



CHEST *Physician*

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Dr. Gregory A. Poland of the Mayo Clinic endorsed the concept of recommending flu vaccination for the entire U.S. population.

ACIP: Give Flu Shot to Kids Up to 5 Years Old

BY MIRIAM E. TUCKER
Elsevier Global Medical News

ATLANTA — All children aged 6-59 months should be immunized annually against influenza, the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices recommended unanimously at its winter meeting.

The new recommendation, which is expected to be approved and published by the CDC prior to the next flu season, expands the age group to be targeted for routine influenza immunization beyond the current 6-23 months to include all children aged 6-59 months, as well as their household contacts. The committee also voted to add coverage of influenza vaccine for 24- to

59-month-olds in the Vaccines for Children Program.

The American Academy of Pediatrics' Committee on Infectious Disease is expected to endorse the recommendation later this year, Dr. Carol J. Baker, the AAP liaison to ACIP, said in an interview.

Among the data leading to the ACIP vote were those presented by Dr. Katherine A. Poehling, of Vanderbilt University, Nashville, Tenn., showing that during two recent influenza seasons, rates of outpatient and emergency room visits for children aged 2-5 years were nearly identical to those for children aged 6-23 months.

Indeed, during 2002-2003, the

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T Cell Type Could Be New Target for Asthma Treatment

Findings may have 'far-reaching effects.'

BY KATE JOHNSON
Elsevier Global Medical News

Invariant natural killer T cells exist abundantly in the lungs of people with asthma and could be a new target for asthma therapies, according to a group of asthma researchers.

According to Omid Akbari, Ph.D., of Harvard Medical School, Boston, and colleagues, "invariant natural killer T cells are virtually absent from the lungs of controls and patients with sarcoidosis but are present in high numbers in the lungs of patients with asthma" (N. Engl. J. Med. 2006;354:1117-29).

These T cells, when activated, can lead to airway inflammation and asthma, they reported. And "therapies for asthma that target pulmonary invariant natural killer T cells may be highly effective."

The findings come from a study of 25 subjects, 14 of whom had moderate-to-severe persistent asthma. Six healthy asymptomatic volunteers served

as controls, and five other subjects had stage II sarcoidosis, a respiratory inflammatory disease.

All study subjects underwent blood drawing, spirometry, and fiberoptic bronchoscopy. When bronchoalveolar-lavage fluid was examined, it revealed a high proportion of natural killer T cells in the asthma patients, but not in the controls or in those with sarcoidosis.

In addition, the predominance of natural killer T cells in asthma patients are found in their lungs, with only low levels in their peripheral blood, noted the authors. "Our study indicates that the immunology of asthma must be studied not by the examination of peripheral blood but, rather, by the evaluation of cells from within the lung," they wrote.

The number of natural killer T cells did not appear to be significantly reduced with inhaled corticosteroid therapy, they

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MedPAC Calls for More Medicare Pay

BY TODD ZWILLICH
Elsevier Global Medical News

The committee advising Congress on Medicare payments has called for reimbursement increases for physicians and hospitals next year, but is proposing to slow the growth rate for hospital payments.

In its March report, the Medicare Payment Advisory Commission (MedPAC) called for a 2.8% increase in payments to doctors, instead of the 4.6% cut required by law next year. Doctors narrowly dodged a similar cut in January when Congress repealed it in the budget bill.

Congress approved \$6.4 billion in cuts to Medicare over 5 years in February. The White House budget called for \$36 billion more in cuts by 2011.

The American Medical Association praised MedPAC's call for higher physician payments. "If enacted by Congress, this new MedPAC recommendation will help physicians continue to treat Medicare patients," AMA board member Dr. Duane Cady said in a statement.

But the group is likely to be less impressed by a renewed MedPAC recommendation that calls for a new committee to

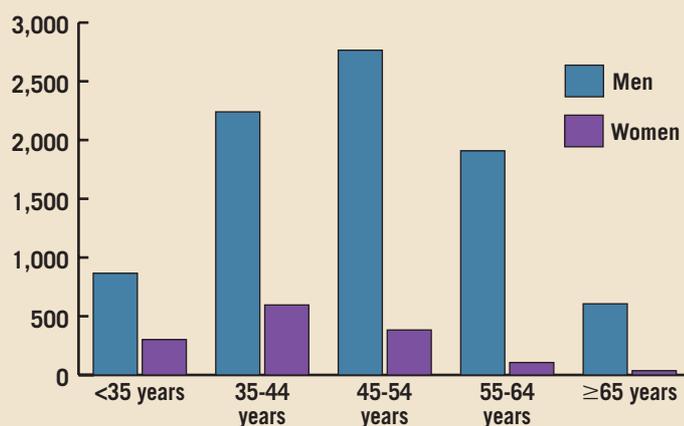
advise Medicare on the resource-based relative value scale (RBRVS) that sets reimbursement for medical services.

An AMA panel, called the RVS update committee (RUC), currently makes recommendations on payment updates for hundreds of treatment and diagnostic codes. But MedPAC chair Glenn Hackbarth told

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VITAL SIGNS

Women Make Gains in Pulmonary Medicine



Note: Based on 8,385 male pulmonologists and 1,422 female pulmonologists in the United States in 2004.
Source: American Medical Association

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More T Cell Research Needed

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reported. Ten of the 14 patients with asthma had received potent inhaled corticosteroid therapy for 6 months or longer prior to the study—yet their level of pulmonary natural killer T cells was similar to that in the asthma patients who had not received corticosteroids.

The authors noted that natural killer T cells are activated by glycolipid antigens, which can be synthetic or endogenous, or can be found in plant pollens and bacteria. Identifying the glycolipids, as well as “understanding the processes by which glycolipids are generated and activate invariant natural killer T cells, will probably provide important insights into asthma pathogenesis and perhaps reveal a host of new pathways amenable to new treatments specifically for asthma,” they wrote.

The findings are exciting, and “may have far-reaching consequences for patient care,” wrote Dr. A. Barry Kay in an

accompanying editorial (N. Engl. J. Med. 2006;354:1186-8).

He noted that targeting natural killer T cells is an obvious treatment approach, but this must be done selectively to avoid “the consequences of disturbing cells that may benefit the overall immune response (for example, by performing tumor surveillance).” In mouse models, in addition to contributing to pathologic processes, “invariant natural killer T cells facilitate a wide range of beneficial host responses, including tumor surveillance, protection from various infectious agents, prevention of autoimmune diseases ... and maintenance of self-tolerance,” he wrote.

Thus, a treatment that targets natural killer T cells by inhibiting CCL25 or CCR9 would be preferable over a treatment that inhibits V α 24 cells, which play a beneficial role, he suggested.

The study is extremely important, “as it

truly brings this body of research to the forefront and could possibly have far-reaching effects,” said Dr. Richard J. Martin, FCCP, a leading researcher in the field and acting chair of the department of medicine at National Jewish Medical and Research Center, Denver. “But much research needs to be done to both verify and understand these results before any targeted treatment is undertaken,” he said in an interview.

The fact that the authors noted no reduction in natural killer T cells in the lungs of patients who had been treated with corticosteroids contrasts with previous research suggesting that natural killer T cells in the peripheral blood of asthma patients are in fact responsive to this therapy, said Dr. Martin, The CHEST Foundation/GlaxoSmithKline Distinguished Scholar in Respiratory Health.

“The lungs’ cells may have changed to become nonresponsive, or the amount and duration of steroids were not sufficient, or other factors are occurring. All of this needs to be worked out,” Dr. Martin said. ■

Congress Considers Medicare Raise

MedPAC • from page 1

reporters that physicians on the RUC tend to counsel for increases, and that MedPAC members want a new committee within the Centers for Medicare and Medicaid Services to review the AMA’s work and make “independent” recommendations on code values.

Mr. Hackbarth said MedPAC members worry that rising code values for some services, particularly specialty care, are robbing resources from the primary care and preventive services that Medicare is now hoping to emphasize.

If an additional expert panel is appointed to help identify services to be reviewed by the RUC, “it should represent current practicing physicians,” Dr. J. Edward Hill, the AMA president, said in a statement.

In addition, MedPAC recommended

that hospitals get a 2.95% increase for treating Medicare’s 42 million beneficiaries. That would pare back the projected growth in hospital payments by nearly half a percent. The commission noted that a slowdown was needed to help control the program’s rising costs.

The proposal is in line with the White House fiscal 2007 budget, which calls for \$480 million in hospital payment cuts for 2007 as part of efforts to control entitlement spending. Hospitals have complained bitterly that they already lose money on Medicare, and that further cuts could drive some of them out of business.

Payment Proposals, Political Realities Physicians and hospitals may have little to fear—or to hope for—this year, according

to several key members of Congress.

At a Capitol Hill hearing, Rep. Nancy L. Johnson (R-Conn.) said that half of hospitals already operate in the red on money from Medicare patients. In an earlier interview, Rep. Johnson, who chairs the House Ways and Means subcommittee on health, said that President Bush’s budget is likely to be “substantially rewritten” by Congress.

California Rep. F. Pete Stark, Rep. Johnson’s democratic counterpart, suggested that Congress will be unwilling to back any more significant changes to Medicare in an election year. “They’re not going to give the raises the doctors want, and the hospitals aren’t going to get cut as much as they think,” he said in an interview.

Sen. Gordon H. Smith (R-Ore.) agreed. “It’s very bleak for doing anything. In sessions that precede elections, it’s all politics all the time,” said Mr. Smith, a member of the Senate Finance Committee. ■

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Panel Expands Vaccination Ages

ACIP • from page 1

combined rates of laboratory-confirmed influenza outpatient clinic visits and emergency room visits were identical for these age groups, at 60 per 1,000.

During 2003-2004, a more severe influenza season, the rates were 164/1,000 for the 6- to 23-month-olds and 111/1,000 for those aged 24-59 months.

Similar outpatient visit rates also were seen in children older than 5 years, of which 80% were associated with antibiotic use, Dr. Poehling noted.

Influenza vaccine manufacturers have indicated that they plan to produce between 100 million and 120 million doses for the 2006-2007 flu season, which should be enough to cover the additional 5.3 million healthy children aged 2-5 years in the United States.

In a separate vote, ACIP also advised against "tiering" of influenza risk groups in the absence of a supply decrease or delay, as has been done in previous seasons in anticipation of such problems.

Dr. Baker pointed out that expanding the age of universal influenza immunization up to age 5 years will reduce rates in the overall population, given recent data suggesting that these children are the vectors of influenza transmission to their contacts. While the ACIP did include household contacts in their recommendation, their immunization rates are typically far lower than for other groups designated as high risk.

"This new recommendation should protect our patients and has the potential for protecting their parents and their older siblings. Immunizing contacts often doesn't happen. This [recommendation provides]

an infrastructure [for immunization of contacts] to happen," Dr. Baker told this newspaper.

Dr. Baker also announced during the meeting a new "Call to Action" initiative of the National Foundation for Infectious Diseases that will be aimed at improving influenza immunization rates among the 6 million children in the United States with asthma.

Currently, only one-third of that high-risk group are immunized against influenza, despite long-standing recommendations that they receive a flu shot annually, said NFID president-elect Dr. Baker, of Baylor College of Medicine, Houston.

The NFID initiative, which is supported by a list of other professional societies including the AAP, the CDC, the American College of Emergency Physicians, the American Medical Association, and the American Thoracic Society, will provide guidance for physicians in increasing patient demand for the vaccine, enhancing access to it, and overcoming practice barriers.

More information is available at www.nfid.org.

'THIS NEW RECOMMENDATION SHOULD PROTECT OUR PATIENTS AND HAS THE POTENTIAL FOR PROTECTING THEIR PARENTS AND THEIR OLDER SIBLINGS.'

While these latest measures should help reduce the burden of influenza in the United States in the near future, ACIP's Prevention and Control of Influenza statement for the 2006-2007 season will contain a statement of the committee's intention to move toward a universal recommendation for influenza vaccine for the entire U.S. population.

That decision came after a strong endorsement of the concept from panel member Dr. Gregory A. Poland, of the Mayo Clinic.

"Health care workers and the public are immensely frustrated and confused regarding who should get vaccinated. 'It seems every year you guys add another risk group' is a refrain I continually hear. Do we really want a policy of 'preventing incrementalism'? It's time to be bold," he said.

The committee fell just short of voting to "encourage" influenza vaccine for everyone, with a nearly tied vote. Some committee members, while voicing support for the idea, felt uncomfortable supporting it without more data on efficacy, safety, cost effectiveness, and supply issues. An ACIP task force will now work on gathering those data.

Dr. LeRoy M. Graham, FCCP, comments: *Universal influenza vaccination for children aged 6-59 months and their household contacts is strongly supported by health resource utilization data. Adding coverage of influenza vaccine for 24- to 59-month-olds under the Vaccines for Children Program is essential to make this recommendation a reality. This policy would also reduce influenza rates among adults, in that the preschool child serves as an important vector of transmission.*

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 LEVOPLOXACIN 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 following 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 appropriate 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 a 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, LEVOPLOXACIN 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 physician;
- 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 Videx® (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 skin reactions, a rapid heartbeat, difficulty in swallowing or breathing, any 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 Videx® (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, Videx® (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 was observed. However, concurrent 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 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 if 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 $t_{1/2}$ 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 27-33% and 30% higher, respectively, while CL/F and CL_e 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 receiving concomitant treatment 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 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 a non-toxic-carcinogen under 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 mutagenicity assay (*S. typhimurium* and *E. coli*), CHO/HGPRT forward mutation assay, 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 (CHLJU 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 (11%) were 75 years 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, and these 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, hypotension aggravated, hypotension, postural hypotension; Central and Peripheral Nervous System Disorders: Convulsions (seizures), hyperesthesia, hyperreflexia, 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, GI hemorrhage, glossitis, intestinal obstruction, pancreatitis, tongue edema, melena, stomatitis; Hearing and Vestibular Disorders: Earache, ear disorder NOS, tinnitus; Heart Rate and Rhythm Disorders: Arrhythmia, arrhythmia ventricular, atrial fibrillation, bradycardia, cardiac arrest, ventricular fibrillation, heart block, palpitation, supraventricular tachycardia, ventricular tachycardia, tachycardia; Liver and Biliary System Disorders: Abnormal hepatic function, cholelithiasis, cholelithiasis, hepatic enzymes increased, hepatic failure, jaundice; Metabolic and Nutritional Disorders: Hypomagnesemia, 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, thrombocytoma; 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, anxiety, confusion, depression, hallucination, impotence, nervousness, paranoia, sleep disorder; Reproductive System Disorders: 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 lenticular 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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Panel: Give Pertussis Shot to Health Care Workers

BY MIRIAM E. TUCKER
Elsevier Global Medical News

ATLANTA — Health care workers in hospitals or ambulatory care settings and those who have direct patient contact should receive the adolescent/adult formulation of the tetanus-diphtheria-acellular pertussis vaccine, the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention voted at its winter meeting.

