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BRUCE JANCIN/ELSEVIER GLOBAL MEDICAL NEWS

"These new treatments will contribute to the life expectancy in cystic fibrosis," explained Dr. Paula J. Anderson, FCCP.

New Therapies Begin To Fill CF Pipeline

BY BRUCE JANCIN
Elsevier Global Medical News

SAN DIEGO — The drug development pipeline for cystic fibrosis is chock full of promising agents that address a wide range of key aspects of the disease.

A few of these products have already been approved in the European Union and Canada, and are now under review by the Food and Drug Administration. Others are in phase III trials, Dr. Paula J. Anderson, FCCP, said at the annual meeting of the American College of Chest Physicians.

"It's really a very exciting time to be a researcher in the area of cystic fibrosis. These new treatments will contribute to the life expectancy in cystic fibrosis and may have applications in other diseases, like non-CF bronchiectasis and perhaps other genetic diseases," noted Dr. Anderson, professor of medicine and director of the adult cystic fibrosis program at the University of Arkansas, Little Rock.

Here are some of the most promising of the emerging therapies:

► **Modifiers of the CF transmembrane conductance regulator (CFTR).** These agents constitute the most exciting advance in CF in 15 years, in Dr. Anderson's view, because they address the central underlying disease deficit. The CFTR is essentially a chloride channel sitting in the membrane of cells in the airway, gastrointestinal tract, and sweat glands. Defects in the CFTR result in distorted chloride and sodium flux, with resultant thick, viscous, dysfunctional secretions.

Ataluren (PTC Therapeutics Inc.) overcomes class I nonsense step mutations in the CFTR gene so the CFTR protein can be properly translated and delivered to the airway epithelium. Phase II studies showed that ataluren, which is an oral agent, resulted in improvement in sweat chloride and nasal potential difference. It is now in a

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FDA Takes Tougher Line on Labeling for LABAs in Asthma

Agency says earlier efforts not enough.

BY ELIZABETH MECHCATIE
Elsevier Global Medical News

The Food and Drug Administration is requiring major changes to the prescribing information of inhaled long-acting beta-agonists as part of a risk management plan to address the ongoing safety issues associated with the products' use in children and adults with asthma, the agency announced last month.

The long-acting beta-agonist (LABA) products approved in the United States are Serevent (salmeterol) and Foradil (formoterol), which contain the LABA alone, and Advair (salmeterol plus fluticasone) and Symbicort (formoterol plus budesonide), which contain the LABA and an inhaled corticosteroid (ICS).

The required label changes are as follows:

► LABAs are not asthma controller medications and are contraindicated without the use of an asthma controller medication, such as an ICS. Single-agent LABAs should be used only with a controller medication, never alone.

► A LABA should be used only as long-term treatment in patients whose asthma cannot be adequately controlled on asthma controller medications.

► Children and adolescents who need a LABA with an ICS should be prescribed one of the combination products, to ensure that a LABA is not used alone.

► LABAs should be used for the shortest period of time possible to achieve symptom control. As soon as a patient's asthma is under control, the LABA should be discontinued "if possible," and the patient should be maintained on an

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INSIDE

Lung Cancer Biomarker Tests Underway

BY SUSAN LONDON
Elsevier Global Medical News

CORONADO, CALIF. — A variety of lung cancer–associated biomarkers are being tested in assays that may improve diagnosis and treatment of this disease, according to three studies reported at a joint conference of the American Association for Cancer Research and the International Association for the Study of Lung Cancer.

A blood-based biomarker profile discriminates well between patients who have early-stage lung cancer and those individuals who are cancer free but at high risk, reported Dr. Gina Lee, a pulmonary and critical care physician at the University of California, Los Angeles.

She and her colleagues hypothesized that molecular changes in the developing tumor environment would be reflected in changes in levels of inflammatory, angiogenic, and tumorigenic proteins that can be detected in peripheral blood.

They used a bead-based multiplex immunoassay to assess

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Biomarker Assays Enter Trials

Lung Cancer • *from page 1*

levels of 40 biomarkers in serum samples from 90 patients who had lung cancer of any stage and from 56 cancer-free controls who were at high risk because of lengthy former smoking status and older age.

Levels of 21 biomarkers differed significantly between the 28 patients with stage I lung cancer and the cancer-free controls (*P* less than .05 for each). For distinguishing between these groups, this panel had an area under a receiver operating characteristic curve of 0.92.

In a logistic regression model focusing on selected biomarkers, participants were more likely to have stage I cancer if they had higher levels of interleukin 2 (odds ratio, 51.4; $P = .003$), interleukin 3 (OR, 11.0; $P = .002$), and macrophage-derived chemokine (OR, 10.9; $P = .002$). For distinguishing between patients with stage I lung cancer and at-risk controls, a panel consisting of these three biomarkers had an area under the curve of 0.93, a sensitivity of 97%, and a specificity of 77%.

"Our results suggest that we can find tumor-associated biomarkers that are differentially expressed in stage I vs. at-risk controls," Dr. Lee said. "However, we are also interested in the clinical scenario where individuals present to clinicians with a lung nodule seen on chest x-ray or a CT scan of indeterminate significance."

Therefore, she and her colleagues will evaluate the 40 biomarkers in pre- and postresection serum samples from patients in the ACOSOG (American College of Surgeons Oncology Group) Z4031 trial. Roughly one-fifth of patients undergoing resection for lung nodules in that trial were found to have benign lung disease.

Dr. Lee reported that she had no conflicts of interest related to the study.

High-Throughput Protein Assay

A protein signature identified by a high-throughput assay correctly classified the large majority of patients with and without lung cancer, reported Dr. Rachel Ostroff, clinical research director at SomaLogic Inc., a diagnostic development company in Boulder, Colo.

The SOMAmer technology used in the study relies on aptamers (oligonucleotides that bind to specific proteins with high affinity) to measure 825 proteins in serum simultaneously with subpicomolar sensitivity, she explained.

The investigators analyzed more than 1,300 serum samples from patients with stage I-III non–small cell lung cancer (20%) and two control groups: individuals with benign calcified pulmonary nodules (40%) and long-term smokers with no evidence of cancer (40%). They were divided into training and verification sets.

Analyses identified a signature of 12 proteins that were differentially expressed between the groups with and without lung cancer, including cell adhesion molecules, cytokines, angiogenesis markers, and tyrosine kinases, among others.

The signature had an area under the curve of 0.91 in the training set and 0.90 in the verification set, Dr. Ostroff reported. In the training set, sensitivity was 91% for cancer of all stages (90% for stage I) and specificity was 84%. In the verification set, sensitivity was 89% for cancer of all stages (87% for stage I) and specificity was 84%.

"We are currently validating this [signature] in independent sample sets," she commented.

The signature has also been tested in breast, prostate, and other cancers. "Certainly, some of the markers are also differentially expressed in those cancers, as you would expect," Dr. Ostroff said.

A protein signature correctly classifies the large majority of patients with lung cancer.

DR. OSTROFF

"But …when you combine all of those 12 markers together, it is much more specific for lung cancer than those others."

Tumor MicroRNA Analysis

A trio of tumor microRNAs predict de novo resistance to first-line chemotherapy among patients with small cell lung cancer, reported Dr. Glenn J. Weiss, a pulmonary oncologist with Scottsdale (Ariz.) Healthcare and the Translational Genomics Research Institute (TGen) in Phoenix.

"Small cell lung cancer patients have not had key breakthroughs for improved therapy in years, in part, because a one-size-fits-all approach for treatment is the current standard," he commented in an interview.

In the study, which was funded in part by the TGen Foundation, he and his colleagues extracted RNA from formalin-fixed, paraffin-embedded tumor specimens obtained from 34 patients with small cell lung cancer before they started chemotherapy, which was a platinum-based regimen in most cases.

Study results, reported in a poster, showed that of 21 evaluable patients, 4 patients (19%) had chemoresistance (defined as progression despite receiving chemotherapy).

MicroRNA array analyses identified 16 microRNA biomarkers as possible predictors of progression. Polymerase chain reaction analyses validated that three of them—miR-92a-2* ($P = .01$), miR-147 ($P = .02$), and miR-574-5p ($P = .04$)—were indeed associated with progression, according to Dr. Weiss, who has filed patents to use them as "theranostics."

Comorbidities were prevalent in the study population at baseline. None of them was significantly associated with chemoresistance.

The investigators are currently assessing how the identified microRNAs may reduce a tumor's sensitivity to chemotherapy, according to Dr. Weiss.

"If we can independently validate our findings in other tumor sample sets collected from small cell lung cancer patients, we can begin to explore [by] using these microRNAs to design better clinical trials and perhaps find new therapies that help patients at higher risk for resistance to current standard chemotherapy treatment," he concluded.

Dr. Weiss has filed patents for the use of microRNAs as theranostics, and has received funding from the Sylvia-Chase Foundation, the American Cancer Society, the IBIS Foundation of Arizona, the TGen Foundation, and Scottsdale Healthcare to conduct this work. ■

Dr. W. Michael Alberts, FCCP, comments: *These are very exciting findings. The "to be answered" question is how these tests will work in the daily practice of medicine. Will they perform with sufficient sensitivity and specificity to allow decisions to be made on individual patients? I, for one, hope that their obvious promise translates to practical success in the clinic.*

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CHEST PHYSICIAN

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ACIP Recommends Newly Licensed 13-Valent Vaccine

BY MIRIAM E. TUCKER
Elsevier Global Medical News

ATLANTA — The 13-valent pneumococcal conjugate vaccine is now recommended to replace the current 7-valent vaccine for routine immunization in children.

Licensure of the 13-valent pneumococcal conjugate vaccine (PCV13), Pfizer's Prevnar 13, was announced by a representative from the Food and Drug Administration at a meeting of the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices.

CHILDREN WHO PREVIOUSLY RECEIVED ONE OR MORE DOSES OF PCV7 SHOULD COMPLETE THE SERIES WITH PCV13.

The vaccine is indicated for the prevention of invasive pneumococcal disease caused by all of its 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F), and for prevention of otitis media caused by the serotypes in the 7-valent vaccine (4, 6B, 9V, 14, 18C, 19F, and 23F).

The committee then voted on recommendations for its routine use in previously unvaccinated children aged 2-59 months of age (the primary series is routinely given at 2, 4, 6, and 12-15 months of age) and in high-risk children aged 60-71 months, as well as on guidelines for transitioning to PCV13 in children who previously received one or more doses of PCV7.

In general, children who previously received one or more doses of PCV7 should complete the series with PCV13.

Children aged 14-59 months who were completely vaccinated with four doses of PCV7 should receive a single "supplemental" dose of PCV13, but this can occur at the next regularly scheduled office visit. There is no need to recall children for it, said Dr. Pekka Nuorti of the CDC's respiratory diseases branch.

The committee also voted PCV13 into the Vaccines for Children Program.

A representative from Pfizer Inc. announced that the company will issue credit to providers for unused doses of PCV7. The first supplies are expected to be shipped out in mid-March, he said. ■

Pandemic Strain Gets Nod For 2010-11 Flu Vaccine

BY ELIZABETH MECHCATIE
Elsevier Global Medical News

BETHESDA, MD. — The influenza vaccine for the 2010-2011 influenza season in the United States should include a pandemic influenza A(H1N1) strain, instead of one of the two seasonal influenza A strains in the current vaccine, a Food and Drug Administration Advisory Panel recommended on Feb. 22.

At a meeting of the FDA's Vaccines and Related Biological Products Advisory Committee, the panel unanimously voted 12 to 0 that the current influenza A(H1N1) strain included in the 2009-2010 seasonal flu vaccine, an A/Brisbane/59/2007 (H1N1)–like virus, should be replaced with a pandemic A(H1N1) vaccine virus, an A/California/7/2009–like virus, the component of the monovalent pandemic vaccine that has been used this season.

