Proteomic analysis can uncover specific protein clusters that are differentially expressed in the urine of children with obstructive sleep apnea.

Background/Objective: Because of the relative expense, inaccessibility, and labor-intensive nature of sleep studies, the authors examined whether the urinary proteome uncovers specific clusters that are differentially expressed in the urine of children with obstructive sleep apnea (OSA).

Methods: 2-dimensional differential in-gel electrophoresis (2D-DIGE) and mass spectrometry proteomics was followed by validation with western blot ELISA testing. Morning urine proteins from 60 children with polysomnographically confirmed obstructive sleep apnea and from match children with primary snoring (n=30) and control subjects (n=30) were examined.

Results: A total of 16 proteins that are differentially expressed in OSA were identified, and 7 were confirmed by either immunoblots or ELISA. Among the latter, receiver-operator curve analyses of urinary concentrations of uromodulin, urocortin-3, orosomucoid-1, and kallikrein demonstrated favorable predictive properties to these proteins. Furthermore, combined approaches indicated that the presence of values beyond the calculated cutoff concentrations for 3 or more of the proteins yielded a sensitivity of 95% and a specificity of 100%.

Conclusions: Pediatric OSA is associated with specific and consistent alterations in urinary concentrations of specific protein clusters. Further studies aiming to validate this approach as a screening method of habitually snoring children appear warranted.

Reviewer's Comments: Proteomics is defined in the Merriam-Webster Medical Dictionary as "a branch of biotechnology concerned with applying the techniques of molecular biology, biochemistry, and genetics to analyzing the structure, function, and interactions of the proteins produced by the genes of a particular cell, tissue, or organism, with organizing the information in databases, and with applications of the data (as in medicine or biology)." We are seeing the genesis of a new application, based on a simple urine test, which may hold the promise of saving profound financial resources in the evaluation of children suspected of having OSA. Whether this information will prove generalizable to adults is yet to be demonstrated. (Reviewer-A. Gray Bullard, MD).
Objective: To evaluate the effect of adjuvant radiation therapy on outcomes in patients treated with sublobar resection for non-small cell lung cancer (NSCLC).

Methods: 32,751 cases were identified between 1988 and 2003 from the Surveillance, Epidemiology, and End-Results (SEER) database who had stage T1-2N0M0 NSCLC. All were ≥20 years old. Histologies were reviewed. Exclusion criteria included brachytherapy, refusal of adjuvant radiation therapy and unknown status of radiation therapy. A total of 5908 cases were identified that underwent sublobar resection. Variables reviewed were age, gender, laterality, race, era of treatment, number of nodes examined, tumor size, histology, grade, and distal involvement of the mainstem bronchus. End point was death from any cause. The disease-specific end point was death from coding of "Lung and Bronchus." Other causes of death were censored.

Results: 493 patients (8.3%) received external beam radiation therapy (XRT). The median follow-up was 40 months. The median survival was 49 months, but 31 months for those receiving XRT and 51 months for those not receiving XRT. Survival rates at 1, 3, and 5 years were higher for those not receiving XRT. The median disease-specific survival was 91 months, 45 months for those receiving XRT and 98 months for those not receiving XRT. Again, 1-, 3-, and 5-year survival rates favored those not receiving XRT. Although gender, race, era of treatment, histology, tumor grade, tumor size, bronchus involvement, number of nodes examined, and use of XRT were all survival predictors, the use of XRT was the most significant of these.

Conclusions: XRT as adjuvant therapy in patients undergoing sublobar resection for NSCLC reduces survival.

Reviewer's Comments: This is a very nice study. Would data from 2003 to 2010 be the same? This study reminds us that comorbidities, as well as treatment modalities, must be considered when recommending therapy to patients who cannot tolerate lobectomy. Quality of life after treatment and the cost of treatment are important in this group. (Reviewer-Allan R. Goldstein, MD).

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Keywords: Early-Stage Lung Ca, Sublobar Resection, Survival, Radiation Tx

Print Tag: Refer to original journal article
The use of ipratropium bromide has been associated with an increased risk of adverse CVEs.

**Background:** In 2002, the Lung Health Study Research Group reported on patients who had been prescribed ipratropium bromide when compared to placebo and exhibited a trend toward increased cardiovascular mortality and supraventricular tachycardia that necessitated hospitalization. Subsequently, additional studies also suggested an association between adverse cardiovascular events (CVEs) and the use of ipratropium bromide.

**Objective:** To evaluate the possible relationship between the use of ipratropium and CVEs.

**Design:** Cohort study of 82,717 U.S. veterans.

**Design/Methods:** The authors performed a cohort study of >82,000 U.S. veterans with a new diagnosis of COPD established between 1999 and 2002. They again utilized the Veteran's Health Administration healthcare database. After a diagnosis was established, the patients were followed until a hospitalization for CVEs, death, or the end of the study in September 2004. The CVEs were acute coronary syndrome, heart failure, or cardiac arrhythmia. Patients were classified as exposed if they had been given anticholinergics during the year prior to an adverse CVE. Cumulative exposure was calculated as the number of standard 30-day equivalents of inhaled anticholinergics potentially used during the past year.

**Results:** 6,200 CVEs that occurred during the study period were identified. Exposure to anticholinergics was associated with a 29% higher risk of CVEs over the past year when compared to no exposure to an anticholinergic. In patients whose anticholinergic exposure was within the past 6 months and the exposure was ≥4 30-day equivalents of an anticholinergic agent, there was a 40% increase in the risk of CVEs compared to no exposure. If the exposure within past 6 months was <4 30-day equivalents of an anticholinergic agent, there was a 23% increase in risk of CVEs compared to no exposure.

**Conclusions:** The authors conclude that having a prescription filled for ipratropium bromide within 6 months is associated with increased risk of adverse CVEs, which include acute coronary syndrome, heart failure, and cardiac arrhythmias.

**Reviewer's Comments:** Ipratropium bromide is a widely prescribed medication for COPD. The mechanisms by which a short-acting anticholinergic agent (ipratropium bromide) would cause an increased risk of CVEs are speculative. (Reviewer-Richard A. Nusser, MD).

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Keywords: Cardiovascular Events, Ipratropium Bromide

Print Tag: Refer to original journal article
Objective: To evaluate the hemodynamic effects of positive end-expiratory pressure (PEEP) in a more physiological manner in order to determine any additional mechanisms that might be present.

