

ABSTRACTS

**META-ANALYSIS OF INCREASED DOSE OF INHALED
STERIOD OR ADDITION OF
SALMETEROL IN SYMPTOMATIC ASTHMA (MIASMA)****Stephen Shrewsbury, Setephen Pyke, Mark Britton**

Objective: To examine the benefits of adding salmeterol compared with increasing dose of inhaled corticosteroids.

Design: Systematic review of randomized, double blind clinical trials. Independent data extraction and validation with summary data from study reports and manuscripts. Fixed and random effects analyses.

Setting: EMBASE, Medline, and Glaxo Wellcome internal clinical study registers.

Main outcome measures: Efficacy and exacerbations.

Results: Among 2055 trials of treatment with salmeterol, there were nine parallel group trials of ≥ 12 weeks with 3685 symptomatic patients aged ≥ 12 year taking inhaled steroid in primary or secondary care. Compared with response to increased steroids, in patients receiving salmeterol morning peak expiratory flow was greater at three months (difference 22.4 (95% confidence interval 15.0 to 30.0) litre/min, $P < 0.001$) and six months (27.7 (19.0 to 36.4) litre/min, $P < 0.001$). forced expiratory volume in one second (FEV_1) was also increased at three months (0.10 (0.04 to 0.16) litres, $P < 0.001$) and six months (0.08 (0.02 to 0.14) litres, $P < 0.01$), as were mean percentage of days and nights without symptoms (three months: days-12% (9% to 15%), nights-5% (3% to 7%); six months: days-15% (12% to 18%), nights-5% (3% to 7%); all $P < 0.001$) and mean percentage of days and nights without need for rescue treatment (three months: days-17% (14% to 20%, nights-9% (7% to 11%); six months: days-20% (17 to 23%), nights-8% (6% to 11%); all $P < 0.001$). Fewer patients experienced any exacerbation with salmeterol (difference 2.73% (0.43% to 5.04%), $P = 0.02$), and the proportion of patients with moderate or severe exacerbations was also lower (2.42% (0.24% to 4.60%), $P = 0.03$).

Conclusion: Addition of salmeterol in symptomatic patients aged 12 and over on low to moderate doses of inhaled steroid gives improved lung function and increased number of days and nights without symptoms or need for rescue treatment with no increase in exacerbations of any severity.

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**A MULTICENTER TRIAL WITH A SOMATOSTATIN
ANALOG ^{99m}Tc DEPREOTIDE IN THE
EVALUATION OF SOLITARY PULMONARY NODULES***

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Neal Rinne, MD, FCCP; and the NeoTect Solitary Pulmonary Nodule Study Group†**

Objective: The affinity of various malignant neoplasms including small cell and non-small cell lung cancer for peptide analogs of somatostatin has been well documented. Depreotide is such an analog and can be complexed with technetium-99m (^{99m}Tc depreotide) for optimal imaging properties. Using this radiopharmaceutical, solitary pulmonary nodules (SPN) were previously evaluated in a successful phase II/III trial. The

results of the larger multicenter phase III study using ^{99m}Tc depreotide to differentiate malignant and benign etiologies in SPN are now presented.

Methods: Patients with SPN ≤ 6 cm on chest radiograph were referred for evaluation. One hundred fourteen individual who had an absence of a benign pattern of calcification on CT scan, age > 30 years, and no demonstrable radiographic stability for the prior 2 years were studied. All underwent single-photon emission CT (SPECT) with ^{99m}Tc depreotide and subsequent tissue histologic examination. Three nuclear medicine specialists blinded to histologic findings examined the SPECT images and scored them as positive or negative based on the presence or absence of activity in the radiographic region of the SPN. The final result was determined by the majority score, which was then compared with the histologic result.

Results: Of the 114 individual studied, 88 had a histologic result compatible with malignant neoplasm. ^{99m}Tc depreotide scintigraphy correctly identified 85 of this group, with three false-negative determinations compared with histology. There were seven false-positive determinations, including six granulomas and one hamartoma. ^{99m}Tc scintigraphy correctly excluded malignancy in 19 of 26 patients with benign histologic findings. The sensitivity of this method was 96.6% with a specificity of 73.1%.