Also included in the vaccine should be an A/Perth/16/2009 (H3N2)–like virus and a B/Brisbane/60/2008–like virus (B/Victoria lineage), the panel said.

The panel's recommendation is based on the finding that the vast majority of influenza A(H1N1) viruses circulating worldwide have been the pandemic strain. At the meeting, Nancy Cox, Ph.D., director of the influenza division, at the Centers for Dis-

THE VAST MAJORITY OF INFLUENZA A(H1N1) VIRUSES CIRCULATING WORLDWIDE HAVE BEEN THE PANDEMIC STRAIN.

ease Control and Prevention, Atlanta, told the panel that there has been very little evidence of circulating seasonal A(H1N1) influenza viruses, which "most likely pose a low risk" in the forthcoming season in the northern hemisphere.

The panel meets every year at this time to make preliminary recommendations on the components of the trivalent vaccine for the forthcoming influenza season in the northern hemisphere. It considered information on the strains circulating worldwide as well as recommendations announced Feb. 18 by the World Health Organization for the 2010-2011 influenza vaccine to be used in the northern hemisphere.

The panel voted to replace the influenza A(H3N2) strain included in the current vaccine, with a southern hemisphere vaccine virus A/Perth/16/2009 (H3N2)–like virus. Dr. Cox said that activity of seasonal A(H3N2) viruses has been "relatively low" worldwide, compared with previous years, and what has been circulating antigenically is related closely to the A/Perth/16/2009 virus.

The panel voted to retain the influenza B component that is in the current vaccine, a B/Brisbane/60/2008–like virus (B/Victoria lineage). Influenza B viruses have been circulating at low levels in many countries, but Victoria lineage viruses continue to predominate, Dr. Cox said. She pointed out that it is always difficult to predict which lineage of influenza B viruses will predominate, however.

The panel's recommendations were the same as the WHO recommendations for the three components of the influenza vaccine for the forthcoming season in the northern hemisphere. ■

Nosocomial Sepsis, Pneumonia Deemed Preventable Killers

BY MARY ANN MOON
Elsevier Global Medical News

Health care–associated sepsis and pneumonia accounted for an estimated 48,000 patient deaths, 2.3 million hospitalization days, and $8.1 billion in in-hospital expenses in 2006, according to a report in the Archives of Internal Medicine.

The investigators based their estimates on a review of 69 million discharge records during 1998-2006 from hospitals throughout 40 states in the federal government's Nationwide Inpatient Sample (NIS) database. That provided a study population "much larger than those used in previous studies" of nosocomial illness, one that "captures a greater diversity of hospitals and geographic locations," said Michael R. Eber of the Center for Disease Dynamics, Economics, and Policy, Resources for the Future, Washington, and his associates (Arch. Intern. Med. 2010;170:347-53).

Even the "substantial" number of health care–related infections they discovered is an underestimate, because hospital-acquired infections that did not manifest themselves until after discharge were not included. Many surgical-site infections fall into that category, Mr. Eber and his colleagues said.

"The magnitude of harm from these infections is disconcerting, and the knowledge that patients continue to experience harm from their interactions with the health system is unconscionable," added Dr. David J. Murphy and Dr. Peter J. Pronovost of Johns Hopkins University, Baltimore, in an editorial comment accompanying the report. (Arch. Intern. Med. 2010;170:353-5).

The NIS is an administrative database that does not directly record hospital-acquired infections. The investigators had to use analytic techniques to exclude infections that may have predated hospitalization. They also excluded data on any patients who entered the hospital with an infectious disease or a potentially immunocompromised state, as well as any who transferred from another facility where they may have acquired an infection.

That left a cohort of 58,701,608 cases of hospitalization during the study period, in which there were 493,250 cases of health care–associated sepsis, 79,835 cases of health care–associated pneumonia, and 15,118 cases of both sepsis and pneumonia.

Outcomes of those infections varied across different groups of patients. "We found that the attributable hospital length of stay and hospital costs of health care–associated sepsis and pneumonia cases were at least 40% higher in patients who underwent invasive procedures than in those who did not," Mr. Eber and his associates wrote.

For patients who underwent invasive surgery, the mean length of stay attributed to nosocomial sepsis was 10.9 days, mean in-hospital cost was $32,900, and mortality was 19.5%. The mean length of stay attributed to nosocomial pneumonia in invasive surgery patients was 14 days, mean in-hospital cost was $46,400, and mortality was 11.4%.

"In the subgroup of electively admitted surgery patients, the attributable costs of hospital-acquired infections were even higher," the investigators added.

"What is glaringly obvious is that preventable harm remains a substantial problem and that investments in research to reduce these harms are woefully inadequate given the magnitude of the problem," Dr. Murphy and Dr. Pronovost said in their editorial comment. "We have invested little in rigorous methods to measure and improve quality of care," they added.

"The United States spends a penny studying the delivery of health care for every dollar it spends studying basic and clinical research," Dr. Murphy and Dr. Pronovost noted.

"We must invest in the science of health care quality and safety, which requires developing methods to measure these infections, identifying and implementing interventions to prevent them, and evaluating their impact," they said.

"This will require new skills for many physicians and researchers because few have formal training in the sciences of quality improvement and patient safety," they added.

The Robert Wood Johnson Foundation supported the study. Mr. Eber reported no financial conflicts of interest. Dr. Pronovost reported receiving grant support from the Agency for Healthcare Research and Quality to reduce central line–associated bloodstream infections and honoraria from various health care organizations to speak on patient safety and quality-related topics. ■

Severe Flu During Pregnancy Tied to IgG Subclass

BY BRUCE JANCIN
Elsevier Global Medical News

KEYSTONE, COLO. — The explanation for pregnancy as a risk factor for severe pandemic influenza A(H1N1) infection may lie in a newly described association between the severity of H1N1 disease and the presence of IgG2 subclass deficiency.

This finding by Australian investigators, if confirmed, may not only shed new light on the pathogenesis of severe H1N1 infection but also prove to have important therapeutic implications, Dr. Gwen Huitt observed at a meeting on allergy and respiratory diseases.

Early in the pandemic, pregnant women were identified as being at particularly high risk for severe infection requiring ICU admission. Other high-risk groups included children less than 2 years of age, the obese, and individuals with chronic lung, heart, or kidney disease. The mechanisms underlying this increased risk have been unclear, said Dr. Huitt, professor of medicine at the University of Colorado and director of the adult infectious disease care unit at National Jewish Health, both in Denver.

Investigators in Melbourne decided to assess total IgG and IgG subclasses in a consecutive series of patients requiring ICU admission for pandemic flu. The impetus for their study came when they noted IgG2 subclass deficiency in a pregnant woman admitted to the ICU for severe H1N1 disease.

The study population consisted of 39 patients hospitalized for H1N1 infection and 17 healthy pregnant controls. A total of 19 patients had severe infection, meaning they required mechanical ventilation and ICU admission. Twenty others had moderate H1N1 disease, defined by hospitalization without ICU care. In all, 7 of the 19 patients with severe infection were pregnant, as were 2 of 20 with moderate infection.

Fifteen of the 19 patients with severe H1N1 infection had low IgG2, with a mean value of 1.8 g/L, as did 5 of the 20 with moderate infection. Furthermore, 10 of the 17 healthy pregnant controls had mildly low IgG2, although their diminished levels were nonetheless significantly higher than those of the pregnant women hospitalized for H1N1 infection.

Severe H1N1 infection was also associated with low total IgG, anemia, and hypoalbuminemia, although multivariate analysis revealed that the associations were significant only for low mean IgG2 and hypoalbuminemia.

Follow-up of 15 surviving H1N1-infected, IgG2-deficient patients showed that 11 remained IgG2-deficient at 90 days, well after recovery from their acute disease episode. In contrast, hypoalbuminemia typically resolved within 30 days (Clin. Infect. Dis. 2010;50:672-8).

The investigators argued that long-term follow-up may be warranted in patients sick enough to require hospitalization for H1N1 infection, since the late implications of lingering IgG2 deficiency in this population are unclear. For example, it is not known whether such patients will have a diminished immunologic response to influenza vaccination. "This is something that needs a lot more work," Dr. Huitt said at the meeting, which was sponsored by the National Jewish Medical and Research Center.

The study was funded by the National Health and Medical Research Council of Australia. Dr. Huitt reported having no relevant financial interests. ■

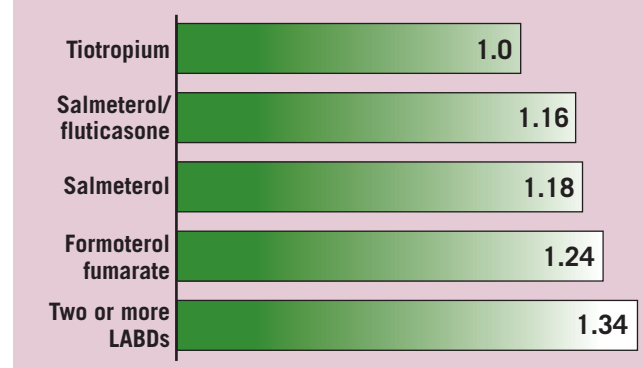
Tiotropium Linked to Fewer COPD Hospitalizations

BY BRUCE JANCIN
Elsevier Global Medical News

SAN DIEGO — Patients with chronic obstructive pulmonary disease that was treated with tiotropium monotherapy had significantly fewer disease-related hospitalizations during a 12-month window than did those on other long-acting bronchodilator regimens, a large national study shows.

The retrospective study looked at COPD-related inpatient admissions in Thomson MarketScan, a large U.S. administrative claims database. The analysis involved 52,274 commercially insured patients with COPD who had one or more prescription claims for a long-acting bronchodilator (LABD) in 2004-2006, Emily D. Durden, Ph.D., reported at the annual meeting of the American College of Chest Physicians.

12-Month Risk of COPD-Related Hospitalization



Notes: Based on analysis of 52,274 patients. Admission rate in tiotropium group was significantly lower than other groups.
Source: Dr. Durden

ELSEVIER GLOBAL MEDICAL NEWS

The COPD patients were categorized into five LABD regimens. Those on monotherapy with tiotropium (Spiriva) had significantly lower rates of disease-related hospital admissions during 12 months of follow-up than those on salmeterol (Serevent), formoterol fumarate (Foradil), salmeterol/fluticasone propionate (Advair), or combination therapy with two or more LABDs, said Dr. Durden of Thomson Reuters, Austin, Tex. (See chart.)

The association between LABD regimen and COPD-related hospital admissions was evaluated in a multivariate analysis that adjusted for potential confounders including age, gender, urban vs. rural location, comorbid conditions, insurance type, emergency department use, and respiratory hospitalizations during the 6 months immediately prior to the 12-month study period.

The tiotropium-only patients had significantly more comorbidities than those in the other study arms. They also were more likely to have been vaccinated against influenza. Mean health care costs in the 6-month pre-period were lowest in the salmeterol group at $12,885 and highest in the combination LABD group, at nearly $17,100.

Dr. Durden noted that the retrospective, nonrandomized nature of her study means that it can't provide proof that tiotropium actually caused the lower hospitalization rate.

However, Dr. Donald P. Tashkin, FCCP, described a new meta-analysis he and his coworkers have conducted that incorporated data from 30 placebo-controlled clinical trials of tiotropium for COPD, including the massive 4-year Understanding Potential Long-Term Impacts on Function With Tiotropium (UPLIFT) trial (Chest 2010;137:20-30).

This meta-analysis indicates that tiotropium provided a 12% reduction in the risk of all-cause mortality relative to placebo and a 17% reduction in the risk of composite cardiovascular events, including stroke and MI, said Dr. Tashkin, professor emeritus of medicine at the University of California, Los Angeles. The relative risks of acute MI and of heart failure were reduced by 23% and 17%, respectively, in this analysis.

