B. Hinshaw, medical director of the palliative care consult team at the Ann Arbor (Mich.) VA Medical Center, said the increasing presence of palliative care programs in the nation’s hospitals “gives us an opportunity to keep that message out there that this [component of care] is not just a matter of fighting disease. It’s really about caring for the whole person who might have a bad disease,” he said. “We may not always be able to cure their problem, but we should always try our best to provide comfort and relief of distress and symptoms.”

For-profit hospitals, however, are significantly less likely to have programs, according to the study. Dr. Morrison said part of the reason may be the fact that palliative care programs started in academic medical centers and branched out to teaching hospitals. “The majority of teaching hospitals in the United States are still not-for-profit,” he said. “I don’t think there is a lot of communication [about palliative care programs] between the not-for-profit sector and the for-profit sector, but it’s something we’d like to address.”

Dr. Dunn called the current funding landscape for hospital-based palliative care programs “tenuous” even though numerous demonstration projects have shown

them to be cost-effective. “What will be a challenge in 5-10 years will be the physician staffing of these [programs],” he said. “Very shortly the American Board of Hospice and Palliative Medicine is expecting to receive credentialing from the American

Board of Medical Specialties. Once that happens, that is going to put a pretty narrow lock on the pool of people who are considered certified and qualified to run these programs. I’m concerned that with this rapid proliferation of programs, how are we going to fill the demand for physicians who have some degree of training in this to do it?”

Dr. Morrison’s study noted that there were 1,892 certified palliative medicine physicians as of July 2005 and 5,500 certified palliative nurses as of March 2005. It also noted that the number of postgraduate palliative medicine fellowships increased from 17 in 2000 to 53 in 2005.

Dr. Morrison said that the cost of a hospital-based palliative care program is directly related to the size of the hospital. At Mount Sinai Medical Center, which is a 1,000-bed teaching hospital, the palliative care program consists of two full-time physicians, four full-time nurse-practitioners, two full-time social workers, and consultation with chaplaincy and physical therapy.

“The expense of the program is far outweighed by the cost savings to our hospital for having it,” said Dr. Morrison, whose study was funded by the Robert Wood Johnson Foundation. “For a 300-bed hospital, the team is probably going to be a physician, a nurse, a social worker, and consultation with other core services. For a 50-bed rural hospital, it may be that the primary person is a nurse-practitioner with a part-time physician as backup in consultation with other services in the hospital.”

To access a financial calculator that helps you estimate the cost of a palliative care program and the cost savings to your hospital, visit the Center to Advance Palliative Care’s Web site at www.capc.org. Look for the “CAPC Impact Calculator” icon.



‘The expense of the program is far outweighed by the cost savings to our hospital for having it.’

DR. MORRISON

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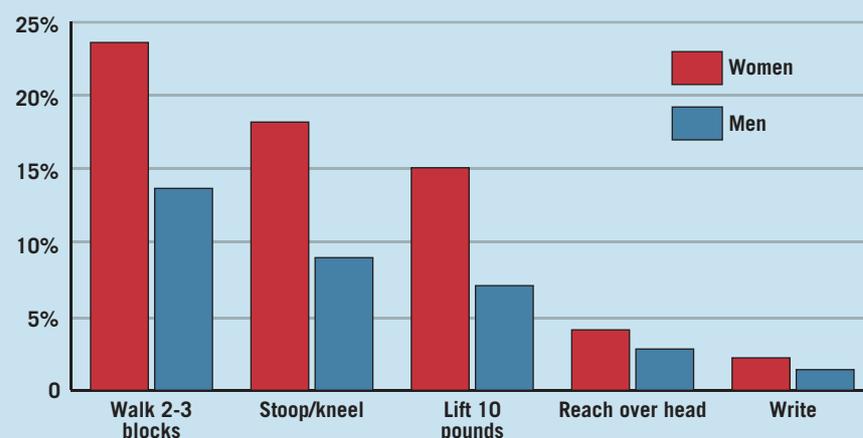
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DATA WATCH

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Note: Rates reported are for enrollees aged 65 years and older in 2003.

Source: Centers for Medicare and Medicaid Services, Medicare Current Beneficiary Survey

Surgery May Correct Sleep Apnea In Cases of Chiari Malformation

BY JEFF EVANS

Elsevier Global Medical News

Surgical decompression may help to relieve central sleep apnea in patients with Arnold-Chiari malformation type 1 and syringomyelia, according to the results of a study on a small series of patients.

The study, conducted by Dr. Frédéric Gagnadoux and his colleagues at the Centre Hospitalier Universitaire, Angers, France, builds on previous reports of isolated cases of reduced central sleep apnea after surgical decompression.

Surgical decompression is thought to relieve the congenital or acquired herniations of the cerebellum through the foramen magnum that characterize Arnold-Chiari malformations (ACMs). Hernial compression of the brainstem is thought to depress the respiratory center or the reticular activating system.

Of 16 patients with ACM type 1 and syringomyelia, 12 had sleep apnea syndrome as defined by an apnea-hypopnea index of 10 or greater; 48% of the apnea episodes that occurred in these patients were classified as central

apneas (*Neurology* 2006;66:136-8).

The investigators surgically decompressed 8 of those 12 patients. In six patients on whom full-night polysomnography was performed before surgery and an average of 203 days after surgery, central apnea was reduced from 14.9 episodes/hour of sleep to 1.3, and microarousal indices from 37.2 episodes/hour of sleep to 26.2. Epworth Sleepiness Scale (ESS) scores, however, did not improve significantly in these patients.

