Patients with a lower respiratory infection who are managed with a procalcitonin algorithm receive fewer antibiotics and have less adverse events without an increase in morbidity.

**Objective:** To determine if the use of a biomarker procalcitonin (PCT) algorithm can help determine when antibodies could be discontinued without causing any adverse effects to patients with lower respiratory tract infections.

**Design:** This was a multicenter, noninferiority, randomized, controlled study.

**Methods:** Patients were enrolled if they had a lower respiratory tract infection and presented to the emergency department of 1 of 6 different tertiary care hospitals. Patients were required to have at least 1 respiratory symptom (cough, sputum production, dyspnea, tachypnea, or pleuritic pain) plus at least 1 additional sign of infection (elevated temperature, shivering, or elevated white count). Community-acquired pneumonia (CAP) was confirmed by chest radiograph. Exclusion criteria were active intravenous drugs or immunosuppression therapy, life-threatening other medical conditions, death, or acquisition of pneumonia in the hospital in addition to a chronic infection. PCT levels were measured using a rapid sensitive assay. Results were made available to the clinician within 1 hour. Patients were not placed on antibiotics if the PCT level was <0.1; antibiotics were discouraged if the level was <0.25; and initiation of antibiotics was encouraged if the levels were ≥0.5. If the antibiotics were withheld, the level was repeated 24 hours later. Patients were reassessed on days 3, 5, and 7 for the presence of infection. Antibiotics were stopped when the PCT level decreased by 80%. Clinicians were able to override the protocol if the patient’s clinical condition was significantly compromised and data could not be obtained rapidly enough. The end point of the study was a composite of overall adverse outcomes within 30 days of the emergency department admission. A total of 1359 patients were randomized.

**Results:** A total of 103 patients in the PCT group achieved 1 of the end points versus 130 patients in the control group. The data, therefore, suggested that there were no increased adverse effects associated with using the PCT protocol since the mortality rates were similar in both groups. Significant reductions in antibody exposure occurred in the PCT group compared to the control group. The overall reduction ranged from 25.7% to 38.7%. Antibiotic adverse effects were significantly reduced in patients who received management using PCT (19.8% vs 28.1%).

**Conclusions:** In patients with lower respiratory infections, the use of PCT guidelines can result in reduced antibiotic exposure and adverse effects from the antibiotics.

**Reviewer’s Comments:** Many patients who present with signs and symptoms of a lower respiratory tract infection actually do not have one. These patients, therefore, are needlessly exposed to antibiotics. Additionally, infection may respond more rapidly than standard antibiotic regimens in some patients, resulting in extra needless antibiotic days. The data in the study strongly suggest that the use of the biomarker PCT can help identify patients with sepsis requiring antibiotics and, in addition, can help determine when antibiotics may be discontinued without causing harmful effects. (Reviewer-Eric H. Gluck, MD, JD).

© 2009, Oakstone Medical Publishing

**Keywords:** Community-Acquired Pneumonia, Procalcitonin

**Print Tag:** Refer to original journal article
Arterial stiffness is a problem in patients with chronic obstructive pulmonary disease.

**Objective:** To evaluate vascular function in patients with chronic obstructive pulmonary disease (COPD) compared to smokers without COPD.

**Participants/Methods:** 18 men with COPD were compared to 17 healthy men. Patients were matched for age and smoking history. All subjects were between 40 and 80 years of age and had at least a 10-year history of smoking cigarettes. Patients with significant comorbid medical conditions were excluded. Controls had normal spirometry and no history of respiratory symptoms. COPD patients (study group) had airflow limitation on spirometry and symptoms consistent with COPD. Their disease was stable for at least 6 weeks, and patients were not on regular oral steroid therapy or long-term oxygen. Arterial stiffness studies were performed as described. Venous occlusion plethysmography was also performed. As part of these studies, IV infusions of bradykinin, acetylcholine, sodium nitroprusside, and verapamil were used to evaluate vasodilatation. Blood was sampled for hemoglobin/hematocrit, white blood cell (WBC) count, C-reactive protein (CRP), arterial oxygen tension glucose, lipids, and endothelial tissue plasminogen activator (t-PA). All data were then analyzed.

**Results:** Patients with COPD were found to have lower saturation, increased resting heart rate, higher WBC and higher-sensitivity CRP. Arterial stiffness was found to be higher in COPD patients. Carotid-femoral pulse wave velocity was also increased in the COPD group. Aortic pulse wave velocity was correlated with systolic and airflow obstruction. No relationship was found with systemic inflammation or arterial oxygen tension. No difference in response to vasodilators was found between groups. In addition, no differences were found in release of t-PA between groups.

**Conclusions:** There is an increase in arterial stiffness directly related to the presence of COPD and not smoking. This stiffness is not a problem related to endothelial dysfunction or an increase in inflammation. The exact mechanism of this stiffness is unclear. It is suggested that a structural abnormality in the vascular extracellular matrix may be the cause.