Dr. Tashkin's meta-analysis and Dr. Durden's study were both funded by Boehringer Ingelheim and Pfizer, which comarket tiotropium. Dr. Tashkin is a consultant to both companies. Dr. Durden reported having no financial conflicts. ■

SLEEP STRATEGIES

Sleep Technician Training and Credentialing: An Update

BY DR. BARBARA PHILLIPS, MSPH, FCCP
Co-Chair, ACCP Sleep Institute

The technologists who work in sleep centers are essential for the safety of our patients and for the quality and validity of the data that we use to make clinical decisions. As the field of sleep medicine has matured, training and credentialing of these clinicians has evolved.

One of the topics of discussion emerging from this evolution has been whether the work of polysomnography data collection and sleep apnea treatment falls under the scope of respiratory care.

This plays out from time to time at the level of state legislatures and licensing bodies, where several states have passed legislation requiring additional training, certification, and credentialing of already-licensed respiratory therapists in order for those therapists to work as sleep lab technicians. In some cases, language is inserted that specifically states that an individual must have passed the Board of Registered Polysomnography Technology (BPRT) examination or the A-STEP program in order to work in a sleep center.

Chest physicians may be asked to comment on or to support legislation regulating licensure or scope of practice of sleep lab technicians, including respiratory therapists. In evaluating such proposed legislation, it may be helpful to review the ACCP's position on this issue, published in 2007 (www.chestnet.org/practice/advocacy/positionPapers/07archives.php, accessed 11/5/09).

Dr. James Parish, FCCP
Section Editor,
Sleep Strategies

The paper states: "Currently, the Commission on Accreditation of Allied Health Education Programs (CAAHEP), the nationally recognized accreditation body for educational programs for various allied health professionals, provides unbiased oversight of the educational process for polysomnographic technologists. Licensure for polysomnographic personnel must require attendance at an education and training program accredited by CAAHEP through one of its member Committees on Accreditation, namely CoAPSG (polysomnography), CoARC (respiratory care), or CoAEND (electroneurodiagnostic technology). Educational programs, such as the AASM-A-STEP (American Academy of Sleep Medicine – Accredited Sleep Technology Program), were designed as stopgap measures to maintain a workforce flow in regions where CAAHEP accreditation programs are not readily available. This type of program is a temporary measure and should not become a primary path to testing for credentialing.

Competency testing for the credentialing of individuals performing polysomnography ensures the knowledge level of technologists entering the field. The National Commission for Certifying Agencies (NCCA) is the accreditation body of the National Organization for Competency Assurance (NOCA) and establishes standards for credentialing agencies. Acceptable credentials must be those granted through validated examinations administered by NCCA-accredited credentialing organizations, such as the Board of Registered Polysomnographic Technologists (BRPT), the National Board for Respiratory Care (NBRC), or an equivalent entity. Additional certification beyond those of the relevant allied health disciplines must not be required."

The ACCP's position is that all personnel working in sleep centers should be well-trained and qualified to perform high quality work that best serves the needs of the patient. The College recognizes that there is a variety of pathways to become a well-qualified sleep technologist and that respiratory therapists should not be excluded if they have proper training and are able to pass a recognized certifying examination. With that background, it is also useful to understand the characteristics of the CoARC (Committee on Accreditation for Respiratory Care) training program for respiratory therapists with the AASM A-STEP program.

CoARC's current standards are at www.coarc.com/standards.htm, and state (line 179) that polysomnography is part of the scope of respiratory care.

To be licensed, a respiratory therapist must have completed, at a minimum, an associate degree education program accredited by the Commission on Accreditation of Allied Health Education Programs (CAAHEP) in collaboration with the Committee on Accreditation for Respiratory Care (CoARC), as well as having obtained a professional respiratory therapist credential from the National Board for Respiratory Care (NBRC) upon passing of a competency examination for respiratory therapists administered by the NBRC. Training in respiratory therapy includes some education in sleep disorders, testing, and treatment. Respiratory therapists are qualified to become sleep technologists with additional training and experience.

The A-STEP program is sponsored by the AASM as a temporary measure to help increase the supply of qualified sleep technologists. The program consists of an 80-hour, on-the-job training course, with an additional 14 online modules (45 to 90 min per module) to be taken while working in a sleep facility. Although the program has not received CAAHEP accreditation, the program is serving a useful function in providing needed education to sleep technologists.

With regard to formal credentialing, chest physicians need to know that there is now an alternative to the Registered Polysomnographic Technologist (RPSGT) certifying exam for respiratory therapists. The new credential is called the Sleep Disorders Specialist (SDS), and it is offered through the NBRC.

A comparison of content emphasized by the SDS and RPSGT examinations also is instructive. Most of the competencies overlap and are covered by the two examinations. Both examinations include a set of competencies that cover skills before a sleep study begins. Competencies described for the RPGST examination start with the physician's order and do not necessarily involve skills in recognizing patients at risk for sleep disorders.

Comparing the relative emphasis of competency domains was a bit complicated. The matrix (Table) illustrates the comparison.

The biggest difference is that the RPSGT emphasizes competencies related to performance of sleep studies more than the SDS examination. The SDS examination gives more emphasis to pretesting information, administration of the sleep center, and support of patient treatments for sleep disorders.

Both examinations use what is called a single compensatory passing point. Scores from item responses across domains described in the matrix below are aggregated into one broad score respectively reflecting competence. In other words, candidates do not have to separately pass each domain. In fact, they can enjoy some degree of benefit by compensating for weak areas by doing better in other domains.

The ACCP's position statement on sleep lab technician licensure states: "The ACCP only supports non-exclusionary legislation that requires rigorous, unbiased, and independent training, accreditation, and credentialing, conforming to accepted national standards."

This is useful guidance when we are asked to evaluate or support legislation relating to sleep technician licensure. ■

Comparison of RPSGT and SDS Examinations

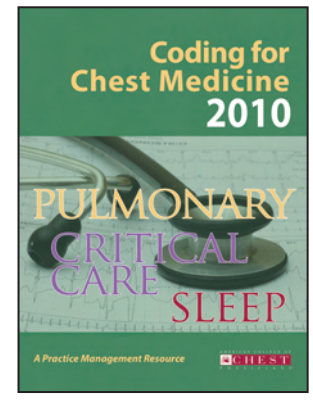
Domain	BRPT RPSGT Examination	NBRC SDS Examination
Pretesting Information	7.5%	12.0%
Sleep Study Performance	50.0%	30.0%
Study Analysis/Scoring	29.0%	31.0%
Management/Administration	5.5%	9.0%
Treatment Support	8.0%	18.0%
Total	100.0%	100.0%

Source: Dr. Barbara Phillips, MSPH, FCCP

PRODUCT OF THE MONTH

Coding for Chest Medicine 2010

Specialty Medicine. Specialty Codes.
For a coding resource as precise and specialized as the medicine you practice, turn to *Coding for Chest Medicine 2010*.



The updated 14th edition features chapters on allergy and immunology, bronchoscopy, critical care, consultations, electronic medical records, ICU procedures, malpractice issues, pay for performance, pediatric pulmonary medicine (new chapter), pulmonary function testing, pulmonary rehabilitation, rapid response teams, and thoracic surgical procedures.

New in 2010:

- New codes for bronchial placement of fiducial markers, navigational bronchoscopy, pleural fibrinolysis, and infant PFTs
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Submission Deadline: May 4

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October 30 - November 4
Vancouver, BC, Canada

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Kalpalatha K. Guntupalli MD FCCP

Sincerely,
Kalpalatha K. Guntupalli, MD, FCCP
President, American College of Chest Physicians

Abstract Topic Areas of Interest

Adult Pulmonary
- AIDS/Immunocompromised Patients
- Asthma
- Bronchoscopy and Interventional Procedures
- COPD
- Cystic Fibrosis/Bronchiectasis
- Cytokines/Cellular Interactions
- DVT/PE/Pulmonary Hypertension
- Education and Teaching in Pulmonary Medicine
- Imaging
- Interstitial Lung Disease
- Lung Cancer
- Lung Transplantation
- Occupational/Environmental Lung Disease
- Physiology/PFTs/Rehabilitation
- Pleural Disease
- Respiratory Infections
- Sleep
- Tobacco Cessation and Prevention
- Women's Health
- Other

Adult Critical Care
- Airway Management
- ARDS/Lung Injury
- Diagnostic Procedures
- Education and Teaching in Critical Care
- End-of-Life Care
- ICU Infections
- Invasive Procedures and Hemodynamic Monitoring
- Nonpulmonary Critical Care
- Nutrition in the ICU
- Outcomes/Quality Control and Improvement
- Pharmacology in the ICU
- Respiratory Support
- Sedation
- Sepsis and Septic Shock

Cardiovascular Diseases and Critical Care
- Arrhythmias
- Coronary Artery Disease/ Coronary Syndromes
- Heart Failure and Cardiogenic Shock
- Other

Thoracic and Cardiovascular Surgery
- Cardiac Surgery
- Postoperative ICU Issues
- Thoracic Surgery
- Other

Pediatric Chest Diseases
- Asthma
- Congenital Lung Disease
- Cystic Fibrosis
- Infections
- Pediatric Critical Care
- Other

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Affiliate members of the ACCP are invited to submit case reports for presentation. Experts will moderate sessions, allowing you and other attendees to closely interact and discuss issues.

Submit at www.chestnet.org.

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NETWORKS

Commercial Drivers, Pediatric Disease, and Mentorship

Occupational and Environmental Health

Commercial Motor Vehicle Drivers and Sleep-Disordered Breathing: An Opportunity for Intervention by Chest Physicians

In the United States, there are approximately 1.6 million commercial motor vehicle drivers who operate vehicles weighing more than 10,001 pounds or vehicles placarded to be carrying hazardous material.

Drivers are allowed to drive for 11 out of 14 h per day and then must have a 10-h break. In the 3 h that they are not driving, they perform the fatiguing tasks of inspecting, fueling, loading, and unloading their vehicles.

While drivers are required to have a 10-h break away from work, they are not required to sleep. EEG studies have shown that during the 10-h break, drivers spend an average of 5.18 h in bed and sleep for 4.78 h (Mitler et al. *N Engl J Med*. 1997;*337*[11]:755). In addition to the problems of fatigue from long work shifts, commercial motor vehicle drivers are at risk for starting their workweek fatigued, as many curtail their usual sleep pattern in the 24 h prior to beginning their shift (Philip et al. *Sleep Med*. 2002;3[6]:507). As an example, a driver who sleeps from 10:00 PM to 6:00 AM on Friday and Saturday may begin his or her workweek at midnight on Sunday.

Of the 1.6 million drivers, approximately 96% are men, and 27% are older than 55 years of age. Commercial drivers also have a high prevalence of ever smoking (67%) (Jain et al. *Am J Ind Med*. 2006;49[12]:755) and obesity (53%) (Wiegand et al. *Traffic Inj Prev*. 2009;10[6]:573). All of these factors increase the risk of obstructive sleep apnea, and prevalence of obstructive sleep apnea in commercial drivers has been estimated at 12% to 17% (Parks et al. *J Occup Environ Med*. 2009;51[3]:275).

Fatigue and sleepiness are related to motor vehicle accidents in commercial drivers due to the prevalence of fatigue from long shifts, poor sleep quality during breaks, and circadian rhythm disturbances. Obstructive sleep apnea is felt to be responsible for only 4% of commercial motor vehicle accidents (Häkkänen et al. *Sleep* 2000; *23*[1]:49).

Chest physicians, especially those with an interest in sleep, occupational medicine, or public health, can become active in their own communities by screening truck drivers during their biannual commercial driver examination and by educating trucking operators on the risks associated with driving while fatigued.

Dr. Richard Evans, FCCP
Steering Committee Member

Pediatric Chest Medicine

The first meeting of the subcommittee on the Pulmonary Care of Patients With Neuromuscular Disease, hosted by the Pediatric Chest Medicine NetWork, was held at CHEST 2009. Members of the Home Care, Respiratory Care, Palliative and End-of-Life Care, and Allied Health Care NetWorks joined colleagues from the Pediatric Chest Medicine NetWork to discuss ways to advance an agenda to make the College the preeminent source for issues pertaining to this important aspect of chest medicine.