The lack of a significant improvement in sleepiness may be explained by the persistence of severe obstructive sleep apnea syndrome in two patients who were eventually treated with continuous positive airway pressure and in one patient who exhibited a normalized apnea-hypopnea index after surgery but had worsening sleepiness due to a depressive syndrome, according to the investigators.

“Our results suggest sleep-disordered breathing should be investigated in patients with ACMs associated with a complaint of daytime sleepiness or an ESS score greater than 10,” Dr. Gagnadoux and his associates wrote. ■

Sleep Apnea Worsened by Supine Position in Children Under Age 3

BY CHRISTINE KILGORE

Elsevier Global Medical News

Young children with sleep apnea showed more respiratory disturbance when they slept on their backs than in all other positions combined, according to new findings from a chart review.

Dr. Kevin D. Pereira and his associates at the University of Texas Health Science Center at Houston reviewed the sleep studies of 60 children aged 3 years and younger who underwent polysomnography to evaluate obstructive sleep apnea syndrome (OSAS).

They found that the mean respiratory disturbance index (RDI) of children sleeping in the supine position was significantly greater than the total RDI, defined as the RDI of children when all positions were included (14 vs. 11). As the amount of total sleep time spent in the supine position increased, so did the RDI.

Rapid eye movement sleep also correlated with an increased RDI, compared with non-REM results (21 vs. 6).

The results “indicate that supine sleep does correlate with an increase in RDI as well as with OSAS in patients younger

than 3 years,” the investigators said.

Previous studies have shown no correlation between sleep position and OSAS in children, and some have suggested that children younger than 10 years breathe better when they sleep in the supine position.

However, “our observations suggest that toddlers have sleep characteristics that are different from those of older children,” Dr. Pereira and his associates said.

Very few infants were included in the study, they noted (*Arch. Otolaryngol. Head Neck Surg.* 2005;131:1014-6).

The severity of obstructive sleep apnea can be underestimated in very young children—and sleep-disordered breathing can be underdiagnosed—if patients do not spend much time in the supine position. “Lack of adequate supine sleep may be an important factor in symptomatic children with normal sleep study results,” they said.

Pediatric OSAS is most commonly caused by enlarged tonsils and adenoids, and patients usually have “an excellent response” to adenotonsillectomy, the investigators noted. The children whose PSG data was analyzed in this study subsequently underwent the procedure. ■

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Admission BNP Predicted Mortality in Acute Heart Failure

BY BRUCE JANCIN
Elsevier Global Medical News

DALLAS — An elevated B-type natriuretic peptide level upon admission for acute decompensated heart failure is an independent predictor of in-hospital mortality, Dr. Gregg C. Fonarow reported at the annual scientific sessions of the American Heart Association.

Moreover, B-type natriuretic peptide (BNP) is an equally robust predictor of in-hospital mortality regardless of whether the patient has preserved or reduced left ventricular systolic function, added Dr. Fonarow, professor of cardiovascular medicine at the University of California, Los Angeles, and director of the Ahmanson-UCLA Cardiomyopathy Center.

"These data suggest that the BNP assay should be part of the standard admission assessment of the acute decompensated heart failure patient," he said.

Dr. Fonarow analyzed the relationship

between admission BNP level and in-hospital mortality in 48,629 hospitalizations for acute decompensated heart failure during 2003-2004 at more than 275 U.S. hospitals participating in the Acute Decompensated Heart Failure National Registry (ADHERE).

He found a near-linear relationship between BNP quartile and in-hospital mortality. The relationship was similar in the 52% of patients with a left ventricular ejection fraction of less than 40% and in those with preserved systolic function.

The median hospital length of stay rose from 4.0 days in patients in the lowest quartile of BNP to 4.9 days in those in the top quartile, a difference that was highly significant because of the huge number of patients involved in the study. ICU admission was required for

12.8% of patients in BNP quartile 1, compared with 19.6% in quartile 4.

In an earlier ADHERE study, Dr. Fonarow and coworkers developed and validated a practical bedside tool for mortality risk stratification in patients with acute decompensated heart failure (JAMA 2005; 293:572-80).

The strongest in-hospital mortality predictors in this risk stratification method were admission blood urea nitrogen level, systolic blood pressure, and serum creatinine. Other significant predictors included in the bedside assessment tool were age, gender, serum sodium, pulse, and the presence of dyspnea at rest.

After adjustment for all of these other predictive factors, admission BNP quartile remained a highly significant independent

predictor of in-hospital mortality. In fact, patients in the highest BNP quartile were 2.2-fold more likely to die during that hospitalization than were those in the lowest quartile, even after adjusting for the other eight predictors.

BNP has previously been shown to facilitate diagnosis of heart failure and to predict long-term mortality risk in patients with chronic heart failure. However, the lab assay's prognostic utility in acute decompensated heart failure hadn't previously been studied.

The next step will be to see whether acutely decompensated patients with higher admission BNP levels benefit from a more aggressive monitoring and treatment strategy. If this hypothesis is shown to be sound, then it's possible that treatment regimens will be stratified based upon a patient's admission BNP, according to Dr. Fonarow.

The ADHERE Registry is funded by Scios Inc. ■



The BNP assay should be part of the standard admission assessment of the heart patient.
DR. FONAROW

Lowering of Central Aortic Pressure Gives Advantage to Amlodipine

BY MITCHEL L. ZOLER
Elsevier Global Medical News

DALLAS — Brachial blood pressure measurements may not be the best way to assess the effects that antihypertensive drugs have on blood pressure.