**Reviewer's Comments:** This is a very challenging article from a physiologic standpoint. The authors suggest that increased arterial stiffness can lead to a greater central aortic systolic pressure, increased left ventricular afterload, and decreased diastolic coronary filling. Perhaps this explains why some patients with COPD do not have reduced dyspnea until treated empirically for cardiac disease. (Reviewer-Allan R. Goldstein, MD).
Long-term CPAP treatment in moderate to severe OSA with ischemic stroke is associated with a reduction in mortality.

**Background/Objective:** Obstructive sleep apnea (OSA) is known to be an independent risk factor for stroke and cardiovascular health. The prevalence of OSA in stroke victims is high. The role of continuous positive airway pressure (CPAP) on mortality in stroke patients with OSA, is heretofore unknown. This Spanish study analyzes the impact of long-term CPAP treatment on mortality in patients with ischemic stroke.

**Design/Participants:** This was a prospective observational study in 166 patients admitted with ischemic stroke.

**Methods:** Results of sleep studies 2 months after the acute event and CPAP treatment were obtained in moderate to severe OSA cases. Patients were followed up for 5 years to analyze the risk of mortality. Thirty-one patients had an apnea-hypopnea index (AHI) of <10; 39 patients had an AHI between 10 and 19; and 96 patients had an AHI of ≥20. CPAP treatment was offered when AHI was ≥20. Outpatient follow-up at 1, 3, and 6 months and every 6 months thereafter for 5 years was obtained.

**Results:** The mean age of subjects was 73.3 ±11 years (59% males); the mean AHI was 26 for patients with predominance of obstructive events. Patients with an AHI of ≥20 who did not tolerate CPAP (n=68) showed an increased adjusted risk of mortality (HR, 2.69; 95% CI, 1.32 to 5.61) compared to patients with an AHI of <20 (n=70), and an increased adjusted risk of mortality (HR, 1.58; 95% CI, 1.01 to 2.49; \( P =0.04 \)) compared to patients with moderate to severe OSA who tolerated CPAP (n=28). No differences in mortality were observed among patients without OSA, patients with mild disease, and patients who tolerated CPAP.

**Conclusions:** Long-term CPAP treatment in moderate to severe OSA and ischemic stroke is associated with a reduced risk of mortality.

**Reviewer’s Comments:** Placing a stroke victim with OSA on CPAP therapy seems, to many of us, a bit like closing the barn door after the horse has gotten away. Those with more urbane sentiments may simply wonder if adding CPAP therapy in this way is cost-effective at all. This study confirms that CPAP treatment lowers the risk of mortality in patients with ischemic stroke. Furthermore, we learn that patients with ischemic stroke and moderate to severe OSA have increased mortality, which should redouble our efforts to identify patients with OSA who are at risk for stroke (which may turn out to be all of them). (Reviewer-A. Gray Bullard, MD).

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Keywords: CPAP Therapy, Stroke, Obstructive Sleep Apnea

Print Tag: Refer to original journal article
Objective: To determine the rate and outcome of *Clostridium difficile* infection in mechanically ventilated patients.

Methods: Data from 2005 were obtained from the Healthcare Utilization Project/Nationwide Inpatient Sample (NIS) from the Agency for Healthcare Research and Quality. The data used represented information from nearly 1000 hospitals. Identification of prolonged acute mechanical ventilation (PAMV) and *C. difficile*-associated disease (CDAD) were based on the ICD-9-CM codes. Outcomes of CDAD+ and CDAD- were compared.

Results: 5.3% of 64,910 patients were CDAD+. This was the principal diagnosis in 142 patients. CDAD+ patients were older, with the rate stabilizing after age 70 years. CDAD discharged patients were more likely to be women and non-white. Trauma as a cause of admission occurred less often in the CDAD+ group. Admission from another health care facility was more common in the CDAD+ group. Comorbidity burden was the same in both CDAD groups, although respiratory failure was the most common principal diagnosis. A geographical difference in the incidence of CDAD+ patients was noted, with the highest proportion of cases in the South but the greatest number of cases in the Northeast. There was a higher incidence in teaching hospitals than in non-teaching hospitals. No difference in hospital mortality was found between CDAD+ and CDAD- patients. The median length of stay was 8 days greater in CDAD+ patients. In addition, median costs were 33% higher in the CDAD+ group. Those being discharged to nursing homes were statistically more likely to be CDAD+.

Conclusions: CDAD+ patients are more common in those receiving PAMV. Although mortality is not increased, length of stay and costs are significantly higher. Older patients with respiratory failure are at an increased risk, especially if being admitted from a long-term care facility.