The subcommittee was created to become a center of excellence that encompasses clinical care, education, research, and advocacy, incorporating the multidisciplinary aspects required to optimize the pulmonary health of children and adults with neuromuscular disease. The subcommittee will identify areas in need of study, develop educational materials for health-care professionals, and advocate for these patients at various levels, including the ACCP, medical communities, and government agencies. It will work with the ACCP to develop external partnerships that will facilitate project development and fulfillment of these goals. The subcommittee plans to meet again at CHEST 2010.

Anyone interested in this subcommittee should contact Dr. David Birnkrant, FCCP; Dr. Girish Sharma, FCCP; or e-mail networks@chestnet.org.

Dr. Howard Panitch, FCCP
NetWork Chair

Women's Health

Mentorship refers to a personal developmental relationship in which a more experienced or more knowledgeable person helps a less experienced or less knowledgeable person. Mentoring is a process for the informal transmission of knowledge, experience, and support that aids the receiver's professional development.

The importance of mentorship has been proven through the ages. In Greek mythology, Mentor provided guidance to Odysseus's son, Telemachus, when Odysseus set out on his famous adventures. Many researchers have identified mentoring as an important tool in fostering academic excellence in students and junior faculty. Having a mentor is a predictor for career satisfaction among academic physicians. Unfortunately, women are underrepresented in the mentoring process, as they are in medicine.

During CHEST 2009, the idea of establishing a mentoring program to help link young ACCP women physicians with members of the Women's Health NetWork was discussed. This project could be a collaborative effort between the Affiliate NetWork and the Women's Health NetWork.

This proposed program would provide mentoring in such areas as career choices, research interests, and work/life balance. It would also provide an avenue for these young physicians to maintain a lifelong association with the ACCP and foster the future generation of leaders.

Dr. Suryakanta Velamuri, FCCP
Steering Committee Member

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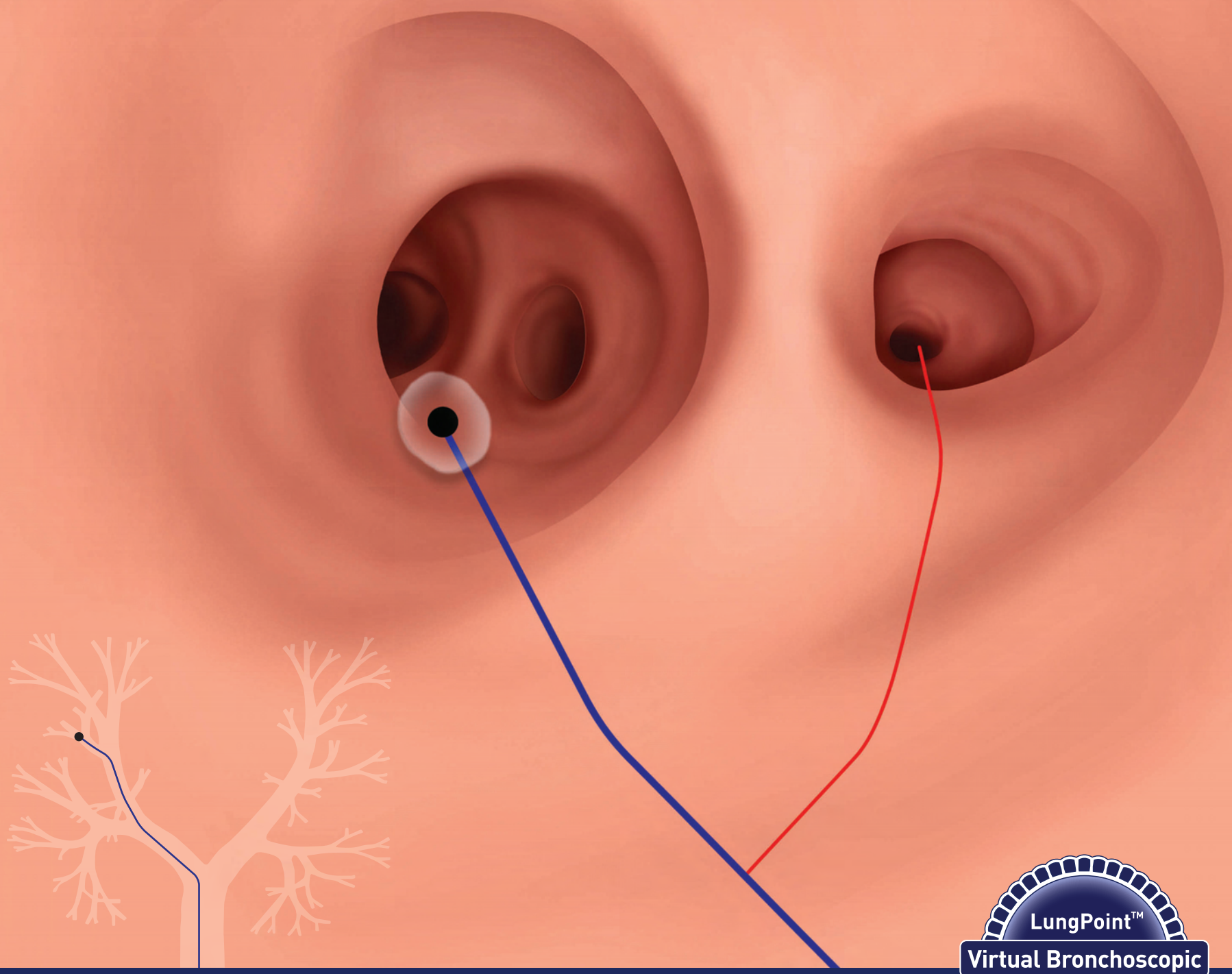

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Pandemic Influenza A(H1N1): Lessons Learned So Far

BY BRUCE JANCIN
Elsevier Global Medical News

KEYSTONE, COLO. — Two large waves of pandemic influenza A(H1N1) have swept across the country, and now viral respiratory disease experts are assessing what the health care community did right—and wrong—to improve response should a third wave hit.

Topping the list of mistakes was the poor distribution of vaccine. The H1N1 vaccine was quickly developed, successfully tested, and manufactured in impressive fashion. It created an excellent antibody response in normal hosts. But there was a major breakdown in distribution, Dr. Gwen A. Huitt said at a meeting on allergy and respiratory diseases.

Another big problem was "woefully inadequate" viral testing methodology. So many people had a negative rapid test—even though they had classic symptoms of H1N1 infection—that the testing was basically abandoned. Rapid, reliable, and relatively inexpensive polymerase chain reaction (PCR) tests are being developed and will soon be available. But the new PCR tests are unlikely to find their way into most physicians' offices or smaller clinic facilities, said Dr. Huitt, director of the adult infectious disease care unit at National Jewish Health and professor of medicine at the University of Colorado, both in Denver.

So many people had a negative H1N1 rapid test that the testing was basically abandoned.

DR. HUITT

Other areas in need of improvement include the following:

► **Poor education.** Only about one-third of the general population has been vaccinated to date. Most of the public was not persuaded by the case for immunization made in the vaccination campaign.

More effective pandemic H1N1 education needs to be aimed not only at the public but also at health care workers, said Dr. Huitt at the meeting, which was sponsored by the National Jewish Medical and Research Center. Despite data showing that in most health care settings, surgical masks are just as protective as the more expensive N-95 masks (N. Engl. J. Med. 2009;361:1823-5), there was considerable resistance to the surgical masks on the part of unionized health care workers.

► **Treatment issues.** Physicians learned too slowly that the antiviral agents are less effective in special populations. For example, it was discovered that higher doses of oseltamivir (Tamiflu) are required in obese patients—which was one of the groups at high risk of hospitalization and severe complications of H1N1.

► **Legal issues regarding mandatory vaccination.** "We're still dealing with this. Many institutions have mandated that health care workers, including docs, get vaccinated against influenza or lose their job. I can tell you there's ongoing litigation on this issue," she said.

What did the medical community get right in the pandemic? Pandemic preparedness algorithms were already in place before case counts started rising. Antiviral agents were available in adequate quantities. Physicians and public health officials were quick to recognize that testing methods were inadequate and couldn't be relied on. And the vaccine was protective.

Dr. Huitt indicated she has no relevant financial relationships. ■

Dr. Mark L. Metersky, FCCP, comments: *Other aspects that the medical community got right were the immediate dissemination of information by Mexican public health authorities when the novel strain was detected, and the performance of several high-quality prospective clinical and epidemiologic studies that were made possible by the advance knowledge of a likely pandemic.*

LABA Use in Asthma

FDA • *from page 1*

asthma controller medication, such as an ICS. That is a change from current asthma treatment guidelines.

Safety concerns regarding LABA therapy date back to a major study reported more than 7 years ago, and were reinforced by a 2008 FDA meta-analysis. That meta-analysis indicated that treatment with LABAs—either alone or when combined with an ICS—is associated with an increased risk of severe asthma symptoms and hospitalizations, as well as deaths in children and adults with asthma, when compared with people not on a LABA.

Previous efforts to address the risks—including the addition of a boxed warning in 2003—have not adequately addressed the safety issue, said Dr. Janet Woodcock, director of the FDA's Center for Drug Evaluation and Research (CDER). So, the FDA now will require more changes to the drug's label as part of a risk evaluation and mitigation strategy (REMS) for the products.

New data and analyses indicate the risks apply broadly to children and adults, Dr. Woodcock added, yet "the products currently are not being used as safely as possible."

The LABA products' REMS includes a revised medication guide for patients that explains the product risks with each filled prescription, a plan to educate health care providers about the appropriate use of LABAs, and a requirement that the manufacturers conduct more studies of the safety of the LABA-ICS combination products.

Currently, there are insufficient data to conclude whether combining LABAs with an ICS "reduces or eliminates the risk of asthma-related death and hospitalizations," according to the FDA.

In addition, under a new FDA drug safety initiative, the agency will monitor use of the medication to determine whether LABAs are still being used without a controller medication.

The new requirements do not apply to the use of LABAs for chronic obstructive pulmonary disease or intermittent exercise-induced bronchospasm. ■

The full statement is available at www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm200776.htm.

Dr. Burt Lesnick, FCCP, comments: *The FDA has advised against using combination products that include LABAs as a first-line therapy for mild to moderate asthma. In keeping with current NHLBI and GINA guidelines, patients under good asthma control should have a trial stepping down from such combination products to inhaled corticosteroids alone.*

Infectious Disease Expert Spells Out Influenza Concerns

BY BRUCE JANCIN
Elsevier Global Medical News

KEYSTONE, COLO. — Where has all the seasonal influenza gone?

That's one of the questions preoccupying flu watchers during this unprecedented 2009-2010 influenza season. Other key questions they're pondering include: Will we see a third wave of the influenza A(H1N1) pandemic? And what's going to happen if—or more likely, when—the extremely deadly avian influenza A(H5N1) virus reassorts with H1N1?

Seasonal flu in the United States ordinarily follows a predictable pattern. It arrives in force in January, peaks in February, and then tails off in March. This year, seasonal influenza didn't show up anywhere in the United States in January, aside from a few sporadic cases of no epidemiologic significance, Dr. Gwen Huitt said at a meeting on allergy and respiratory disease.

Instead, the Centers for Disease Control and Prevention's Outpatient Influenza-Like Illness Surveillance Network reported a huge peak during October, 4 months earlier than usual, that was the crest of the second wave of the H1N1 pandemic. The first wave came in June 2009.

"That was a paradigm shift. It was far different from anything seen in recent history," recalled Dr. Huitt of the department of medicine at the University of Colorado, who is also an infectious disease specialist at National Jewish Health, both in Denver.

