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## Rivista recensita su Index Medicus e/o Science Citation Index

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Tommasi S.,  
Paradiso A.In: *American Journal  
of Respiratory and Critical  
Care Medicine*;  
Epub 2007; Oct. 25.3P MICROSATELLITE SIGNATURE IN EXHALED BREATH CONDENSATE  
AND TUMOR TISSUE OF LUNG CANCER PATIENTS.

**Rationale:** Our group has recently demonstrated the possibility of studying microsatellite alterations (MAs) of 3p in the DNA of exhaled breath condensate (EBC) of patients with non-small cell lung cancer (NSCLC). **Objectives:** To verify whether MAs analyzed in DNA from EBC reflect a profile of alterations present in tumor tissue of NSCLC.

**Methods:** Fifty-nine subjects undergoing histologic diagnosis for clinical suspicion of lung cancer entered the study: 41 were found to have NSCLC and 18 to have nonneoplastic diseases. All subjects underwent allelotyping on DNA from whole blood, EBC, and lung tissue removed for histologic diagnosis by analyzing a panel of five microsatellites located in chromosomal region 3p. Results obtained from DNA of the three biological sites and nonneoplastic tissues from controls were compared.

**Measurements and Main Results:** MAs in DNA from tumor tissues and EBC of each patient with cancer presented an overlapping profile of loss of heterozygosity and microsatellite instability. An MA profile of DNA of lung tissue reflecting the DNA of EBC profile from controls was also confirmed. Smoking status was associated with the presence of MAs in patients with NSCLC and in control subjects.

**Conclusions:** We demonstrated that MAs in DNA from EBC of patients with NSCLC are significantly more frequent than in control subjects. More interesting, the MA profile of DNA from EBC corresponds to that from lung cancer tissue of each patient with NSCLC.

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Depalo A.,  
Foschino Barbaro M.P.In: *American Journal  
of Rhinology*; 2007; 21;  
5: 542-546.EXHALED INFLAMMATORY MARKERS IN ASPIRIN-INDUCED ASTHMA  
SYNDROME.

**Background:** Interleukin (IL)-4 and IL-6, respectively, markers of neutrophilic and eosinophilic inflammation, were analyzed in nasal and oral exhaled breath condensate to understand the inflammation of upper and lower airways in subjects with aspirin-induced asthma (AIA) syndrome, evaluating possible differences between AIA and the single pathological conditions included in AIA syndrome.

**Methods:** Twelve patients with AIA, 17 patients with mild asthma (MA), 12 patients with nasal polyposis (NP), 11 patients with mild asthma + nasal polyposis (MA + NP), and 10 healthy subjects (HSs) were enrolled. Nasal and oral exhaled IL-4 and IL-6 were measured by enzyme immunoassay kit.

**Results:** Higher levels of nasal and oral exhaled IL-4 and IL-6 were observed in AIA compared with MA, NP, MA + NP, and HSs. Moreover, a positive correlation was identified between nasal exhaled IL-4 and IL-6 and, respectively, the number of neutrophils and eosinophils and in nasal scraping.

**Conclusion:** The concentration of eosinophilic and neutrophilic markers in upper and lower airways of subjects with AIA syndrome is higher compared with HS and subjects with MA, NP, and MA + NP.

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Foschino Barbaro M.P.In: *Oncology Research*;  
2007; 16; 8: 375-381.IL-2, TNF-ALPHA, AND LEPTIN: LOCAL VERSUS SYSTEMIC CONCENTRATIONS  
IN NSCLC PATIENTS.

One recent line of cancer research shows increasing interest for biological factor such as IL-2, TNF-alpha, and leptin, which have been found to participate in the development and progression of non-small cell lung cancer (NSCLC). The aim of this study was to measure IL-2, TNF-alpha, and leptin concentrations in the airways and in the systemic circle of patients with NSCLC, investigating the role of these factors in the lung tumors. We enrolled 32 patients (17 men, 71 ± 7 years) with a histological diagnosis of NSCLC and 20 healthy ex-smoker controls, negative for computed tomography of the chest (14 men, 69 ± 8 years). IL-2, TNF-alpha, and leptin levels were measured in the serum, the urine, the bronchoalveolar lavage, the induced sputum, and exhaled breath condensate (EBC) of patients enrolled by means of a specific enzyme immunoassay kit. Higher concentrations of IL-2, TNF-alpha and leptin were found in NSCLC patients than in controls (p < 0.0001). A statistically significant increase of IL-2, TNF-alpha, and leptin concentrations was observed in patients from stage I to stage III of NSCLC. These findings suggest that IL-2, TNF-alpha, and the leptin play an important role in the cancerogenesis of NSCLC. Their measure in the EBC could be proposed as noninvasive markers for an early detection of NSCLC and in the follow-up of this tumor.

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Dragonieri S.,  
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Sterk P.J.

In: *The Journal of Allergy  
and Clinical Immunology*;  
2007; 19.