Reviewer's Comments: This paper should alert all of us to the significant cost associated with CDAD+ patients. Increased surveillance and preventive procedures should be in place to avoid this common problem. Patients admitted from long-term care facilities, in particular, should be suspected of harboring *C. difficile*. (Reviewer-Allan R. Goldstein, MD).

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Keywords: *Clostridium difficile*, Acute Mechanical Ventilation

Print Tag: Refer to original journal article
Objective: To evaluate dynamic hyperinflation, exercise tolerance, and airway oxidative stress as related to physical activity in chronic obstructive pulmonary disease (COPD).

Participants/Methods: 110 patients with moderate to severe COPD were studied. All patients had FEV₁/FVC% <0.7, postbronchodilator FEV₁ <80%, smoking history of >20 pack-years, stable disease for at least 2 months, and optimal medical therapy for at least 8 weeks. Clinical evaluation (St. George’s Respiratory Questionnaire, exhaled IL-6, TNF-α receptor, and 8-isoprostane concentrations), physical activity measurements and pulmonary function measurements (arterial blood gas, spirometry, body plethysmography, DLCO, and 6-minute walk tests) were obtained on all enrollees. In addition, end expiratory lung volumes (EELVs) were determined.

Results: The more severe the COPD, the less the daily activity. Physical activity was found to be related to symptoms, quality of life, and exercise tolerance. Daily physical activity was related to the ventilatory response to exercise. This response was the development of dynamic hyperinflation. This was manifested by an increase in the EELV. The 89 patients with an increase in the EELV performed less activity than did the 21 patients who did not have an increase in EELV. Activity was inversely related to EELV. Airway oxidative stress measurements also showed an inverse relationship to physical activity. Physical activity was unrelated to age, sex, smoking habits, comorbid conditions, inspiratory capacity, desaturation during the 6-minute walk test, or inflammatory markers.

Conclusions: Reduced daily activity in COPD is related, at least in part, to dynamic hyperinflation as measured by the increase in EELV. Although not measured in this study, one must also consider psychological, behavioral, social, and personality factors.

Reviewer’s Comments: This study is very provocative. It is not unusual for patients to report less dyspnea with activity with no apparent change in spirometry. Some literature has suggested that the physiologic change is a reduction in residual volume. This study would support that theory. In clinical practice, relief of dyspnea is a major goal. This study gives us a better idea of the possible mechanism for this improvement in symptoms. Patients want to be more active and less symptomatic. We should try to accommodate them. (Reviewer-Allan R. Goldstein, MD).

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Keywords: Dyspnea, Daily Activity

Print Tag: Refer to original journal article
The combination of budesonide/formoterol plus tiotropium is better in all aspects for COPD patients than tiotropium alone.

**Objective:** To determine if the combination of budesonide/formoterol plus tiotropium improves outcomes in patients with chronic obstructive pulmonary disease (COPD).

**Design:** This was a randomized, double-blind, parallel group multicenter study. The study was conducted in 102 centers in 9 different countries.

**Methods:** Patients entered into the study met the eligibility criteria for COPD and had an FEV\(_1\) <50% of predicted. All patients also had a previous history of exacerbation. Prior to enrollment, patients stopped their medication for up to 4 weeks depending on the type and then were maintained on tiotropium. Patients were randomized to receive tiotropium plus budesonide/formoterol or placebo. Terbutaline was used as the rescue therapy. A total of 660 patients were randomized.

**Results:** Combination therapy improved FEV\(_1\) to a significantly greater extent than tiotropium alone. There was a 6% improvement in FEV\(_1\) with combination therapy compared to tiotropium alone. In addition, combination therapy provided a more rapid onset of effect than did the single agent. Quality-of-life health status improved by 3.8 units in the combination group compared to only 1.5 units in the tiotropium-only group. The improvement in FEV\(_1\) was maintained throughout the 12-week study. A significant improvement was seen in symptom scores, including reduction of breathlessness, nighttime awakening, chest tightness, and cough. There was also a significant reduction in the need for using a rescue medication. In the combination group, 7.6% of the patients had severe exacerbations versus 18.5% in the control group. A significant reduction was also seen in the number of hospitalizations and emergency department visits and in the need for antibiotic therapy. Both treatment regimens were well tolerated. There was a very low incidence of any adverse effects in either group.

**Conclusions:** In patients with COPD, adding budesonide/formoterol to tiotropium results in more rapid onset of action and significant improvement in lung function status, respiratory symptoms, and exacerbation rate.

**Reviewer’s Comments:** This well-done multicenter study clearly demonstrated that adding budesonide/formoterol to tiotropium had a significant impact on many aspects of COPD. The tolerability was quite high. Although it would be a significant cost for the extra medication, the reduction in the need for antibiotics, emergency department visits, and hospitalizations would appear to offset this additional cost. In patients with significant COPD, this combination therapy should be strongly considered. (Reviewer-Eric H. Gluck, MD, JD).
The recognition of daytime hypercapnia in obstructive sleep apnea is vital.