Participants/Methods: Patients were included if they met the criteria for acute respiratory distress syndrome (ARDS). All patients were receiving a tidal volume of 6 mL/kg. The PEEP was adjusted to improve oxygenation while maintaining the plateau pressure to ≤30. The respiratory rate and inspiratory-to-expiratory (IE) ratio were adjusted to avoid hypercapnia. Initially, the PEEP was set at 5 cm following which measurements were performed. Standard hemodynamic measurements were obtained from a pulmonary artery (PA) catheter, and standard hemodynamic formulas were used to make calculations. A transesophageal echocardiogram was performed in all patients at both the high and low levels of PEEP.

Results: 21 patients were included in the study. At baseline, PEEP was 5 and plateau pressure was 22. A plateau pressure of 30 was achieved by setting the end expiratory pressure to 13. The static compliance was identical at both levels of PEEP. At low levels of PEEP, 3 patients experienced acute cor pulmonale. Increasing the PEEP significantly reduced cardiac index. Oxygen delivery, therefore, fell as well. However, heart rate and mean arterial pressure were not changed significantly. Pulmonary arterial resistance increased. When PEEP was increased, 18 additional patients developed acute right heart dilation. Changes in the left ventricle were less significant. Passive leg raising resulted in improvement in cardiac output and pulmonary vascular resistance at the high level of PEEP. The effect of the low level of PEEP was significantly smaller.

Conclusions: These data suggest that in patients with ARDS, a PEEP increase, still limited by tidal volume and plateau pressure, reduced cardiac output by increasing pulmonary vascular resistance. This suggests that pulmonary microvessels were collapsed by the increased end-expiratory pressure and that the passive leg raising increased central blood volume resulting in the improvement.

Reviewer's Comments: This study is quite interesting and very well done. The most blatant criticism would be the small number of patients studied. The authors demonstrated that even following lung protective strategies for PEEP and tidal volume, hemodynamic effects can occur. They further elucidated that most likely these are due to compression of small blood vessels in the lung increasing right ventricular afterload. Increasing central blood volume by passive leg raising ameliorated these effects suggesting that volume loading might be beneficial in these patients. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: PEEP, ARDS, Hemodynamics, Volume Status

Print Tag: Refer to original journal article
Airflow limitation is common in patients with CVD/CAD; under diagnosis and under treatment are significant.

**Objective:** To determine the prevalence of airflow limitation (AL) in patients who have cardiovascular disease (CVD).

**Participants/Methods:** Male and female patients between 42 and 81 years of age were randomly selected based on the presence or absence of CVD. Exclusions included only an inability to perform pulmonary function tests (PFTs) or refusal to sign the informed consent form. Dyspnea, cough, sputum production, and previous diagnosis of chronic obstructive pulmonary disease (COPD) were determined by questionnaire. Comorbidities were determined, and body mass index (BMI) was recorded. Spirometry was performed and staged by Global Initiative for Obstructive Lung Disease (GOLD) guidelines. Statistical methods are described.

**Results:** 1113 patients from the general population and 120 patients from the hospital were originally included. Quality PFT was obtained in 51% from the general population and 73% from the hospital group. Clinical information was analyzed for 621 patients. The 3 groups were no CVD, nonhospitalized patients with CVD, and hospitalized patients with coronary artery disease (CAD). Sociodemographics and clinical characteristics differed in these groups, and the differences are reported. Dyspnea was more common in the hospitalized CAD group. Cough and sputum incidence were the same in all groups. Hospital patients and non-hospital patients with CVD had lower post-bronchodilator FEV₁ than patients without CVD. A previous diagnosis of COPD was uncommon but more frequent in the nonhospitalized CVD group. AL was seen in 18% of non-CVD patients, 19% nonhospital CVD patients, and 34% hospital CVD patients. Severity was similar in all groups. Under diagnosis was high in all groups with a range of 60% to 87%. Reasons for under diagnosis included being a former smoker, fewer symptoms, and mild AL. Under treatment was 60% in all groups. Short-acting bronchodilators were the most frequently used respiratory medications.

**Conclusions:** AL is common in those with CVD/CAD. Underdiagnosis and undertreatment are significant. The authors feel that this is correctable and recommend screening spirometry in smokers or ex-smokers with CVD.

**Reviewer's Comments:** This is a very important study. Many patients with CVD/CAD have complications of AL/COPD that go unrecognized or untreated until some medical or surgical event occurs. By then, they are a greater risk of morbidity and mortality with greater costs of care and significant reduction in quality of life. Early identification of AL could lead to fewer acute events and lower costs of care. (Reviewer-Allan R. Goldstein, MD).

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Keywords: CVD, Airflow Limitation, Prevalence

Print Tag: Refer to original journal article
Inhaled corticosteroids may not prevent exacerbations in patients with COPD.

**Objective:** Evaluation of the efficacy of inhaled corticosteroids (ICS) in preventing chronic obstructive pulmonary disease (COPD) exacerbations.

**Methods:** A meta-analysis was done of articles published between 1988 and 2008 relating to the use of ICS in COPD. Studies included were confirmed cases of COPD, had at least 1 year follow-up, were randomized controlled trials comparing ICS and placebo, and were peer reviewed publications. Items extracted included publication details, details on randomization and drop out, dosages and ICS devices used, demographics, and definition of exacerbation. Statistical methods and explanations are included.

**Results:** The final number of studies used was 11, and they encompassed 8164 patients, 4241 patients who received ICS and 3923 patients who received placebo. The mean age was 62 years, with the FEV\(_1\) being <50% in 7 of the 11 studies. The definition of an exacerbation varied between studies, but the authors felt it was consistent with the definition used in clinical practice. The pooled results showed an 18% reduction in exacerbations with the use of ICS. Using the sensitivity analysis and accounting for heterogeneity, the beneficial effect was found only in those with an FEV\(_1\) of <50%. Metaregression analysis did not show a linear relationship between FEV\(_1\) values and decline in COPD exacerbations with the use of ICS.

**Conclusions:** This study fails to show a significant reduction in exacerbations of COPD in patients using ICS as opposed to a placebo. The authors note that their results differ from previous reviews. Metaregression may account for this difference.