Conclusion: ^{99m}Tc depreotide scintigraphy is a safe and useful method for the noninvasive evaluation of SPN with a sensitivity and accuracy comparable to that reported for fluorine-18 fluorodeoxyglucose positron emission tomography.

(*CHEST 2000; 117:1232-1238*)

WHO GETS CHEMOTHERAPY FOR METASTATIC LUNG CANCER?*

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And Jane C. Weeks, MD, MSc

Study objectives: To determine the prevalence and factors associated with chemotherapy use in elderly patients presenting with advanced lung cancer.

Design: A retrospective cohort study using administrative data.

Setting and patients: We analyzed the medical bills for the 6,308 Medicare patients > 65 years old with diagnosed stage IV non-small cell lung cancer (NSCLC) in the 11 SEER (survival, epidemiology, and end results) regions between 1991 and 1993. The main outcome measure, chemotherapy administration, was identified by the relevant medical billing codes. Patient sociodemographic and disease characteristics were obtained from the SEER database and census data.

Results: Almost 22% of patients received chemotherapy at some time for their metastatic NSCLC. As expected, younger patients and those with fewer comorbid conditions were more likely to receive chemotherapy. However, several nonmedical factors, such as nonblack race, higher socioeconomic status, treatment in a teaching hospital, and living in the Seattle/Puget Sound or Los Angeles SEER regions, also significantly increased a patient's likelihood of receiving chemotherapy.

Conclusion: Compared to previous reports, the prevalence of chemotherapy use for advanced NSCLC appears to be increasing. However, despite uniform health insurance coverage, there is wide variation in the utilization of palliative chemotherapy among Medicare patients, and nonmedical factors are strong predictors of whether a patient receives chemotherapy while it is impossible to know the appropriate rate of usage, nonmedical factors should only influence a patient's likelihood of receiving treatment if they reflect patient treatment preference. Research to further clarify the costs, benefits, and patient preferences for chemo-

therapy in this patient population is warranted in order to minimize the effect of nonmedical biases on management decisions.

(*CHEST 2000; 117:1239-1246*)

EPIDEMIOLOGY AND CLINICOPATHOLOGY OF AORTIC DISSECTION*

A Population-Based Longitudinal Study Over 27 Years

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Study objective: To determine the incidence and mortality as well as to analyze the clinical and pathologic changes of aortic dissection.

Design and setting: A population-based longitudinal study over 27 years on a study population of 106,500, including 66 hospitalized and 18 nonhospitalized consecutively observed patients.

Measures: Analysis of data from the medical, surgical, and autopsy records of patients with aortic dissection.

Results: Altogether, 86 cases of aortic dissection were found in 84 patients, corresponding to a 2.9/100,000/yr incidence. Sixty-six of the 84 patients (79%) were admitted to the hospital, and 18 patients (21%) died before admission. Their ages ranged from 36 to 97 years, with a mean of 65.7 years. The male/female ratio was 1.55 to 1. A total of 22.7% of the hospitalized patients died within the first 6 h, 33.3% within 12 h, 50% within 24 h, and 68.2% within the first 2 days after admission. Six patients were operated on, with a perioperative mortality of two of six patients and a 5-year survival of two of six patients. All patients who were not operated on died. Pain was the most frequent initial symptom. Every patient had some kind of cardiovascular and respiratory sign. Neurologic symptoms occurred in 28 of 66 patients (42%). Five patients presented with clinical pictures of acute abdomen and two with acute renal failure. Trunk arteries were affected in 33 of the 80 autopsied cases (41%), and rupture of aorta was seen in 69 cases (86%). In five cases, spontaneous healing of dissection was also found. The ratio of proximal/distal dissections was 5.1 to 1. All 18 prehospital cases were acute. Fifty-nine cases (89.4%) were acute at admission, and 7 cases (10.6%) were chronic dissections. Hypertension and advanced age were the major predisposing factors.