**Objective:** To determine the risk factors associated with daytime hypercapnia in obstructive sleep apnea (OSA).

**Design:** A MEDLINE search was performed on 42 years of articles dealing with OSA. Fifteen articles that were relevant to the purpose of this paper were selected.

**Methods:** Risk factors were identified for both eucapnic and hypercapnic patients. Those factors identified were gender, age, body mass index (BMI), apnea-hypopnea index (AHI), FEV₁%, vital capacity, FEV₁/FVC%, total lung capacity, residual volume, mean overnight pulse oximetric saturation (SpO₂), and percentage of total sleep time with SpO₂ <90% (% total sleep time SpO₂ <90%). Data collected were then analyzed for relevance.

**Results:** No difference was found between the 2 groups when looking at age or gender. BMI was 3.13 kg/m² in the hypercapnic group, and AHI was 12.51 higher in this group. Analysis of pulmonary function data revealed a greater degree of abnormality that was restrictive in nature. The hypercapnic group had an overnight oximetry 5% less than in the eucapnic group. This group also had a much greater sleep time with O₂ saturation <90%. All results were to the exclusion of any finding of chronic obstructive pulmonary disease (COPD).

**Conclusions:** Daytime hypercapnia in OSA, in the absence of COPD, is directly related to: (1) the severity of OSA based on AHI and nocturnal desaturation; (2) BMI; and (3) the degree of chest wall restriction. Both the severity of the OSA and the abnormal chest wall mechanics are directly related to the degree of obesity. If a patient also has COPD, the problem could be accentuated. Therefore, in obese COPD patients, the contribution of each problem should be determined.

**Reviewer's Comments:** This is an important article. It reminds us that there are 2 groups of patients with OSA. Both have increased morbidity and mortality based on obesity alone. However, daytime hypercapnia adds an additional dimension of risk. All patients identified as obese, especially those with OSA, need full pulmonary and gas exchange studies. (Reviewer-Allan R. Goldstein, MD).

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Keywords: Hypercapnia, Obstructive Sleep Apnea

Print Tag: Refer to original journal article
Complex Sleep Apnea Simplifies With Therapy

The Prevalence and Natural History of Complex Sleep Apnea.

Javaheri S, Smith J, Chung E:


CPAP-emergent CSA is generally transitory and disappears within 8 weeks of CPAP therapy.

**Background:** Complex sleep apnea is generally defined as central sleep apnea (CSA) emerging during titration of continuous positive airway pressure (CPAP) in patients with obstructive sleep apnea (OSA), or CSA otherwise persisting despite CPAP therapy for OSA.

**Objective:** To determine the prevalence and natural history of CPAP-emergent CSA.

**Design:** This retrospective study of 1288 patients with newly diagnosed OSA undergoing CPAP treatment over 12 months yielded 84 patients with a CSA index of ≥5 per hour while on CPAP.

**Results/Conclusions:** The incidence of CSA ranged from 3% to 10% monthly, with an overall incidence of 6.5%. Of the 84 patients, 42 returned for a second CPAP titration; in 33 patients, CSA was no longer present. In the remaining 9 patients, the CSA index remained ≥5 per hour (mean, 13). These patients had the most severe OSA, and 5 had a central apnea index of ≥5 per hour at baseline. Two of the 9 patients were on opioids, and 6.5% of patients in this study had CPAP-emergent or persistent CSA. However, CPAP-emergent CSA was generally transitory and was eliminated within 8 weeks of CPAP. The prevalence of CPAP-persistent CSA was 1.5%. OSA severity, central apnea index of ≥5 per hour, and opioid use were risk factors.

**Reviewer's Comments:** The question increasingly at the forefront of the minds of those who care for large numbers of OSA patients in the context of CPAP clinics is this: "Must we order a more extensive and expensive positive airway pressure machine to care for CPAP-emergent central (complex) sleep apnea?" On the basis of this study's results, the authors recommend a strategy of: (1) early return to clinic (within a few days of the titration study) for patients who have CSA on CPAP; (2) a pressure decrease if the patient complains of symptoms of excessive pressure; (3) encouragement of patients to continue to use CPAP and be assured that CSA is generally transitory; and (4) for the minority of patients with clinical problems such as excessive daytime sleepiness or poor adherence with CPAP, pressure-assisted servo-ventilation (eg, assisted servo-ventilation should be used to eliminate residual CSA events. A reasonable inference is that patients found by titration study to have complex sleep apnea who also use narcotics, have baseline severe OSA, or have baseline CSA should be considered for pressure support servo-ventilation. This article implies that patients with complex sleep apnea who do not have these factors may be considered for more standard (non-CSA) CPAP or bi-level positive airway pressure modalities of therapy for OSA. Should we restudy these complex patients later, as was done in this study? The authors do not recommend this, but acknowledge that the long-term effects of persistent CSA in asymptomatic patients is unknown; so, too, is the answer to the question—for now. (Reviewer-A. Gray Bullard, MD).