**Reviewer's Comments:** This study flies in the face of other studies that I have reviewed. It is also totally contrary to my personal experience with patients that I treat with ICS who have COPD. My patients have many fewer emergency department visits, hospitalizations, and unplanned office visits since on ICS. In addition, their quality of life is better. My recommendation is that dyspnea, sputum production, and sputum volume rather than FEV\(_1\) be used to guide the initiation of ICS. This study, in my opinion, should not cause pulmonologists to cease using ICS in COPD patients. I think recent industry-sponsored studies would support that recommendation. (Reviewer-Allan R. Goldstein, MD).

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Keywords: COPD Exacerbations, Inhaled Corticosteroids

Print Tag: Refer to original journal article
Confusional behavior arising from a sleep apnea patient in stage N3 (slow-wave) sleep is likely to represent a confusional arousal and is less likely to represent NFLE.

**Background/Objective:** To describe the features of arousal parasomnias and identify features that can be used to reliably distinguish parasomnias from nocturnal frontal lobe epilepsy (NFLE).

**Methods:** A systematic semiologial analysis of 120 events from 44 subjects (parasomnias and NFLE seizures recorded on video-electroencephalogram [EEG] monitoring) was undertaken to determine the presence or absence of 68 elemental clinical features in parasomnias and NFLE seizures. Qualitative and statistical analysis of behavior patterns and ictal EEG was undertaken.

**Results:** Elemental clinical features strongly favoring parasomnias included interactive behavior, failure to wake after event, and indistinct offset (all $P < 0.001$). Cluster analysis confirmed differences in the frequency and combination of elemental features in parasomnias and NFLE. A diagnostic decision tree generated from these data correctly classified 94% of events. While sleep stage at onset was discriminatory (82% of seizures occur during stage 1 or 2 sleep, with 100% of parasomnias occurring from slow-wave sleep) ictal EEG features were less useful. Video analysis of parasomnias identified 3 principal behavioral patterns: arousal behavior (92% of the events); non-agitated motor behavior (72%); and distress emotional behavior (51%).

**Conclusions:** Confusional arousals, somnambulism, and nightmares form a prototypical, hierarchical continuum of behavior patterns of NREM parasomnias.

**Reviewer’s Comments:** Confusional arousals are the mildest parasomnias and are common in obstructive sleep apnea. The others are somnambulism, sleep terrors, and sleep-related behavior related to either eating or sex, collectively known as NREM parasomnias to distinguish them from REM behavior disorder. However mild, confusional arousals can cause confusion for the physician as well as the patient. They occur during the transition between sleep and wakefulness and are characterized by disorientation, slow speech and mentation, or inappropriate behavior. Cognition is disturbed despite the motor behavior of wakefulness, resulting in complex behavior without conscious awareness. It is important to distinguish these behaviors from other types of parasomnias and especially from seizures occurring out of sleep (specifically, NFLE). Confusional arousals with an inability to attain full alertness or automatic behavior following an extended period of sleep are referred to as sleep drunkenness. Although there is usually amnesia for the event, vivid dreamlike mentation may occasionally be experienced and reported. These disorders may actually begin in adulthood, and disorders of arousal occur in up to 4% of all adults. Febrile illness, alcohol, prior sleep deprivation, emotional stress, and medications may trigger any of the disorders of arousal in susceptible individuals. It is of interest that in this study, 100% of confusional arousal events occurred out of slow-wave sleep rather than lighter stages of sleep. Furthermore, the study establishes that NFLE is most likely to occur out of stage I or II sleep, which is helpful, as ictal EEGs in NFLE are frequently nondiagnostic. (Reviewer-A. Gray Bullard, MD).

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Keywords: Parasomnia, Obstructive Sleep Apnea

Print Tag: Refer to original journal article
Reduced tumstatin in asthma is responsible for hyperresponsiveness and angiogenesis of airways.

**Objective:** To study tumstatin in airways of asthmatics and nonasthmatics and determine its role in angiogenesis and airway hyperresponsiveness.

**Participants:** 25 asthmatics and 44 nonasthmatics.

**Methods:** Studies were performed to determine levels of tumstatin in the study subjects. Studies included immunochemistry, dot blot, in vitro angiogenesis assays, and a murine model of allergic airways disease. Methodology is complex, but it is clearly and fully explained in the text.

**Results:** 10 basic findings were noted. (1) Subjects with asthma had increased angiogenesis in airways. (2) Lung and airway tissue of asthmatics were negative for tumstatin, but tumstatin was found in tissue from nonasthmatics, cystic fibrosis, chronic obstructive pulmonary disease, and bronchiectasis. (3) Vascular endothelial growth factor (VEGF) was found in asthmatic airways, but VEGF and tumstatin were both found in nonasthmatics. (4) Serum and bronchoalveolar lavage fluid (BALF) levels were similar in both groups. (5) Tumstatin inhibits primary pulmonary endothelial cell tube formation. (6) Tumstatin peptides inhibit primary pulmonary endothelial cell proliferation. (7) Tumstatin prevents angiogenesis and VEGF in a mouse model. (8) Tumstatin improves airway hyperresponsiveness in a mouse model. (9) Tumstatin inhibits airway inflammation in a mouse model. (10) Tumstatin inhibited interleukin 13 accumulation in a mouse model.

**Conclusions:** Tumstatin is an antiendogenous angiogenesis factor. Its absence allows proendogenous angiogenesis factors to be overexpressed leading to inflammation, hyperresponsiveness, and angiogenesis of asthmatic airways.

**Reviewer's Comments:** This is a very interesting and provocative study. It takes time to read, study, and understand. However, it makes one realize how little we really know about the asthmatic airway. New drugs aimed at tumstatin stability and deficiency may prevent severe problems with bronchospasm and the problems associated with remodeling. (Reviewer-Allan R. Goldstein, MD).
The use of tiotropium is associated with a decrease in all-cause mortality, cardiovascular mortality, and adverse cardiovascular events.

**Background:** Much of the literature suggesting an association between adverse cardiovascular events (CVEs) and the use of an inhaled anticholinergic have involved ipratropium. However, in a meta-analysis published by Singh and colleagues in 2008, these investigators suggested that both ipratropium and tiotropium were associated with a significantly increased risk of cardiovascular death, myocardial infarction (MI), or stroke in chronic obstructive pulmonary disease (COPD) patients.

**Objective:** To evaluate the association between the use of tiotropium and adverse events, particularly cardiovascular mortality and selected CVEs.