"We're treading uncharted territory right now, but the thing we're all concerned about is whether or not we'll have a third wave. The 1918 Spanish flu H1N1 pandemic had three waves. The second was the worst, and the third was almost as bad. So we're just waiting to see what happens," Dr. Huitt said at the meeting sponsored by National Jewish Health.

The CDC has reported 59 documented cases of oseltamivir (Tamiflu)-resistant H1N1 through January of this year. A third wave of the pandemic could turn oseltamivir resistance into a major problem. Availability of another oral drug in addition to oseltamivir and zanamivir (Relenza) would be most welcome. Unfortunately, the only anti-influenza drug in phase III testing is intravenous peramivir, although it does look promising.

Seasonal influenza A isn't being seen on a significant scale anywhere in the world right now. However, an upsurge in seasonal influenza B is underway in China. "Fortunately, it's a strain included in our seasonal influenza vaccine, so I think our population should be fairly well covered if that virus starts appearing in North America," she said.

The biggest concern now, Dr. Huitt said, is the prospect of genetic reassortment between avian influenza and the H1N1 virus. The avian H5N1 virus has an extremely high mortality rate—around 50%—but poor human-to-human transmissibility. The H1N1 virus has a much lower death rate—certainly less than 10%—but is highly transmissible.

Egypt and Indonesia are the hotbeds of H5N1 activity right now, with large outbreaks in both poultry and humans. Workers from the CDC and the World Health Organization are on the scene, trying to figure out the next move.

Pigs are susceptible to both avian influenza and H1N1 and are thought to be a frequent source of new human viral strains. And, in underdeveloped areas of the world, pigs and flocks of poultry often live underneath or in human dwellings.

"All it takes is two gene reassortments. One has already taken place. So we're waiting for the other shoe to drop, and if that occurs, then you've got a supervirus that's quite lethal. … and easily transmissible from human to human," the physician said.

Dr. Huitt reported having no relevant financial interests. ■

Critical Care in a Pay-for-Performance World

BY DAMIAN McNAMARA
Elsevier Global Medical News

MIAMI BEACH — Critical care societies and individual physicians should drive the implementation of pay-for-performance measures in critical care, because they are most familiar with the complex care processes in this setting, Dr. J. Randall Curtis, FCCP, said.

Pay for performance (P4P) presents "unique challenges to critical care," Dr. Curtis, president of the American Thoracic Society (ATS), said at the Society of Critical Care Medicine: Critical Care Congress. For example, intensive care unit outcomes depend on simultaneous, multiple processes. In addition, it can more difficult to quantify clinical outcomes in this setting. "We take care of syndromes, such as ARDS [acute respiratory distress syndrome], rather than acute diagnoses, like acute myocardial infarction," he said.

Although the ideal P4P measures are evidence-based, there is a paucity of data in the critical care literature about the validity of performance measures, Dr. Curtis said. Most studies focus on primary-care, heterogeneous programs, and use heterogeneous quality indicators. "It is hard to summarize these studies into one answer," he noted.

A combined effort is underway through the Critical Care Societies Collaborative to devise these performance measures with input from the ATS, the American College of Chest Physicians (ACCP), the Society of Critical Care Medicine, and the American Association of Critical-Care Nurses.

"We are very excited about this—we are actually at ground level of developing a performance measure," ACCP president Dr. Kalpalatha K. Guntupalli, FCCP, said during a presentation at the meeting.

Clinicians should be the ones to develop and implement these quality measures, Dr. Curtis said. "We need to find a way to do this without just adding to the burden of busy critical care physicians." Dr. Curtis is professor of medicine at the University of Washington and section head of pulmonary and critical care medicine at Harborview Medical Center, both in Seattle. He had no relevant financial disclosures.

In response to one meeting attendee's comment that, "in our ICU, if we have another thing to do, many feel our heads will explode," Dr. Guntupalli replied, "I understand. We are all under pressure and time constraints. My advice is to pick the highest-risk or highest-volume patients … and identify your priorities."

Dr. Guntupalli is a professor and chief, pulmonary/critical care and sleep section, at the Baylor College of Medicine in Houston. She had no financial disclosures.

The primary goals of pay for performance should be improving health outcomes and expanding access to high-quality care. Cost reduction is an appropriate secondary goal, according to the ATS pay-for-performance working group, which will publish a statement in April in the American Journal of Respiratory and Critical Care Medicine.

CLINICIANS NEED TO DEVELOP AND IMPLEMENT QUALITY MEASURES WITHOUT ADDING TO THE BURDEN OF CRITICAL CARE PHYSICIANS.

Despite these laudable goals, Dr. Curtis cautioned about potential unintended consequences. "Improvements may come at the expense of unmeasured quality indicators." In other words, if pay-for-performance initiatives focus on a few factors that are easy to measure, it may draw attention away from other important but harder to measure components of clinical care, he said.

Other possible pitfalls of pay-for-performance initiatives are enrollment of fewer sick patients to avoid worse outcomes, upcoding of illness severity, and improved documentation without changes in quality of care, Dr. Curtis added. "There also is concern about penalizing physicians caring for minority or underserved populations. We have to make sure these initiatives do not worsen disparities," he noted.

Choice of quality measure is important. "It has to be clinically important, reliable, responsive, interpretable, and valid, especially if it is tied to pay for performance," Dr. Curtis said

Dr. Guntupalli agreed. "Basically, it does work when you take an outcome measure that is well thought out."

For example, she noted, an evidence-based intervention to decrease catheter-related bloodstream infections in the ICU successfully reduced the rate by up to 66% at 18 months (N. Engl. J. Med. 2006;355:2725-32). Dr. Guntupalli said this worked in part because "there was buy in from hospitals, buy in from MDs, and it was funded by the Agency for Healthcare Research and Quality."

"It is fair to say that pay for performance is here, and it's here to stay. The concept of reimbursing quality rather than quantity is sound," Dr. Curtis said. ■

Extended VTE Prophylaxis Helpful After Surgery

BY BRUCE JANCIN
Elsevier Global Medical News

SAN DIEGO — Two-thirds of patients placed on thromboprophylaxis after total hip or knee replacement surgery receive it for 2 weeks or less—and their venous thromboembolic event rate is markedly higher than in patients on prophylaxis for longer, according to a retrospective study of more than 3,000 patients.

Moreover, the rate of major bleeding in this study was fourfold greater among patients on prophylaxis for 14 days or less than in those on longer-term prophylaxis, contrary to the conventional wisdom that major bleeding risk rises with increasing duration of prophylaxis, Dr. Philip Wells said at the annual meeting of the American College of Chest Physicians.

The shorter-duration prophylaxis group had more than a twofold rate of deep venous thrombosis.

DR. WELLS

He reported on a study of 3,195 adults in a large U.S. managed care database who underwent total hip or knee replacement in 2004-2006 and received prophylaxis against venous thromboembolic events (VTE) with an ACCP-recommended agent for at least 1 day, beginning within 24 hours after surgery. These patients represented only 43% of hip/knee replacement patients in the database, meaning that most patients hospitalized for major orthopedic surgery did not receive any guideline-recommended VTE prophylaxis.

ACCP guidelines recommend extending thromboprophylaxis beyond 10 days and up to 35 days after total hip or knee replacement surgery, but the findings suggest that "the concept of extended prophylaxis may not have filtered into widespread clinical use," said Dr. Wells, professor of medicine at the University of Ottawa and chair of the department of medicine at Ottawa Hospital.

A total of 67% of patients received shorter-duration prophylaxis of 14 days or less. Their incidence of VTE during the next 3 months was 3.96%, significantly greater than the 1.43% rate among patients with extended-duration prophylaxis for 15 days or longer.

The shorter-duration prophylaxis group had more than a twofold rate of deep venous thrombosis, a sixfold incidence of pulmonary embolism, and a fourfold rate of major bleeding. (See chart.) These differences achieved significance, but the difference in minor bleeding rates—a 3.91% incidence with shorter-duration prophylaxis vs. 2.98% with extended prophylaxis—did not.

Upon adjustment for potential confounders including age, baseline comorbidity, and oral vs. injectable prophylaxis, extended-duration prophylaxis remained advantageous. The adjusted risk of VTE with extended prophylaxis was 60% lower than with shorter-duration therapy. The adjusted risks of pulmonary emboli and major bleeding in the extended prophylaxis group were one-fifth and one-quarter, respectively, of those who had shorter-duration prophylaxis.

When outcomes were compared between the 831 patients who received more than 21 days of thromboprophylaxis and those with 1-21 days of prophylaxis, extended prophylaxis still provided significant advantages. These included deep venous thrombosis and pulmonary embolism rates of 1.2% and 0.12%, respectively, compared with 2.7% and 1.06% in patients who had up to 21 days of prophylaxis.

A total of 58% of major bleeding events in the shorter-duration prophylaxis group occurred during the first 3 weeks post surgery, and roughly half of these early major bleeds happened in the first 2 days.

Dr. Wells said his first thought in looking at the data was that the increased VTE rate in patients with shorter-duration prophylaxis was related to the higher bleeding rate in this group. Perhaps, he reasoned, when patients had a bleeding event, their prophylaxis was stopped, with a resultant increase in clotting events. But this proved not to be the case. Even when he excluded all patients who had a major bleeding event, there was still a significant difference in VTEs between the shorter- and extended-duration prophylaxis groups.

"It wasn't that the bleeders were the ones getting the clots. Shorter-duration prophylaxis definitely seems to be associated with a higher risk of clotting," according to Dr. Wells.

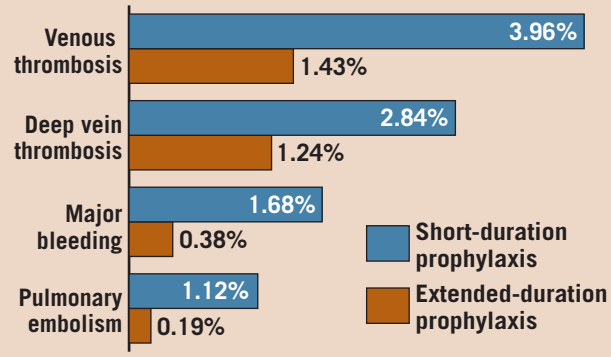
Several audience members expressed frustration that decisions about postsurgical VTE prophylaxis is typically rest in the orthopedic surgeons' hands.

The audience members complained that many surgeons are reluctant to employ the guideline-recommended prophylaxis because if a patient on prophylaxis develops bleeding, it will be laid at the surgeon's doorstep.

"These data show that in actual life, bleeding is not a risk with extended prophylaxis. The surgeons make the decision. All you can do is show them the information and hope they believe it. It's their patient. But if they don't believe real data, what can I say?" Dr. Wells replied.

The study was funded by Johnson & Johnson and Bayer Corp. Dr. Wells serves as a paid consultant to and is on the speakers bureaus for both firms. ■

Postsurgical Thromboembolic Event Rates Drop With Longer Prophylaxis

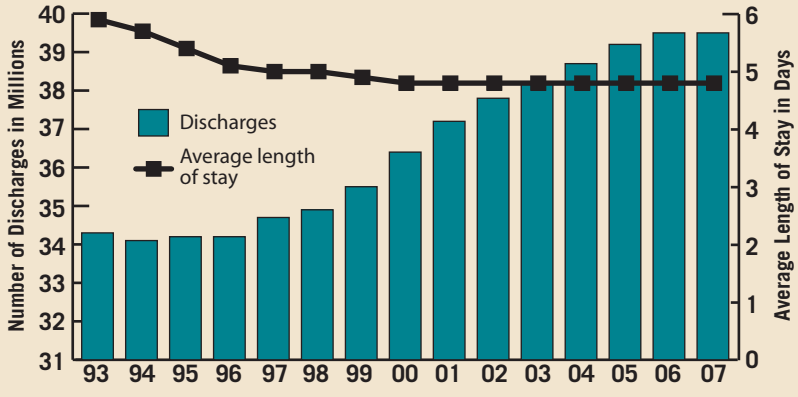


Note: Based on a retrospective study of 3,195 adults.
Source: Dr. Wells

ELSEVIER GLOBAL MEDICAL NEWS

DATA WATCH

Average Length of Inpatient Stays Stabilized in 2000; Number of Stays Continued to Rise



Note: Based on data from the Nationwide Inpatient Sample. From 1998 to 2006, growth in the number of discharges exceeded population growth.
Source: Agency for Healthcare Research and Quality

ELSEVIER GLOBAL MEDICAL NEWS

New Drugs for CF Enter Trials

Pipeline • *from page 1*

definitive, 48-week, phase III clinical trial whose primary end point is change in forced expiratory volume in 1 second (FEV_1). Only about 10% of CF patients have the type of class I mutation for which ataluren will be effective, but in these patients, it is likely to bring major benefits.