## AN ELECTRONIC NOSE IN THE DISCRIMINATION OF PATIENTS WITH ASTHMA AND CONTROLS.

*Background:* Exhaled breath contains thousands of volatile organic compounds (VOCs) that could serve as biomarkers of lung disease. Electronic noses can distinguish VOC mixtures by pattern recognition. *Objective:* We hypothesized that an electronic nose can discriminate exhaled air of patients with asthma from healthy controls, and between patients with different disease severities.

*Methods:* Ten young patients with mild asthma ( $25.1 \pm 5.9$  years; FEV(1),  $99.9 \pm 7.7\%$  predicted), 10 young controls ( $26.8 \pm 6.4$  years; FEV(1),  $101.9 \pm 10.3$ ), 10 older patients with severe asthma ( $49.5 \pm 12.0$  years; FEV(1),  $62.3 \pm 23.6$ ), and 10 older controls ( $57.3 \pm 7.1$  years; FEV(1),  $108.3 \pm 14.7$ ) joined a cross-sectional study with duplicate sampling of exhaled breath with an interval of 2 to 5 minutes. Subjects inspired VOC-filtered air by tidal breathing for 5 minutes, and a single expiratory vital capacity was collected into a Tedlar bag that was sampled by electronic nose (Cyrano 320) within 10 minutes. Smellprints were analyzed by linear discriminant analysis on principal component reduction. Cross-validation values (CVVs) were calculated.

*Results:* Smellprints of patients with mild asthma were fully separated from young controls (CVV, 100%; Mahalanobis distance [M-distance], 5.32), and patients with severe asthma could be distinguished from old controls (CVV, 90%; M-distance, 2.77). Patients with mild and severe asthma could be less well discriminated (CVV, 65%; M-distance, 1.23), whereas the 2 control groups were indistinguishable (CVV, 50%; M-distance, 1.56). The duplicate samples replicated these results.

*Conclusion:* An electronic nose can discriminate exhaled breath of patients with asthma from controls but is less accurate in distinguishing asthma severities.

*Clinical implication:* These findings warrant validation of electronic noses in diagnosing newly presented patients with asthma.

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Foschino Barbaro M.P.,  
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In: *International Journal  
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and Pharmacology*; 2007;  
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## INFLAMMATION, OXIDATIVE STRESS AND SYSTEMIC EFFECTS IN MILD CHRONIC OBSTRUCTIVE PULMONARY DISEASE.

Chronic obstructive pulmonary diseases (COPD) is a pulmonary disease characterized by systemic abnormalities. The aim of this study is to investigate inflammation and systemic effects in mild COPD. Twenty-seven mild stable smoking related COPD patients and 15 age-matched healthy subjects were enrolled in the study. IL-6, TNF-alpha and IL-4 in plasma, sputum and exhaled breath condensate were measured. We also measured exhaled nitric oxide (NO) and pH in sputum and in breath condensate. Moreover, fat-free mass, body mass index (BMI), respiratory muscle strength, plasma oxidative stress and C-reactive protein (CRP) were measured. Higher concentrations were found of CRP, of diacron reactive oxygen metabolites (DROMs) and of IL-6, TNF-alpha and IL-4 either in plasma or in supernatant of induced sputum or in exhaled breath condensate of COPD subjects compared to healthy controls. Furthermore, higher concentrations were observed of exhaled NO and lower exhaled pH in breath condensate of COPD when compared with healthy subjects. In the group of COPD patients, the subjects with airway reversibility showed an increase of sputum eosinophils and exhaled NO, whereas the subjects without airway obstruction reversibility showed an increase in sputum neutrophils, TNF-alpha and IL-6. We also found a trend towards a decrease in fat-free mass and respiratory muscle strength in COPD compared to healthy subjects and a negative correlation between these systemic indices (fat-free mass, maximal inspiratory pressure, maximal expiratory pressure) and TNF-alpha concentrations in the blood, sputum and breath condensate. We conclude that mild COPD subjects present an increase in inflammatory markers in blood and in airways of similar pattern and furthermore, the neutrophilic pattern of airway inflammation observed in the group of COPD subjects without an airway obstruction reversibility makes it more likely that systemic features are present.

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Iozzo R.V.,  
Ludwig M.S.*In: American Journal  
of Physiology. Lung  
cellular and molecular  
physiology; 2007; 293;  
5: L1111-L1117.***EFFECT OF PEEP ON INDUCED CONSTRICTION IS ENHANCED IN DECORIN-DEFICIENT MICE.**