The new recommendation is aimed at protecting health care workers as well as their patients. "Preventing pertussis among health care workers will decrease exposures and secondary cases in both pediatric and adult care settings," said Dr. Trudy Murphy of the CDC's National Immunization Program.

Like the tetanus-diphtheria (Td) vaccine that it replaces, the tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine, adsorbed (Tdap) is routinely recommended at intervals of 10 years for all adults.

But an interval as short as 2 years is now advised for the Tdap dose among health care workers in ambulatory and acute care settings, including physicians, nurses, aides, respiratory therapists, medical and other students, social workers, and clerical workers, among others.

Priority should be given to vaccination of health care workers who have direct contact with infants who are less than 12 months of age and have not yet received all three doses of the infant formulation diphtheria-tetanus-acellular pertussis vaccine (DTaP). Hospitals and ambulatory facilities are strongly encouraged to provide Tdap for health care workers and to use approaches that maximize vaccination rates, according to the draft document that the committee unanimously approved. The document must be adopted by the director of Centers for Disease Control and Prevention before it becomes official.

The move follows ACIP's October 2005 vote to replace the old 10-year Td booster with Tdap (marketed by Sanofi Pasteur as Adacel) as a routine adult immunization and the committee's June 2005 recommendation to use Tdap among 11- to 12-year-olds at the routine adolescent visit (using either Adacel, which is licensed

for use in persons aged 11-64 years, or GlaxoSmithKline's Tdap, Boostrix, which is licensed for ages 10-18 years).

The routine childhood immunization wears off after about 10 years, so nearly all adults are currently susceptible to pertussis. Although the disease is rarely fatal in adults (as it can be in infants), it does cause prolonged cough lasting for 3 or more weeks in 80%-100% of adults, and post-tussive vomiting in 50%. Missed work for illness or medical care occurs in 78% of adults for a mean of 9.8 days, Dr. Tejpratap Tiwari of the CDC's National Immunization Program reported at the meeting.

In one previous study, 90% of 62 pediatric hospitals that responded to a survey mailed to 93 hospitals reported having identified pertussis cases within the past 5 years. In 11% of the hospitals, a physician had contracted the disease after exposure to a patient (*Infect. Control Hosp. Epidemiol.* 1997;18:400-4). A serosurvey of 145 health care workers conducted at a tertiary care hospital between 1992 and 1994 identified infection in 7.6% of 39 emergency department employees and in 2% of 106 resident physicians (*Infect. Control Hosp. Epidemiol.* 1999;20:120-3).

In a third study, health care workers made up 8% of 384 adults with pertussis from a total of 664 adolescent and adult pertussis cases that occurred in Quebec in 1998 (*J. Infect. Dis.* 2000;182:174-9). In that setting, the risk of pertussis among health care workers was 1.7 times greater than the risk among the general adult population.

"Limited data suggest a substantial rate among health care workers, higher than the general population," Dr. Tiwari said.

Often, the disease is passed between patients, hospital visitors, health care workers, ancillary staff, and their outside contacts in the community before it is detected, resulting in late diagnosis, delayed treatment, and late implementation of control measures.

And once a pertussis outbreak is detected, the process of identifying contacts, providing postexposure prophylaxis, testing and treating symptomatic patients and employees, and furloughing symptomatic employees during the first 5 days of treatment becomes "very labor intensive, destructive, and costly," Dr. Tiwari said.

In a separate vote, the committee rejected



"Preventing pertussis among health care workers will decrease exposures and secondary cases in both pediatric and adult care settings," said Dr. Trudy Murphy.

a proposal from its pertussis working group to recommend off-label use of Adacel in adults over 64 years of age, despite limited data suggesting high rates of infection in that age group, as well as no evidence of increased adverse events in a study from Austria in which a similar vaccine containing the

same Tdap composition was given to 252 healthy adults aged 59-91 years.

Still, some ACIP members expressed discomfort about making a recommendation for off-label use without more specific data. Sanofi-Aventis expects to provide that data within 2-3 years. ■

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Bosentan Labeling Adds Liver Warning

Reported cases of hepatotoxicity associated with bosentan therapy have prompted changes to the pulmonary arterial hypertension drug's prescribing information.

Actelion Pharmaceuticals US Inc., which manufactures bosentan (Tracleer), made the changes to highlight the importance of monthly liver function monitoring for the duration of bosentan treatments and the need to adhere to the new recommended dosage adjustment and monitoring guidelines. The new treatment and monitoring recommendations include:

► For alanine aminotransferase/aspartate aminotransferase (ALT/AST) levels greater than three and up to five times the

upper limit of normal, confirm by another aminotransferase test. If confirmed, reduce the daily dose or interrupt treatment and monitor aminotransferase levels at least every 2 weeks.

► For ALT/AST levels greater than five and up to eight times the upper limit of normal, confirm by another aminotransferase test. If confirmed, stop treatment and monitor aminotransferase levels at least every 2 weeks.

► For ALT/AST levels greater than eight times the upper limit of normal, treatment should be stopped and reintroduction of the drug should not be considered.

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—Kerri Wachter

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BMI Affected Response to Two Asthma Medications

Beclomethasone provided greater asthma control than montelukast in normal-BMI but not obese patients.

BY JOHN R. BELL
Elsevier Global Medical News

Montelukast maintained a consistent level of asthma control regardless of patients' body mass index, while beclomethasone's level of control declined as BMI increased, reported Dr. Marc Peters-Golden of the University of Michigan, Ann Arbor, and colleagues.

In a post hoc analysis of data from four studies of adult asthmatics, BMI was "an important determinant of response to active treatment," the researchers said.

Moreover, differences in response to montelukast and beclomethasone corresponding to BMI "may be important in considering treatment choices in individual adult asthmatics," they wrote (*Eur. Resp. J.* 2006; 27:1-9).

The investigators analyzed data from four previous multicenter, randomized, parallel-group studies of 3,073 adult patients with moderate asthma. The analysis compared results achieved with 10 mg of the leukotriene antagonist montelukast

taken four times daily; 200 mcg of the inhaled corticosteroid beclomethasone taken twice daily; and placebo taken either once daily as a tablet or four times each day via inhalation.

The double-blind treatment period was 6 weeks in two of the trials and 12 weeks in the other two studies. Pooling studies of differing durations was justified, the authors explained, because the two active drugs in the comparison achieved their maximum efficacy by 6 weeks.

In all four studies, participants were limited to nonsmokers of either sex and at least 15 years of age, with at least a 1-year history of asthma symptoms and an average β -agonist use of more than two puffs per day. Current asthma treatment could include only a short-acting β -agonist at randomization, and only one study allowed inhaled corticosteroids. Patients were required to have a forced expiratory volume in 1 second (FEV_1) of greater than 50% and less than 85% of predicted value at rest, as well as at least a 15% increase in FEV_1 after treatment with a β -agonist.

Participants in the four studies filled out diary cards with information on asthma symptoms, presence or absence of asthma attacks, nighttime awakening, and number of inhalations of β -agonist. Days with none of those symptoms and with no more than two puffs of β -agonist (including before exercise) counted as asthma control days.

The proportion of study days meeting the criteria for asthma control days was the primary end point. Secondary end points were percentage change in FEV_1 , percentage of nights with awakenings, and percentage change in number of daily β -agonist puffs.

Patients were classified in three groups according to BMI: normal (less than 25 kg/m², 52% of patients), overweight 25-29.9, 32% of patients), and obese (30 or greater, 16% of patients). The investigators used a modified intent-to-treat approach, with all patients ascribed one intent-to-treat measurement.

Montelukast showed similar asthma control in all three BMI classes. Beclomethasone, however, showed less control as BMI increased. The percentage of asthma control days achieved with beclomethasone

was significantly greater than with montelukast for normal-BMI patients (19% vs. 10%) but not for overweight (19% vs. 16%) or obese (14% vs. 16%) patients.

Further analysis confirmed the initial finding that the efficacy of montelukast was comparable across all BMI groups but that the results achieved with beclomethasone and placebo declined as BMI increased. Because montelukast is a leukotriene antagonist, this might mean that asthma in overweight and obese patients "may be a more [leukotrienes]-driven form of asthma than in individuals of normal BMI," the investigators said.

Analysis for secondary end points showed no differences in FEV_1 among the three BMI groups. For nocturnal awakenings, the investigators' findings confirmed significant differences for the BMI groups by treatment. The overweight and obese groups had more nights with awakenings than the normal-BMI patients in both treatment groups; but for each group, there were more nocturnal awakenings with montelukast than with beclomethasone. In regard to β -agonist use, there were no significant differences by BMI group. ■

DIFFERENCES IN RESPONSE TO THE TWO DRUGS CORRESPONDING TO BMI MAY BE IMPORTANT IN CONSIDERING TREATMENT CHOICES IN ADULT ASTHMATICS.

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Omalizumab Cut Steroid Use For Severe Allergic Asthma

BY PATRICE WENDLING
Elsevier Global Medical News

MIAMI — Omalizumab maintained control of severe allergic asthma and reduced the need for inhaled corticosteroids during 3 years of treatment in an analysis of data from a 52-week open-label extension study.

The findings extend the results of previous studies by showing that asthma control and a favorable safety and tolerability profile were maintained during long-term treatment with the anti-IgE monoclonal antibody, Dr. Jacques Hébert and associates reported in a poster at the annual meeting of the American Academy of Allergy, Asthma, and Immunology.

The study was supported by Genentech Inc. and Novartis Pharmaceuticals Corp., which comarket omalizumab (Xolair). The drug gained federal approval in June 2003 for the treatment of moderate to severe asthma in patients age 12 years and older.

In the core 32-week study of 341 patients, omalizumab significantly reduced the use of inhaled corticosteroids and rescue medications while improving symptom scores and quality of life, compared with placebo. A first extension to this trial showed that these favorable efficacy and safety findings were sustained for a further 96 weeks of treatment.

In a second extension of the trial, researchers enrolled 178 patients, of whom

149 (84%) completed the study. Patients underwent a washout period of 12 weeks or more before receiving omalizumab subcutaneously at a dose of 0.016 mg/kg or more per IU/mL of IgE every 2 weeks or 4 weeks for up to 52 weeks.

Mean forced expiratory volume in 1 second (FEV_1) showed no decline between the start of the first extension (baseline) and week 52 of the second extension (2.24 L vs. 2.26 L). Good or excellent asthma control, based on the physician's overall assessment, was sustained from baseline to week 52 in 121 of the 149 (81%) patients.

During the same period, inhaled corticosteroid doses decreased about 20% among 96 patients who received the same inhaled corticosteroid throughout the first and second extensions and were not taking oral corticosteroids, reported Dr. Hébert, director of the Centre de Recherche Appliquée en Allergie, Quebec City. He has no financial interest in either of the study's sponsors.

Of the 178 patients who enrolled in the second extension, 134 (75%) had at least one adverse event, generally of mild or moderate severity. The incidence was similar to that reported during the core study (80%) and the first extension (88%). Respiratory events were the most frequent adverse events: asthma not otherwise specified in 49 patients (27.5%), and nasopharyngitis in 41 (23%). No drug-related deaths and no new safety issues were identified during the study. ■

Infusion Protocol Cuts Time To Target Glucose Levels

The Yale protocol, which includes drip rate and blood glucose change velocity, is being increasingly adopted.

BY MIRIAM E. TUCKER
Elsevier Global Medical News

WASHINGTON — More hospitals are implementing standardized insulin infusion protocols, many of which emulate the Yale protocol, Dr. Philip A. Goldberg said at a consensus conference sponsored by the American Association of Clinical Endocrinologists, American College of Endocrinology, and the American Diabetes Association.

Dr. Goldberg, a postdoctoral fellow at Yale University, New Haven, Conn., said the protocol was introduced in 2001 after the publication of the landmark Leuven, Belgium study (N. Engl. J. Med. 2001; 345:1359-67). Until then, the “state of the art” in the intensive care unit had been to tolerate blood glucose levels as long as they did not exceed 200 mg/dL and to rarely address plasma glucose elevations. Glucose levels were rarely checked in nondiabetic patients, and existing “sliding scale” insulin orders took into account only the current blood glucose. In contrast, the Yale protocol incorporated two other essential elements: The velocity of change (based on both the current and previous values) and the current infusion rate. “If you don’t incorporate all three of those, your drip will not be successful,” he said.

In the first 69 insulin drips used in 52 medical ICU patients with a baseline mean glucose of 299 mg/dL, the median time to achieve target blood glucose levels of 100-139 mg/dL (now 90-119 mg/dL) was 9 hours, and the median drip duration was 61 hours. The protocol worked equally well in diabetic and nondiabetic patients, and was not influenced by the severity of illness.