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Keywords: Complex Sleep Apnea

Print Tag: Refer to original journal article
Airway disease in farmers can be an occupationally related disease.

**Objective:** To determine the cause of increased respiratory morbidity and mortality in farmers.

**Participants/Methods:** 4735 Norwegian farmers were evaluated using spirometry, blood testing, and a respiratory questionnaire. Of these, 1213 were tested for atopy. All study participants were active farmers without another job that would expose them to respiratory irritants, had never changed farm production due to dust-related respiratory symptoms, and had complete information available. Farmers who had left farming in the past 4 years and farmers who changed farm production in the past 10 years due to respiratory symptoms were compared to the study group. Both crop and livestock/crop farmers were included. Exposures were measured over 4 years and included all seasons. Sampling was done during the handling of harvest, tending animals, and handling of manure. Analysis was performed for dust, fungi, endotoxin, specific antigens, silica, mites, ammonia, hydrogen sulphide, and glucans. The questionnaire used looked at respiratory symptoms, specific tasks, hours performing specific tasks, and whether the farmer was a crop or livestock/crop farmer. Laboratory studies included spirometry and measurement of specific IgE. All data were analyzed for exposure and respiratory symptoms/disease.

**Results:** For agents with published occupational limits, no excess level was found. Risk levels previously published for fungal spores were exceeded. Endotoxin levels were above published levels. Exposure levels were similar in men and women, but women had less COPD and chronic bronchitis. COPD and chronic bronchitis were more common in livestock farmers as opposed to crop farmers. Chronic bronchitis was associated with all agents except glucans and hydrogen sulfide. COPD was associated with organic dust, endotoxins, mites, ammonia, and hydrogen sulfide. FEV₁, but not FVC, was related to several agents. Atopy caused a lower FEV₁, but was not associated with COPD or chronic bronchitis. Farmers who left farming had a lower FEV₁ and a higher prevalence of COPD and chronic bronchitis. Farmers who changed crops due to respiratory symptoms had a higher incidence of asthma.

**Conclusions:** Farmers, especially livestock farmers, have a higher incidence of respiratory symptoms, COPD, and chronic bronchitis directly related to occupational exposure as opposed to smoking. In those who have left farming or changed crops, it is not uncommon to have respiratory illness.

**Reviewer's Comments:** This very nice study alerts us to yet another occupation that can lead to significant respiratory impairment. Work history is vital. The question to be answered is whether this study is applicable to American farmers. I don't see why it should not be. (Reviewer-Allan R. Goldstein, MD).

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**Keywords:** Biological Agents, Farmers, Lung Function

**Print Tag:** Refer to original journal article
Changes in AHI are strongly associated with changes in weight and waist circumference.

**Background:** Obesity is the most important risk factor for obstructive sleep apnea (OSA), and both obesity and OSA are increasing public health burdens. However, although included in clinical guidelines, no randomized controlled studies have been performed regarding the effects of weight reduction in mild OSA.

**Objective:** This is the first randomized study on the effects of an intensive lifestyle intervention with a weight-reduction program and supervised lifestyle counselling in overweight patients with mild OSA.

**Design/Participants:** This was a randomized, clinical 1-year follow-up Finnish trial of 72 patients with a body mass index (BMI) of 28 to 42 who also had mild OSA.

**Methods:** The patients in the intervention group (n=35) received a 1-year lifestyle intervention, including an initial weight-reduction program with a 12-week very-low-calorie diet (VLCD) and supervised lifestyle counselling. The control group (n=37) received routine lifestyle counselling. The supervised lifestyle counselling was an active intervention informing patients about the following: general health risks associated with OSA and obesity; deleterious effects of smoking and alcohol use; the provision of group-based VLCD (eg, Nutrifast for 12 weeks) based on a baseline 3-day food diary; discussion of previous attempts/failures to lose weight; visits with nutritionists every other week for compliance; and advice upon completion of VLCD to reduce fats to no more than 30% of total energy by dietary modification emphasizing fruits and vegetables, with 1-year intervention. Change in symptoms and the 15D-Quality-of-Life tool were used as subjective measurements.