**Design:** Compilation of placebo, double-blind trials.

**Participants:** The Understanding Potential Long-term Impacts on Function with Tiotropium (UPLIFT) trial was a 4-year, randomized, placebo-controlled trial of tiotropium involving approximately 6,000 patients with COPD. Celli and colleagues combine the UPLIFT Trial with all other tiotropium double-blind, placebo-controlled trials that lasted at least 4 weeks. There were 30 completed clinical trials involving >19,000 patients; 8,699 patients received placebo and 10,846 patients received tiotropium. At the time of randomization, 34% of patients were smoking.

**Results:** Serious adverse events were experienced by 24% of patients. The risk of a serious adverse event was significantly lower in the tiotropium group. Tiotropium was not associated with an increased risk for serious adverse CVEs. The rate ratio for any serious cardiac event for tiotropium was 0.83, and the rate ratio for any serious cardiac event for placebo was 1.15. A rate ratio of <1 indicates a decreased risk, while a rate ratio >1 indicates an increased risk. There was a 12% reduction in the risk of experiencing a fatal adverse event in the tiotropium group relative to placebo. There was a 17% reduction in the risk of a major cardiovascular event in the tiotropium group relative to placebo.

**Conclusions:** Tiotropium is associated with a reduction in the risk of all-cause mortality, cardiovascular mortality, and adverse CVEs.

**Reviewer's Comments:** It has been suggested that the short-acting anticholinergic agents might be more frequently overused by patients. These data would suggest that tiotropium is the preferred anticholinergic agent. (Reviewer-Richard A. Nusser, MD).

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Keywords: Drug Safety, Tiotropium

Print Tag: Refer to original journal article
Tiotropium is associated with decreased mortality in patients with COPD.

**Objective:** To describe the effect of tiotropium on survival in patients with chronic obstructive pulmonary disease (COPD).

**Design/Participants:** 4-year, randomized double-blind, placebo-controlled study in COPD patients.

**Methods:** All usual medications, except inhaled anticholinergics, were allowed. Primary outcomes were yearly reduction in pre- and post-bronchodilator pulmonary function tests (PFTs) until the end of the double-blind treatment. Secondary end points were quality-of-life (QOL) score, COPD exacerbations and related hospitalizations, and mortality. Participation was based on diagnosis of COPD, age ≥40 years, a minimum of a 10-pack year smoking history, post-bronchodilator FEV₁ <70%, and FEV₁/FVC <70%. After the baseline visit, the patients were seen at 1 and 3 months and then every 3 months for a total of 4 years. All usual medications and the trial drug were used for 1440 days. At that time, the study drug was stopped and tiotropium given at 2 actuations 4 times a day for 30 days. Patients were then evaluated. This paper was devoted to evaluating the effect of tiotropium on mortality, which was determined at 45 to 49 months. Adverse effects, serious or fatal, were recorded. Spirometry was performed at baseline, at 30 days, and then every 6 months until the study ended. Exacerbation was defined, and all episodes were recorded.

**Results:** 3006 placebo and 2987 treatment patients were included. Baseline demographics have been previously reported. Mean age, FEV₁, smoking incidence, discontinuation rate, and baseline medications are again noted. Tiotropium-treated patients had a significantly lower mortality rate than placebo patients. This finding was consistent across subgroups except for body mass index. The most common causes of death were lower respiratory disorders, lung cancer, and general disorders including cardiac disease.

**Conclusions:** In addition to previous reports relating a reduction in COPD exacerbations with tiotropium use, this study showed a reduction in mortality associated with that drug. QOL improvement is again noted.

**Reviewer's Comments:** This paper should further justify the use of tiotropium in COPD. Of course, the proper patients, nonemphysema predominant, should be our focus. Improved QOL, reduced mortality, fewer exacerbations — sounds like a winner. (Reviewer-Allan R. Goldstein, MD).

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Keywords: Tiotropium, Effects, Mortality

Print Tag: Refer to original journal article
Patients with restrictive lung disease should be afforded pulmonary rehabilitation.

**Objective:** To assess the effectiveness and feasibility of pulmonary rehabilitation in patients with restrictive lung disease (RLD).

**Participants:** Patients studied were >18 years old, clinically stable, had an FEV1 <60%, and met 2 of the following criteria: maximum workload (Wmax) <90 W, 6-minute walk distance (6MWD) <70%, <100 points on the Chronic Respiratory Questionnaire or <20 points on the domain dyspnea, a quadriceps force (QF) <70%, or an inspiratory or expiratory muscle force of <70% (PImax, PEmax, respectively). Excluded were patients with cancer or cardiac, neurologic or orthopedic illnesses that limited exercise. Demographics and functional variables were measured at baseline, 12 weeks, and 24 weeks. Studies performed were complete pulmonary function tests (PFTs), maximal exercise capacity, PImax and PEmax, QF, and dyspnea. The rehabilitation program was a maximum of 60 sessions over 24 weeks. Sessions included 90 minutes of reconditioning and 30 minutes of occupational therapy (OT), nutritional support, patient education, or psychological support. The exercise program is clearly described in the article as are the data analysis methods.

**Results:** Diagnoses of the patients are noted. 6MWD, maximal oxygen consumption, Wmax, QF, PImax, and PEmax all improved at 12 and 24 weeks relative to baseline. Dyspnea, fatigue, and emotion all showed improvement. Patients who required oxygen due to exercise desaturation did not differ from those not requiring oxygen relative to outcome. In those with chest wall deformity, the 6MWD did not improve to the same degree as the interstitial lung disease group but did improve significantly. All other measurements were similar in the 2 groups.

**Conclusions:** In this prospective, nonrandomized, noncontrolled study, dyspnea, fatigue, emotional status, and exercise ability improved over time. Interstitial lung disease and chest wall diseases both benefitted.

**Reviewer’s Comments:** This is an intriguing study. It demonstrates that pulmonary rehabilitation is valuable as a treatment tool not only in COPD but also in restrictive lung diseases. One might criticize the noncontrolled, nonrandomized protocol, but the results should be of interest to all clinicians and to those looking for ways to reduce unscheduled office visits, emergency department visits, and hospitalizations. Further study looking at those parameters is indicated. (Reviewer-Allan R. Goldstein, MD).

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Keywords: Restrictive Lung Dz, Pulmonary Rehabilitation, Effects

Print Tag: Refer to original journal article
In the ICU, compliance with hand hygiene and glove-and-gown procedures may be good, but improvements may be needed in adequate backrest elevation, tracheal cuff pressure, and oral hygiene to prevent VAP.