VX-809 (Vertex Pharmaceuticals Inc.) is a CFTR corrector that works on class II mutations, such as F408del. "This is huge, because we have so many patients with that mutation," Dr. Anderson observed. VX-809 allows the CFTR protein to be released from the endoplasmic reticulum and move to the apical membrane. It is now in phase II studies.

VX-770 (Vertex) is a CFTR potentiator rather than a corrector. It opens chloride channels and overcomes class III mutations. The drug is now in phase III clinical trials. In a phase II study, it resulted in improved sweat chloride and FEV_1 in patients with the relatively uncommon G551D mutation.

► **Airway surface liquid enhancers.** Denufosol (Inspire Pharmaceuticals Inc.) is the agent furthest along in this category. It improves viscous airway liquids by working through the P2Y receptor to increase chloride secretion. In phase II studies, denufosol improved FEV_1. The drug, which is inhaled three times daily, is now nearing completion of phase III trials.

► **Osmotic therapy.** This type of treatment is designed to improve mucociliary clearance and decrease CF exacerbations. Hypertonic saline aerosol 7% is an agent approved for this purpose that is already widely used in adults and older children; first-ever trials in infants are ongoing.

Inhaled mannitol (Bronchitol, Pharmaxis Ltd.) is a novel, inhaled dry powder. This medication is in phase III CF trials, and also is under study for the treatment of non-CF bronchiectasis.

► **Anti-inflammatory agents.** These drugs are the holy grail of CF therapy, according to Dr. Anderson. The inflammation of CF is neutrophilic and has a large number of mediators.

Numerous agents are in phase I and II studies, including simvastatin, inhaled glutathione, pioglitazone, sildenafil, oral *N*-acetylcysteine, docosahexaenoic acid, and GlaxoSmithKline's SB 656933. It is too early to tell whether any of them will be beneficial.

"Right now, high-dose ibuprofen is the only recommended therapy, and it's not in widespread use, mainly because of toxicities and dosing issues," Dr. Anderson said.

The median life expectancy of patients with CF now stands at 37 years. Audience member Dr. Daniel Schidlow, professor of pediatrics at Drexel University, Philadelphia, predicted that "a really good anti-inflammatory drug for CF would probably prolong our patients' lives by another 20 years.

"That's the silver bullet in 2010: a corticosteroid-like drug in its efficacy, but without the side effects," added Dr. Schidlow, who is also physician-in-chief at St. Christopher's Hospital for Children, Philadelphia.

'A REALLY GOOD ANTI-INFLAMMATORY DRUG FOR CF WOULD PROBABLY PROLONG OUR PATIENTS' LIVES BY ANOTHER 20 YEARS.'

► **Inhaled antimicrobials.** Here the pipeline is particularly plentiful. And that's good news, as at present the sole approved agent for use in CF in the United States is inhaled tobramycin solution (TOBI).

Inhaled aztreonam lysine (Cayston, Gilead Sciences Inc.) is probably closest to hitting the U.S. market. It is already approved in the EU and Canada, and is now under review at the FDA. In published studies, Cayston improved FEV_1, bacterial density, and quality of life scores. It is administered three times daily.

Colistimethate sodium (Colobreathe, Forest Laboratories Inc.) is under review in the EU, having completed phase III trials. Tobramycin inhaled powder (Novartis) is a once- or twice-daily drug that has also completed phase III trials.

Liposomal amikacin (Arikace, Transave Inc.) has completed phase II studies. Its once-daily dosing is a strong plus. This agent appears to penetrate biofilms, which would be a boon in pseudomonal infections. Inhaled levofloxacin (Aeroquin, Mpex Pharmaceuticals Inc.) also has finished phase II testing.

Inhaled fosfomycin/tobramycin (Gilead) is a twice-daily agent with broad-spectrum coverage that is in ongoing phase II studies. Ciprofloxacin also is undergoing phase II trials.

Many of the investigational agents are delivered by the novel eFlow nebulizer (PARI Pharma GmbH), a battery-powered, portable device that can give a dose of medication in about 3 minutes.

"I'm hoping that in the future we won't have to throw IV antibiotics in a nebulizer and use them [off label] without any advanced testing of the effects in the lungs or dosing," Dr. Anderson said.

► **Gene therapy.** It's not dead, but it has proved much more difficult than imagined. Indeed, the only clinical trial of gene therapy for CF going on anywhere is a 3-year, 100-patient U.K. study that is testing the viability of a plasmid DNA formulation.

There is a sense within much of the research community that modulation of the CFTR mght be a more effective way of addressing the underlying disease defect than is gene transfer, Dr. Anderson said. Agents such as ataluren and VX-809 are among the earliest viable examples of pharmacogenetics, in which specific drugs are designed to address different types of mutations.

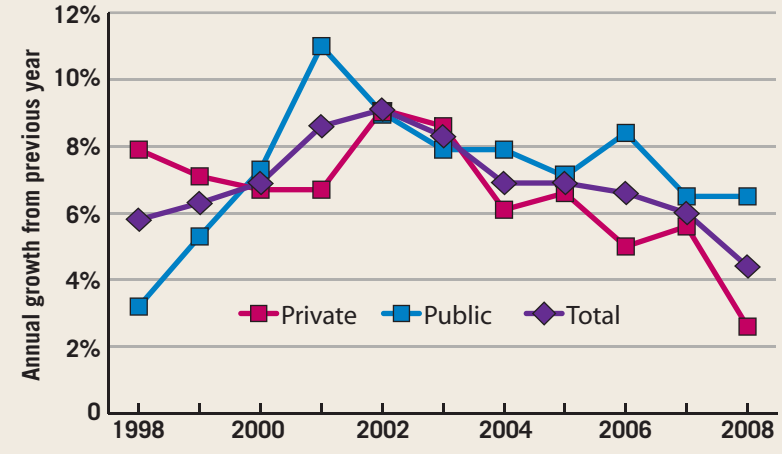
It's worth noting, however, that nearly 1,500 mutations have been identified so far in the CF gene since it was first described in 1989.

Dr. Anderson disclosed that she serves on the advisory board of Bayer Healthcare Pharmaceuticals and has received grants to conduct research on behalf of Bayer, Gilead Sciences Inc., Inspire Pharmaceuticals Inc., and the Cystic Fibrosis Foundation. ■

Dr. Philip Marcus, MPH, FCCP, comments: *Cystic fibrosis, an illness well understood mechanistically, has remained difficult to treat. We have been able to extend the life of those with the disease into early adulthood, primarily by the use of better antibiotics and mucus clearing agents. This report shows that there is greater hope for the future. Of course, agents developed for use in the CF population will extend into other populations and increase the profitability for drug development.*

DATA WATCH

U.S. Health Care Spending Growth Continues to Decelerate



Source: Centers for Medicare and Medicaid Services

Lung Cancer Setback Aids Trials of New Drug Class

BY SUSAN LONDON
Elsevier Global Medical News

CORONADO, CALIF. — Growing interest in the relationship between insulin signaling and cancer has not been dimmed by the recent failure of a phase III trial testing an insulin-like growth factor I receptor inhibitor in lung cancer.

Along with disappointment, the trial has generated information that researchers hope will improve the safety and efficacy of this class of agents, according to Dr. Michael Pollak of McGill University in Montreal.

Two dozen drugs, mainly tyrosine kinase inhibitors and antireceptor antibodies, have been developed to target the IGF-IR, Dr. Pollak told attendees at a joint conference of the American Association for Cancer Research and the International Association for the Study of Lung Cancer. About a third of them are in clinical trials.

Many human cancers, including lung cancer, express insulin receptors, IGF-IR, and hybrid receptors.

DR. POLLAK

Many human cancers, including lung cancer, express insulin receptors, IGF-IR, and hybrid receptors. "These receptors are highly homologous to the oncogenes of the tyrosine kinase class," Dr. Pollak said. Despite some toxicity, the safety data thus far have been encouraging, he said. Anti–IGF-IR antibodies have been associated with modest hyperglycemia. Unexpectedly, the tyrosine kinase inhibitors do not cause severe metabolic toxicity, even though they target insulin receptors in addition to IGF receptors. This may be because they do not accumulate in muscle, which has a high level of insulin-dependent glucose uptake.

The drug advancing furthest clinically—Pfizer Inc.'s figitumumab (CP-751,871)—is an anti–IGF-IR antibody. It showed promising activity when it was combined with chemotherapy to treat advanced squamous cell lung cancer in a phase II trial (ASCO 2009, abstract 8072). This led to the disappointing phase III trial (NCT00596830) of figitumumab with carboplatin and paclitaxel in non–small cell lung cancer that was closed early because of lack of efficacy.

One of the most plausible explanations is acquired resistance, according to Dr. Pollak. He noted that blockade of IGF-IR in normal tissues in the body induces a compensatory response leading to increased levels of growth hormone, with a resultant rise in levels of IGF-I, glucose, and insulin. "Now we have higher insulin levels, but we have not blocked the insulin receptor," he said. "So this is an obvious candidate resistance mechanism."

In the diabetes field, trials of inhaled insulin were stopped, in part, because it was linked to a higher incidence of lung cancer, Dr. Pollak further noted. "It gives us some reason to think that… insulin is relevant to lung cancer."

Tolerability was also problematic in the phase III trial, with some patients unable to withstand the hyperglycemia associated with the therapy.

Several next steps have been proposed to improve the efficacy and tolerability of IGF-IR–targeted therapy for lung cancer, said Dr. Pollak. One is to coadminister the antidiabetic agent metformin (Glucophage) or the growth hormone antagonist pegvisomant (Somavert). With one of these added drugs, "we might be able to interfere with some of these potentially undesired metabolic compensations."

Studies from the diabetes field have also found that the cancer risk in diabetics is lower among those taking metformin, "so there are many reasons these combinations deserve our attention."

To further address tolerability, trial enrollment could be restricted to metabolically robust patients, especially when the anti-IGF-IR therapy will be combined with chemotherapy and steroids, he said. Alternatively, the therapy could be combined with treatments other than chemotherapy, which would avoid the need for high-dose steroids; for example, figitumumab has been found to radiosensitize non–small cell lung cancer in preclinical testing.

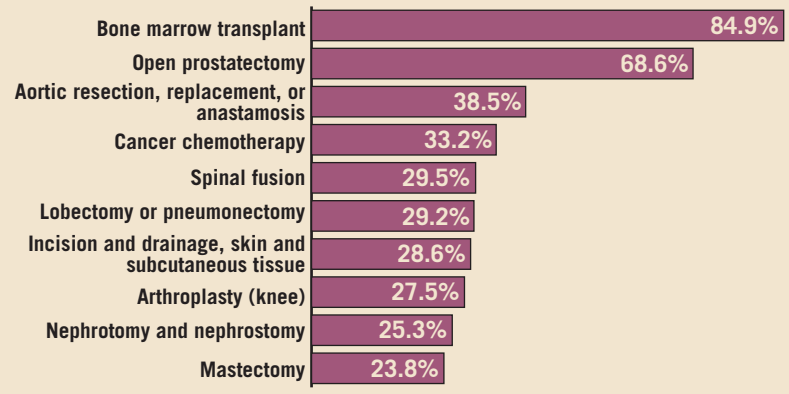
Finally, IGF-IR–targeted therapy might be improved by identifying predictors of response. To that end, preliminary data suggest that patients having a high fraction of free IGF-I in blood have the greatest improvement in outcome when they're treated with figitumumab (ASCO 2009, abstract 3539). "This is a paradigm shift in a sense, or a new kind of paradigm applicable to this target, where the predictive biomarker may not be on the tumor; it may be in the blood," Dr. Pollak observed.