**Results:** The supervised lifestyle intervention effectively reduced body weight (-10 ± 6.5 kg; BMI, -3.5 ± 2.1). There was a statistically significant difference in the average apnea-hypopnea index (AHI) between groups (P =0.017). The adjusted odds ratio for having mild OSA was markedly lowered in the intervention group (OR, 0.24; 95% CI, 0.08 to 0.72; P =0.11). OSA symptoms and some quality-of-life features improved after the lifestyle intervention. Apnea-hypopnea index (AHI) changes were strongly associated with changes in waist circumference and weight. In the intervention group, a 40% AHI reduction was achieved from baseline, and 2 of every 3 patients had an AHI of <5 events per hour at follow-up. The achieved beneficial outcomes were maintained at 1 year.

**Conclusions:** A very-low-calorie-diet combined with active lifestyle counselling resulting in marked weight reduction is a feasible and effective treatment for most patients with mild OSA.

**Reviewer’s Comments:** As clinicians, we are often nihilistic about obese patients and their ability or willingness to lose weight, and for good reason: We see weight loss success very infrequently. When 32% of adults in the United States have a BMI >30, it seems like a losing battle. Exacerbating our nihilism is the nagging suspicion in the corner of our minds that even if obese sleep apnea patients lost weight, OSA would not go away. This study should dispel our pessimism and spark our determination to use well-run weight-loss programs. (Reviewer-A.Gray Bullard, MD).

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Keywords: Obstructive Sleep Apnea, Weight Loss

Print Tag: Refer to original journal article
Approximately 71% of the cases are identified during the first sputum result and in an additional 17%, during the second. Only 42% of the lymph nodes that are cultured result in a positive result for TB.

**Background:** It is often difficult to make the diagnosis of tuberculosis in patients with human immunodeficiency virus (HIV) disease. The World Health Organization has recently revised its recommendations for diagnosis in this patient population.

**Objective:** To evaluate the performance of the standard sputum smear and culture in the HIV-patient population.

**Methods:** The study was performed in Southeast Asia. All patients with HIV, irrespective of symptomatology, were enrolled in the study. Patients who were enrolled were required to produce 3 different sputum specimens, urine specimens, a blood specimen, and if there was adenopathy present, a biopsy. If any of these cultures were positives, they were considered actively infected with tuberculosis. A total of 1060 patients were enrolled in the study.

**Results:** Almost 14% of patients were eventually diagnosed as having tuberculosis. Using 3 smears instead of 2 smears resulted in just a 2% increase in the identification of a case of tuberculosis; 71% of the cases were identified during the first sputum result and in an additional 17% during the second. Only 42% of the lymph nodes that were cultured resulted in a positive result for tuberculosis. Of all the techniques involved, sputum specimens resulted in the highest yield in this patient population.

**Conclusions:** The authors conclude that 2 sputum specimens are probably the optimal way to determine the diagnosis of active tuberculosis in patients who are HIV-positive, especially if they have minimal access to healthcare situations. In the event of these negative cultures of the specimens, especially lymph nodes will result in a large incremental yield in positive testing results.

**Reviewer's Comments:** These data were interesting based on the fact that they were obtained in patients who had limited access to health care and also had HIV disease. The take-home message here, however, is actually a message that has been prevalent for the diagnosis of TB for 30 years now—that is sputum specimens of the highest yield followed by culture and then followed by biopsies of suspicious tissues. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Diagnostics, Acid-Fast Smear, Mycobacterial Culture, HIV

Print Tag: Refer to original journal article
Buffering pH During Hypercapnic Permissive Hyperventilation

Infection Induced Lung Injury Is Worsened After Renal Buffering of Hypercapnic Acidosis.

Nichol AD, O’Cronin DF, et al:


Animals that were buffered had significantly increased lung injury when exposed to endotoxin when compared to the controls.

**Background**: During lung protective strategies, patients are often subjected to hypercapnic respiratory acidosis. Data have suggested that this actually protects against sepsis-induced lung injury. Unfortunately, once the kidneys buffer the data are less clear and, in fact, may suggest that lung injury is enhanced during this period of time. Oftentimes, clinicians aid the kidneys in buffering this respiratory acidosis by giving IV bicarbonate. Obviously this would be inappropriate if lung injury was enhanced by the buffering of the respiratory acidosis. **Design/Subjects**: This was a prospective randomized animal study performed in rats at a university research center.

**Methods**: 1 group of animals was subjected to hypercapnea by exposing them to concentrations of increased carbon dioxide during ventilation for 3 days prior to the induction of lung injury. The control group was maintained in a normal carbon dioxide status. Both animals were injured using the intra-tracheal inoculation of *Escherichia coli* endotoxin. Animals that were buffered had significantly increased lung injury when they were exposed to endotoxin compared to the controls. They experienced decreased oxygen levels in the blood, a reduction in lung compliance, an increase in pro-inflammatory cytokine concentrations measured in the lung, and a worsening of structural damage to the lung. Although 1 of the postulates for the protection induced by hypercapnea from lung injury was neutrophil function, which was not different between the 2 groups.