An amlodipine-based regimen was much better than atenolol-based treatment for lowering central aortic pressure in a substudy of a trial that involved a total of more than 19,000 patients, Dr. Bryan Williams said at the annual scientific sessions of the American Heart Association.

The results "demonstrate for the first time in a large, clinical-outcomes trial that blood pressure-lowering drugs have profoundly different effects on central aortic pressures and hemodynamics despite a similar impact on brachial blood pressure," said Dr. Williams, a professor of medicine at the University of Leicester (U.K.).

Amlodipine's ability to reduce central aortic pressure is likely a major reason that the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) showed that an amlodipine-based regimen led to a 16% relative reduction in the incidence of total cardiovascular events and procedures, compared with an atenolol-based regimen during an average follow-up of 5.5 years (Lancet 2005;366:895-906).

Central aortic pressures were obtained for 2,199 of the patients enrolled in ASCOT. These measures were obtained via a commercially available device that calculates central aortic pressures after transcutaneously measuring the radial artery waveform through an external transducer wand that's placed on a patient's wrist.

"Systolic pressure is not constant throughout the arterial tree, and clinically relevant changes may not be measured by brachial-cuff blood pressure," commented

Dr. Joseph L. Izzo Jr., professor of medicine and pharmacology at the State University of New York at Buffalo.

The ASCOT substudy was done at five participating hospitals in the United Kingdom and Ireland. Participating patients had their central aortic pressures measured at baseline and during multiple follow-up examinations using the SphygmoCor Px system. Like all participants in ASCOT, these hypertensive patients were randomized to treatment with either of two regimens: amlodipine, followed by perindopril when a second drug was needed to reach the goal brachial-artery pressure, or atenolol, with the diuretic bendroflumethiazide and potassium added when a second drug was needed.

During treatment, the amlodipine group maintained a central aortic systolic pressure that averaged 4.3 mm Hg lower than that of the atenolol group, and a central

aortic pulse pressure that averaged 3.0 mm Hg lower, reported Dr. Williams. Both cuts in pressure were significant. In contrast, systolic pressure measured by brachial cuff averaged 0.7 mm Hg lower in the amlodipine group than in the atenolol group, and diastolic pressure averaged 1.6 mm Hg lower with amlodipine.

Dr. Williams and his associates analyzed the role of central aortic pressure and other variables on the incidence of 305 cardiovascular events, procedures, or episodes of renal impairment that occurred in the 2,199 patients during follow-up. Central aortic pulse pressure was the only factor that produced a significant, independent effect on the rate of these outcomes.

The ASCOT study and substudy were sponsored by Pfizer Inc. which markets amlodipine (Norvasc). Dr. Williams has been a consultant to and has received research grants from Pfizer. ■

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Free Curbside Consults Can Add Up for ID Specialists

BY SHERRY BOSCHERT
Elsevier Global Medical News

SAN FRANCISCO — Infectious disease specialists at one institution provided over \$93,000 worth of curbside consultations without reimbursement, Dr. Christopher J. Grace said at the annual meeting of the Infectious Diseases Society of America.

Members of the specialty “need to get a handle on this. We’re giving away the farm,” said Dr. Grace of the University of Vermont, Burlington.

A 1-year prospective study at Fletcher Allen Health Care, a 500-bed community and tertiary care center in Burlington, found that infectious disease specialists gave 1,001 curbside consultations, which are defined as advice or suggestions given to another physician without seeing the patient. Curbside consultations took place in person or by telephone, letter, or e-mail.

Without the physicians or nurses who requested the curbside consultations knowing it, the infectious disease specialists assigned a CPT code to each event based on whether the patient in question was an inpatient or outpatient, whether the consultation dealt with initial care or subsequent care, and how complex the case was.

They then gave a physician-work relative value unit, or RVU (used by the Centers for Medicare and Medicaid Services [CMS] to calculate reimbursements) to each curbside consultation based on the CPT code, and multiplied the aggregate RVUs by the 2005 CMS conversion factor of \$37.89 per RVU to estimate costs.

In 98% of cases, curbside consultations focused on a specific patient, rather than on theoretical patients or general topics. Among consultations for patients, 34% were for inpatients and 66% were for outpatients.

Events were coded as initial consultations in 96% of cases.

The main clinical topics of consultations focused on skin disease in 16% of cases, pulmonary disease in 8%, bone or joint infection in 8%, and bacteremia in 7%.

The curbside consultations accounted for 21% of all infectious disease consultations that year and were equally as complex as formal consultations, Dr. Grace said.

The curbside consultations generated a total of 2,462 RVUs, which would have meant \$93,285 “if we were paid the standard Medicare reimbursement fee,” he said.

Formal consultations in the same time period generated 9,409 RVUs worth \$356,507. The number of RVUs per consultation was higher for curbside (2.46) than for formal consultations (1.22)

because the former had a higher proportion of initial consultations.

Who asked for curbside consultations? Questions came about equally from the health center’s staff and from community physicians with medical privileges at the center. More questions came from general internists than other specialists.

A physician in the audience urged Dr. Grace to share the results with colleagues in other specialties at his institution. “When you do, they’ll be horrified that they’re using you this way. It tends to

bring your formal consults up,” he said, based on his own experience.

Dr. Grace noted that some physicians requesting the curbside consultations practiced 20-150 miles away, making formal consultations more difficult.