**Background:** Evidence-based guidelines aimed at the prevention of ventilator-associated pneumonia (VAP) in the ICU are often poorly implemented. Whether educational and other interventions improve long-term compliance with these guidelines is not known.

**Objective:** To determine the long-term impact of a multifaceted intervention program on compliance with measures to prevent VAP in the ICU.

**Design:** Prospective observational study of compliance with preventive measures both before and after implementation of an intervention program for the medical ICU of a teaching hospital in France.

**Methods:** The intervention program included a task force, educational sessions, performance observations (with feedback), technical improvements, and reminders. Compliance with VAP preventive measures was assessed before the intervention and at 1, 6, 12, and 24 months after implementation of the intervention. The intervention program involved all health-care workers in the medical ICU.

**Results:** 1649 ventilator-days were observed. Of the 102 staff members who completed the educational portion of the intervention, 84 were still working in the ICU after 12 months. Compliance with hand-hygiene and glove-and-gown procedures was high at baseline and remained high throughout all post-intervention assessments. The intervention program was associated with significant improvements in compliance with adequate backrest elevation (baseline compliance, 5%; 24-month compliance, 58%), maintenance of adequate tracheal cuff pressure, adequate oral hygiene with chlorhexidine, orogastric tube use (rather than nasogastric tube use), avoidance of gastric overdistention, and elimination of nonessential tracheal suction. The prevalence rate of VAP decreased 51% after implementation of the intervention in this ICU.

**Conclusions:** A multifaceted intervention program aimed at improving simple clinical processes associated with VAP reduction can provide significant improvements in infection control. Compliance with VAP prevention measures depends on the bedside performance of health-care workers in the ICU. A multidisciplinary approach to improving compliance can provide long-term success.

**Reviewer's Comments:** This study demonstrates what has been noted before, that adherence to guidelines will be poor unless there is a unit or hospital wide effort for implementation. Just writing the guidelines does not make them happen. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Ventilator-Associated Pneumonia, Prevention, Compliance Improvement

Print Tag: Refer to original journal article
Conjugate Vaccine Protects Against IPD in HIV Patients

A Trial of a 7-Valent Pneumococcal Conjugate Vaccine in HIV-Infected Adults.

French N, Gordon SB, et al:


A 7-valent protein conjugate pneumococcal vaccine can generate protective responses in HIV-infected adults and adolescents, even in those with baseline CD4+ counts <200 cells/mm3.

Background: Preventing invasive pneumococcal disease (IPD) in HIV-infected patients is important because it is the leading cause of death in these patients, especially in sub-Saharan Africa. The case fatality rate associated with IPD is ≥8% overall and is approximately 50% in African populations with meningitis. Vaccines are good preventive measures, but the suboptimal activity of the 23-valent pneumococcal polysaccharide vaccine has lead to the recommendation that it not be used in Africa.

Objective: To determine the clinical efficacy of a 7-valent protein conjugate vaccine in the prevention of recurrent IPD in African patients infected with HIV.

Design: Double-blind, randomized, placebo-controlled clinical trial.

Participants: 439 HIV-infected patients aged ≥15 years who resided in Malawi (in southeast Africa) and who had recovered from a confirmed episode of IPD.

Methods: Participants were randomly assigned to receive 2 doses of either 7-valent pneumococcal protein conjugate vaccine or placebo given 4 weeks apart. All participants were then evaluated at 3-month intervals for episodes of recurrent IPD. The primary end point was an episode of IPD caused by 1 of the vaccine’s serotypes. Patients were encouraged to receive antiretroviral therapy and other related care provided at public clinics.

Results: The follow-up analysis included 239 HIV-infected patients. Overall, 67 episodes of recurrent IPD occurred in 52 patients. Of these, 5 cases in the vaccinated group and 19 cases in the placebo group were caused by a serotype found in the vaccine. This translates to a vaccine efficacy of 74% in HIV-infected patients (hazard ratio, 0.26). Among HIV-infected patients with baseline CD4+ T-cell counts <200 cells/m3, the vaccine’s efficacy was 86%. On multivariate analysis, a baseline CD4+ T-cell count of 200 cells/m3 was associated with a 7.1 times increased risk of recurrent IPD compared with a baseline count of >500 cells/m3. Deaths from any cause occurred in 63 patients from the placebo group and in 73 patients from the vaccine group (hazard ratio for vaccine, 1.18). This difference in mortality was not statistically significant.

Conclusions: The 7-valent protein conjugate pneumococcal vaccine prevents 74% of recurrent episodes of IPD caused by vaccine serotypes in HIV-infected patients. The risk of recurrent IPD is highest in HIV-infected patients with a baseline CD4+ T-cell count of 200 cells/m3. The vaccine did not appear to significantly affect the mortality rate.

Reviewer’s Comments: It is interesting that despite reducing the likelihood of getting a common form of pneumonia, there was no change in the overall mortality. Does this mean that preventing one cause of death in this group exposes them to another? (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Invasive Pneumococcal Disease, Prevention, Vaccination

Print Tag: Refer to original journal article
Concomitant HIV, TB Therapies Improve Survival

Timing of Initiation of Antiretroviral Drugs During Tuberculosis Therapy.

Abdool Karim SS, Naidoo K, et al:


In patients coinfected with HIV and TB, concomitant antiretroviral and TB therapies reduce the mortality rate by 56%. Current WHO guidelines should be expanded to include cotreatment of HIV and TB in selected patients.

Background: The number of HIV patients coinfected with tuberculosis (TB) is increasing rapidly, and TB coinfection is the most common cause of death in HIV patients in developing countries. Guidelines from the World Health Organization (WHO) recommend treating the 2 diseases at the same time (concomitant or integrated therapy). However, antiretroviral therapy is sometimes delayed until after TB treatment is completed due to worries about drug interactions. The effect that deferred antiretroviral therapy has on mortality for patients coinfected with HIV and TB is unknown.

Objective: To determine the mortality rates associated with deferred antiretroviral therapy versus concomitant antiretroviral and TB therapy in patients coinfected with HIV and TB.

Design: Open-label, randomized, controlled trial.

Participants: 643 patients coinfected with HIV and TB who underwent treatment in Durban, South Africa.

Methods: Patients were randomly assigned to 1 of 3 treatment protocols, which included initiation of antiretroviral therapy at 4 weeks after start of TB therapy (early integrated-therapy group), at 4 weeks after completion of intensive phase of TB therapy (late integrated-therapy group), or at 4 weeks after completion of TB therapy (sequential-therapy group). For 24 months, patients were evaluated monthly for adherence to antiretroviral therapy and for clinical status. CD4+ cell counts, radiologic changes, and sputum conversion were monitored at regular intervals and when clinically indicated.