**Conclusions**: During a model of infection-induced lung injury in animals, buffering of hypercapnic acidosis was independently associated with worse physiologic outcomes and worse pathological outcomes.

**Reviewer’s Comments**: While we do not usually report many animal studies, I am aware of the controversy of using bicarbonate solutions in patients who are undergoing lung protective ventilatory strategies, so I thought that these data might be useful to our readership in order to make more informed decisions about the treatment of these patients. Obviously, there are severe limitations in trying to analogize between animal data and human data. Hopefully, in the future, studies in patients in the ICU will take place and will help us answer this question. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Acute Lung Injury, Infection, Renal Buffering, Hypercapnic Acidosis

Print Tag: Refer to original journal article
New Assay Determines MIs Earlier

Early Diagnosis of Myocardial Infarction With Sensitive Cardiac Troponin Assay.

Reichlin T, Hochholzer W, et al:


A new cardiac component assay is significantly better than the standard one, particularly in patients who present to the emergency department early on in their symptomatology of acute MI.

**Background:** Diagnosis of MI in the emergency department (ED) is impaired by the fact that oftentimes, troponin levels are not elevated at the time of presentation.

**Objective:** To evaluate a new, more sensitive marker of troponin that increases more rapidly and, therefore, would be positive even early on during acute MI.

**Design/Participants:** Multicenter study in the ED on > 700 patients whose symptoms suggested acute MI.

**Methods:** Cardiac troponin levels were performed in a standard fashion and then using 4 different high sensitivity assays. The diagnosis was established by 3 independent cardiologists.

**Results:** 17% of the patients had a final diagnosis of acute MI. The 4 high-sensitivity cardiac troponin assays had significantly greater area under the curve characteristics than the standard measurement. These areas ranged from 0.94 to 0.98. The standard area under the curve ranged from 0.86 to 0.94. Patients who presented very early on in the course of the MI demonstrated a significant benefit as well from the more sensitive assay demonstrating an area under the curve of between 0.88 and 0.99 for the sensitive assays, but only 0.64 to 0.88 for the standard assay.

**Conclusions:** The diagnostic accuracy and sensitivity of this new cardiac component assay is significantly better than the standard one, particularly in patients who present to the ED early on in their symptomatology.

**Reviewer's Comments:** Chest pain is one of the most common presenting symptoms in U.S. EDs, and many patients have to spend 4 to 6 hours in the ED awaiting the results of their laboratory tests to confirm or refute the occurrence of acute MI. The new sensitive assay would actually benefit this presentation to be able to make a diagnosis in <1 hour in most instances. This would result in earlier interventions for these patients as well as decreased crowding in the ED. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: MI Diagnosis, Cardiac Troponin Assay

Print Tag: Refer to original journal article
One-year patient outcomes for prolonged mechanical ventilation are significantly worse than expected by the patient's surrogates and in fact by the physicians as well.

**Background:** Respiratory failure can become a chronic condition requiring placement of the patient on a long-term ventilator unit. Oftentimes, the prognosis is poor for liberation from mechanical ventilation. Surrogates often have to make decisions since the patient affected is often incapable of doing so.

**Objective:** To evaluate the expectations of the surrogates as well as the physicians and to evaluate the actual outcome of the patient 1 year after tracheotomy then long-term ventilation support.

**Design/Participants:** A prospective, observational, cohort study done at a single academic medical center. Over 100 patients who were receiving prolonged mechanical ventilation or with various respiratory insults were included.

**Methods:** Participants were interviewed at the time of tracheostomy about their expectations for their future well-being. In addition, the physicians were also interviewed at the time and were required to respond to 3 major areas that included patient survival, functional status, and quality-of-life.

**Results:** In follow-up, only 11 of 126 patients were alive and independent of any major functional status limitations. Interestingly, there was a significant discordance between the surrogate’s expectations and the physician’s expectations, but, in fact, both of them were poorly correlated with the actual outcome. Surrogates believed >70% of the time that the patient would have survived, have a reasonable functional status, and a reasonable quality-of-life. Physicians believed survival was likely approximately 43% of the time, but felt that most patients would have functional limitations and a poor quality-of-life even so. Interestingly, this information was not transmitted to the surrogates. Only 26% reported that the physician discussed with them what their patient’s expectations might be at the time of the tracheostomy.

**Conclusions:** The authors conclude that 1-year patient outcomes for prolonged mechanical ventilation are significantly worse than expected by the patient's surrogates and, in fact, by the physicians as well. There is a significant lack of ability to prognosticate on the physician’s part, and there is discordance between surrogates and physicians regarding the outcomes. Surrogates appear to be unreasonably optimistic.