Hospitals, insurers, and others need to integrate curbside consultations into productivity measures and compensation measures, he said.

Many in the audience agreed. “We all should have done this 30 years ago, and we’d have more leverage with

the payers,” one physician said.

Another suggested refusing to do curbside consultations. “At some point we just need to draw the line. If you offend the people who are curbsiding you, you lose nothing,” he suggested.

The definition of curbside consultation in the study excluded consultations for infection control, antibiotic restriction efforts, follow-up on formal consultations, education of students or residents, and curbside consultations that converted to formal consultations on the same day. ■

LEVAQUIN® (levofloxacin) TABLETS LEVAQUIN® (levofloxacin) ORAL SOLUTION LEVAQUIN® (levofloxacin) INJECTION LEVAQUIN® (levofloxacin in 5% dextrose) INJECTION

Brief Summary
The following is a brief summary only. Before prescribing, see complete Prescribing Information in LEVAQUIN Tablets/Oral Solution/Injection labeling.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of LEVAQUIN® (levofloxacin) and other antibacterial drugs, LEVAQUIN should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

CONTRAINDICATIONS: Levofloxacin is contraindicated in persons with a history of hypersensitivity to levofloxacin, quinolone antimicrobial agents, or any other components of this product.

WARNINGS: (THE SAFETY AND EFFICACY OF LEVOFLOXACIN IN PEDIATRIC PATIENTS, ADOLESCENTS (UNDER THE AGE OF 18 YEARS), PREGNANT WOMEN, AND NURSING WOMEN HAVE NOT BEEN ESTABLISHED.) (See **PRECAUTIONS: Pediatric Use, Pregnancy, and Nursing Mothers** subsections.)

In immature rats and dogs, the oral and intravenous administration of levofloxacin resulted in increased osteochondrosis. Histopathological examination of the weight-bearing joints of immature dogs dosed with levofloxacin revealed persistent lesions of the cartilage. Other fluoroquinolones also produce similar erosions in the weight bearing joints and other signs of arthropathy in immature animals of various species. The relevance of these findings to the clinical use of levofloxacin is unknown. (See **ANIMAL PHARMACOLOGY** in full Prescribing Information.)

Convulsions and toxic psychoses have been reported in patients receiving quinolones, including levofloxacin. Quinolones may also cause increased intracranial pressure and central nervous system stimulation which may lead to tremors, restlessness, anxiety, lightheadedness, confusion, hallucinations, paranoia, depression, nightmares, insomnia, and, rarely, suicidal thoughts or acts. These reactions may occur during the first dose. If these reactions occur in patients receiving levofloxacin, the drug should be discontinued and appropriate measures instituted. As with other quinolones, levofloxacin should be used with caution in patients with a known or suspected CNS disorder that may predispose to seizures or lower the seizure threshold (e.g., severe cerebral arteriosclerosis, epilepsy) or in the presence of other risk factors that may predispose to seizures or lower the seizure threshold (e.g., certain drug therapy, renal dysfunction). (See **PRECAUTIONS: General, Information for Patients, Drug Interactions and ADVERSE REACTIONS.**)

Serious and occasionally fatal hypersensitivity and/or anaphylactic reactions have been reported in patients receiving therapy with quinolones, including levofloxacin. These reactions often occur following the first dose. Some reactions have been accompanied by cardiovascular collapse, hypotension/shock, seizure, loss of consciousness, tingling, angioedema (including tongue, larynx, throat, or facial edema/swelling), airway obstruction (including bronchospasm, shortness of breath, and acute respiratory distress), dyspnea, urticaria, itching, and other serious skin reactions. Levofloxacin should be discontinued immediately at the first appearance of a skin rash or any other sign of hypersensitivity. Serious acute hypersensitivity reactions may require treatment with epinephrine and other resuscitative measures, including oxygen, intravenous fluids, antihistamines, corticosteroids, pressor amines, and airway management, as clinically indicated. (See **PRECAUTIONS and ADVERSE REACTIONS.**)

Serious and sometimes fatal events, some due to hypersensitivity, and some due to uncertain etiology, have been reported rarely in patients receiving therapy with quinolones, including levofloxacin. These events may be severe and generally occur following the administration of multiple doses. Clinical manifestations may include one or more of the following: fever, rash or severe dermatologic reactions (e.g., toxic epidermal necrolysis, Stevens-Johnson Syndrome), vasculitis, arthralgia, myalgia, serum sickness, allergic pneumonitis, interstitial nephritis, acute renal insufficiency or failure; hepatitis; jaundice; acute hepatic necrosis or failure; anemia, including hemolytic and aplastic; thrombocytopenia, including thrombotic thrombocytopenic purpura; leukopenia; agranulocytosis; pancytopenia; and/or other hematologic abnormalities. The drug should be discontinued immediately at the first appearance of a skin rash or any other sign of hypersensitivity and supportive measures instituted. (See **PRECAUTIONS: Information for Patients and ADVERSE REACTIONS.**)

Peripheral Neuropathy: Rare cases of sensory or sensorimotor axonal polyneuropathy affecting small and/or large axons resulting in paresthesias, hypoesthesia, dysesthesias and weakness have been reported in patients receiving quinolones, including levofloxacin. Levofloxacin should be discontinued if the patient experiences symptoms of neuropathy including pain, burning, tingling, numbness, and/or weakness or other alterations of sensation including light touch, pain, temperature, position sense, and vibratory sensation in order to prevent the development of an irreversible condition.

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including levofloxacin, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of any antibacterial agent.