Conclusion: Aortic dissection was the initial clinical impression in only 13 of the 84 patients (15%). Thus, 85% of the patients did not receive immediate appropriate medical treatment. For this reason, these late-recognized and / or unrecognized cases may be regarded as an untreated or symptomatically treated group, whose course may resemble the natural course of aortic dissection.

(*CHEST 2000; 117:1271-1278*)

PNEUMOTHORAX*

Experience With 1, 199 Patients

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Objective: To study the outcome of pneumothorax managed in a university-affiliated metropolitan medical center.

Design: A retrospective review.

Setting: Busy metropolitan medical center.

Patients and methods: Records of 1,199 patients with pneumothorax were reviewed and analyzed.

Results: Primary spontaneous pneumothorax occurred in 218 patients, secondary spontaneous pneumothorax occurred in 505, traumatic in 403, and iatrogenic in 73. Ninety-six patients with small pneumothorax (8%) were managed by observation, and 1,103 patients (92%) were managed by tube thoracostomy. Drainage of the pleural cavity was continued for 1 to 7 days in 893 patients (81%), 8 to > 10 days in 176 patients (16%), and 10 days in 34 patients (3%). Drainage for > 10 days was classified as persistent pneumothorax. In these 34 patients and in 132 others with a second ipsilateral recurrence (a total of 166 patients), direct pleuroscopy was performed. The pleuroscopy findings and further management are outlined in the algorithm.

Conclusions: Pneumothorax is a common condition affecting all age groups. If the volume of the pneumothorax is > 20% of the pleural space, pleural drainage is indicated. For management of persistent or recurrent pneumothorax, the use of pleuroscopy (direct or video-assisted) is of great value and should be part of routine management.

(*CHEST* 2000; 117:1279-1285)

THE EFFECT OF CORONARY VASOSPASM ON THE DIRECTION OF ST-SEGMENT DEVIATION IN PATIENTS WITH BOTH HYPERTROPHIC CARDIOMYOPATHY AND VASOSPASTIC ANGINA*

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Background: There has been no report of ECG changes during anginal attacks in patients with coexistent hypertrophic cardiomyopathy (HCM) and vasospastic angina.

Study objectives: To elucidate the change in ST-segment during anginal attacks in patients with coexistent HCM and vasospastic angina (the HCM group) in comparison with that of patients with vasospastic angina and no left ventricular hypertrophy (the non-HCM group).

Design: Retrospective study.

Patients: Twelve patients in the HCM group, and 28 patients in the non-HCM group.

Measurement: The direction of ST segment shift, either ST-segment elevation or depression, on the ECGs recorded during vasospastic anginal attacks with severe vasoconstriction in the epicardial coronary artery after intracoronary injection of acetylcholine.

Results: Age, male gender, and distribution of coronary arteries in which the vasospasm occurred were similar between the two groups. Collateral circulation to the affected arteries was absent in all the study patients. The prevalence of anginal attacks associated with ST-segment elevation was 2.7 times higher in the non-HCM group than in the HCM group (51.5% [17 of 33 attacks] vs 18.8% of 16 attacks], respectively; $p = 0.03$).

Conclusions: In the HCM group, myocardial ischemia associated with a transmural injury pattern seen on the ECG, which is represented as ST-segment elevation, seldom develops during vasospastic anginal attacks because of marked left ventricular hypertrophy.

(CHEST 2000; 117:1300-1308)

IS NEBULIZED AEROSOL TREATMENT NECESSARY IN THE PEDIATRIC EMERGENCY DEPARTMENT?*

Comparison With a Metal Spacer Device for Metered-Dose Inhaler

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Background: Infants and small children admitted to the pediatric emergency department (PED) with acute wheezing episodes (AWE) are currently treated with nebulized wet aerosol (NWA).