Dr. Pollak reported that he had no direct conflicts of interest related to his presentation. ■

Dr. W. Michael Alberts, FCCP, comments: *Although targeted therapies have proven beneficial in some circumstances, not all such therapy or strategies are successful. While the results of trials with figitumumab are disappointing, at times, more may be learned from failed studies than from successes.*

VITAL SIGNS

Commonly Performed Procedures With the Greatest Increases in Inpatient Costs, 2004-2007



Note: Costs for 2004 adjusted to 2007 dollars using overall Consumer Price Index.
Source: Agency for Healthcare Research and Quality

ELSEVIER GLOBAL MEDICAL NEWS

Transplant Candidates Require Special Flu Management

BY MARK S. LESNEY
Elsevier Global Medical News

Guidelines issued by the International Society for Heart and Lung Transplantation recommend giving cardiothoracic transplant candidates vaccination for both seasonal and pandemic influenza A(H1N1) as soon as they become available, according to an ISHLT advisory.

Because the H1N1 virus causes a viral infection of the respiratory tract, it is especially challenging for cardiothoracic transplant teams. Surgeons and hospitals that interact with organ procurement organizations must be aware of the multiple issues involved in using organs from donor patients who have been infected and treated for the virus, according to a report published in the Journal of Heart and Lung Transplantation.

In addition, the unique needs of organ recipients and the post-transplant patient population must be taken into account in the management of both seasonal influenza and the H1N1 variant, according to Dr. Lara A. Danziger-Isakov and her colleagues for the ISHLT Infectious Diseases Council.

The guidelines present the following five categories for organ procurement decision making as well as the treatment of both donor and recipients:

► Category 1 comprises potential donors who have died of proven novel H1N1 virus, in which case neither the lung nor the heart should be used for transplant.

► Category 2 comprises potential donors with confirmed concomitant diagnosis of the novel H1N1 virus, who may be eligible to donate hearts if they have received at least 2 days of appropriate antiviral therapy. Recipients must be given appropriate antiviral drugs, and immunosuppression must be managed in the immediate postoperative period.

► Category 3 comprises potential donors who have suspect diagnosis of the virus with signs and symptoms in the donor and either strong or weak contact history. Appropriate antiviral treatment of both donor and recipient is recommended along with changes in the immunosuppression regimen. In this category, only hearts should be considered for transplant, according to the guidelines.

► Category 4 comprises donors with a previous history of novel H1N1 virus who have been treated for at least 5 days. Both the lungs and the heart may be used, and recipients should be observed clinically after the transplant, according to the guidelines.

► Category 5 comprises donors who may have been exposed to positive cases in the hospital ward or ICU. In such cases, both heart and lungs may be transplanted, but antiviral treatment of recipients may be considered until confirmatory tests are available. Immunosuppression should be treated as in category 2.

In all cases, the ISHLT recommends that all organ recovery decisions be made at the discretion of the transplanting surgeon or center and on a case-by-case basis with the assistance of an infectious disease or clinical microbiology expert (J. Heart Lung Transplant. 2009;28:1341-7).

All patients who are called in for transplant, whether they have positive symptoms or not, should be tested for the virus; transplant may proceed if the results are negative. If rRT-PCR (real-time reverse transcriptase polymerase chain reaction) testing—the ultimate test of choice—later shows that either the donor or the recipient had incubating virus, then posttransplant recipients should receive appropriate antiviral treatment and adjustments to their immunosuppression regimen.

Patients who are admitted to the hospital for non-influenza-like illnesses and who are not immediately post transplant should be treated according to the standard of care and given antiviral prophylaxis only in the case of an outbreak in the hospital, according to the report. Recipients exposed at home to close contacts may be considered for postexposure prophylaxis.

In addition, the writers said, "the transplant team can encourage and empower transplant recipients by education to protect themselves and report early illness symptoms."

The authors reported that they had no disclosures regarding this manuscript. ■

BY DR. KALPALATHA K. GUNTUPALLI, FCCP

PRESIDENT'S REPORT

Combating a Scourge to Our National Health

As health-care professionals responsible for the cardiopulmonary health of our patients, we are well aware of the toll lung cancer takes on our patients and their families.

Although we may eventually diagnose some of our patients with lung cancer, many are under our care for other smoking-related diseases, such as chronic bronchitis, emphysema, and coronary artery disease. We establish close relationships with these patients and their families, experiencing their ups and downs alongside them. It is these patients' stories that should motivate us to continue our fight against smoking and its consequences.

Take Annie, my favorite patient. Annie had emphysema and was part of our practice for many years. Although her FEV_1 barely hovered around 25%, and she knew that the damage to her lungs was irreparable, she did not lose her zest for life.

Annie started smoking while in college as a challenge from her "cool" friends. She tried to quit smoking so many times, she lost count. She was so proud when she did not smoke for a year or so.

Unfortunately, I was a mute witness to the constant struggle between her body and her mind. Even after her body was ravaged by the effects of emphysema—her legs swollen from cor pulmonale and she became wheelchair-bound—Annie continued to speak her mind and maintained a great sense of humor.

It lifted my spirits to see Annie and hear her voice on a busy day. I wondered how someone could be so full of life when faced with meager resources and deteriorating health. Annie was the first to volunteer for any of our clinical research studies and was a crowd favorite as a patient volunteer for teaching programs conducted at our facility. She loved being interviewed and would tell it like it is, especially when it came to the curses of smoking!

Once, Annie was scheduled to meet a group of visitors learning about COPD but was in the hospital with a COPD exacerbation. She still came—in her wheelchair, wearing a hospital wristband, and with her oxygen and IV pole in tow.

It was a devastating loss to me and my colleagues when she died in her sleep. Annie, I miss you! Now, there will be no Annie to say, "Dr. Kay, I will go to Washington with you and talk to those Congressmen!"

Smoking-related diseases do not spare those with higher education or success. My father-in-law, an ophthalmologist, also suffered from emphysema. I stood witness as he struggled to breathe, and his once active and athletic body was replaced with skin and bones. Eventually, the effects of smoking took their toll on the simple necessities of daily living. Emphysema took away my father-in-law's life 20 years after he had given up tobacco.

There are many celebrities and public figures who have smoked and, subsequently, succumbed to lung cancer: Peter Jennings, Sammy Davis Jr, Yul Brynner, Ed Sullivan, Groucho Marx, Walt Disney, Gary Cooper, Jesse Owens, John Wayne, George Harrison, Rosemary Clooney, Edward Morrow, and Vincent Price, to name a few. There are so many celebrity spokespersons for many diseases, and we should admire their devotion to these causes.

However, in the United States, nearly 20,000 more women die of lung cancer than of breast cancer each year. Nonetheless, only 2% of cancer research dollars is allocated to lung cancer research. This obvious disparity in funding is in part due to lack of public awareness. How is it that the public is so aware of breast cancer when more women die of lung cancer than breast cancer? Despite so many high profile celebrities dying of lung cancer, why is there no spokesperson to draw attention to this preventable cancer?

The answers, I suspect, are many.

First, celebrities do not want to publicly admit that they are ex-smokers. Second, there is no good screening tool for lung cancer. Katie Couric raised awareness of colon cancer prevention by nationally televising her own screening colonoscopy, but what test would a smoker promote?

The staggering financial, emotional, and health costs of tobacco use need to reach the forefront of the health-care debate. This is one area of preventive care that has the potential to save billions of health-care dollars.

A leader in lung cancer education, the American College of Chest Physicians has published a number of provider and patient resources related to lung cancer, including evidence-based lung cancer guidelines and tobacco prevention education materials.

Throughout the 2010: The Year of the Lung campaign, the ACCP will build on the strong foundation of its lung cancer guidelines to increase awareness regarding lung cancer prevention, diagnosis, and management.

The ACCP also will provide educational material for clinicians, patients, and patient families regarding critical care units and end-of-life and critical care family assistance programs.

The Grim Statistics

Lung cancer is the leading cause of cancer deaths in men and women in the United States and throughout the world, yet it is the least funded.

Lung cancer causes more deaths than the next four most common cancers combined, including breast, colon, pancreas, and prostate. Furthermore, of the five leading cancer killers, lung cancer has one of the lowest 5-year survival rates, second only to pancreatic cancer.

We all should be aware that in the United States, lung cancer receives just $1,200 of federal funding per death, while breast cancer receives more than $27,000 per death, followed by $14,000 for prostate cancer and $6,500 for colon cancer.

I would like to take this opportunity to invite the membership to suggest ways to start a concerted effort to at least reduce the prevalence of this evil. I very strongly believe that, together, we can make some inroads in combating this scourge to our national health. ■

How Do I ...

Download an app?
Be sure to check the ACCP Web site for the latest blogs. Steve Welch, Vice President of Publications and Editorial Resources and Executive Editor of *CHEST,* has an ongoing blog entitled, "It Ain't Rocket Surgery." One of his goals is to highlight online tools that could make your life and retrieval of information on the Web easier.

Read Steve's February 10, 2010, blog, and find out all about downloading apps: **www.chestnet.org/accp/blogs/steve%20welch.**

Get ACCP-SEEK for my iPhone?
Study on the go; no connectivity is needed to instantly access the ACCP-SEEK™ app (Pulmonary, Critical Care, and Sleep Medicine) once it is purchased. Go to **www.chestnet.org/iSEEK/** for more information or go directly to the iTunes store at **http://itunes.apple.com/us/app/accp-seek-american-college/id331597123.**

Submit an abstract for CHEST 2010?
Abstract and case report submission is FREE and EASY. Pass the word, and get those abstracts and case reports in before the May 4 deadline: **www.chestnet.org/accp/chest/call-abstracts-case-reports.**

Submit a manuscript to *CHEST*?
CHEST makes it easy to submit a manuscript for publication. Just go to the journal's Web site at **http://chestjournal.chestpubs.org,** and click on "Submit a Manuscript" in the right column.

Create your account, and you are on your way. ■

This Month in *CHEST*: Editor's Picks

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

▶ **Occurrence of Coronary Collateral Vessels in Patients With Sleep Apnea and Total Coronary Occlusion.** *By Dr. S. Steiner, et al.*

▶ **The Relationship Between Chest Tube Size and Clinical Outcome in Pleural Infection.** *By Dr. N. M. Rahman, et al.*

Special Feature

▶ **The Incidence of Dysphagia Following Endotracheal Intubation: A Systematic Review.** *By S. A. Skoretz, et al.*

ACCP Consensus Statement

▶ **Management of Dyspnea in Patients With Advanced Lung or Heart Disease.** *By Dr. D. A. Mahler, FCCP, et al.*

Commentary

▶ **The Master Settlement Agreement and Its Impact on Tobacco Use 10 Years Later: Lessons for Physicians About Health Policy Making.** *By Dr. W. J. Jones; and Dr. G. A. Silvestri, FCCP.*

www.chestjournal.org

FDA Sets New Safety Requirements for LABAs

BY DR. JAY PETERS, FCCP
Chair, Airways Disorders NetWork

Due to safety concerns, the FDA is requiring changes to how long-acting beta-agonists are used in the treatment of asthma and has planned a risk management program called "Risk Evaluation and Mitigation Strategy" (REMS) for these products (see story on page 1). The REMS will include a plan to educate health-care professionals about the appropriate use of LABAs and an updated Medication Guide for patients.