The protocol was complex enough to achieve strict glycemic control in critically ill patients and practical enough to be implemented by busy ICU nurses without the need for continuous expert supervision (Diabetes Care 2004;27:461-7). Importantly, the protocol also was readily accepted by the nursing staff, with 73% rating it as “very easy” or “somewhat easy” to use.

“It’s only complex the first two or three times you do it. Once you actually run an ICU nurse through this protocol a few times, it’s not complex at all compared to the other things they do,” Dr. Goldberg said.

Since then, other institutions have created their own versions of the Yale protocol—some including computerized algorithms—with similar success rates. “Everybody’s institution has different local climates and needs to adjust these things... It’s nice to see that people are taking our drip, adapting it to their local environment, and having some success with it,” Dr. Goldberg noted.

And in 2004, the Yale group again updated its protocol following the publication of the first American Association of Clinical Endocrinologists’ national guideline on inpatient diabetes and metabolic control (Endocr. Pract. 2004;10:77-82) and the American Diabetes Association’s technical review (Diabetes Care 2004;27:553-91). The blood glucose targets were lowered to 90-119 mg/dL and the IV bolus was increased by about 40% to gain more rapid control. Also, the terminology was modified to conform to the standards of the Joint Commission on Accreditation of Healthcare Organizations (Diabetes Spectrum 2005;18:188-91).

In 54 consecutive cardiothoracic ICU patients, mean blood glucose levels were another 12-13 mg/dL

lower on average with the new protocol and with no concomitant increases in hypoglycemia. Similarly, mean glucose level was 118 mg/dL among 47 consecutive medical ICU patients receiving 63 drips.

With the old protocol, levels averaged 123 mg/dL. The new protocol halved to 4.5 hours the median time to reach a glucose level below 140 mg/dL (the old target).

These results would have been impossible without “buy in” from the nursing staff, Dr. Goldberg emphasized. “The ICU nurses are the ones who are doing this. You have to recognize that up front.”

A major barrier still to be overcome is the long-held fear of hypoglycemia. Many hospital personnel believe that levels of 150-200 mg/dL are “normal” and that anything below 100 mg/dL is cause for concern. “There is a ‘culture of hyperglycemia,’ with a fear of hypoglycemia, or even of low normal,” he said.

To address these concerns, inservice training at Yale consists of 35 minutes addressing the “why” of the protocol and just 10 minutes for the “how.” The trainers review the published data and reinforce the message that most hypoglycemic episodes are benign and treatable.

It’s also important to acknowledge to the nursing staff that the infusions will cause them extra work, Dr. Goldberg said. Some of the impact can be minimized with efficient use of ancillary staff, additional glucose meters, and use of lines in place for other reasons to sample venous or arterial blood for glucose measures.

In the future, continuous glucose monitoring systems—currently approved for use only in diabetic outpatients—might also prove useful in the ICU setting. In a preliminary study, the Yale group found good correlation between values obtained with Medtronic Minimed’s CGMS system and capillary glucose levels in 22 medical ICU patients (Diabetes Technol. Ther. 2004;6:339-47).

THE PROTOCOL ACHIEVED STRICT GLYCEMIC CONTROL IN PATIENTS AND WAS ‘PRACTICAL ENOUGH TO BE IMPLEMENTED BY BUSY ICU NURSES.’

Morbid Obesity Complicates Airway Management

BY ROBERT FINN
Elsevier Global Medical News

SAN FRANCISCO — Despite attempts at optimal positioning, it’s significantly more difficult to intubate patients who are morbidly obese than those of normal weight, according to a poster presentation by Dr. Thomas C. Mort at the annual congress of the Society of Critical Care Medicine.

In a retrospective analysis of more than 1,200 patients, 72% of patients with body mass indexes below 25 kg/m² could be intubated on the first try, compared with just 52% of those with BMIs greater than 40. At least three attempts were required for 18% of the morbidly obese (MO) patients, compared with 10.5% of the normal-weight patients.

Accessory airway devices were required far more often in MO patients. Of MO patients, 58% required one of these devices, compared with 22% of normal-weight patients. Bougies were required 21% of the time in MO patients, compared with 10% of normal-weight patients. Similarly significant differences were noted for laryngeal mask airways (28% vs. 4%), but no significant differences were noted in the use of fiberoptic bronchoscopes or Combitubes.

The study involved 1,253 consecutive emergency intubations over a 12-year period from 1994 to 2005. Dr. Mort, of Hartford (Conn.) Hospital, isolated those cases in which emergency airway management took place outside the operating room. Fourteen percent of the

cohort (174 patients) had BMIs greater than 40, and they were compared with a cohort of normal-weight patients.

Members of the medical team routinely built a ramp with blankets to optimize head and neck position and to improve the thoracic-cervical spine relationship.

The groups differed significantly in Mallampati class, which relates tongue size to pharyngeal size. A total of 90% of the normal-weight patients were Mallampati class 1 or 2, compared with 16% of MO patients. Fully 42% of MO patients were Mallampati class 4, compared with 2.6% of nonobese patients.

Mild hypoxemia was found in 33% of the MO group, significantly greater than the 17% of the normal-weight patients. Likewise, severe hypoxemia was more common in MO patients (11% vs. 2%).

No significant differences were noted in the rates of esophageal intubation or regurgitation. Dr. Mort attributed this to the more frequent use of accessory devices in the morbidly obese.

Dr. Susan M. Harding, FCCP, comments: *Although this is a retrospective study, it shows that morbidly obese individuals (BMI of greater than 40 kg/m²) are more likely to require multiple intubation attempts and accessory airway device use for successful intubation. With the increased prevalence of obesity in our society, we need to ensure that intubation kits in our practicing hospitals have accessory airway devices, including bougies and laryngeal mask airways.*

Medication Errors in ICU Stem From Communication Lapses

Medication errors in the intensive care unit are most often due to communication failures and improper use of intravenous pumps, according to a report compiled by the U.S. Pharmacopeia.

The USP analyzed records from 503 hospitals, and likely just touched on the error problem because there are more than 5,500 hospitals in the United States, John P. Santell, R.Ph., director of educational program initiatives for the Center for the Advancement of Patient Safety at USP, said at a press briefing sponsored by the organization.

The reports to USP are voluntary and are compiled in the “Medmarx Data Report: A Chartbook of 2000-2004 Findings From Intensive Care Units and Radiological Services,” available on-line to hospital subscribers.

Over 5 years, USP received reports of 38,371 errors. One-third, or 12,861 errors, were intercepted before they reached the patient, but 22,691 (59.1%) did reach the patient and 1,270 (3.3%) resulted in harm. Among the harmful errors, 1,063 (84%) resulted in temporary harm. There were 68 serious errors and 14 fatalities, said Mr. Santell.

Communications problems included verbal orders that were misinterpreted, incomplete or poor transcription, illegible handwriting, wrong or unreadable abbreviations, and inappropriate use of decimal points in written orders, said Mr. Santell.

In the intensive care unit, errors of omission were the most frequently reported and were committed by nurses, physicians, and pharmacists, said Mr. Santell. Patients were also administered the wrong dose or the wrong drug. These two errors plus the omissions accounted for 72% of errors in the ICU, he said.

Intravenous pump problems—usually tubing mix-ups or improper programming—were the second largest area of errors.

Insulin, heparin, and albuterol were most often involved in ICU errors.

Surgical ICUs had the most errors involving harm to the patient. General ICUs had the lowest percentage of errors reaching the patient (53%), but the highest percentage of medication errors (17%), the report said.

—Alicia Ault

More Pediatric Status Asthmaticus Cases Visit PICU

'We need to ask ourselves if we're prepared for the increase in admissions that is certainly ahead.'

BY ROBERT FINN
Elsevier Global Medical News

SAN FRANCISCO — The number of hospital admissions for pediatric status asthmaticus seems to be decreasing, but at the same time both the number and the proportion of patients with status asthmaticus who are admitted to the ICU appear to be increasing, Dr. Mary E. Hartman said at the annual congress of the Society of Critical Care Medicine.

In New Jersey over the 10-year period from 1992 to 2001, ICU admissions for status asthmaticus increased from 10 per 100,000 children to 18 per 100,000, an increase of 80%, said Dr. Hartman of the University of Pittsburgh.

At the same time, total hospital admissions for status asthmaticus declined from 4,170 in 1992 to 2,361 in 2001, a decline of 43%.

Dr. Hartman and her colleagues examined an administrative database from New Jersey that tabulated every pediatric hospitalization in the state's hospitals. For the years 1992, 1995, 1999, 2000, and 2001, the

investigators identified all admissions with the ICD-9 codes for status asthmaticus. The database included demographic information as well as information on admission characteristics such as length of stay and whether the child was admitted to an ICU.

The investigators were also able to determine which of the 108 hospitals had a pediatric ICU (PICU) and which had only an adult ICU or no ICU at all.

During the 10-year period, there were 17,066 pediatric status asthmaticus admissions. Fifty-nine percent of the children were male, and 70% were less than 10 years old. The proportion of uninsured children was 8.1%. These demographic characteristics did not change appreciably over the study period.

Overall, 9.3% of status asthmaticus admissions involved an ICU stay. But

that increased from 4.4% in 1992 to 17.7% in 2001.

This pattern of increased ICU use did not reflect overall trends in hospitalization during that period. When all hospitalizations and all ICU admissions were considered, total pediatric hospitalizations decreased just 9%, compared with 43% for status asthmaticus. Likewise, total pediatric ICU cases increased by 51%, compared with 127% for status asthmaticus.

Deaths were infrequent during the study period and remained stable over time. A total of eight children died during the 5 years studied. On the other hand, the number of children who required mechanical ventilation declined steadily from 1995 to 2001.

"The drop in ventilated cases corresponds to an increase in ICU admissions during that time, and we believe that these data represent a trend in increased vigilance ... toward more aggressive management of status asthmaticus patients in the ICU," Dr. Hartman said.

One of the more interesting aspects of the study concerned whether children were admitted to a PICU or to an adult ICU. Despite the fact that only 17 of 108 hospitals had a PICU, three-quarters of the children with status asthmaticus who needed intensive care were seen in PICUs. In 1992, only 8% of all admissions for status asthmaticus received intensive care in PICU hospitals. By 2001, 40% of all such admissions ended up in the PICU.

"If there's one take-home point I'd like you all to remember today, it's that ICU admissions for status asthmaticus are increasing linearly over time," she continued. "We need to ask ourselves if we're prepared for the increase in admissions that is certainly ahead. Second, I think this study clearly raises questions about the regionalization of ICU care. Children's hospitals have changed in ways adult hospitals have not." ■

Dr. LeRoy M. Graham, FCCP, comments: Severe pediatric status asthmaticus requiring PICU admission is unfortunately increasing while overall hospitalization for pediatric asthma is decreasing. Increased PICU capacity as well as support for children's hospitals with unique pediatric expertise and effective triage practices are critical issues in health care planning.

'WE BELIEVE THAT THESE DATA REPRESENT A TREND ... TOWARD MORE AGGRESSIVE MANAGEMENT OF STATUS ASTHMATICUS PATIENTS IN THE ICU.'

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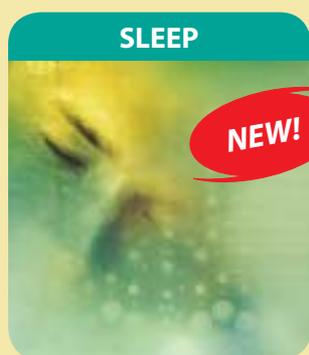
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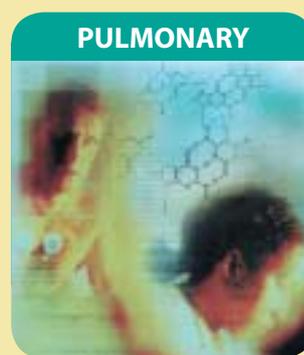
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Maternal Vitamin D Intake May Cut Kids' Asthma Risk

BY PATRICE WENDLING
Elsevier Global Medical News

MIAMI BEACH — High maternal vitamin D intake in pregnancy may help protect children from asthma and wheezing illnesses during early childhood, results of a large, prospective study suggest.

In multivariate analyses, every 100 IU increase in maternal vitamin D intake was associated with about a 10% lower risk for any wheeze (an odds ratio of 0.90) and with nearly a 20% lower risk of having a child at high risk for asthma (an odds ratio of 0.82).

This inverse association between vitamin D intake and asthma risk was present whether vitamin D came from diet or nutritional supplements and remained after controlling for 10 confounding factors, Dr. Carlos A. Camargo Jr., FCCP, reported at the annual meeting of the American Academy of Allergy, Asthma and Immunology.

The best explanation is that vitamin D influences IL-10 secretion by regulatory T cells.
DR. CAMARGO

hear more and more about in the years ahead," Dr. Camargo told reporters at the meeting.

"Already this year there is a lot of discussion going on about vitamin D and cancer. But to link this to asthma and allergic diseases is very exciting," Dr. Camargo explained.

The best explanation for the observed protective effect is that vitamin D, which is known to have some immunologic effects, influences IL-10 secretion by regulatory T cells, explained Dr. Camargo, who is with the department of epidemiology at Harvard Medical School in Boston.

The findings suggest that vitamin D insufficiency is a reality, particularly in northern parts of the country.

Exactly what the correct amount of daily vitamin D intake is remains unclear, in part because of emerging data from this and studies in other specialties, Dr. Camargo said.

"Most people in the field would recommend 800-1,000 IU/day, and yet you'll see recommendations of 200-400 IU in the literature," he said.

Dr. Camargo added that the Institute of Medicine's recommendations should be revisited.

The mean vitamin D intake by mothers during pregnancy was 548 IU/day in the study, which included 1,194 mother-child pairs in Project Viva. Project Viva is a prospective prepartum cohort study in Massachusetts.

Maternal intake of vitamin D was assessed by study researchers using a validated food questionnaire in the first and second trimesters and was averaged for analyses.