Objective: To determine the efficacy of MDI with Nebuchamber (Astra AB; Lund, Sweden), a nonelectrostatic spacer device (NESD), as compared to NWA in the treatment of an unselected population of babies and small children with AWE.

Design: Randomized, double-blind, placebo-controlled trial. Forty-two children referred to the PED (median age $\pm$ SD, 16 ± 15 months) with AWE received either placebo MDI through a NESD (four puffs) and salbutamol 0.5 mL (2.5 mg) as a NWA (group I, $n = 19$), or salbutamol MDI and 0.5 mL of saline solution administered in the same manner as above (group II, $n = 23$). This treatment was repeated three times every 20 min.

Results: The respiratory rates (RRs) at baseline were as follows: group I, 45 ± 112 breaths/min; and group II, 52.3 ± 11.3 breaths/min ($p =$ not significant [NS]). After the first, second, and third interventions, the percent fall from baseline of the RR were as follows: group I, 8.9, 13.1, and 17.9%, respectively; group II, 8.6, 14.6, and 18.6%, respectively. There was no significant difference at any time in the results between the two groups. The clinical scores (CSs) at baseline were as follows: group I, 6.6 ± 1.3 ; group II, 6.8 ± 1.49 ($p =$ NS). After the first, second, and third interventions, the percent fall from baseline of the CS were as follows: group I, 9.1, 17.9, and 23.2%, respectively; group II, 8.6, 18.9, and 24.7%, respectively. These results, also, did not differ significantly at any time between the two groups. Hospitalization rate and side effects did not differ between the two groups.

Conclusions: We conclude that even in the group of unselected very young children (mean age < 2 years) with AWE, the use of MDI with NESD is at least as effective as the use of NEA. As opposed to data from an adult population, no plateau was reached in the dose-response curve using the above doses over time.

(CHEST 2000; 117:1309-1313)

THE PROTECTIVE EFFECT OF SALBUTAMOL INHALED USING DIFFERENT DEVICES ON METHACHOLINE BRONCHOCONSTRICTION*

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Study objective: To determine the protective effect of salbutamol, 100 µg, inhaled by different devices (pressurized metered-dose [pMDI; Ventolin; GalxoWellcome; Greenford, UK], pMDI + spacer [Volumatic; GalxoWellcome], or breath-activated pMDI [Autohaler; 3M Pharmaceuticals; St. Paul, MN]) on bronchoconstriction induced by methacholine.

Design: Randomized, double-blind, cross-over, placebo-controlled study.

Patients: Eighteen subjects with stable, moderate asthma, asymptomatic, receiving regular treatment with salmeterol, 50 µg bid, and inhaled beclomethasone dipropionate, 250 µg bid, in the last 6 months, with high hyperreactivity to methacholine (baseline provocative dose of methacholine causing a 20% fall in FEV₁ [PD₂₀] geometric mean [GM], 0.071 mg). Subjects were classified into two groups: subjects with incorrect (n=5) pMDI inhalation technique, and subjects with correct (n=13) inhalation technique.

Methods and measurements: After cessation of therapy for 3 days, all subjects underwent four methacholine challenge tests, each test 1 week apart, each time 15 min after inhalation of salbutamol, 100 µg (via pMDI, pMDI + spacer, or Autohaler), or placebo. The protective effect on methacholine challenge test was evaluated as the change in the PD₂₀, and expressed in terms of doubling doses of methacholine in comparison with placebo treatment.

Results: The PD₂₀ was significantly higher after salbutamol inhalation than after placebo inhalation, but no significant difference was observed among the three different inhalation techniques. Only when salbutamol was inhaled via pMDI + spacer, PD₂₀ was slightly but not significantly higher (pMDI GM, 0.454 mg; pMDI + spacer GM, 0.559 mg; and Autohaler GM, 0.372 mg; not significant [NS]) than other inhalation techniques. Similar results (mean ± SEM) were obtained with doubling doses of methacholine (pMDI, 2 ± 0.47; pMDI + spacer, 3 ± 0.35; and Autohaler, 2.4 ± 0.40; NS). No significant difference was found among techniques when subjects with correct or incorrect inhalation technique were separately considered.