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of “antibiotic-associated colitis.”

After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against *C. difficile* colitis. (See **ADVERSE REACTIONS.**)

Tendon Effects: Ruptures of the shoulder, hand, Achilles tendon, or other tendons that required surgical repair or resulted in prolonged disability have been reported in patients receiving quinolones, including levofloxacin. Post-marketing surveillance reports indicate that this risk may be increased in patients receiving concomitant corticosteroids, especially the elderly. Levofloxacin should be discontinued if the patient experiences pain, inflammation, or rupture of a tendon. Patients should rest and refrain from exercise until the diagnosis of tendonitis or tendon rupture has been confidently excluded. Tendon rupture can occur during or after therapy with quinolones, including levofloxacin.

PRECAUTIONS: General: Prescribing LEVAQUIN in the absence of proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria. Because a rapid or bolus intravenous injection may result in hypotension, LEVOFLOXACIN INJECTION SHOULD ONLY BE ADMINISTERED BY SLOW INTRAVENOUS INFUSION OVER A PERIOD OF 60 OR 90 MINUTES DEPENDING ON THE DOSAGE. (See **DOSAGE AND ADMINISTRATION** in full Prescribing Information.)

Although levofloxacin is more soluble than other quinolones, adequate hydration of patients receiving levofloxacin should be maintained to prevent the formation of a highly concentrated urine.

Administer levofloxacin with caution in the presence of renal insufficiency. Careful clinical observation and appropriate laboratory studies should be performed prior to and during therapy since elimination of levofloxacin may be reduced. In patients with impaired renal function (creatinine clearance <50 mL/min), adjustment of the dosage regimen is necessary to avoid the accumulation of levofloxacin due to decreased clearance. (See **CLINICAL PHARMACOLOGY and DOSAGE AND ADMINISTRATION** in full Prescribing Information.)

Moderate to severe phototoxicity reactions have been observed in patients exposed to direct sunlight while receiving drugs in this class. Excessive exposure to sunlight should be avoided. However, in clinical trials with levofloxacin, phototoxicity has been observed in less than 0.1% of patients. Therapy should be discontinued if phototoxicity (e.g., a skin eruption) occurs.

As with other quinolones, levofloxacin should be used with caution in any patient with a known or suspected CNS disorder that may predispose to seizures or lower the seizure threshold (e.g., severe cerebral arteriosclerosis, epilepsy) or in the presence of other risk factors that may predispose to seizures or lower the seizure threshold (e.g., certain drug therapy, renal dysfunction). (See **WARNINGS and Drug Interactions.**) As with other quinolones, disturbances of blood glucose, including symptomatic hyper- and hypoglycemia, have been reported, usually in diabetic patients receiving concomitant treatment with an oral hypoglycemic agent (e.g., glyburide/glibenclamide) or with insulin. In these patients, careful monitoring of blood glucose is recommended. If a hypoglycemic reaction occurs in a patient being treated with levofloxacin, levofloxacin should be discontinued immediately and appropriate therapy should be initiated immediately. (See **Drug Interactions and ADVERSE REACTIONS.**)

Torsades de pointes: Some quinolones, including levofloxacin, have been associated with prolongation of the QT interval on the electrocardiogram and infrequent cases of arrhythmia. Rare cases of torsades de pointes have been spontaneously reported during post-marketing surveillance in patients receiving quinolones, including levofloxacin. Levofloxacin should be avoided in patients with known prolongation of the QT interval, patients with uncorrected hypokalemia, and patients receiving class IA (quinidine, procainamide), or class III (amiodarone, sotalol) antiarrhythmic agents.

As with any potent antimicrobial drug, periodic assessment of organ system functions, including renal, hepatic, and hematopoietic, is advisable during therapy. (See **WARNINGS and ADVERSE REACTIONS.**)

Information for Patients
Patients should be advised:

- Patients should be counseled that antibacterial drugs including LEVAQUIN® (levofloxacin) should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When LEVAQUIN is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by LEVAQUIN or other antibacterial drugs in the future.
- that peripheral neuropathies have been associated with levofloxacin use. If symptoms of peripheral neuropathy including pain, burning, tingling, numbness, and/or weakness develop, they should discontinue treatment and contact their physicians;
- to drink fluids liberally;
- that antacids containing magnesium, or aluminum, as well as sucralfate, metal cations such as iron, and multivitamin preparations with zinc or Vitec® (didanosine) should be taken at least two hours before or two hours after oral levofloxacin administration. (See **Drug Interactions.**)
- that levofloxacin oral tablets can be taken without regard to meals;
- that levofloxacin oral solution should be taken 1 hour before or 2 hours after eating;
- that levofloxacin may cause neurologic adverse effects (e.g., dizziness, lightheadedness) and that patients should know how they react to levofloxacin before they operate an automobile or machinery or engage in other activities requiring mental alertness and coordination. (See **WARNINGS and ADVERSE REACTIONS.**)
- to discontinue treatment and inform their physician if they experience pain, inflammation, or rupture of a tendon, and to rest and refrain from exercise until the diagnosis of tendonitis or tendon rupture has been confidently excluded;
- that levofloxacin may be associated with hypersensitivity reactions, even following the first dose, and to discontinue the drug at the first sign of a skin rash, hives or other allergic reactions, a rapid heartbeat, chest pain, swelling of the face, tongue, or swelling suggesting angioedema (e.g., swelling of the lips, tongue, face, tightness of the throat, hoarseness), or other symptoms of an allergic reaction. (See **WARNINGS and ADVERSE REACTIONS.**)
- to avoid excessive sunlight or artificial ultraviolet light while receiving levofloxacin and to discontinue therapy if phototoxicity (i.e., skin eruption) occurs;
- that if they are diabetic and are being treated with insulin or an oral hypoglycemic agent and a hypoglycemic reaction occurs, they should discontinue levofloxacin and consult a physician. (See **PRECAUTIONS: General and Drug Interactions.**)
- that concurrent administration of warfarin and levofloxacin has been associated with increases of the International Normalized Ratio (INR) or prothrombin time and clinical episodes of bleeding. Patients should notify their physician if they are taking warfarin.
- that convulsions have been reported in patients taking quinolones, including levofloxacin, and to notify their physician before taking this drug if there is a history of this condition.