Dr. Camargo and his colleagues defined any wheeze as a mother-reported wheeze or physician-diagnosed asthma, wheezing, or reactive airway disease at ages 1, 2, or 3 years.

High risk of asthma was defined by the researchers as the subset of children who experienced two or more reports of wheezing at 1, 2, or 3 years, plus either parental history of asthma or child diagnosis of eczema.

Multivariate analyses were performed controlling for gender, birthweight,

income, maternal age, prepregnancy body mass index, passive smoking exposure, breast-feeding duration at 1 year, number of children younger than 12 in the household, and maternal and paternal history of asthma.

The adjusted risk was significantly lower for any wheeze at age 3 years in children who were born to 298 women with the highest vitamin D intake, or about 724 IU/day, than in children who were born to 298 women with the lowest vitamin D intake or about 356 IU/day

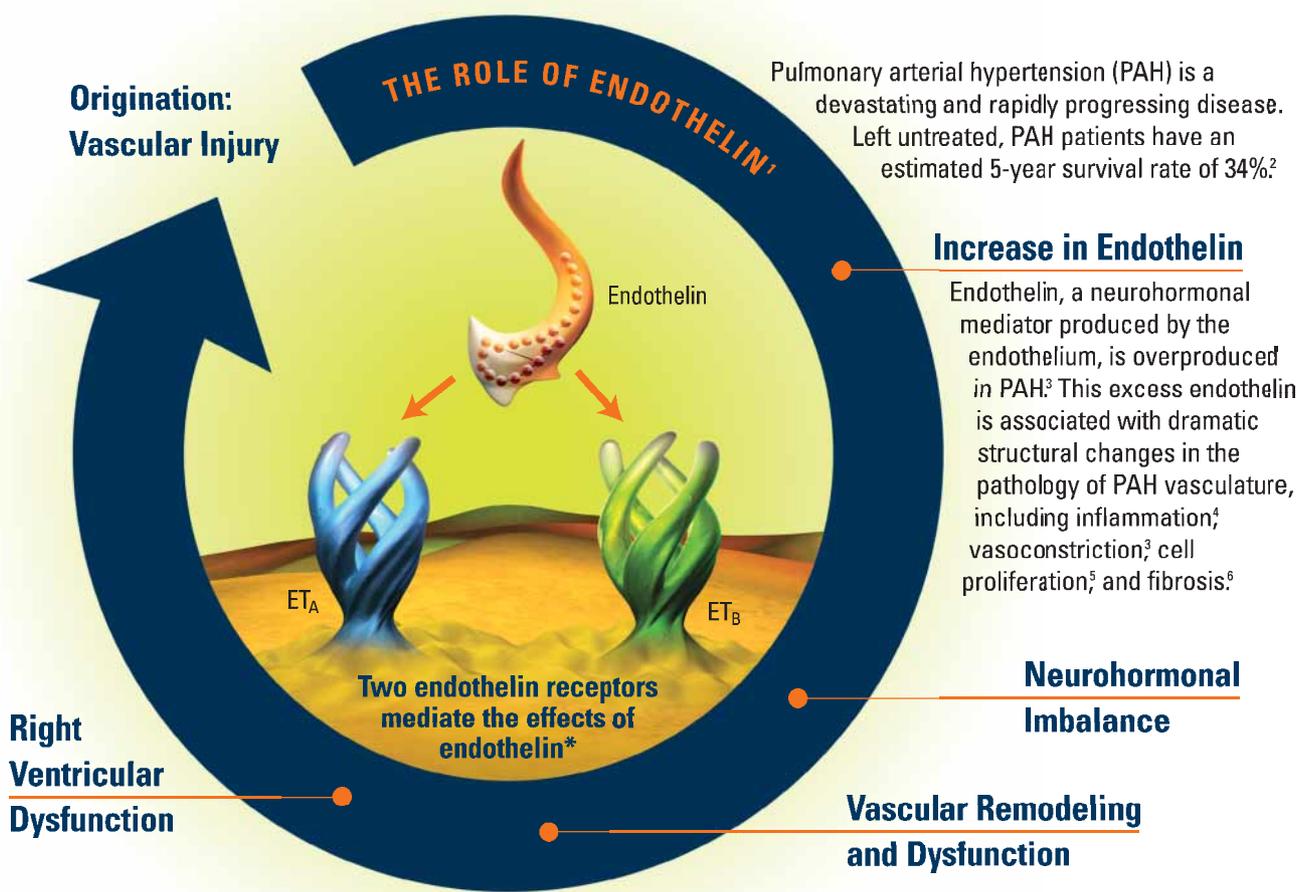
(odds ratio of 0.58 vs. odds ratio of 1).

The chance of having a child who was at high risk of asthma at age 3 years also was significantly lower among the high-intake group (odds ratio of 0.41 vs. odds ratio of 1).

Further adjustment for maternal intake of fruit, vegetables, and fish did not change the results.

Continued follow-up of the cohort will determine if these research findings will translate into decreased asthma risk in later childhood, Dr. Camargo said. ■

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



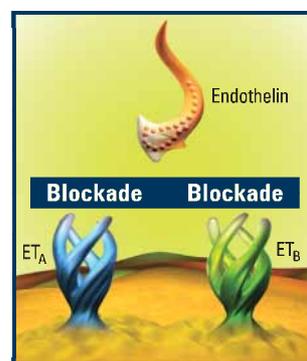
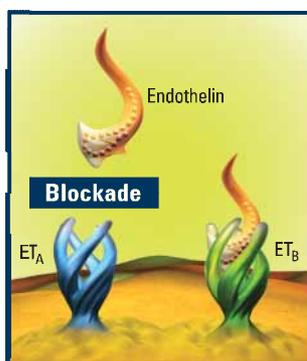
Blockade of Both ET_A and ET_B Receptors Is Critical

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.

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Study Clarifies Algorithms for Preop Cancer Assessment

BY BRUCE K. DIXON
Elsevier Global Medical News

MONTREAL — Lung cancer patients should be assessed for their surgical suitability using algorithms rather than absolute values of forced expiratory volume in 1 second, according to a study conducted at the University of Texas Health Science Center in Houston.

“Algorithms ... that use values of FEV₁ [forced expiratory volume in 1 second] greater than 80% for pneumonectomy or predicted postoperative FEV₁ of 35% or greater are more consistent than predictions for resection using absolute values of FEV₁ in liters,” Dr. M. Yesim Ersoy told the CHEST 2005 annual meeting of the American College of Chest Physicians.

Explaining the “apparent lack of congruency” among methods for preoperative patient selection, Dr. Ersoy and her colleagues cited previously published studies and British Thoracic Society guidelines, which state that an FEV₁ of 2 L or greater is a safe lower limit for pneumonectomy in patients with lung cancer. Others have utilized FEV₁ based on percent of predicted normal—ranging between 60% or higher and 80% or higher—to indicate a patient suitable for resection.

“The most quoted study by the British Thoracic Society [Thorax 2001;56:89-108] says no further respiratory function tests are required for pneumonectomy if FEV₁ is 2 L or higher. Otherwise, based on radionuclide studies, an estimated postoperative FEV₁ greater than 40% predicted is okay; otherwise, consider exercise testing,” said Dr. Ersoy of the University of Texas Health Science Center (UTHSC) in Houston.

There are difficulties with recommendations that use percentage of predicted or estimated postoperative FEV₁. “The literature is heavily based on making predictions for resection using absolute values of FEV₁ in liters, but this approach creates a big bias against older patients, females, and patients of small stature who might tolerate lower levels of lung function,” she said.

Dr. Ersoy and her associates conducted a study that included all patients with unilateral lung cancer referred to the UTHSC pulmonary laboratory for preoperative evaluation between January 2002 and May 2005. The investigators reviewed clinical characteristics, the results of pulmonary function tests, and quantitative regional ventilation-perfusion lung studies. “Tests included spirometry before and after bronchodilators, measurement of lung volumes by body box plethysmography, and single-breath diffusing capacity,” Dr. Ersoy explained. Quantitative radionuclide studies of regional lung ventilation and perfusion in the sitting position were performed the same day. A total of 1,334 patients were studied.

The researchers found that 47% of patients had FEV₁ greater than 2 L (mean 2.64 L). But 49% of those who had FEV₁ greater than 2 L had an FEV₁ less than 80%.

“Another interesting thing was that of those patients who had FEV₁ greater than 2 L, 30% had a predicted postoperative (PPO) FEV₁ of less than 40% and 13% had a ... PPO less than 35%,” Dr. Ersoy said.

When the researchers looked at FEV₁ in percent predicted, only 11% of those patients had PPO FEV₁ under 40%, and only 2% of those had a reading under 35%.”

“We also looked at patients with FEV₁ over 60% and under 80%, and this was even worse: 41% of them had predicted postoperative FEV₁ less than 40%, and 26% had PPO FEV₁ less than 35%,” she said. “About one-third of patients with an FEV₁ higher than 2 L would have been deemed ineligible for pneumonectomy based on PPO FEV₁ less than 40%,” Dr. Ersoy said.

“I agree completely that we need to get away from absolute values, and we need to get away from this preoperative percent of normal and really go through a predicted postoperative value as the cutoff,” said Dr. Frank C. Detterbeck, FCCP, chief of thoracic surgery at the Yale University Cancer Center in New Haven, Conn.

Regarding mortality figures, he said that the “numbers we have for a predicted postoperative FEV₁ of less than 40% pertain to an open lobectomy or an open pneumectomy. If you look at data from

series that used open segmentectomies or open wedge resections in patients with very limited pulmonary function, mortality results are consistently below 5%.

“So we have to be careful about using these numbers to say that patients will not tolerate a segmentectomy or wedge resection,” Dr. Detterbeck said. He also noted that there is no good definition of exactly how high the risk is for patients below a particular level. “So a 15% operative mortality might be appropriate in some patients who have a very curable cancer.” ■

CRITICAL INSIGHTS INTO THE NATURE OF NICOTINE ADDICTION

A SUMMARY OF KEY LEARNINGS TO DATE

With all the public awareness efforts that have been made, and with all the truths that have come to light over the last several decades about the dangers of smoking, one obvious question lingers: **Why are people still smoking?**

Understanding nicotine addiction

Most experts agree at this point that smoking is a chronic, relapsing condition—an addiction similar in nature to that seen in cocaine and heroin users.^{1,2} Following are 4 criteria the Surgeon General has used to define addiction, along with an explanation of how nicotine—specifically smoking—meets these criteria.²

1. Addiction leads to compulsive use, despite adverse consequences

According to a 1988 Surgeon General’s report, “highly controlled or compulsive use indicates that drug-seeking and drug-taking behavior is driven by strong, often irresistible urges. It can persist despite a desire to quit or even repeated attempts to quit.”² Smoking statistics show that approximately **70% of current smokers report that they want to quit**; however, only about 5% of smokers who try to quit without medical aid succeed.^{3,4} For those who finally do quit, it is usually only after **6 to 9 failed attempts**.⁵ It is common for people to continue smoking despite known negative health consequences. In fact, smoking behavior often persists even after the presentation of comorbid conditions.^{2,6,7}

2. Addiction involves a psychoactive substance with reinforcing properties

The psychoactive (mood-altering) properties of nicotine are substantially related to its effect on the mesolimbic dopaminergic system. For delivery of nicotine, smoking is the most efficient mechanism. In a matter of seconds, nicotine from inhaled smoke crosses the blood-brain barrier and begins altering brain chemistry through binding to

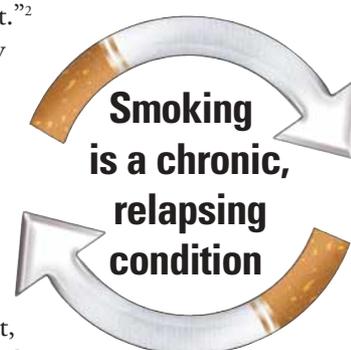
cholinergic receptors normally activated by acetylcholine. Dopamine is released in the nucleus accumbens, triggering central nervous system effects such as pleasure, relief of anxiety, better task performance, and improved memory. These rewards serve to reinforce smoking behavior.^{2,8-10}

Complicating this effect is that the routines associated with smoking, such as smoking in social environments, can also come to be reinforced through the pleasure response. Eventually, the pleasure associated with smoking in these settings acts as a subconscious trigger, making it hard for the smoker to dissociate the behavior from the addiction. **This explains why successful quit attempts often require some degree of behavioral modification.**^{2,11,12}

3. The addicted subject develops tolerance

Nicotine initiates its action by competitively binding at the nicotinic acetylcholine receptors (nAChRs), ligand-gated ion channels on the cell membrane. Compared with the endogenous agonist acetylcholine, nicotine causes a prolonged activation of nAChRs. The activation is followed by a desensitized state in which the receptors are unresponsive to agonists. This process has been compared to tripping a circuit breaker.^{10,11,13}

Chronic use of nicotine leads to chronic desensitization of nAChRs. As more nicotine is consumed, and more receptors become desensitized, **the user experiences a diminished pleasure effect with each subsequent cigarette smoked**. As the response decreases, increasing levels of nicotine are required to achieve a consistent, desired effect.^{2,10-12} These are defining characteristics of tolerance.¹⁴



'New Era' of Drugs Approaching for Atrial Fibrillation

BY MITCHEL L. ZOLER
Elsevier Global Medical News

BOSTON — Two drugs for preventing atrial fibrillation that were being considered for approval by the Food and Drug Administration in early 2006 headed the list of new antiarrhythmia agents that could change atrial fibrillation treatment over the next few years.

A "new era" of drug treatment is approaching, Dr. Peter Kowey said at an international symposium on atrial fibrillation

that was sponsored by Massachusetts General Hospital.

Drugs that may be part of that era include:

► **Azimilide.** This agent blocks both rapid and slow potassium channels in the heart and is one of the drugs under FDA review. Azimilide is being considered as a way to prevent shocks from an implanted cardiac defibrillator.