Conclusions: Our data show that the protective effect of salbutamol, 100 µg, on methacholine induced bronchoconstriction is not affected by the different inhalation techniques, although inhalation via pMDI + spacer tends to improve the bronchoprotective ability of salbutamol. These data confirm the clinical efficacy of salbutamol, whatever the device, and the patient's inhalation technique.

(CHEST 2000; 117:1319-1323)

IMPACT OF AIRWAY LABILITY, ATOPY, AND TOBACCO SMOKING ON THE DEVELOPMENT OF ASTHMA-LIKE SYMPTOMS IN ASYMPTOMATIC TEENAGERS*

The Odense Schoolchild Study

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- **Aim:** To investigate the impact of airway lability, atopy, and tobacco smoking on the development of asthma-like symptoms in asymptomatic subjects.

Methods: In this prospective, community-based study, 271 asymptomatic adolescents with an average age at inclusion of 13.9 years were followed for 6.4 years. Airway lability was assessed at baseline by three tests, including exercise challenge, airway provocation with methacholine, and monitoring of peak expiratory flow. Atopy was defined by one or more positive reactions (≥ 3 -mm weal) to 10 common aeroallergens by skin prick testing. The influence of airway lability, atopy, and smoking on the development of asthma-like symptoms was assessed by logistic regression.

Results: During the 6-year study period, 68 of the previously asymptomatic teenagers (25%) developed asthma-like symptoms. Among those, 50% reported cough only, 29% reported wheezing only, and 21% reported both wheezing and coughing. Hyperresponsiveness to methacholine (odds ratio [OR], 3.5; 95% confidence interval [CI], 1.1 to 11.6), smoking (OR, 2.1; 95% CI, 1.2 to 3.8), and atopy (OR 3.5; 95% CI, 1.8 to 6.8) each contributed independently to explain symptom development (wheezing and cough together). Girls, but not boys, with airway lability were less likely to take up smoking, compared with subjects of that set with no airway lability (32% vs 51%; $p < 0.05$). No effect of airway lability on the likelihood of giving up smoking could be demonstrated, nor did the presence of atopy have any significant impact on smoking behavior.

Conclusion: Hyperresponsiveness to methacholine, atopy, and smoking were independent risk factors for the development of asthma-like symptoms during adolescence. The presence of airway lability may prevent girls from taking up smoking.

(*CHEST 2000; 117:1330-1335*)

RACIAL DIFFERENCES IN PHYSIOLOGIC PARAMETERS RELATED TO ASTHMA AMONG MIDDLE-CLASS CHILDREN*

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Background: Asthma morbidity and mortality are higher in the United States for African American (AA) children when compared to European-American (EA) children.

Study objectives: To explore racial differences in physiologic factors associated with pediatric asthma severity.

Design: Cross-sectional.

Methods: We analyzed data from two groups of children in suburban Detroit, one of which contains non-urban, middle-class AA children, a group not usually included in childhood asthma studies. All children were 6 to 8 years of age. Clinical evaluations included medical history, physical examination, skin testing, spirometry, and methacholine challenge.

Results: The study population ($n = 569$) was 14% African American, 51% of the participants were male, and the mean age was 6.8 ± 0.4 years. Socioeconomic status (parental education) was similar overall by race, although some strata-specific differences were observed. The prevalence of physician-diagnosed asthma was 10% for both AA and EA groups. AA children were more reactive to methacholine than EA children (42% vs 22%, respectively; $p = 0.001$), and had significantly higher total IgE than EA children (geometric mean, 60.6 vs 27.5 IU/mL; $p = 0.001$). Serum IgE was related to methacholine reactivity in EA children ($p = 0.001$), but not AA children ($p = 0.73$). These differences remained after adjustment for gender, age, parental education, parental smoking, and maternal smoking during pregnancy.