Results: Baseline age, CD4+ cell counts, and HIV RNA levels were similar for all treatment groups. At the end of the study, 134 patients had completed follow-up, 338 were still being followed up, and 52 had died (8.1%). The median follow-up was 12.1 months. Adherence rates for antiretroviral therapy were approximately 97% in both groups. The mortality rate was approximately 5.4 deaths/100 person-years in the integrated-therapy groups and approximately 12.1 deaths/100 person-years in the sequential-therapy group. The hazard ratio in the combined integrated-therapy groups was 0.44, reflecting a 56% reduction in the mortality rate.

Conclusions: In patients coinfected with HIV and TB, the survival rate is significantly better with concomitant antiretroviral and TB therapy than with deferment of antiretroviral therapy until after the completion of TB therapy.

Reviewer's Comments: Nice, simple study that discloses the best way to handle the problem of concomitant TB and HIV disease. Not surprising that starting antiretroviral treatment right away improves outcomes. Prior study in the ICU demonstrated the same thing. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: TB & HIV Coinfections, Antiretroviral Therapy, Timing

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**A Little Dietary Salt Reduction Gives Large Benefits**

*Projected Effect of Dietary Salt Reductions on Future Cardiovascular Disease.*

Bibbins-Domingo K, Chertow GM, et al:

N Engl J Med 2010; 362 (February 18): 590-599

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Among U.S. adults, a 3-g/day reduction in salt intake would reduce annual health-care costs by up to $24 billion, and a 1-g/day reduction in salt intake would be a cost-effective method of lowering hypertension.

**Background:** Excess intake of dietary salt is associated with increased blood pressure and increased risk of cardiovascular disease (CVD). The recommended daily intake of dietary salt is <5.8 g for most Americans and 3.7 g and for adults aged >40 years. However, between 2005 and 2006, the estimated consumption was 10.4 g/day for men and 7.3 g/day for women. Most of this dietary salt comes from the consumption of processed foods.

**Objective:** To determine if modest population-wide reductions in dietary salt intake are associated with improvements in hypertension and the risk of CVD.

**Design:** Computer simulation analysis using the Coronary Heart Disease (CHD) Policy Model, which models heart disease in U.S. adults.

**Methods:** Population-wide reductions of up to 3.0 g/day in dietary salt were modeled. Various subgroups were defined by age, gender, and race. The rates and costs of CVD were estimated in the various subgroups based on dietary salt reductions.

**Results:** Reductions of 3 g/day in dietary salt were associated with significant nationwide reductions in the number of new cases of CHD, stroke, and myocardial infarction (MI). Although all population members would benefit from this modest reduction in dietary salt, those who would likely benefit the most included blacks, women, older adults, and younger adults. Reducing the population-wide salt intake would provide benefits similar to those seen with reductions in smoking, obesity, and cholesterol levels. The analysis projected that a 3-g/day reduction in salt intake would reduce annual health-care costs by $10 billion to $24 billion and that a 1-g/day reduction in salt intake would be a more cost-effective method of lowering hypertension than would current medication usage.

**Conclusions:** In the U.S., modest population-wide reductions in dietary salt intake among adults would be associated with substantial reductions in the rates of cardiovascular events, mortality rates, and medical costs.

**Reviewer’s Comments:** A reduction in salt improves outcome for the population in general for some major health care issues. However, reducing salt by 3 gm per day is not a trivial task. An adherence study should be done to see if a group of people can sustain a salt reduction in their diet. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Cardiovascular Disease, Dietary Salt Reductions, Effects

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For patients presenting with fever to the ED, PCT levels provide additional prognostic information on the duration of IV administration of antibiotics and admission to a special care unit.

**Background:** For patients presenting with fever, conventionally used markers to help distinguish infectious versus noninfectious causes include C-reactive protein (CRP) and leukocyte counts. Procalcitonin (PCT) has been proposed as a good marker to help diagnose bacterial infection in critically ill patients. However, the use of PCT is not yet established, partially because it is unknown if PCT adds any significant diagnostic value to markers already in common use.

**Objective:** To determine if PCT adds significant value in the diagnosis of bacterial infection in patients presenting with fever and to determine the prognostic values associated with PCT and CRP.

**Methods:** Various analytical techniques were used to determine the diagnostic value of PCT in an emergency department (ED) setting.

**Participants:** 211 nonpregnant adults with a complaint of fever who presented to an ED in the Netherlands; patient ages ranged from 18 to 85 years.  

**Methods:** Fever was defined by a tympanic temperature of ≥38.0°C. Patient medical records were reviewed by 2 blinded medical investigators. Cases were identified as "confirmed bacterial infection" (defined by positive cultures), "possible bacterial infection" (defined by positive imaging or visual findings), or "negative bacterial infection" (defined by negative culture and imaging findings or a confirmed alternative diagnosis). CRP and PCT levels were measured in a blinded fashion without knowledge of each patient's clinical status. CRP and PCT levels were correlated with outcomes.

**Results:** 73 patients had confirmed bacterial infections, 58 cases were considered likely for bacterial infection, 46 cases could not have the possibility of bacterial infection excluded, and 34 cases were negative for bacterial infection. On multivariate analysis, CRP and the presence of chills were strongly associated with confirmed bacterial infection. When PCT was added to CRP and the presence of chills as markers of infection, the model "fit" improved significantly. CRP and PCT levels were each associated with length of hospital stay and duration of antibiotic treatment. In addition, PCT levels were also associated with duration of IV antibiotic administration and admission to a special care unit.

**Conclusions:** PCT measurements provide additional valuable diagnostic and prognostic information for patients presenting to the ED with a complaint of fever. PCT may provide significant additional diagnostic value when added to the currently used markers of infection in the ED.

**Reviewer's Comments:** This is another study in a stream of studies (some reviewed here previously) that tout the benefits of PCT as a biomarker for sepsis. Improving the diagnostic yield raises the number of patients correctly diagnosed while allowing antibiotics not be used on patients who are not infected. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Infection Biomarkers, Procalcitonin

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Reduce Sepsis-Related Mortality by Applying Guidelines

The Surviving Sepsis Campaign: Results of an International Guideline-Based Performance Improvement Program Targeting Severe Sepsis.