However, although it is a "very potent" drug for suppressing atrial fibrillation, the results of one major trial failed to

demonstrate that treatment produced a survival benefit, said Dr. Kowey, professor of medicine at Thomas Jefferson University, Philadelphia.

► **Dronedarone.** Also before the FDA, dronedarone is an amiodarone congener and the first from a line of amiodarone-like compounds that are under development. These agents are attracting interest because amiodarone is the most effective antiarrhythmic medication that is currently available but it is also associated with adverse effects and weaknesses,

Dr. Kowey said at the symposium, also sponsored by the Academy of Health Care Education.

Dronedarone avoids the thyroid and pulmonary toxicity that is seen with amiodarone. The two agents have not been compared with each other in a head-to-head study, but if dronedarone were to be approved, it would be "extraordinarily useful" for relatively young patients who are being considered for amiodarone treatment, perhaps because they have already failed treatment with a class 1C drug such as flecainide or propafenone, he said.

Dronedarone should not be used in patients who have severe heart failure because of a suggestion of safety problems in the clinical trials so far. The drug also should be avoided in patients who are suffering from severe renal dysfunction. For patients with severe left ventricular hypertrophy, amiodarone remains the best drug.

► **RSD-1235.** Some phase III testing has been completed for this atrial-selective drug, but other studies are still in progress.

The drug's manufacturer says that it plans to apply for FDA licensing early this year with an intravenous formulation for termination of acute arrhythmia. An oral form is still in clinical trials.

Dronedarone avoids the thyroid and pulmonary toxicity that is seen with amiodarone.
DR. KOWEY

Atrial-selective agents are a major area of development because adverse electrical effects on ventricles are the biggest reason for toxicity of existing drugs for atrial arrhythmia, said Dr. Kowey. Another atrial-selective drug, AVE-0118, is just starting clinical studies.

Atrial repolarizing delaying agents also are just entering clinical studies and must show their potential in proof-of-concept tests. Gap-junction modulators are in pre-clinical development, although the main focus now for these drugs is ventricular arrhythmias. Stretch-activated channel blockers also are being studied.

Some drugs already on the market have also shown signs of possible efficacy for atrial fibrillation. β -Blockers are a promising class. Carvedilol in particular showed signs of efficacy for preventing atrial arrhythmia in patients with ischemic heart disease in the Carvedilol Postinfarct Survival Control in Left Ventricular Dysfunction (CAPRICORN) trial. Certain ACE inhibitors and angiotensin-receptor blockers have also shown signs of efficacy for preventing fibrillation in completed trials, and the efficacy of some angiotensin-active drugs as primary therapy for atrial fibrillation is now being tested in randomized controlled trials.

Other agents that have shown hints of efficacy include anti-inflammatory drugs, especially statins, which significantly reduced the incidence of atrial fibrillation episodes in two retrospective studies. ■

4. An addictive substance causes physical dependence, as evidenced by withdrawal and relapse

The symptoms of nicotine withdrawal have been clearly identified and confirmed. For most smokers, these symptoms include at least one, if not several, of the following: craving, irritability, insomnia, headache, anxiety, depression, and impaired concentration.^{11,14} These withdrawal symptoms have been identified as key contributors to relapse, as the smoker often "self-medicates" with nicotine to return to a perceived state of normalcy.¹²

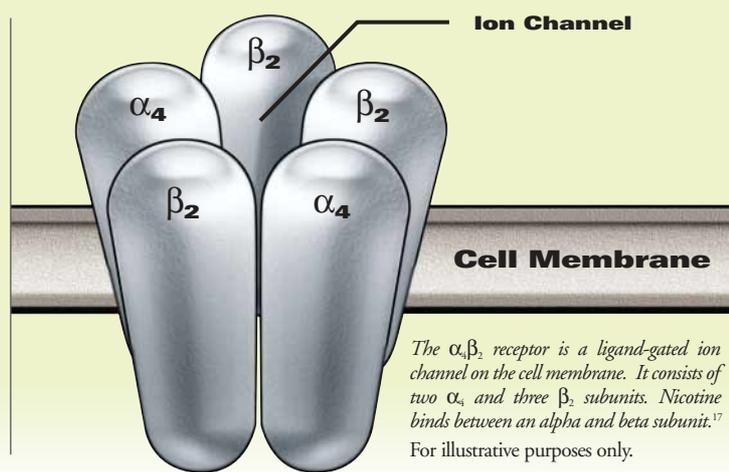
Additionally, chronic stimulation at the receptor site is believed to be responsible for upregulation (an increase) in the number of receptors expressed at the cell surface.^{8,10,12} This is likely a result of the brain compensating for the desensitization of existing receptors, as described earlier.

As nicotine leaves the system, however, desensitized receptors can return to an "open" state in which they are once again susceptible to stimulation.^{10,11} The combination of these factors—ie, a greater number of available, sensitized receptors—may create "an excess excitability of the nicotinic cholinergic systems of smokers."¹² This hyperexcitable state is believed to contribute to the smoker's motivation to smoke another cigarette (craving).^{9,12}

Hyperexcitability may also explain why the first cigarette smoked following a period of abstinence provides a more intense pleasure response for the smoker.^{11,12} Note, for example, that most smokers derive the greatest pleasure from their first cigarette of the day.^{10,12} **In fact, smoking a single cigarette following a cessation attempt often prompts a complete relapse to heavy smoking.**^{10,11}

The $\alpha_4\beta_2$ receptor

Recent evidence suggests that scientists have identified a specific nAChR in the brain that is believed to act as a primary mediator of the addictive properties of nicotine—the $\alpha_4\beta_2$ receptor.¹⁵⁻¹⁷ The isolation and characterization of this receptor is a significant advancement in the understanding of the neurobiology of smoking addiction.



Conclusion

Smoking is a chronic, relapsing condition. For most smokers, the compounding effects of behavioral, psychological, and physical triggers make overcoming their addiction extremely difficult. However, given the high morbidity and mortality related to smoking,^{3,8} getting smokers to quit is important. Proactive medical intervention for smokers may be beneficial.¹ Recent advancements in the study of nAChRs—specifically the identification and characterization of the $\alpha_4\beta_2$ receptor—represent a significant advancement in the understanding of the nature of nicotine addiction.

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Pulmonary Perspectives

The World Health Organization Framework Convention on Tobacco Control: Where Are We Now?

In this one bowl, there is rice from a thousand households." The saying of Zen poet Ryokan (1758–1831) well describes the contribution of many parties toward the Framework Convention on Tobacco Control (FCTC): the World Health Organization (WHO), other United Nations agencies, member states, nongovernmental organizations (NGOs), academia, the media, and even the tobacco industry.

The FCTC came into effect on February 27, 2005. It was signed by 168 countries and has now been ratified by 116. This makes it one of the fastest track international treaties of all time, enjoying widespread support around the world. This new treaty is the first international legal instrument designed to promote national action to reduce the growth and spread of the global tobacco epidemic. It will place countries under international legal obligation to curb tobacco use by implementing tobacco control laws, taxation policies, and programs. The treaty provisions are outlined in the table below.

There is no disagreement on the health evidence that led to the treaty. The main concern of countries has been economic—whether or not the FCTC would have an effect on their tobacco farmers and other tobacco workers and tax revenues. Reassuringly, analysis of economics and trade by the World Bank, the Food and Agriculture Organization of the United Nations,

and other health economists concludes that neither the FCTC nor any tobacco control measures will harm economies, even those of major tobacco-growing countries, such as China or Brazil. With the number of smokers predicted to rise from the current 1.3 billion to 1.6 billion by 2020 (principally due to increases in global population), no tobacco farmers will be out of work for decades to come.

Economists have pointed out that many tobacco control measures cost nothing. For example, these include legislation requiring warnings labels on cigarette packets, the creation of smoke-free areas, or simple advice on quitting from a health professional.

Other actions may have some cost, but are cost-effective, such as bans on advertising and promotion and the provision of quitting services, including nicotine replacement treatment. Price measures, such as increased tobacco tax and a crackdown on smuggling, will actually increase government tax revenue, while reducing the numbers of young smokers and encouraging adults to quit.

The FCTC is, as its name suggests, an initial framework. Over time, countries will negotiate and conclude more specific protocol agreements designed to implement the goals of the framework convention. The late Paul Szasz, a United Nations expert on international law, said, "Expect a convention to please no one, but hope it will be acceptable to everyone," and that is what we got. The lengthy process and the interminable discussions at many meetings were often wearisome but had the advantage of gradually emerging with a consensus and buy-in from the key players, especially the member states.

Even before it was adopted by the World Health Assembly in May 2003, the process itself had mobilized technical and financial resources for tobacco control, encouraged governments to take action ahead of the finalization of the

convention, and raised awareness among other government ministries.

Because the convention is ratified by national governments, an important result of the FCTC is that it has "kicked tobacco upstairs" in governments, requiring an ongoing commitment from all government departments, not just ministries of health, but also those of economics and trade, development and planning, foreign affairs, law, and customs. This widespread involvement was evident even in the negotiating process.

China's team, for example, included members from a wide range of government departments. Similarly, the convention expanded responsibility for tobacco issues from WHO to other United Nations agencies, some of which had hitherto been minimally involved with tobacco.

The FCTC has had a major impact on NGOs, as well. Prior to 1993, there were only a handful of international and regional NGOs devoted solely to tobacco issues, and most of them functioned independently of one another. The FCTC changed this isolation, giving birth to alliances and coalitions throughout the NGO community. NGOs attended all the working group and intergovernmental negotiating body meetings, some as members of government delegations. They were highly creative in their lobbying, supported or criticized governments with daily "orchid" or "dirty ashtray" awards to the best or worst performance of the day, and ran an effective media campaign. The Death Clock (see photo), run by the NGOs, was one example of their constant efforts. The published comments on the Chair's text were used extensively by delegates. NGOs will be crucial in the implementation stage ahead.

Not surprisingly, the tobacco industry was not in favor of a strong, legally binding FCTC and, instead, sought to promote self-regulating marketing mechanisms and voluntary agreements. The industry complained it was not invited to be an integral part of the negotiations, but there have been many avenues for it to make its views known, *ie*, directly to governments, as members of delegations, at the public hearings on the FCTC in Geneva in October 2000, and through its public relations machinery.

The FCTC now makes it more difficult for the tobacco industry and its allies to try

to derail national tobacco control legislation, as the convention indicates that the tide of tobacco control action is international, unstoppable, and a necessary public health measure, good for the wealth and health of nations.

There are lengthy procedures ahead, involving further ratifications by remaining countries, establishment of a Conference of the Parties, development of protocols, and creation of a reporting mechanism.

The first session of the Conference of the Parties to the FCTC took place from February 6–17, 2006, in Geneva, between ratifying states. Other states, for example those who had signed but not ratified the FCTC (such as the United States), participated as observers. NGOs in official relations with WHO and international intergovernmental organizations also participated as observers.

During this first session of the Conference of the Parties, parties decisions were taken in technical, procedural, and financial matters relating to the implementation of the treaty, such as the establishment of the permanent secretariat, funding and financial support, monitoring and reporting on implementation progress, and protocols.

Ongoing information on the process can be found at the following sites: WHO, www.who.int/tobacco/framework/en; and the Framework Convention Alliance, fctc.org. ■

Professor Judith L. Mackay
Director, Asian Consultancy on
Tobacco Control
Hong Kong SAR, China

At-a-Glance: FCTC Main Provisions

Regulation of:

- ▶ Contents, packaging, and labeling of tobacco products
- ▶ Prohibition of sales to and by minors
- ▶ Illicit trade in tobacco products
- ▶ Smoking in work and public places

Reduction in consumer demand by:

- ▶ Price and tax measures
- ▶ Comprehensive ban on tobacco advertising, promotion, and sponsorship
- ▶ Education, training, raising public awareness, and assistance with quitting
- ▶ Protection of the environment and the health of tobacco workers
- ▶ Support for economically viable alternative activities
- ▶ Research, surveillance, and exchange of information
- ▶ Support for legislative action to deal with liability



The Death Clock was run by the nongovernmental organizations during the negotiations for the FCTC.

COURTESY JUDITH L. MACKAY

Dr. Deborah Shure, Master FCCP
Editor, *Pulmonary Perspectives*

Dr. Aymar Robles, FCCP
Deputy Editor, *Pulmonary Perspectives*

Editor's Insight

Dr. Mackay provides an important and timely update on the status of the FCTC. The convention is the result of untiring work and perseverance by many, including Dr. Mackay. Since the ACCP and The CHEST Foundation have played a major role in tobacco control in the United States and have a strong international interest in tobacco control, this reminder of the status of the FCTC is particularly relevant. That the US government has not ratified the convention is a sign of the power and ongoing influence of the tobacco industry and a strong reminder of our need for continued work in this area. The fight is not over. The FCTC is, however, an extraordinary measure in the ongoing fight.

—Editor

NEWS FROM THE COLLEGE



PRESIDENT'S REPORT

Meeting Practice Management Challenges Together

I have just returned from the clinic after seeing an urgent add-on patient who needed to be seen before planned surgery.

He has esophageal cancer and had been enrolled in a clinical trial of neoadjuvant chemotherapy and radiation therapy prior to resectional surgery. Unfortunately, a repeat CT scan of the chest, done before surgery, revealed a number of centimeter-sized pulmonary nodules that was not visible on the previous scan, some 6 weeks earlier. I relate this story, because it explains why I missed the scheduled 2:30 pm Practice Management Committee conference call.

Although I am not as successful as I would like to be (have to keep my day



BY DR. W. MICHAEL ALBERTS, FCCP

job), I try to attend as many of the administrative committee and NetWork steering committee conference calls as possible. I receive the minutes of committee, task force, and NetWork calls and meetings, but there is nothing like actually participating to stay on top of things. It is tough to do, as the ACCP

currently has 16 administrative committees and 26 NetWork steering committees, along with a number of *ad hoc* task forces and working groups. I am continually amazed (and very pleased) at the amount of time and effort our members are willing to devote to College activities and initiatives.