Conclusions: Our data support previous reports of racial differences in lung volume, airway responsiveness, and serum IgE concentrations. We found a racial difference in the relationship between total serum IgE and airway responsiveness that is unreported elsewhere. Overall, our results suggest that AA children may be predisposed to asthma.

(*CHEST 2000; 117:1336-1344*)

ANTIBIOTICS ARE ASSOCIATED WITH LOWER RELAPSE RATES IN OUTPATIENTS WITH ACUTE EXACERBATIONS OF COPD*

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Background: COPD is a complex disease with exacerbations characterized by worsening of symptoms resulting in deteriorating lung function.

Study objective: To assess predictive factors of relapse for patients with acute exacerbations of COPD (AECB).

Design: Retrospective cohort analysis of visits for AECB.

Setting: Veterans Affairs Medical Center.

Patients: Three hundred sixty-two visits (173 patients) with documented COPD treated as outpatients for AECB.

Measurements: Severity of underlying COPD, severity of AECB, comorbid conditions, therapy, and relapse rates (return visit within 14 days with persistent or worsening symptoms).

Results: Each visit was analyzed individually (referred to as a patient-visit). One group received antibiotics, and the second group (92 patient-visit) did not. Both groups had similar demographics and severity of underlying COPD. The overall relapse rate was 22%. The majority of patient-visits (95%) with severe symptoms at presentation were prescribed antibiotics vs only 40% of those with mild symptoms. Twenty-nine of 92 patient-visits (32%) were followed by relapse in the group that was not given antibiotics, whereas only 50 of 270 (19%) treated with antibiotics relapsed ($p < 0.001$). Those treated with amoxicillin had an even higher relapse rate (20 of 37 patient-visit, or 54%) than those who did not receive antibiotics ($p = 0.006$).

Conclusions: Relapse from AECB was not related to the severity of underlying disease or to the severity of

the acute exacerbation. Patients treated with antibiotics had significantly lower relapse rates than those who did not receive antibiotics. However, the specific choice of antibiotics is important because those treated with amoxicillin had the highest relapse rates of all groups.

(CHEST 2000; 117:1345-1352)

TUMOR NECROSIS FACTOR GENE COMPLEX IN COPD AND DISSEMINATED BRONCHIECTASIS*

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Background: Tumor necrosis factor (TNF) is a potent proinflammatory cytokine with increased levels in the sputum of COPD subjects. Two biallelic TNF gene complex polymorphisms have been described: Lt α NcoI, in the first intron of the lymphotoxin α (previously referred to as TNF- β) gene, and TNF-308, in the promoter region of the TNF- α gene. Higher levels of TNF production are associated with allele 1 of Lt α NcoI (Lt α NcoI*1) and with allele 2 of TNF-308 (TNF-308*2).

Study objectives: To study the frequencies of the two TNF gene complex polymorphisms in patients with COPD and bronchiectasis.

Design: Association study.

Subjects and methods: We studied the frequencies of these polymorphisms in 66 subjects with COPD and in 23 subjects with disseminated bronchiectasis and compared them to the frequencies in 98 healthy control subjects and 45 subjects with nonobstructive pulmonary disease. Genomic DNA samples were extracted, and TNF- α and Lt α NcoI polymorphisms were detected after polymerase chain reaction by restriction digestion.

Results: We found the following frequencies: the TNF-308*2 allele was detected in 11% of COPD individuals, 15% of bronchiectasis patients, 10% of healthy control subjects, and 18% of subjects with nonobstructive pulmonary disease. The Lt α NcoI*1 allele was detected in 28% of COPD individuals, 30% of bronchiectasis patients, 29% of healthy control subjects, and 29% of subjects with nonobstructive pulmonary diseases. We found evidence of linkage disequilibrium between the two loci ($\Delta = 0.068$).

Conclusions: We conclude that the TNF gene complex, at least in Caucasoid individuals and for the considered polymorphisms, does not seem to play a major role as genetic risk factor in COPD and bronchiectasis.