Drug Interactions: Antacids, Sucralfate, Metal Cations, Multivitamins

LEVAQUIN Tablets: While the chelation by divalent cations is less marked than with other quinolones, concurrent administration of LEVAQUIN Tablets with antacids containing magnesium, or aluminum, as well as sucralfate, metal cations such as iron, and multivitamin preparations with zinc may interfere with the gastrointestinal absorption of levofloxacin, resulting in systemic levels considerably lower than desired. Tablets with antacids containing magnesium, aluminum, as well as sucralfate, metal cations such as iron, and multivitamins preparations with zinc or Vitec® (didanosine) may substantially interfere with the gastrointestinal absorption of levofloxacin, resulting in systemic levels considerably lower than desired. These agents should be taken at least two hours before or two hours after levofloxacin administration.

LEVAQUIN Injection: There are no data concerning an interaction of intravenous quinolones with oral antacids, sucralfate, multivitamins, Vitec® (didanosine), or metal cations. However, no quinolone should be co-administered with any solution containing multivalent cations, e.g., magnesium, through the same intravenous line. (See **DOSAGE AND ADMINISTRATION** in full Prescribing Information.)

Theophylline: No significant effect of levofloxacin on the plasma concentrations, AUC, and other disposition parameters for theophylline was detected in a clinical study involving 14 healthy volunteers. Similarly, no apparent effect of theophylline on levofloxacin absorption and disposition was observed. However, concomitant administration of other quinolones with theophylline has resulted in prolonged elimination half-life, elevated serum theophylline levels, and a subsequent increase in the risk of theophylline-related adverse reactions in the patient population. Therefore, theophylline levels should be closely monitored and appropriate dosage adjustments made when levofloxacin is co-administered. Adverse reactions, including seizures, may occur with or without an elevation in serum theophylline levels. (See **WARNINGS and PRECAUTIONS: General.**)

Warfarin: No significant effect of levofloxacin on the peak plasma concentrations, AUC, and other disposition parameters for R- and S-warfarin was detected in a clinical study involving healthy volunteers. Similarly, no apparent effect of warfarin on levofloxacin absorption and disposition was observed. There have been reports during the post-marketing experience in patients that levofloxacin enhances the effects of warfarin. Elevations of the prothrombin time in the setting of concurrent warfarin and levofloxacin use have been associated with episodes of bleeding. Prothrombin time, International Normalized Ratio (INR), or other suitable anticoagulation tests should be closely monitored. Levofloxacin is administered concomitantly with warfarin. Patients should also be monitored for evidence of bleeding.

Cyclosporine: No significant effect of levofloxacin on the peak plasma concentrations, AUC, and other disposition parameters for cyclosporine was detected in a clinical study involving healthy volunteers. However, elevated serum levels of cyclosporine have been reported in the patient population when co-administered with some other quinolones. Levofloxacin C_{max} and K_e were slightly lower while T_{max} and t_{1/2} were slightly longer in the presence of cyclosporine than those observed in other studies without concomitant medication. The differences, however, are not considered to be clinically significant. Therefore, no dosage adjustment is required for levofloxacin or cyclosporine when administered concomitantly.

Digoxin: No significant effect of levofloxacin on the peak plasma concentrations, AUC, and other disposition parameters for digoxin was detected in a clinical study involving healthy volunteers. Levofloxacin absorption and disposition kinetics were similar in the presence or absence of digoxin. Therefore, no dosage adjustment for levofloxacin or digoxin is required when administered concomitantly.

Probenecid and Cimetidine: No significant effect of probenecid or cimetidine on the rate and extent of levofloxacin absorption was observed in a clinical study involving healthy volunteers. The AUC and t_{1/2} of levofloxacin were 27-35% and 30% higher, respectively, while CL/F and CL_R were 21-35% lower during concomitant treatment with probenecid or cimetidine compared to levofloxacin alone. Although these differences were statistically significant, the changes were not high enough to warrant dosage adjustment for levofloxacin when probenecid or cimetidine is co-administered.

Non-steroidal anti-inflammatory drugs: The concomitant administration of a non-steroidal anti-inflammatory drug with a quinolone, including levofloxacin, may increase the risk of CNS stimulation and convulsive seizures. (See **WARNINGS and PRECAUTIONS: General.**)

Antidiabetic agents: Disturbances of blood glucose, including hyperglycemia and hypoglycemia, have been reported in patients treated concomitantly with quinolones and an antidiabetic agent. Therefore, careful monitoring of blood glucose is recommended when these agents are co-administered.