Let me take the opportunity to mention one of our committees, the

Practice Management Committee (PMC). As I mentioned in my inaugural address, these are not easy times to practice medicine, particularly chest medicine. One must simultaneously deliver state-of-the-art care, stay up-to-date on new developments, and try to run a business. Today's medical practice is very much a business, and most of our members have not received formal business training. The PMC is working to make sure that the College becomes an increasingly important resource to members as they seek information, training, and assistance in managing their practice. Each PMC conference call addresses relevant items, such as proposed current procedural terminology (CPT) changes and the Relative Value Update Committee (RUC) deliberations. A particularly impressive outcome of the committee's work is the 2006 version of the *Appropriate Coding for Critical Care*

Services and Pulmonary Medicine book, edited by Dr. Scott Manaker, FCCP. Also, Web-based practice management education, a 14-volume CD-ROM series, entitled *Solutions in Practice Management*, is available now.

I hesitate to single out the PMC in this report, as very important and impressive work comes from the Continuing Education Committee, the Health and Science Policy Committee, the Government Relations Committee, among many others. Equally notable is the quality of work coming from the NetWork steering committees.

The greatest strength of the College is, and always has been, its members. The successes of the past could not have been possible, and the promise of the future could not become reality, without dedicated members willing to contribute their time and expertise. ■

ACCP NetWorks: Planned Surveys, Roundtables Keep Groups Busy

Pulmonary Vascular Disease

Interest in pulmonary vascular disease continues to grow among members of the ACCP. This was clearly reflected by the record attendance at the NetWork Open Meeting at CHEST 2005.

We invite you to www.chestnet.org/networks/pvd/index.php, our NetWork Web page that features a curriculum with links to selected abstracts. We continue to update the curriculum and add new material.

The NetWork will conduct a survey to assess the training provided in pulmonary vascular disease during fellowships in pulmonary and critical care medicine. The findings of this survey will enable us to identify and address specific levels of need within the field of pulmonary vascular disease.

We continue to explore ways to facilitate communication and discussion among NetWork members through clinical roundtable discussions and other means. To contact us regarding new projects, e-mail the NetWork chair at Namita.Sood@osumc.edu.

Respiratory Care

The Respiratory Care NetWork serves to connect the ACCP with other professional organizations that focus on respiratory care. These include the National Board for Respiratory Care (NBRC), the Committee on Accreditation of Respiratory Care (CoARC), the AARC Board of Medical Advisors (BOMA), and NAM-DRC. The liaisons, as well as leaders from these organizations, meet with the Respiratory Care NetWork Steering Committee at the annual CHEST meeting. Each reports on the current activities of that organization.

An important group that is missing

from this list of liaisons comprise the physicians who are the Medical Directors of the nearly 400 respiratory care training programs throughout the country. A forum is needed for these Medical Directors to share their ideas, successes, and failures.

We hope to meet this need by inviting Medical Directors, who also are ACCP members, to participate in roundtable discussions during CHEST 2006. If you are a Medical Director of a respiratory care training program, please submit your name, e-mail address, and other contact information to Lee Ann Fulton at lfulton@chestnet.org to receive additional information.

Sleep Medicine

More than 50 members of the Sleep Medicine NetWork participated in the NetWork's open meeting at CHEST 2005 in Montréal. A presentation by Dr. Bela Patel on "The Nose and Sleep-Disordered Breathing" was followed by discussions on the activities of the NetWork during the past year, which included an educational slide set project; an update on certifications by the American Board of Sleep Medicine (ABSM) and the American Board of Medical Specialties (ABMS); the change in fellowship accreditation from the American Academy of Sleep Medicine (AASM) to the Accreditation Council for Graduate Medical Education (ACGME); a report on the activities of the Board of Registered Polysomnographic Technologists; and an update on joint activities between the Sleep Medicine NetWork and the ACCP Sleep Institute, Academy of Sleep Medicine, American Thoracic Society, American Sleep Apnea Association,

and American Society of Anesthesiologists. For more information on the Sleep Medicine NetWork, visit www.chestnet.org/networks/sleep/.

Thoracic Oncology

The Thoracic Oncology NetWork has sent a survey to ACCP member pulmonologists and thoracic surgeons in the United States. This survey is a Time II assessment of lung cancer diagnosis and treatment practices and beliefs. The original survey results were summarized in an article in *CHEST* (Schroen et al. *Chest* 2000; 118:129), before the publication and dissemination of the *Diagnosis and Management of Lung Cancer: ACCP Evidence-Based Guidelines* in January 2003. Pulmonologists and thoracic surgeons are the primary point of care for patients with lung cancer. They have significant influence over the subsequent care patients receive and the patient's attitude toward his or her disease. In addition to assessing changes in attitude since the previous survey, this project seeks to gauge current beliefs regarding the treatment of non-small cell lung cancer in the United States. Dr. Frank Detterbeck, FCCP, chairs this NetWork project. For further information or to learn about other projects of this NetWork, contact Dr. Sandra Zelman Lewis, staff liaison, at slewis@chestnet.org.

**Transplant**

The Transplant NetWork continues to be busy, with excellent sessions planned for CHEST 2006, including collaborations with several other NetWorks. In this spirit of collaboration, several members of the Transplant NetWork are serving along with members of the Interstitial and Diffuse Lung Disease NetWork, on the Health and Science Policy Committee's review panel for the evidence-based guideline, "Monitoring of Immunomodulatory Drugs in Patients With Diffuse Lung Disease and/or Transplant."

Members of our NetWork serve on the review committee for The American Society of Transplantation (AST)/CHEST Foundation Clinical Research Award in Lung Transplantation. This 1-year award in lung transplantation will fund research that provides improvements and/or new information on the care and treatment of lung transplant patients. The application deadline is April 28, 2006. Information is available at www.chestfoundation.org/researchAwards/index.php.

Our Web page, www.chestnet.org/networks/transplant/index.php, features a patient guide to lung transplantation and links to online transplant resources.

We are working on a guide for community physicians on management of lung transplant recipients that will be available online. ■

INSIDE THE ACCP
The CHEST Foundation: Helping Your Patients Live and Breathe Easier

For over 10 years, The Foundation has provided funding to reach thousands of patients and communities.

BY MARILYN LEDERER

Vice President and COO,
The CHEST Foundation

Ten years ago, a committed group of ACCP members, led by ACCP Past President Dr. Bart Chernow, Master FCCP, had a vision to create a philanthropic arm of the College to address the needs of patients and their communities in the area of cardiopulmonary and critical care medicine. In 1996, The CHEST Foundation was created as ACCP's supporting foundation. For the past decade, with the assistance of ACCP members, donors, staff, and strategic partners, The Foundation has made a significant impact in improving patient care and lung health for the College's global membership.

Unlike other foundations that focus on specific diseases or public health issues, The CHEST Foundation solely exists to support the College and its members. Its mission and programs derive from the expressed needs of ACCP members who serve on The Foundation's Board of Trustees and working committees. The Foundation concentrates its efforts in four key areas—critical care, tobacco prevention, humanitarian services, and clinical research—to develop programs and resources that help you promote better health for your patients and their families. Over the past 10 years, The Foundation has provided funding to reach thousands of patients and communities.

What kind of resources is The Foundation providing for ACCP members?

▶ The Critical Care Family Assistance

Program (CCFAP) is designed and implemented in nine hospitals across the United States and is changing the way care is delivered to ICU patients and their families. With the CCFAP toolkit, promotional video, and the September 2005 supplement to *CHEST*, any ACCP member can

replicate this important program in his or her hospital.

▶ Lung Lessons™ and the Speakers Kit on Women & Girls, Tobacco, & Lung Cancer reflect The Foundation's knowledge that

smoking kills and its commitment to tobacco prevention for children and adults. With these ready-to-use resources, any ACCP member can use the materials for grand rounds or to make a presentation in a child's classroom.

▶ The Humanitarian Awards Program annually provides grants to organizations in which ACCP members volunteer their time and expertise to provide care to those who otherwise could not afford their services. Over the past 6 years, The Foundation conferred almost \$600,000 in grants to organizations around the world.

▶ Beyond the First Response provides disaster relief in times of manmade and natural disaster. In the past year, with support from ACCP members and staff, The Foundation has provided assistance in the aftermath of the Asian tsunami and Hurricanes Katrina and Rita on the Gulf Coast of the United States.

▶ The CHEST Foundation has provided over \$3 million in clinical research awards since 1997 and annually grants almost \$500,000 in awards to ACCP members to promote turning research into practice.

To ensure that its valuable programs are implemented, The CHEST Foundation works through the College's NetWorks and committees. In addition, for the past 5 years, the Ambassadors Group, made up of ACCP members' spouses and family mem-

bers, has been educating, networking, and volunteering on behalf of The CHEST Foundation. The Ambassadors Group has completed projects, such as *Stories at the End of Life* and the Love Your Lungs™ wristbands, and uses The CHEST Foundation tobacco prevention materials to make presentations to elementary and high school students around the world.

This year commemorates The CHEST Foundation's 10th anniversary. The impact that its founders envisioned a decade ago has been realized. The Foundation's 10th anniversary theme is "Imagine the Power of 10." I hope that we can count on ACCP members to help The CHEST Foundation multiply its impact exponentially in the next 10 years.

For more information about The CHEST Foundation, or to make a charitable contribution, please go to www.chestfoundation.org. ■



2006 CHEST Foundation Awards Program

Each year, through its extensive awards program, The CHEST Foundation confers awards to ACCP members for 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.

Apply today!

Applications for all awards are being accepted now.
Access more details at www.chestfoundation.org.



The CHEST Foundation's 2006 Award Opportunities

The clock is ticking... apply now!

Clinical Research

▶ The CHEST Foundation Clinical Research Award in Women's Health
 DEADLINE: May 15, 2006

▶ The CHEST Foundation and the LUNgevity Foundation Clinical Research Award in Lung Cancer
 DEADLINE: April 28, 2006

▶ Alpha-1 Foundation/CHEST Foundation Clinical Research Award in Alpha-1 Antitrypsin (AAT) Deficiency
 DEADLINE: April 28, 2006

▶ The American Society of Transplantation (AST)/CHEST Foundation Clinical Research

Award in Lung Transplantation

DEADLINE: April 28, 2006

▶ Clinical Research Trainee Awards
 DEADLINE: May 1, 2006

Humanitarian Awards

▶ Humanitarian Recognition Awards
 DEADLINE: May 15, 2006

▶ Humanitarian Project Development Grants

In 2006, special Humanitarian Project Development Grants will be given to projects focused on recovery from Hurricanes Katrina, Wilma, and Rita in the United States Gulf Coast area. Please see the application form for more information.

DEADLINE: June 15, 2006

NEWS FROM THE COLLEGE



CRITICAL CARE COMMENTARY

Ultrasonography for the Pulmonary-Critical Care Physician

Ultrasonography has important applications in pulmonary and critical care medicine (PCCM). In the United States, ultrasonography is still considered to be the province of the radiologist, particularly by medical subspecialists, such as the PCCM clinician. This essay will present a basic overview of ultrasound concepts and discuss an alternative approach to ultrasonography—that the proper place of ultrasonography is at the bedside of the patient and in the hands of the PCCM clinician.

Bedside ultrasonography is a powerful clinical tool that has many different uses for the PCCM clinician.

The availability of high quality, portable ultrasonography machines now allows the PCCM clinician to use this method at the bedside for immediate diagnosis, to guide treatment, and to better perform a wide variety of invasive procedures. Using the ultrasonography transducer, the bedside clinician can obtain accurate two-dimensional images in order to assess the anatomy and function of many critical organ systems, while the use of Doppler assesses cardiovascular function. Thoracic ultrasonography includes the pleural space, the mediastinum, and the lung (Beckh et al. *Chest* 2002; 122:1759-1773). Pleural ultrasonography has importance for the diagnosis of pleural disease and for ultrasonography guidance of device insertion. Lung ultrasonography has exceptional utility in management of the critically ill (Lichtenstein. *General ultrasound in the critically ill*. Berlin: Springer-Verlag, 2005). For example, it allows immediate diagnosis of pneumothorax and is superior to standard supine chest radiography in assessing the critically ill patient with ARDS (Lichtenstein et al. *Anesthesiology* 2004; 100:9-15). Echocardiography has great utility in the management of patients with hemodynamic failure in the ICU. It can be used in a goal-directed manner (Manasia et al. *J Cardiothorac Vasc Anesth* 2005; 19:155-159). In its more complete form, it provides 2-D examination with Doppler analysis to yield assessment of hemodynamic function that is superior to standard hemodynamic monitoring. Abdominal ultrasonography has strong utility in the rapid assessment of patients with acute abdominal presentation and in the assessment of acute renal failure. Vascular ultrasonography is useful in guidance of vascular access; strong argument can be made that ultrasonography

should routinely be used for internal jugular venous access (Feller-Kopman. *Crit Care Med* 2005; 33:1875-1877).

Ultrasonography allows the safe guidance of device insertion. Paracentesis, pericardiocentesis, thoracentesis, transthoracic biopsy, mediastinal biopsy, and abscess drainage are readily performed with ultrasonography guidance. Other advantages include its safety, low cost, and reduction of the need to transport critically ill patients for imaging outside of the ICU. It provides immediate information

to the bedside clinician that complements, and may be superior to, other methods of imaging and hemodynamic

monitoring. It can be repeated as often as is needed. Ultrasonography may be viewed as similar to the physical examination: it is performed at a complexity and frequency that is determined by the needs of the patient. It is the dynamic utility of the technique that makes ultrasonography so useful to the PCCM clinician.

Adequate training is the key to safe application of bedside ultrasonography. How can the PCCM clinician obtain adequate training in this important discipline? The following is a summary of some principles in planning training strategy.