In addition, the FDA is requiring the manufacturers to conduct additional clinical trials to further evaluate the safety of LABAs when used in combination with inhaled corticosteroids. These changes are NOT based on any new information about the risk and benefits of LABAs but are based on analyses from the Salmeterol Multicenter Asthma Research Trial (SMART), the Salmeterol Nationwide Surveillance study (SNS), and a meta-analysis conducted by the FDA in December of 2008.

The FDA's meta-analysis was based on 110 studies evaluating the use of LABAs in 60,954 patients with asthma. This meta-analysis used a composite endpoint to measure severe exacerbation of asthma (asthma-related death, intubation, and hospitalization) and found an increased risk for severe exacerbation in patients using LABAs compared with those not using LABAs. The differences were primarily driven by increased rates of hospitalization, with the largest differences seen in children between the ages of 4 and 11.

Other meta-analyses evaluating the safety of LABAs in the treatment of asthma have not shown a significant increase in the risk for severe asthma exacerbations. Despite data suggesting that LABAs used in conjunction with inhaled corticosteroids are safe and reduce the overall risk of severe exacerbations, the FDA concluded that there are insufficient data to determine whether using LABAs with an inhaled corticosteroid (ICS) reduces or eliminates the risk of asthma-related death and hospitalizations.

PERHAPS IT IS BEST SEEN AS A STEP TO REINFORCE THE EVIDENCE-BASED GUIDELINES THAT HAVE BEEN DEVELOPED.

Therefore, the FDA is requiring the manufacturers of LABAs to conduct further studies evaluating the safety of LABAs when used in conjunction with an ICS.

When one reads the FDA's recommendations, it is clear that they really serve to reinforce the NAEPP and GINA guidelines (with one addition):

▶ "The use of LABAs is contraindicated without the use of an asthma controller medication such as an inhaled corticosteroid. Single-ingredient LABAs should only be used in combination with an asthma controller medication; they should not be used alone."

This applies only to asthma and not COPD, where single-agent use of LABAs has been shown to be safe and effective. Unfortunately, despite several studies demonstrating that LABA monotherapy increases the risk of asthma exacerbation, a recent publication showed that over 10% of primary care physicians still consider LABAs alone as the initial therapy for asthma (Karpel et al. *Ann Allergy Asthma Immunol.* 2009;103[4]:304).

▶ "LABAs should only be used long-term in patients whose asthma cannot be adequately controlled on asthma controller medications."

This applies to the concept of "step-up" therapy and suggests mild, easy to control asthma should be treated with a single controller agent, and the patient's use of albuterol should be monitored to assess the need for combination therapy.

▶ "LABAs should be used for the shortest duration of time required to achieve control of asthma symptoms and discontinued, if possible, once asthma control is achieved. Patients should then be maintained on an asthma controller medication."

This applies to the principle of "step-down" therapy that is probably underutilized in the care of patients who have been stable for 3-6 months on combination therapy.

The one new recommendation is based on the concern that the potential risks of LABAs may be greater in the pediatric population. The FDA now recommends:

▶ "Pediatric and adolescent patients who require the addition of a LABA to an inhaled corticosteroid should use a combination product containing both an inhaled corticosteroid and a LABA, to ensure compliance with both medications."

This addresses the issue that patients prescribed a LABA and ICS in separate devices (based on reduced acquisition costs) may have a tendency to underutilize their ICS.

It is clear that the FDA's decision to impose new warnings regarding the use of LABAs will raise both controversy within the medical community as well as questions from our patients.

Perhaps it is best seen as a step to reinforce the evidence-based guidelines that have been developed and a call for additional well-designed studies to further document the safety of LABA/ICS combinations. ■

What Is the Ambassadors Group?

The Ambassadors Group is open to American College of Chest Physician (ACCP) members' families and other committed individuals interested in furthering the goals of The CHEST Foundation, the philanthropic arm of the ACCP. Our members participate in activities aimed at improving patient care and lung health at the local level.

During the past year, the Ambassadors Group has accomplished the following:

▶ Helped The CHEST Foundation develop the "Lung Lessons℠: A Presenter's Guide" DVD to inform members how to present tobacco prevention information and good lung health practices to elementary schoolchildren.

▶ Partnered with the AMA Alliance and their project, Screen Out! that focuses on writing letters and acquiring signatures on petitions to be mailed to movie producers who allow smoking to be included in their movies, even though these movies are rated PG. The intent of this program is to raise the rating of these movies to R.

▶ Donated to support the fourth Ambassadors Group Humanitarian Award. This $5000 award was presented to Martin L. Bauer, MD, FCCP, for his project *Child Care and Conference for Parents Support Group of the Arkansas Center for Technology-Dependent Children* in Little Rock, AR.

▶ Sponsored a poster contest for children, with the winning design displayed on the CHEST 2009 5K Lung Health Walk/Run T-shirts, posters displayed at CHEST 2009, and the cover for the ACCP's 2009 holiday card.

▶ Participated in the ACCP Industry Advisory Council and The CHEST Foundation's Community Outreach Event held at Sycamore Canyon Elementary School, in Santee CA, during CHEST 2009.

The Ambassadors Group dues has remained the same for the past 4 years:

▶ $50 for US and Canadian members

▶ $35 for international members, and

▶ $10 for high-school and college-age youth

Members of The Ambassadors Group (except ACCP members, eg, physicians) are entitled to all the benefits of guests at the annual CHEST meeting without the guest fee! ■

Join the Ambassadors Group Today!
Volunteering. Educating. Networking.
Visit: **www.chestfoundation.org/foundation/ambassadors/index.php**

Meet the Ambassadors Group Chair: Jay Guntupalli, MD

In a seaside town on the east coast of India on the day before India's independence, Jayarama Guntupalli was born. When he was very young, his parents moved to Hyderabad in central India. His two sisters settled in India. After completing his basic education, he attended Osmania Medical College in Hyderabad, where he met his future wife, Dr. Kalpalatha Guntupalli, FCCP, ACCP's current President. Since he and his wife believed in securing the best medical education available, they traveled to the United States in 1973 to continue their education.

COURTESY ACCP

Dr. Jay Guntupalli is welcomed by Susan Mathers, outgoing Ambassadors Group Chair.

Both Jay and his wife pursued internal medicine residencies in Washington, DC. Dr. Kay Guntupalli joined the University of Pittsburgh as a fellow in critical care medicine after completing her fellowship in pulmonary medicine. Dr. Jay Guntupalli joined the University of Michigan Medical School as a fellow in nephrology. Traveling 330 miles each weekend to be together only further enhanced their commitment to each other and to their dedication to the practice of medicine.

Both Drs. Guntupalli now work as full-time faculty at Baylor College of Medicine in Houston. They have two sons who are both physicians-in-training. Among Jay's interests, reading is tops, and he has a collection of nearly 1,000 books in his personal library.

During his year of serving as the Ambassadors Group chair, he plans to continue to support The CHEST Foundation's antitobacco education program and work toward making the Ambassadors Group financially self-sufficient. He and his team of volunteers have already gone into 11 schools in India that range from 200 to 500 students each, to bring the antitobacco message using lung models and slides with the anti-smoking messages. ■

Dr. Gerald L. Baum Leaves Lasting Legacy

COURTESY ACCP

Dr. Baum (right) receiving his Master Fellow Award from then ACCP President, Dr. Mark Rosen, FCCP.

From his ambassadorial work and membership recruitment in the Middle East, to his many publications and leading textbook of pulmonary diseases, to his outstanding service to the ACCP throughout many years, Dr. Gerald L. Baum, Master FCCP, has left a legacy of commitment, leadership, and eminence in clinical practice and contributions to medical research. Dr. Baum passed away in Israel, January 11, 2010.

Dr. Baum was Medical Director (Emeritus), Israel Lung Association; and Emeritus Professor of Medicine, Sackler School of Medicine, Tel Aviv University. A member of numerous medical organizations where he had held leadership positions, Dr. Baum served the ACCP in several areas: he was the ACCP College Medalist in 1989 and participated on the Ethics Committee, *CHEST* Editorial Board, and the Palliative and End-of-Life Care NetWork. He was awarded Master Fellowship from the College in 2007.

A consummate ambassador of good will, Dr. Baum worked tirelessly to teach and help others everywhere he went. He initiated many projects and training activities with Palestinian and other international chest physicians and will be remembered as an exemplary role model for establishing good relationships built with the profession of medicine as a common ground. ■

Measuring the Value of The CHEST Foundation's Awards Program

Humanitarian Project Development Grant

Gregory Efosa Erhabor, MBBS, FCCP, was the recipient of one of the $25,000 Project Development Grants in 2008. The name of his project was the "Asthma Campaign in Ile-Ife, Osun State, Nigeria."

Dr. Erhabor reported that The CHEST Foundation Award has contributed immensely to accelerating the work of the Asthma and Chest Care Foundation within the Ile-Ife community and the whole Osun State.

The award funds were used to sponsor comprehensive education seminars that taught the recognition of the symptoms and signs of asthma, the prevention of acute asthma attacks, and patient self-management of asthma.

Among the seminar attendees were physicians, nurses, nursing students, medical students, health-care professionals, and patients with asthma. Funds were also used to print and distribute asthma education brochures and distribute peak flow meters and medications to treat asthma.

Dr. Erhabor says, "Notable within the last year, acute asthma emergencies have been reduced to bare minimum, and mortality from this disease has not been reported."

Clinical Research Awards

Christopher G. Slatore, MD, FCCP, Assistant Professor of Medicine in the Division of Pulmonary & Critical Care Medicine, Portland VA Medical Center, Health Services Research & Development, Portland, OR, was the 2008 recipient of The CHEST Foundation and the LUNGevity Foundation Clinical Research Award in Lung Cancer.

His project was "The Association Between Incident Lung Cancer and Hormone Replacement Therapy in a Large Cohort."

His specific aims were the following: (1) to evaluate the association between incident lung cancer and hormone replacement therapy overall and for estrogen alone and estrogen plus progestin among postmenopausal women; (2) to evaluate the association between incident lung cancer and hormone replacement therapy among postmenopausal women stratified by phytoestrogen intake; and (3) to evaluate the association between different histologic types of incident lung cancer and hormone replacement therapy among postmenopausal women.

He has completed the first year of his 2-year award.

Dr. Slatore writes, "I want to thank The CHEST Foundation and the LUNGevity Foundation for this award granted in 2008. It has provided the needed funds to support my research project. This grant has also assisted me in securing a position as Assistant Professor at the Oregon Health and Science University.

"In evaluating the association of hormone replacement therapy with lung cancer incidence, preliminary results show a small increased risk of lung cancer with long-term use of estrogen plus progestin, a finding that has the potential to affect millions of women and will deserve publication in a high-impact journal.

"In addition, we also plan to evaluate another important concern of patients with lung cancer—the stage of diagnosis." ■

The CHEST Foundation Welcomes New President-Elect

Dr. Stephanie M. Levine, FCCP, began her 1-year term as The CHEST Foundation's President-Elect at CHEST 2009. Dr. Levine has been a committed trustee of The Foundation since 2005.

In addition to the many ACCP offices Dr. Levine has held over the years, she also serves The CHEST Foundation as a member of The Foundation's Awards Committee, becoming the Chair of this important committee in 2006. Under her leadership, The CHEST Foundation's Clinical Research Awards Program has expanded to offer more diverse opportunities for ACCP members. She also spearheaded the conversion of the awards application process to be available solely online at http://mc.manuscriptcentral.com/chest2010, beginning this year.

Dr. Levine will assume the Presidency of The CHEST Foundation following the October 2010 CHEST meeting. Dr. John C. Alexander, Jr., FCCP, will transition to the role of Chair of the Board of Trustees in November 2010.

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