Carcinogenesis, Mutagenesis, Impairment of Fertility: In a lifetime bioassay in rats, levofloxacin exhibited no carcinogenic potential following daily dietary administration for 2 years; the highest dose (100 mg/kg/day) was 1.4 times the highest recommended human dose (750 mg) based upon relative body surface area. Levofloxacin did not shorten the time to tumor development of UV-induced skin tumors in hairless albino (Skh-1) mice at any levofloxacin dose level and was therefore not photo-carcinogenic under the conditions of this study. Dermal levofloxacin concentrations in the hairless mice ranged from 25 to 42 µg/g at the highest levofloxacin dose level (300 mg/kg/day) used in the photo-carcinogenicity study. By comparison, dermal levofloxacin concentrations in human subjects receiving 750 mg of levofloxacin averaged approximately 11.8 µg/g at C_{max}.

Levofloxacin was not mutagenic in the following assays: Ames bacterial mutation assay (S. typhimurium and S. coli), V79 CHO cells, V79 CHO cells, mouse micronucleus test, mouse dominant lethal test, rat unscheduled DNA synthesis assay, and the mouse sister chromatid exchange assay. It was positive in the in vitro chromosomal aberration (CHL cell line) and sister chromatid exchange (CHL/UL cell line) assays. Levofloxacin caused no impairment of fertility or reproductive performance in rats at oral doses as high as 360 mg/kg/day, corresponding to 4.2 times the highest recommended human dose based upon relative body surface area and intravenous doses as high as 100 mg/kg/day, corresponding to 1.2 times the highest recommended human dose based upon relative body surface area.

Pregnancy: Teratogenic Effects. Pregnancy Category C: Levofloxacin was not teratogenic in rats at oral doses as high as 810 mg/kg/day which corresponds to 9.4 times the highest recommended human dose based upon relative body surface area, or at intravenous doses as high as 160 mg/kg/day corresponding to 1.9 times the highest recommended human dose based upon relative body surface area. The oral dose of 810 mg/kg/day to rats caused decreased fetal body weight and increased fetal mortality. No teratogenicity was observed when rabbits were dosed orally as high as 50 mg/kg/day which corresponds to 1.1 times the highest recommended human dose based upon relative body surface area, or when dosed intravenously as high as 25 mg/kg/day, corresponding to 0.5 times the highest recommended human dose based upon relative body surface area.

There are, however, no adequate and well-controlled studies in pregnant women. Levofloxacin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. (See **WARNINGS.**)

Nursing Mothers: Levofloxacin has not been measured in human milk. Based upon data from ofloxacin, it can be presumed that levofloxacin will be excreted in human milk. Because of the potential for serious adverse reactions from levofloxacin in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness in pediatric patients and adolescents below the age of 18 years have not been established. Quinolones, including levofloxacin, cause arthropathy and osteochondrosis in juvenile animals of several species. (See **WARNINGS.**)

Geriatric Use: In phase 3 clinical trials, 1,190 levofloxacin-treated patients (25% were 65 years of age. Of these, 675 patients (14%) were between the ages of 65 and 74 and 515 patients (43%) were 75 years of age or older. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Elderly patients may be more susceptible to drug-associated effects on the QT interval. Therefore, precaution should be taken when using levofloxacin with concomitant drugs that can result in prolongation of the QT interval (e.g. class IA or class III antiarrhythmics) or in patients with risk factors for Torsades de pointes (e.g. known QT prolongation, uncorrected hypokalemia). (See **PRECAUTIONS: GENERAL: Torsades de Pointes.**)

The pharmacokinetic properties of levofloxacin in younger adults and elderly adults do not differ significantly when creatinine clearance is taken into consideration. However, since the drug is known to be substantially excreted by the kidney, the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

ADVERSE REACTIONS: The incidence of drug-related adverse reactions in patients during Phase 3 clinical trials conducted in North America was 6.7%. Among patients receiving levofloxacin therapy, 4.1% discontinued levofloxacin therapy due to adverse experiences. In all Phase III trials, the overall incidence, type and distribution of adverse events was similar in patients receiving levofloxacin doses of 750 mg once daily, 250 mg once daily, and 500 mg once or twice daily.

In clinical trials, the following events were considered likely to be drug-related in patients receiving levofloxacin: nausea 1.5%, diarrhea 1.2%, vaginitis 0.5%, insomnia 0.4%, abdominal pain 0.4%, flatulence 0.2%, pruritus 0.2%, dizziness 0.3%, rash 0.3%, dyspepsia 0.3%, genital moniliasis 0.1%, moniliasis 0.2%, taste perversion 0.2%, vomiting 0.3%, injection site pain 0.2%, injection site reaction 0.1%, injection site inflammation 0.1%, constipation 0.1%, fungal infection 0.1%, genital pruritus 0.1%, headache 0.2%, nervousness 0.1%, rash erythematous 0.1%, urticaria 0.1%, anorexia 0.1%, somnolence 0.1%, agitation 0.1%, rash maculo-papular (<0.1%), dry mouth 0.2%, tremor 0.1%, condition aggravated 0.1%, allergic reaction 0.1%.

In clinical trials, the following events occurred in >3% of patients, regardless of drug relationship: nausea 6.6%, headache 5.8%, diarrhea 5.4%, insomnia 4.6%, constipation 3.1%.

In clinical trials, the following events occurred in 1 to 3% of patients, regardless of drug relationship: abdominal pain 2.5%, dizziness 2.4%, vomiting 2.4%, dyspepsia 2.3%, vaginitis 1.3%, rash 1.4%, chest pain 1.2%, pruritus 1.2%, sinusitis 1.1%, dyspnea 1.3%, fatigue 1.2%, flatulence 1.2%, pain 1.3%, back pain 1.2%, rhinitis 1.2%, pharyngitis 1.1%.