Levy MM, Dellinger RP, et al:

Crit Care Med 2010; 38 (February): 367-374

In hospitalized patients with severe sepsis, decreases in sepsis-related mortality are associated with obtaining blood cultures before initiating broad-spectrum antibiotics and maintaining blood glucose control.

**Background:** As part of the Surviving Sepsis Campaign, evidence-based guidelines were developed, published, and updated in 2008. Because integrating new guidelines into bedside practices in the ICU can be a slow process, the campaign initiated an international registry into which providers could monitor the performance of their institutions.

**Objective:** To perform an analysis of data from this international registry to determine the global impact of implementing these guidelines as it relates to process improvements and patient outcomes in the treatment of severe sepsis and septic shock.

**Methods:** Data were submitted from January 2005 through March 2008 after incorporating a multifaceted performance initiative to improve compliance with selected sepsis-care guidelines in the ICU. In the analysis of these data, the primary outcome was a change in compliance with targeted guidelines over time. Secondary outcomes included hospital mortality and both hospital and ICU length of stay.

**Results:** 15,022 patients from 165 qualifying hospitals (each contributing ≥20 subjects) were entered into the database. Although the magnitude of improvements varied between hospitals, compliance with implementation of the targeted guidelines improved over time by the end of the 2-year campaign. The longer a hospital participated in the Campaign, the greater the risk of death from sepsis decreased. These decreases in sepsis-related hospital mortality were associated with obtaining blood cultures before initiating antibiotics, administration of broad-spectrum antibiotics, and maintaining blood glucose control. Outcomes were also improved when plateau pressure control was achieved in those requiring mechanical ventilation. For patients with septic shock, an association was seen between mortality and the administration of drotrecogin alfa in the first 24 hours but not with the following: use of low-dose steroids, achieving a central venous pressure ≥8 mm Hg, or demonstrating a central venous oxygen saturation of ≥70%.

**Conclusions:** The Campaign's performance improvement initiative successfully changed sepsis treatment behavior in hospitals around the world. Improved compliance with targeted guidelines was associated with significant reductions in hospital mortality in patients with severe sepsis and septic shock.

**Reviewer's Comments:** Hospitals that followed the Surviving Sepsis Campaign guidelines had a significant reduction in mortality. More hospitals are compliant with the protocol. However, overall better adherence is necessary. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Sepsis Care, Guideline Compliance, Outcomes

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TRALI Contributes to Adverse Transfusion Outcomes

Risk Factors and Outcome of Transfusion-Related Acute Lung Injury in the Critically Ill: A Nested Case-Control Study.
Vlaar APJ, Binnekade JM, et al:

Crit Care Med 2010; 38 (March): 771-778

In critically ill patients, TRALI is associated with a high incidence and significantly increased morbidity and mortality.

**Background:** Acute lung injury (ALI) occurring within 6 hours after transfusion is diagnosed as "transfusion-related ALI (TRALI)" if other risk factors for ALI are absent or as "possible TRALI" if a risk factor for ALI is present before transfusion. One hypothesis about TRALI states that the underlying clinical illness primes neutrophils in the pulmonary capillaries, which become activated when antibodies or bioactive lipids in the transfused blood product interact with the neutrophils. The result of this interaction is pulmonary leakage.

**Objective:** To determine the incidence, risk factors, and outcome associated with TRALI in critically ill patients.

**Design:** Retrospective case-control study performed in a university hospital ICU in The Netherlands.

**Participants:** Patients admitted to the ICU for ≥48 hours were included. Control subjects included transfused ICU patients in whom ALI did not develop and patients who were not transfused in whom ALI either did or did not develop.

**Methods:** Cardiogenic pulmonary edema was diagnosed when (1) pulmonary arterial occlusion pressure was >18 mm Hg or (2) when at least 2 of the following were present: central venous pressure >15 mm Hg; history of heart failure/valve dysfunction; ejection fraction <45%; and a positive fluid balance. Numerous risk factors, data regarding patient outcomes, and the association between TRALI and time to death were analyzed.

**Results:** 2235 of 5208 ICU patients were transfused. TRALI was confirmed in 114 patients, and "possible TRALI" was diagnosed in 100 (87%). The incidence of TRALI was 0.9%, the incidence of suspected TRALI was 2.2%, and the incidence of TRALI per transfused patient was 5.1%. Five of the 114 transfused patients died within 48 hours of admission. Overall, 2024 patients stayed >48 hours in the ICU, and TRALI developed in 109 of these patients within 6 hours of transfusion. Multivariate analysis showed that risk factors for TRALI included high APACHE II score, hematologic malignancy, sepsis, mechanical ventilation, massive transfusion, and emergency coronary artery bypass grafting. Compared with transfused control subjects, TRALI patients had a longer ICU stay, were mechanically ventilated for longer times, and had lower survival rates.

**Conclusions:** The incidence of TRALI is high in critically ill patients. Risk factors for the onset of TRALI include emergency coronary artery bypass grafting, hematologic malignancy, and sepsis, in addition to APACHE II score, mechanical ventilation, and massive transfusion. TRALI is associated with significantly increased morbidity and mortality in these critically ill patients.

**Reviewer's Comments:** Although a relatively rare problem without a definite pathophysiology, TRALI is associated with significant morbidity and mortality. There are multiple risk factors, but they typically boil down to the sickest of the patients in the ICU. Therefore, if there is no definite benefit to the use of blood products in an individual patient, one should refrain. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Acute Lung Injury, Transfusions, Survival, Risk Factors

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In the ICU, nosocomial infection rates are influenced by many factors, including severity of underlying illness, duration of hospital stay, diagnostic procedures, device use, and compliance with infection control practices.

**Background:** In ICUs in Germany, the cross transmission of organisms between patients accounts for approximately 15% of nosocomial infections. This reflects a breakdown of infection control practices in the ICU.  

**Objective:** To determine if nosocomial infections caused by patient-to-patient transmission of causative organisms in the ICU are related to length of stay in the ICU, device use, compliance with infection control measures, and/or other factors.

**Design:** Prospective cohort study conducted in 11 ICUs in Germany in the 24-month period encompassing 2003 and 2004.  

**Participants:** All patients admitted to the 11 ICUs during the study interval.  

**Methods:** Health-care workers in the 11 ICUs were asked to follow standard hygiene precautions, including the use of alcoholic hand sanitizers. ICU surveillance consisted of ventilator-associated lower respiratory tract infection, central line-associated bloodstream infection, and catheter-associated urinary tract infection. Microbiological specimens for culture were collected when clinically indicated. In addition, surveillance cultures were performed for methicillin-resistant *Staphylococcus aureus*. "Potential transmission" was declared when genetically identical strains were identified in at least 2 patients from the same ICU during overlapping stays or during ICU stays of no more than 9 days apart.