(CHEST 2000; 117:1353-1358)

QUANTITATING PHYSICAL ACTIVITY IN COPD USING A TRIAXIAL ACCELEROMETER*

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Study objective: To determine the reliability, validity, and stability of a triaxial accelerometer for walking and daily activity measurement in a COPD sample.

Design: Cross-sectional, correlational, descriptive design.

Setting: Outpatient pulmonary rehabilitation program in a university-affiliated Veterans Affairs medical center.

Participants: Forty-seven outpatients (44 men and 3 women) with stable COPD (FEV1, 37% predicted; SD, 16%) prior to entry into a pulmonary rehabilitation program.

Measurements and results: Test-retest reliability of a triaxial movement sensor (Tritrac R3D Research Ergometer; Professional Products; Madison, WI) was evaluated in 35 of the 47 subjects during three standardized 6-min walks (intraclass correlation coefficient[rICC] = 0.84). Pearson correlations evaluated accelerometer concurrent validity as a measure of walking (in vector magnitude units), compared to walking distance in all 47 subjects during three sequential 6-min walks (0.84, 0.85, and 0.95, respectively; $p < 0.001$). The validity of the accelerometer as a measure of daily activity over 3 full days at home was evaluated in all subjects using Pearson correlations with other indicators of functional capacity. The accelerometer correlated with exercise capacity (maximal 6-min walk, $r = 0.74$; $p < 0.001$); level of obstructive disease (FEV1 percent predicted, $r = 0.62$; $p < 0.001$) dyspnea (Functional Status and Dyspnea Questionnaire, dyspnea over the past 30 days, $r = -0.29$; $p < 0.05$); and activity self-efficacy (Activity Self-Efficacy Questionnaire, $r = 0.43$; $p < 0.01$); but not with self-report of daily activity (Modified Activity Recall Questionnaire, $r = 0.14$; not significant). Stability of the accelerometer to measure 3 full days of activity at home was determined by an rICC of 0.69.

Conclusion: This study provides preliminary data suggesting that a triaxial movement sensor is a reliable, valid, and stable measure of walking and daily physical activity in COPD patients. It has the potential to provide more precise measurement of everyday physical functioning in this population than self-report measures currently in use, and measures an important dimension of functional status not previously well-described.

(CHEST 2000; 117:1359-1367)

ACUTE CHEST SYNDROME IN ADULTS WITH SICKLE CELL DISEASE*

Therapeutic Approach, Outcome, and Results of BAL in a Monocentric Series of 107 Episodes

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Study objectives: Acute chest syndrome (ACS) is a frequent and potentially severe pulmonary illness in sickle cell disease (SCD). The aim of the study was to report the clinical features and outcome of consecutive ACS episodes in adult patients in a French SCD center. All patients were treated according to an uniform therapeutic protocol applying transfusion only in the more severe clinical form of ACS.

Results: There were 107 consecutive episodes in 77 adult patients (mean age, 29 ± 7 years; 78% hemoglobin [Hb] SS; 14% Hb SC; and 8% Hb S β + thalassemia) over a 6-year period. Seventy eight percent of our patients had an associated vaso-occlusive crisis that preceded the chest signs in half of the cases. Comparison between acute and baseline levels showed a statistically significant difference in Hb levels (drop of 1.6 to 2.25 g/dL depending on Hb genotype), WBC count (increase of $9.2 \pm 8.3 \times 10^9/L$); platelet count (increase of $67 \pm 209 \times 10^9/L$); and lactate dehydrogenase values (increase of 358 ± 775 IU/L) in ACS patients. Hypercapnia was detected in 42% of patients without sign of narcotic abuse. We identified a high percentage of alveolar macrophages containing fat droplets in 31 of 43 (77%) patients who underwent BAL. Bacterial culture findings were almost always negative, but were performed after starting antibiotic therapy that was administered in 96 episodes. Transfusion was required in 50 of 107 ACS events (47%). Five patients died, and all were transfused.