In clinical trials, the following events, of potential medical importance, occurred at a rate of 0.1% to 0.9%, regardless of drug relationship:

Body as a Whole – General Disorders: Ascites, allergic reaction, asthenia, edema, fever, headache, hot flashes, influenza-like symptoms, leg pain, malaise, rigors, substernal chest pain, syncope, multiple organ failure, changed temperature sensation, withdrawal syndrome. Cardiovascular Disorders, General: Cardiac failure, hypertension, congestive heart failure, hypotension, postural hypotension; Central and Peripheral Nervous System Disorders: Convulsions (seizures), hyperesthesia, hyperkinesia, hypertonia, hypoesthesia, involuntary muscle contractions, migraine, paresthesia, paralysis, speech disorder, stupor, tremor, vertigo, encephalopathy, abnormal gait, leg cramps, intracranial hypertension, ataxia; Gastro-Intestinal System Disorders: Dry mouth, dysphagia, esophagitis, gastritis, gastroesophageal reflux, G.I. hemorrhage, glossitis, intestinal obstruction, pancreatitis, tongue edema, melena, stomatitis; Hearing and Vestibular Disorders: Earache, ear disorder, tinnitus, vertigo; Heart Rate and Rhythm Disorders: Arrhythmia; arrhythmias: ventricular atrial fibrillation, bradycardia, cardiac arrest, ventricular fibrillation, heart block, palpitation, supraventricular tachycardia, ventricular tachycardia, tachycardia; Liver and Biliary System Disorders: Abnormal hepatic function, cholestasis, cholelithiasis, hepatic enzymes increased, hepatic failure, jaundice; Metabolic and Nutritional Disorders: Hypoglycemia, thirst, dehydration, electrolyte abnormality, fluid overload, gout, hyperglycemia, hyperkalemia, hypernatremia, hypoglycemia, hypokalemia, hyponatremia, hypophosphatemia, non-protein nitrogen increase, weight decrease; Musculo-Skeletal System Disorders: Arthralgia, arthritis, arthrosis, myalgia, osteomyelitis, skeletal pain, synovitis, tendonitis, tendon disorder; Myo, Endo, Pericardial and Valve Disorders: Angina pectoris, myocardial infarction; Neoplasms: Carcinoma, thrombocythemia; Other Special Senses Disorders: Parosmia, taste perversion; Platelet, Bleeding and Clotting Disorders: Hematoma, epistaxis, prothrombin decreased, pulmonary embolism, purpura, thrombocytopenia; Psychiatric Disorders: Abnormal dreaming, agitation, anorexia, anxiety, confusion, depression, depression, insomnia, nervousness, paranoia, sleep disorder, somnolence; Red Blood Cell Disorders: Anemia; Reproductive Disorders: Dysmenorrhea, leucorrhoea; Resistance Mechanism Disorders: Abscess, bacterial infection, fungal infection, herpes simplex, moniliasis, otitis media, sepsis, infection; Respiratory System Disorders: Airways obstruction, aspiration, asthma, bronchitis, bronchospasm, chronic obstructive airway disease, coughing, hemoptysis, epistaxis, hypoxia, laryngitis, pleural effusion, pleurisy, pneumonitis, pneumonia, pneumothorax, pulmonary edema, respiratory depression, respiratory disorder, respiratory insufficiency, upper respiratory tract infection; Skin and Appendages Disorders: Alopecia, bullous eruption, dry skin, eczema, genital pruritus, increased sweating, rash, skin disorder, skin exfoliation, skin ulceration, urticaria; Urinary System Disorders: Abnormal renal function, acute renal failure, hematuria, oliguria, urinary incontinence, urinary retention, urinary tract infection; Vascular (Extracardiac) Disorders: Flushing, cerebrovascular disorder, gangrene, phlebitis, purpura, thrombophlebitis (deep); Vision Disorders: Abnormal vision, eye pain, conjunctivitis; White Cell and RES Disorders: Agranulocytosis, granulocytopenia, leukocytosis, lymphadenopathy, WBC abnormal NOS.

In clinical trials using multiple-dose therapy, ophthalmologic abnormalities, including cataracts and multiple punctate epithelial opacities, have been noted in patients undergoing treatment with other quinolones. The relationship of the drugs to these events is not presently established.

Crystalluria and cylindruria have been reported with other quinolones. The following markedly abnormal laboratory values appeared in >2% of patients receiving levofloxacin. It is not known whether this abnormality was caused by the drug or the underlying condition being treated.

Hematology: decreased lymphocytes (2.2%)

Post-Marketing Adverse Reactions: Additional adverse events reported from worldwide post-marketing experience with levofloxacin include: allergic pneumonitis, anaphylactic shock, anaphylactoid reaction, dysphonia, abnormal EEG, encephalopathy, eosinophilia, erythema multiforme, hemolytic anemia, multi-system organ failure, increased International Normalized Ratio (INR)/prothrombin time, peripheral neuropathy, rhabdomyolysis, Stevens-Johnson Syndrome, tendon rupture, torsades de pointes, vasodilation.

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INDEX OF ADVERTISERS

Actelion Pharmaceuticals US, Inc.	
Tracleer	5
Boehringer Ingelheim Pharmaceuticals, Inc.	
Spiriva	6a-6b
Ortho-McNeil Pharmaceutical, Inc.	
Levaquin	19-20