1. Ultrasonography is a valuable tool for all PCCM clinicians. PCCM clinicians are able to achieve a high level of competence with proper training in ultrasonography. However, there is no requirement that a PCCM clinician learn any particular aspect of ultrasonography. The clinician should only pursue training if he/she would find clinical utility in the skill.

2. The clinician should pursue a modular approach to training. The modules of ultrasonography that are relevant to PCCM practice include the following:

- ▶ Transthoracic and transesophageal echocardiography: the basic and advanced levels
- ▶ Abdominal ultrasonography: basic and advanced levels, including ultrasonography-assisted interventions
- ▶ Vascular ultrasonography: ultrasonography-assisted vascular access
- ▶ Vascular ultrasonography: ultrasonography examination for venous thrombosis
- ▶ Thoracic ultrasonography: ultrasonography examination of pleura, lung, and mediastinum, including ultrasonography-assisted interventions
- ▶ Endobronchial ultrasonography: advanced level

Clinicians should pursue the module of ultrasonography that is defined by their clinical needs. For example, the

clinician who is primarily interested in pulmonary medicine might choose ultrasonography skills related to thoracic ultrasonography. On the other hand, the full-time intensivist might be interested in additional modules of ultrasonography, such as abdominal, vascular, and echocardiography. The modular approach permits physicians to train in those aspects of ultrasonography that are important to their practice needs.

3. The concept of basic training and advanced training is valid. Obviously, some aspects of ultrasonography are not amenable to basic-level training in terms of image acquisition. Some modules do not require separation between basic and advanced training: pleural, thoracic, and vascular are sufficiently straightforward, so the distinction is not necessary. Echocardiography and abdominal ultrasonography are best divided into basic and advanced levels, due to the complexity of the field. Clinicians who choose to complete training to an advanced level must follow training strategies that are as demanding and complete, as followed by other expert-level ultrasonography practitioners. Accepting the concept of basic ultrasonography training will foster widespread application of ultrasonography in PCCM, particularly in the ICU environment. At the same time, the clinician who achieves basic-level competence must carefully recognize the limitations of their ultrasonography skills and seek confirmatory study when indicated.

4. The cognitive skills required to perform ultrasonography can be divided into three general areas. The clinician must develop the ability in image acquisition, image interpretation, and factual knowledge of the field. In general, the PCCM clinician will personally perform all aspects of the ultrasonography examination; image acquisition, image interpretation, and clinical application should be the responsibility of the physician in charge of the bedside management of the patient. This has special relevance to ultrasonography in ICU and ultrasonography-assisted procedures. In this situation, the clinician can combine the immediate information of ultrasonography with knowledge of the clinical situation to establish diagnosis and guide ongoing therapy. Implicit to the commitment to personally perform ultrasonography is that training includes heavy emphasis on the technique of image acquisition.

Training in image acquisition requires dedicated practice at the bedside and may require separate training with an experienced teacher.

This is especially important for complex applications of ultrasonography, such as advanced echocardiography. The most practical time to achieve training in these skills is during fellowship training. PCCM clinicians who are already at attending level may find it more difficult to train in ultrasonography, due to time constraints and interspecialty conflict. For PCCM clinicians, it is essential that they find a committed teaching mentor, as image acquisition and interpretation skills are best learned by close cooperation with an expert teacher.

Excellent courses are available, as well as audiovisual training material, but the clinician should not rely completely on these methods of instruction for complex areas of ultrasonography. It is important for the PCCM clinician to obtain his own ultrasonography machine. Mastery of any aspect of ultrasonography requires hands-on practice, and complete control of the ultrasonography machine allows the clinician to rapidly acquire hands-on scanning experience and easily transition

to clinical application of his or her skill. For the factual component of training, standard texts on echocardiography, critical care, thoracic ultrasonography, and other aspects of general ultrasonog-

raphy are available (Otto. *Practice of clinical echocardiography*. 2nd ed. Philadelphia, PA: WB Saunders Co, 2002; Lichtenstein et al, eds. *Atlas of chest sonography*. Berlin: Springer-Verlag, 2003; and Kopman-Feller et al, eds. *Ultrasound-guided procedures and investigations*. New York, NY: Marcel Dekker, 2005). PCCM journals have published comprehensive review articles on many aspects of ultrasonography (Beaulieu et al. *Chest* 2005; 128:881-895, 1766-1781).

The goal of training is competence. How to determine competence in ultrasonography remains controversial. Clearly, the first step in the process is to develop training guidelines. For this reason, the ACCP Critical Care NetWork has sponsored a working group on ultrasonography that is tasked with writing a comprehensive guide to training strategy for ultrasonography performed by the PCCM clinician. In the meantime, this essay serves to outline the justification for ultrasonography performed by the PCCM clinician, as well as reviews some general principles of training to guide the interested physician. ■

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Critical Care Institute
American College of Chest Physicians

ULTRASONOGRAPHY ALLOWS THE PCCM CLINICIAN TO USE THIS METHOD AT THE BEDSIDE FOR IMMEDIATE DIAGNOSIS AND TO GUIDE TREATMENT.

EDUCATION INSIGHTS

How Important Is Continuing Medical Education?

A successful CME educational activity will no longer be defined in terms of participants' satisfaction.

BY ED DELLERT, RN, MBA
Vice President, Educational Resources,
American College of Chest Physicians

How important is CME to physicians? Does CME really support professional development? Can CME be linked to improved patient outcomes? Continuing medical education (CME), by definition, consists of educational activities that serve to maintain, develop, and increase a physician's knowledge throughout his or her entire career.

The American Medical Association (AMA) defines the content of CME as being the body of knowledge and skills generally recognized and accepted by the profession as within the basic medical sciences, the discipline of clinical medicine, and the provision of health

care to the public. The real question becomes, "Does our current CME structure really make a difference?" Could a new and more qualified CME system affect the driving change correlated with improved outcomes?

To address the use of structured time for education, some CME providers have proposed and implemented self-directed learning tools to develop educational programs into learning portfolios, designed to capture learning whenever and wherever it can occur. Learning portfolios can document, describe, and assess learning events, such as answering important clinical questions in order to maintain competence. Strategies such as these are, in part, due to address the seven recommendations to improve physician "life-long learning," as suggested by the Council of

Medical Specialty Societies (CMSS) (www.cmss.org/index.cfm?p=display&detail=Conjoint%20Committee%20on%20CME).

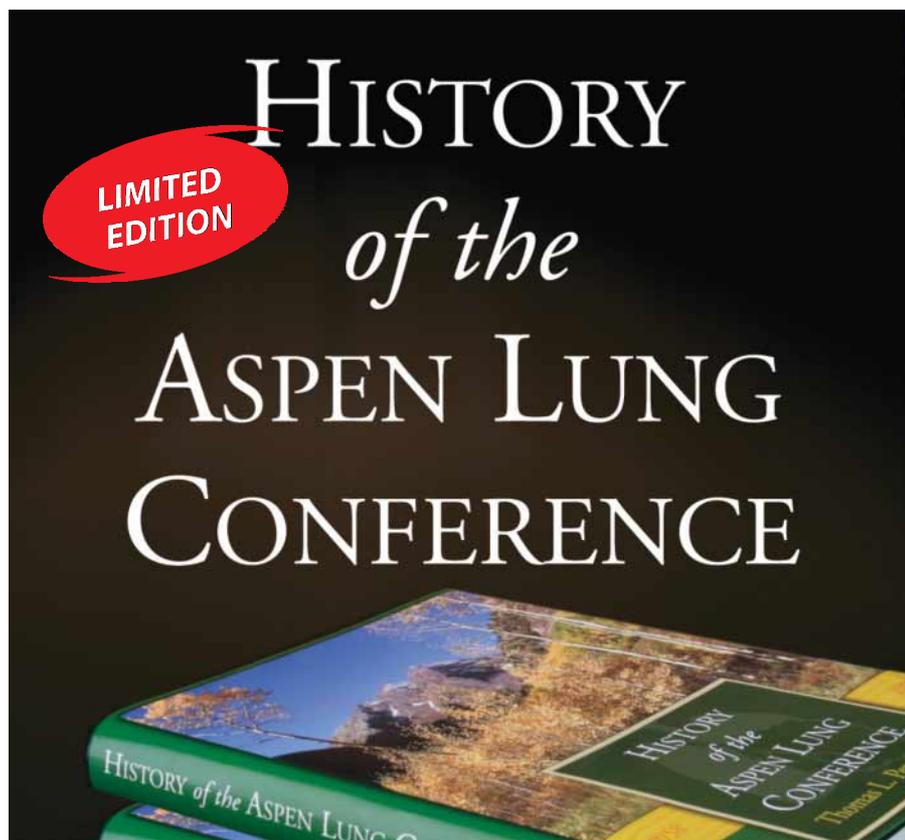
The ACCP Continuing Education Committee (CEC) has had many discussions using the seven recommendations outlined by the CMSS as a benchmark to what ACCP's educational future would look like.

The foundation of ACCP's educational future, however, has indirectly been aligning itself with various adult-learning theories, specifically with that of David Kolb, PhD (www.infed.org/biblio/b-explrn.htm). His work in the early 1970s at Harvard University indicated that adult learners base their learning styles upon the way they perceive and then process an experience. The term "experiential learning" was really created under Dr. Kolb, whereby he highlighted two dimensions that he felt are critical for learning to occur. The first dimension is described as perceiving information, and the second, processing the information. In essence, he created four quadrants, whereby the ideal learning environment takes the learner from one quadrant to another.

The variation in learning styles from one quadrant to the next, exemplifies the "experiential learning" concept.

The ACCP CEC recognizes that the environmental demands are advocating for a change in CME, and change will occur over the next few years. The question for the CEC is to determine what experiential learning concepts they will want to advocate to ACCP membership. Professional societies, such as the ACCP, need to seriously assess the strategies being used in their educational curricula and begin to assess the desired knowledge, skills, behaviors, and patient outcomes that measure attainment of these outcomes. A successful CME educational activity will no longer be defined in terms of participants' satisfaction but rather in terms of clinical performance improvement, improved patient satisfaction, and other desirable implications from these types of educational efforts. The ultimate question is, "Will you be ready to embrace this type of change in CME?"

What is your vision of tomorrow's CME? Let me know via e-mail at edellert@chestnet.org. ■



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Review: History of the Aspen Lung Conference

A SPECIAL NOTE BY
DR. EDWARD C. ROSENOW III,
MASTER FCCP

For those of us who know Dr. Tom Petty, Master FCCP, you know that Tom has many passions for disorders of the lung, particularly regarding education and research.

One of these passions has culminated in **History of the Aspen Lung Conference**, which documents nearly 50 years of the annual Aspen Lung Conference.

Each year, the world's authorities, the giants in pulmonary research and medicine, gather to present and discuss, in a friendly social atmosphere, what is new in a specific area of lung disease, designated the topic for that particular annual session.

The meetings have been held every late spring in Aspen, Colorado, beginning in 1958.

Initially, most of the topics were related to emphysema, but, over the years, topics have included asthma, pulmonary circulation, ARDS (Tom is one of the co-describers of ARDS), pulmonary fibrosis, and lung cancer.

Physiology, molecular biology, immunology, genetics, and other

parameters of research have all played a major part of the content of each conference.

Since the 13th meeting, all the scientific material has been published yearly as a supplement to *CHEST*.

Each annual session is summarized by the leading authority attending the meeting.

Dr. Petty has published the summary of each conference as the basis of recording the **History of the Aspen Lung Conference**.

Since 1990, the conference is now called the Thomas L. Petty Aspen Lung Conference.

This limited edition, beautifully published (only 500 published) 321-page book is one of the best summaries of pulmonary disorders over the last 48 years.

It should be in every academic pulmonary library for its historic benefits, as well serving as a guideline on how to run a unique annual conference.

It can be purchased for \$199 with the proceeds going to the Aspen Lung Conference Endowment (not-for-profit) by calling (303) 996-0868, or write Snowdrift Pulmonary Conference, Inc., 899 Logan Street, Suite 103, Denver, CO, 80203. ■

NEWS FROM THE COLLEGE



Position Statement: Medical Director of Sleep Disorders Center

Definition:

The Medical Director of a sleep center or laboratory shall be a licensed physician who has special interest and knowledge in the diagnosis and treatment of sleep disorders. The Medical Director should be qualified by training and/or experience in the management of sleep disorders and possess an in-depth knowledge of diagnostic equipment, procedures, and techniques. This physician should be responsible for the quality, safety, and appropriateness of the sleep center and/or laboratory services provided and require that these services be ordered by a physician who has medical responsibility for the patient.

Duties:

1. The Medical Director is responsible for the delivery of sleep center and/or laboratory services and is accountable to the medical staff for the quality of patient services delivered by the sleep center staff and all other health professionals providing such care and/or diagnostic testing. As a result, sleep technologists should work under the direction of a qualified Medical Director at all times in order to assure their competency and to maximize their capabilities as described in their scope of practice.
2. The Medical Director provides 24-hour availability, including, where necessary, an appropriately qualified designee(s) to share these responsibilities or assume them in the Director's absence.
3. The Medical Director is readily

available and interacts regularly with sleep laboratory personnel, promoting bedside and laboratory problem-solving and guidance.

4. The Medical Director positions the sleep center and/or laboratory to be successful in the changing health-care environment by championing cost-effective policies and procedures, while assuring optimal delivery of sleep diagnostic and therapeutic services in a continuum, inside and

outside of the hospital. The Medical Director has a special responsibility for developing and managing patient care protocols that guide and permit independent decision-making by sleep technologists, such as protocols for clinical assessment and treatment of patients.

5. The Medical Director participates in the quality improvement program of the sleep center/laboratory and the hospital, assuring proper allocation of sleep disorder therapies and diagnostic services through appropriate audit techniques.
6. The Medical Director participates in the development, evaluation, and introduction of new sleep medicine services, equipment, and procedures and also monitors current sleep medicine services for their continued medical usefulness.