**Reviewer’s Comments:** I think this is a significant problem and I am not sure what the cause is. The data in the literature are resplendent with information suggesting that these patients typically will have a very poor outcome. The question arises is why is this information not made available to the surrogates at the time when a significant medical intervention is about to take place. The evaluation of physician’s attitudes regarding death and dying and the failure of medical therapy for patients is certainly a significantly fertile area for study. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Prolonged Mechanical Ventilation, Expectations, Outcomes

Print Tag: Refer to original journal article
Fat Emulsions Don’t Affect Outcome in Gram-Negative Sepsis

Efficacy and Safety of a Phospholipid Emulsion in Gram-Negative Severe Sepsis: Results of a Phase 2 Multicenter, Randomized, Placebo—Controlled, Dose Finding Clinical Trial.

Dellinger RP, Tomayko JF, et al:

Crit Care Med 2009; 37 (November): 2929-2938

In this study by Dellinger et al, the 28-day mortality rate is not significantly different between patients who received emulsion and those who did not. The mortality rate was 25.8% in the control group and 31.3% in the placebo group.

Background: Patients with sepsis with decreased levels of lipid in their serum appear to have poor outcomes. In addition lipids appear to help bind endotoxin.

Objective: To identify whether a confusing a lipid emulsion might have any beneficial effect on outcomes in patients with sepsis.

Design/Participants: Prospective, randomized, blinded, placebo-controlled study done at 235 medical centers worldwide between September 2004 and April 2006. The study was conducted on almost 1400 patients.

Methods: 598 received low-dose phospholipid emulsion, 599 received placebo, and the high-dose phospholipid solution was stopped based on recommendation of the independent data monitoring committee due to significant serious adverse events.

Results: The 28-day mortality rate was not significantly different between patients who received emulsion and those who did not. The mortality rate was 25.8% in the control group and 31.3% in the placebo group. Approximately 45% of the patients had microbiologic with demonstrated Gram-negative infections.

Conclusions: The authors conclude, unfortunately, that phospholipid emulsion did not improve mortality rates at the 28-day marker. In addition, the phospholipid did not play a significant role in reducing organ failure in patients who had confirmed or suspected Gram-negative severe sepsis.

Reviewer’s Comments: I usually do not like to print negative studies in this journal, but I thought that the physiology and potential of a nonantibiotic approach to the treatment of patients with sepsis might be interesting to look at. The study also brings to bear on the fact that individual laboratory data from animal models cannot necessarily be extrapolated to a human’s overall response to sepsis, as it is a much more complicated physiological expression that has taken hundreds of millions of years to develop and varies from person to person. (Reviewer-Eric Howard Gluck, MD, JD).

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Keywords: Septic Shock, Gram-Negative, Phospholipid Emulsion

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Interestingly, there is an increased likelihood of mortality at 28 days (OR, 2.07) and a decreased odds of discharge from the hospital (OR, 0.53) if a patient has a delayed transfer from the ED to the ICU.

**Background:** Cases of community-acquired pneumonia (CAP) present to the emergency department (ED) with varying degrees of severity. Many patients require direct ICU admission, while some actually continue to deteriorate in the hospital and thus require ICU transfer several days after admission.

**Objective:** To identify outcomes in these 2 different populations of patients.

**Materials/Methods:** These data were obtained from 4 prior studies (2 done in North America and 2 done in Europe) that were originally prospective multicenter cohort analyses of patients with CAP. The cohort for the current study consisted of 453 patients who were transferred from the ED to an ICU within 3 days of admission. Standard criteria were used for the identification of CAP. All patients appeared to receive a similar regimen as far as resuscitation and antibiotic therapy.

**Results:** A total of 138 patients were delayed transfers to the ICU, and 315 were direct transfers to the ICU. Interestingly, delayed transfer was associated with an increased likelihood of mortality at 28 days (OR, 2.07) and a decreased odds ratio of discharge from hospital (OR of discharge, 0.53). In addition, delayed ICU admission patients had a longer median hospital length of stay, at 13 days versus 7 days for patients immediately transferred to the ICU. The results were no different when the 150 patients with an obvious indication for immediate ICU admission were excluded from the analysis.

**Conclusions:** According to the authors, their findings would suggest that severe CAP might benefit from ICU therapy, since the identification of these patients and transfer later in the course of their illness results in a significant decrease in outcome.

**Reviewer's Comments:** It is not obvious why patients who present overtly with criteria requiring ICU admission would fare better than patients who have more subtle indications for ICU care or who deteriorate despite therapy. It is possible that the patients who were admitted to the floor would have fared just as poorly in the ICU environment. In fact, these patients may represent a subset of patients with a genetic predisposition to poor outcomes following respiratory infection. Decreasing the criteria for ICU admission for patients with CAP could have significant effects on the availability of a limited resource. Obviously, further studies are indicated for this problem. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: CAP, ED, ICU, Delayed Admissions, Direct Admissions

Print Tag: Refer to original journal article