Conclusions: These results confirm that fat embolism is probably a frequent mechanism of ACS in adult patients. However, fat embolism was not associated with a more severe clinical course, suggesting that bronchoscopy and BAL have little impact on the management of these patients. Restricting transfusion to the most severe ACS cases does not seem to increase the mortality rate.

(*CHEST* 2000; 117:1386-1392)

SUCCESSFUL TALC SLURRY PLEURODESIS IN PATIENTS WITH NONMALIGNANT PLEURAL EFFUSION*

Report of 16 Cases and Review of the Literature

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Background: Chemical pleurodesis is an effective treatment for malignant pleural effusion and pneumothorax. This mode of therapy is, however, less widely accepted in the treatment of patients with refractory benign or undiagnosed pleural effusion.

Study objectives: To analyze the outcome of talc slurry pleurodesis in patients with nonmalignant pleural effusions.

Design: Retrospective and partly prospective analysis of clinical outcome.

Setting: Hadassah University Hospital, Jerusalem, Israel.

Patients and participants: Between 1992 and 1997, we treated 16 patients with nonmalignant pleural effusion using talc slurry pleurodesis. The cause of effusion was congestive heart failure in 6 patients, liver cirrhosis in 4 patients, yellow nail syndrome in 1 patient, systemic lupus erythematosus in 1 patient, chylothorax in 1 patient, and undiagnosed in 3 patients.

Interventions: Nine patients were hospitalized, and seven patients received treatment in a day-care setting. Follow-up ranged from 2 months to 3 years.

Results: Complete success was observed in 12 cases (75%), partial success in 3 cases (19%), and pleurodesis was ineffectual in 1 case (6%). There were no significant complications after the procedure in any of our patients. A review of the English-language medical literature revealed an additional 110 reported cases of nonmalignant pleural effusion that were treated with chemical pleurodesis. Of these cases, talc was used in 65% with a success rate of nearly 100%.

Conclusions: Chemical pleurodesis, and specifically talc slurry, is an effective treatment for recurrent benign or undiagnosed pleural effusion. This procedure is safe and easily performed and, in selected cases, can be performed in an outpatient day-care setting.

(*CHEST* 2000; 117:404-1409)

SLEEP APNEA AND HYPERTENSION*

The Role of Peripheral Chemoreceptors and the Sympathetic System

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Study objectives: To examine the central inspiratory drive response to hypoxia in patients with obstructive sleep apnea (OSA), according to their circadian BP profile, and in healthy control subjects. Another objective was to evaluate the relationship among sleep architecture, hypoxic sensitivity, urinary catecholamine excretion, and BP in OSA patients.

Patients and interventions: Polysomnography, 24-h ambulatory BP recording, and urinary excretion of catecholamines were simultaneously examined in 24 consecutive OSA patients and 11 healthy subjects. OSA patients were categorized as being normotensive (type 1), having BP elevation only during sleep (type 2), and as being hypertensive with elevated BP at all times (type 3). The response of mouth occlusion pressure at 0.1 s after onset ($P_{0.1}$) to progressive isocapnic hypoxic stimulation was measured.

Results: There was a significant difference in the $P_{0.1}$ response to hypoxia among control subjects ([mean $\pm$ SD] 0.353 ± 0.129 cm H₂O/%) and type 1 (0.228 ± 0.062 cm H₂O/%), type 2 (0.345 ± 0.106 cm H₂O/%), and type 3 (0.508 ± 0.118 cm H₂O/%) OSA patients. In OSA patients, chemosensitivity was related to the apnea-hypopnea index and to the nocturnal excretion of epinephrine. Significant relationships between the nocturnal excretion of epinephrine and BP were noted. On multiple linear regression analysis, the $P_{0.1}$ response to hypoxia was the only variable significantly related to diurnal ($r^2 = 0.364$; $p = 0.005$) and nocturnal mean BP ($r^2 = 0.461$; $p = 0.002$).

Conclusion: The findings of the present study suggest a possible mediating role of the peripheral chemosensitivity in the association between sleep apnea and hypertension.

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