7. The Medical Director facilitates continuing education in the diagnosis and treatment of sleep disorders for physicians, sleep technologists, sleep

technology students, registered nurses, respiratory therapists, administrators, patients, and the community.

8. The Medical Director coordinates and facilitates professional relationships between the sleep center/laboratory and hospital administration, the medical staff, nursing, respiratory care, pharmacy, emergency care unit, critical care units, post-anesthesia recovery rooms, home health agencies, and other departments and agencies that utilize sleep medicine services.

9. The Medical Director audits physician performance in prescribing sleep disorder therapies in conjunction with the appropriate governing body of the medical staff.

10. The Medical Director provides consultation to physicians with respect to availability and appropriateness of requested sleep diagnostic and therapeutic services.

11. The Medical Director shares responsibility with and provides medical expertise to the administrative/technical director of the sleep center/laboratory in matters regarding: equipment, space, personnel, discharge planning, safety, policies and procedures, supplies, patient care protocols, budget, case management, record keeping, preventive maintenance, infection control, fiscal and regulatory agencies.

12. The Medical Director, as the agent of the medical staff, is responsible for seeing that the sleep medicine services are in compliance with federal and state laws and regulations, as well as the requirements of the Joint Commission on Accreditation of Healthcare

Organizations (JCAHO) and the American Academy of Sleep Medicine (AASM).

13. The Medical Director assures the quality and safety of the sleep studies, including:

- a. Ensuring the quality of the testing performed in the sleep laboratory.

- b. Deciding what types of testing will be performed in the laboratory and what equipment will be used.

- c. Selecting the normal reference values appropriate for the patient population studied in the laboratory.

- d. Being responsible for the quality of review and interpretation of test results.

- e. Deciding the training and/or credential requirements and evaluating the performance of the technical personnel of the laboratory.

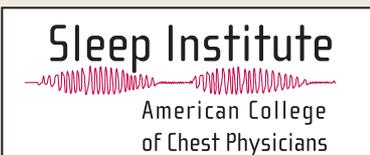
- f. Minimizing any risks to and managing any complications in the patients tested in the laboratory and ensuring the safe performance of sleep diagnostic testing and administration of therapies.

- g. Developing written protocols for all testing procedures.

- h. Being a consultant to other physicians to offer advice on appropriate tests to order in a given clinical situation and appropriate use of the laboratory facilities.

- i. Developing and implementing procedures to prevent the transmission of infection by the laboratory equipment and personnel and to prevent other hazards to patients and staff. ■

Adapted from ACCP Position Statement: "Medical Director of Respiratory Care Department and Pulmonary Function Laboratory: Definition and Duties," revised 2005; www.chestnet.org/institutes/si/index.php.



This Month in CHEST: Editor's Picks

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

► **A Randomized Trial of Different Docetaxel Schedules in Non-small Cell Lung Cancer Patients Who Failed Previous Platinum-Based Chemotherapy**

Dr. Yuh-Min Chen, FCCP, et al

► **High Levels of Medical Utilization by Ambulatory Patients With Vocal Cord Dysfunction as Compared to Age- and Gender-Matched Asthmatics**

Dr. Jeffrey Mikita and Dr. Joseph Parker, FCCP

► **"Tobacco Free With FDNY": The New York**

City Fire Department World Trade Center Tobacco Cessation Study

Dr. Matthew P. Bars, et al

► **Management of Unsuccessful Thrombolysis in Acute Massive Pulmonary Embolism**

Dr. Nicolas Meneveau, et al

► **A Randomized Controlled Trial**

on Office Spirometry in Asthma and COPD in Standard General Practice: Data From Spirometry in Asthma and COPD: a Comparative Evaluation Italian Study

Dr. Mirco Lusuardi, et al

► **The BODE Index After Lung Volume Reduction Surgery Correlates With Survival**

Dr. Stephan Imfeld, et al

► **Applied Medical Informatics for the Chest Physician: Information You Can USE! – Part 3**

Dr. William F. Bria II, FCCP

► **The Uniform Requirements for Manuscripts Submitted to Biomedical Journals Recommended by the International Committee of Medical Journal Editors**

J. Patrick Barron

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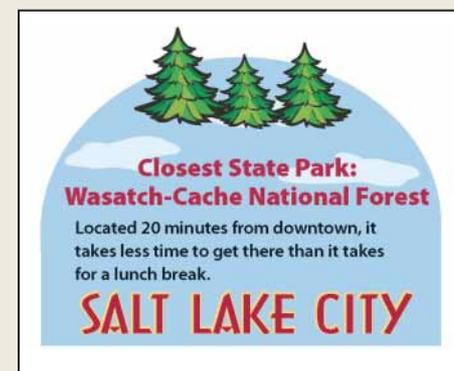
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Treatable Coexisting Rhinitis Is Common in Sleep Apnea

Intranasal corticosteroid use may result in marked improvement in sleep-disordered breathing.

BY BRUCE JANCIN
Elsevier Global Medical News

KEYSTONE, COLO. — All patients with obstructive sleep apnea should be evaluated and treated for rhinitis, an extremely common coexisting condition, Dr. Robert Ballard said at a meeting sponsored by the National Jewish Medical and Research Center.

Several recent studies indicate that intranasal corticosteroids, perhaps in combination with an oral leukotriene modifier, result in marked improvement in sleep-disordered breathing in children. Indeed, in many cases the youths are essentially cured of their sleep apnea. Adults seem less responsive but do experience worthwhile partial improvement, according to Dr. Ballard, director of the sleep disorders program at the Denver center.

Epidemiologic studies indicate the vast majority of patients with obstructive sleep apnea (OSA) have symptoms characteristic of rhinitis: nasal dryness, congestion, postnasal drip, runny nose. That has been Dr. Ballard's clinical experience as well.

As a result, nearly all National Jewish Medical and Research Center patients on nasal continuous positive airway pressure (CPAP) therapy for OSA are on intranasal steroids. It lessens OSA severity, renders the CPAP more tolerable, and improves compliance.

The therapeutic rationale for identifying and treating rhinitis in patients with OSA lies in the notion that the nasal disorder may contribute to the pathophysiology of the sleep disorder. The idea here is that the nasopharynx functions as a Starling resistor. Increased nasal airflow resistance due to rhinitis leads to exaggerated intrapharyngeal pressure during inspiration, which may in turn result in oropharyngeal collapse, much like when one sucks too hard on a straw, Dr. Ballard explained.

There are a couple of published studies demonstrating marked benefit from intranasal steroids in children with OSA, one of which was placebo controlled.

Even more recently, investigators at the University of Louisville (Ky.) reported on 22 children aged 2-10 years with residual mild sleep-disordered breathing at overnight

polysomnography 10-14 weeks following tonsillectomy and adenoidectomy performed as treatment for their OSA. The children were placed on the oral leukotriene modifier montelukast plus intranasal budesonide for 12 weeks, at which point they underwent overnight polysomnography again. Fourteen other children with residual sleep-disordered breathing after tonsillectomy and adenoidectomy whose physicians elected not to resort to medication served as controls.

The mean baseline postsurgical apnea-hypopnea index (AHI) in children in the montelukast/budesonide group was 3.9 events per hour. Although that wouldn't even qualify as mild OSA in adults, in children it does, Dr. Ballard explained.

After 12 weeks of montelukast and intranasal budesonide, their AHI had dropped to 0.3 per hour, considered normal. In contrast, there was no significant

change in AHI among controls. Moreover, the treatment group's nadir arterial oxygen saturation climbed from a mean of 87.3% to 92.5%, a significant improvement, with again no change in the control group (Pediatrics 2006;117:e61-6).

Dr. Ballard noted that a recent study by investigators at University College Dublin demonstrated significant albeit less robust improvement with intranasal steroid therapy in adults with OSA and coexisting rhinitis than in the pediatric studies, which is consistent with his clinical experience.

Thirteen adults with OSA and rhinitis were randomized to 4 weeks of twice-daily intranasal fluticasone or placebo, then crossed over to the other study arm. Their mean AHI was 23.3 per hour after fluticasone, classified as moderate OSA, and 30.3 after placebo, which falls into the low end of the severe category (Thorax 2004;59:50-5).

Risk of Sleep Apnea Is High In Polycystic Ovary Syndrome

BY ROBERT FINN
Elsevier Global Medical News

SAN FRANCISCO — A high risk for sleep apnea was common in women with polycystic ovary syndrome and was linked to high fasting insulin levels, Dr. Esra Tasali reported at a conference sponsored by the American Diabetes Association.

Among the women with normal glucose tolerance, insulin levels in response to oral glucose were twice as high in women at high risk for sleep apnea, compared with those at low risk. This finding suggests that sleep apnea might worsen the metabolic consequences of insulin resistance, accelerating the conversion from normal to impaired glucose tolerance, Dr. Tasali said.

Although the study does not establish causation, Dr. Tasali recommended that women with polycystic ovary syndrome (PCOS) be systematically evaluated for sleep apnea, as its treatment might improve glucose metabolism.

A high risk for sleep apnea was observed in 30 of 40 women with PCOS, and 92% of the women had sleep problems, according to Dr. Tasali and her colleagues at the University of Chicago (J. Clin. Endocrinol. Metab. 2006;91:36-42).

Of the 40 women, 32 had previously been given an oral glucose tolerance test. Glucose tolerance was normal in 19 women. In 22 women at high sleep apnea risk, average fasting insulin levels were significantly higher (168 pmol/L) than they were in the 10 women at low apnea risk (97 pmol/L). Among the 13 women with impaired glucose tolerance, glucose and insulin levels did not differ depending on the level of apnea risk.

A cohort of eight women with PCOS underwent overnight polysomnography

for symptoms suggestive of obstructive sleep apnea. Mean sleep efficiency was 80% in the women with PCOS, compared with 92% in a control group of age-matched, nonobese women. The women with PCOS also had significantly longer mean sleep latency (41 minutes vs. 10 minutes), and significantly shorter total sleep time (323 minutes vs. 442 minutes, a difference of almost 2 hours).

"Sleep apnea might be an intrinsic component of the metabolic disturbances that appear with polycystic ovary syndrome," Dr. Tasali said.

Furthermore, severity of sleep apnea as measured by the apnea-hypopnea index, and the degree of oxygen desaturations during rapid-eye-movement sleep, accounted for more than 90% of the variability in measures of glucose tolerance including hemoglobin A_{1c} levels.

Together, these findings could mean that both glucose tolerance and sleep apnea are strongly influenced by a common mechanism in women with PCOS.

Dr. Tasali disclosed that she had no conflict of interest related to her presentation.



Insulin levels in response to oral glucose were twice as high in women at high risk for sleep apnea.
DR. TASALI

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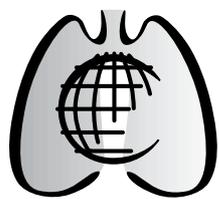
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AMA-Congress Pact Pushes Pay for Performance Ahead

BY JENNIFER LUBELL
Elsevier Global Medical News

Specialty organizations are concerned that the American Medical Association is unilaterally setting performance goals that doctors won't be able to meet.

A recent agreement between the AMA and leaders in Congress outlines an ambitious 2-year time line for establishing performance measures, "to improve voluntary quality reporting to congressional leadership," AMA Chair Duane M. Cady said in a statement.

Dr. Cady signed the pact at the end of last year, although the details weren't publicly disclosed until several months later. The terms were outlined in a Feb. 7 memorandum from AMA Vice President Michael Maves to the state medical associations and national specialty societies.

The agreement was cosigned by Sen. Charles E. Grassley (R-Iowa), chair of the Senate Finance Committee; Rep. Bill Thomas (R-Calif.), chair of the House Ways and Means Committee; and Rep. Nathan Deal (R-Ga.), chair of the House Energy and Commerce subcommittee on health.

The plan calls for physician groups to work with the Centers for Medicare and Medicaid Services (CMS) to agree on a starter set of evidence-based quality measures for a broad group of specialties, with a goal of developing approximately 140 physician measures covering 34 clinical topics by the end of 2006.

A performance improvement consortium convened by the AMA that includes more than 70 national medical specialty and state medical societies has been working with

several groups to test the physician measures. The groups include the Ambulatory Care Quality Alliance, said Dr. Nancy Nielsen, speaker of the AMA's House of Delegates, at a press briefing. The alliance is receiving funding from the Agency for Health Research and Quality and CMS to test 26 measures at six clinical sites, beginning May 1. Those measures include some developed by the consortium, among others. The pilot is crucial, Dr. Nielsen said.

In 2007, doctors who report on three to five quality measures would see increased payments from Medicare. By the end of next year, physician groups should have developed performance measures "to cover a majority of Medicare spending for physician services," the agreement said.

Other initiatives, such as working on methods to report quality data and implementing additional reforms to address payment and quality objectives, also were outlined in the agreement.

Nothing in the agreement with the congressional leaders should be a surprise, Dr. Cady said. "It involved only [those] commitments we had previously outlined to our specialty society colleagues."

Yet some members of the consortium said they had no advance notice of the AMA's plans to sign this pact. "Some groups feel they should have been a part of it," Cynthia A. Brown, director of advocacy and health policy at the American College of Surgeons, said in an interview. While many primary care quality measures have been written, it's a different story for subspecialties, she said.



Pilot testing the measures at six clinical sites is crucial, said Dr. Nancy Nielsen, speaker of the AMA's House of Delegates.

At the press briefing, Dr. Nielsen said the initial measures won't cover all the specialties, but it was necessary to show Congress that the profession was serious about quality improvement, she said.

There's an assumption that the AMA will be responsible for doing all the specialty measures, said Dr. David Nielsen, executive vice president and chief executive officer of the American Academy of Otolaryngology-Head and Neck Surgery. "While those concerns are valid, it isn't going to come to that." These groups need to remember that the AMA's consortium is run by the specialty societies, a process that's consensus based, he said.

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