**Results:** 100,781 patient days were evaluated, and 100,829 microbiological specimens were sampled from 24,362 patients. On 914 occasions, potential patient-to-patient transmissions were identified. If only ICU stays of >48 hours were considered, 462 potential cross transmissions were seen. On correlation analysis of 463 transmissions and 1216 nosocomial infections, no association was found between the incidence of cross transmissions and nosocomial infections, duration of hospitalization, or device use in the ICU.

**Conclusions:** Nosocomial infections in the ICU cannot be explained based only on patient-to-patient transmission of microorganisms. Although compliance with infection control measures is a contributing factor, other important factors may include the severity of underlying illness, a patient's endogenous flora, and invasive procedures. Continued surveillance of nosocomial infections in the ICU is an important infection control tool.

**Reviewer’s Comments:** We know that on occasions mistakes are made and patient-to-patient transmission of bacteria takes place. This study suggests that it is a very small percentage of the causes of nosocomial infection. Other factors need to be identified and remedied. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Nosocomial Infections, Bacterial Cross Transmission

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Background: ICU-acquired weakness (ICU-AW) develops in ICU patients and significantly impedes the recovery process. This complication of critical illness is particularly common in patients undergoing mechanical ventilation (MV). In 2009, the topic of ICU-AW was discussed by numerous clinicians, physician scientists, and investigators at the Brussels Round Table Conference. The authors present a brief summary of these discussions. Summary: The incidence of ICU-AW ranges from 25% to 58% in ICU patients ventilated for >7 days and from 50% to 100% in critically ill patients with sepsis. ICU-AW is associated with a longer duration of mechanical ventilation, which is linked to longer ICU and hospital stays. In addition, ICU-AW appears to be a marker for severity of illness, but it does not appear to be an independent cause of death in critically ill patients. After dismissal from the ICU, ICU-AW is responsible for major functional limitations and disability during recovery, and these limitations may persist for >12 months in many patients. Risk factors for ICU-AW may include severity of illness, systemic inflammatory response syndrome, use of neuromuscular blocking agents or corticosteroids, glycemic control, and immobility. Although the exact pathophysiology of ICU-AW is unknown, several possible explanations are given, including the effect of inactivity on disease processes, pathologic changes in integration of brain function along peripheral nerves to the contractile machinery, and the catabolic breakdown of muscle proteins. Mechanical unloading of muscle can result in fewer actin filaments, causing muscle atrophy. Unloading of the diaphragm is of particular concern for ICU patients on prolonged MV. Diaphragmatic atrophy and contractile dysfunction can occur in as few as 18 hours on controlled MV. MV using pressure support mode may limit the protein catabolism induced by the ventilator. Short periods of intermittent spontaneous breathing during controlled MV may also help limit diaphragmatic dysfunction. Short-term (6 hours) controlled MV is linked to declines in protein synthesis, including a 65% decrease in the rate of myosin heavy chain synthesis. Prolonged controlled MV activates both proteases and the oxidation of key diaphragmatic proteins. Sepsis causes atrophy and reduces the force-generating capacity of muscle, which is of particular concern for the diaphragm. Chronic sepsis may cause a dysregulation of the sodium channels, resulting in sarcolemmal damage and a decrease in muscle contractility. Sepsis-induced changes in skeletal muscle are also linked to activation of proteolytic pathways.

Reviewer's Comments: Weakness in patients who are critically ill is under diagnosed. It can lead to prolonged ventilatory stay and ICU stay and significant post-discharge functional impairment. Further work in this area is certainly needed. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Critical Illness, Neuromuscular Complications, Severe Weakness

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For patients with CAP, racial disparities in treatment quality appear to result from differences in the care administered by various hospitals, with no black/white disparities seen within individual hospitals.

**Background:** Disparity research shows that quality of care for severe infections, such as community-acquired pneumonia (CAP), may vary by patient race and the hospital administering the treatment. Because there is no standard definition for quality of care, evidence-based processes of care must be evaluated alongside other factors such as patient preferences and hospital case-mix.

**Objective:** To determine if racial differences exist regarding CAP treatment quality based on the processes of care administered in the emergency department (ED) and therapeutic interventions used in the hospital and ICU.

**Design:** Large observational cohort study.

**Participants:** 2090 adults with a clinical and radiologic diagnosis of CP who presented to the ED of 28 hospitals from 4 different regions of the United States were included.

**Methods:** Data were analyzed from the Genetic and Inflammatory Markers of Sepsis study of patients with CAP from various regions of the U.S. Treatment quality was evaluated by assessing initial antibiotic therapy administered within 4 hours in the ED, antibiotic use in the first 24 hours of hospital admission, and both admission rates and therapy utilization in the ICU.

**Results:** 1738 white patients and 352 black patients were included in the study. In the ED, blacks were less likely to receive antibiotics within 4 hours than were whites. The antibiotics used in the first 24 hours of hospital admission were less likely to adhere to the 2001 American Thoracic Society guidelines when given to black patients than when given to white patients. Overall, the rates of hospital and ICU admissions were similar for black and white patients. Both hospital and ICU uses of mechanical ventilation were slightly higher for black patients. In the ICU, pulmonary artery catheters were more likely to be placed in black patients, but the frequencies of do-not-resuscitate directives and initiation of comfort measures were similar for the 2 groups.

**Conclusions:** Overall, in the ED, the quality of CAP care provided to black patients was similar to that provided to white patients. However, the quality of care (antibiotic timing) provided to hospitalized black patients was lower than that provided to hospitalized white patients. Racial disparities in CAP treatment quality appear to result from differences in the level of care administered by various hospitals, with no black/white racial disparities seen within each individual hospital. To most effectively reduce racial disparities in CAP treatment, the authors recommend targeting policy and care interventions at the hospitals treating large numbers of black patients.

**Reviewer’s Comments:** Very surprising and troubling study. Seems almost incongruous that a patient admitted to the hospital could receive different treatment based on race. Strict adherence to the guidelines, however, would avoid this problem. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Pneumonia & Hospital Care, Racial Disparities

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