Decorin (Dcn), a small leucine-rich proteoglycan, is present in the extracellular matrix of the airways and lung tissues, contributes to lung mechanical properties, and its deposition is altered in asthma. The effect of Dcn deficiency on airway parenchymal interdependence was examined during induced bronchoconstriction. Studies were performed in C57Bl/6 mice in which the Dcn gene was disrupted by targeted deletion (Dcn<sup>-/-</sup>) and in wild-type controls (Dcn<sup>+/+</sup>). Mice were mechanically ventilated, and respiratory system impedance was measured during in vivo ventilation at positive end-expiratory pressure (PEEP) = 2 and 10 cmH<sub>2</sub>O, before and after aerosol delivery of methacholine (MCh). Length vs. tension curves in isolated tracheal rings were measured in vitro. Dcn distribution in <sup>+/+</sup> mice airways was characterized by immunofluorescence; differences in collagen structure in Dcn<sup>+/+</sup> and Dcn<sup>-/-</sup> mouse lungs was examined by electron microscopy. MCh caused similar increases in airway resistance (Raw) and tissue elastance (H) in Dcn<sup>+/+</sup> and Dcn<sup>-/-</sup> mice. During MCh-induced constriction, increasing PEEP caused a decrease in Raw that was greater in Dcn<sup>-/-</sup> mice and a decrease in H in Dcn<sup>-/-</sup> mice only. Tracheal ring compliance was greater in Dcn<sup>-/-</sup> mice. Imaging studies showed that Dcn was deposited primarily in the airway adventitial layer in Dcn<sup>+/+</sup> mice; in Dcn<sup>-/-</sup> mice, collagen had an irregular appearance, especially in the lung periphery. These results show that lack of Dcn alters the normal interaction between airways and lung parenchyma; in asthma, changes in Dcn could potentially contribute to abnormal airway physiology.

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Salerno F.G.

*In: Giornale Italiano  
di Medicina del Lavoro  
ed Ergonomia; 2007;  
29; 1: 72-73.***INDICI DI OUTCOME.**

La terapia della Broncopneumopatia Cronica Ostruttiva (BCO) e della insufficienza respiratoria acuta e cronica include trattamenti sia farmacologici che riabilitativi. Un problema rilevante è come valutare l'efficacia degli interventi terapeutici. L'approccio corrente è l'utilizzo di indicatori di risultato (o indicatori di outcome), cioè l'utilizzo di variabili che descrivendo in modo sintetico un fenomeno sono capaci di fornire attraverso il confronto con uno standard di riferimento informazioni sull'efficacia di un trattamento.

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Spanevello A.

*In: Giornale Italiano  
di Medicina del Lavoro  
ed Ergonomia; 2007;  
1; 1: 37-39.***PROSPETTIVE DELLA RIABILITAZIONE NELLE MALATTIE RESPIRATORIE.**

Le malattie respiratorie sono fra le prime cause di mortalità e morbilità. In particolar modo la Broncopneumopatia Cronica Ostruttiva (BPCO), tra le malattie respiratorie, si impone oggi, e lo farà ancor di più nel futuro, alla nostra attenzione per la sua rilevanza clinico-epidemiologica e socio-assistenziale fino a costituire una delle aree prioritarie in pubblica sanità. La BPCO è una sindrome clinica eterogenea e complessa caratterizzata da limitazione al flusso espiratorio, nonostante presenti una storia naturale variabile, è una malattia irreversibile ed evolutiva.

Sono molteplici gli approcci terapeutici, farmacologici e non, nel trattamento di tale patologia, aventi come obiettivi principali quello di prevenire e controllare i sintomi, ridurre la frequenza e la gravità delle riacutizzazioni, con conseguente riduzione di ricoveri ospedalieri, migliorare la qualità di vita e la tolleranza allo sforzo. Un ruolo fondamentale è rivestito dalla terapia farmacologica che tuttavia si è rivelata incapace di arrestare e/o modificare la progressiva riduzione del quadro funzionale respiratorio, elemento caratteristico della malattia. Tra le modalità di trattamento non farmacologico emerge, raccomandata da forti evidenze scientifiche che ne documentano l'efficacia, specie in rapporto alla riduzione del numero di riacutizzazioni e quindi di ospedalizzazioni, la Riabilitazione Respiratoria (RR). Approcci globali di trattamento della patologia respiratoria comprendenti Programmi Riabilitativi, si sono sviluppati in questi ultimi anni assumendo un ruolo primario nella gestione dei pazienti, soprattutto se anziani, con problemi respiratori, tanto da avere una influenza preminente nella storia naturale delle malattie respiratorie.

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In: *Monaldi Archives  
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67; 2: 102-105.

**BRITTLE ASTHMA.**

Brittle asthma is a clinical phenotype of the disease at the severe end of the spectrum. Type 1 brittle asthma is characterised by a maintained wide PEF variability ( $> 40\%$  diurnal variation for  $> 50\%$  of the time over a period of at least 150 days) despite considerable medical therapy including a dose of inhaled steroids of at least 1500  $\mu\text{g}$  of beclomethasone or equivalent. Type 2 brittle asthma is characterised by sudden acute attacks occurring in less than three hours without an obvious trigger on a background of apparent normal airway function or well controlled asthma. Mechanisms behind the development of brittle asthma include smooth muscle contraction and edema of the airways, which are supported by chronic airway inflammation. Allergy reactions, impairment of local immunity, respiratory infections, psycho-social disorders and reduced perception of worsening airway function are the risk factors for brittle asthma. The diagnosis is based on the analysis of specific symptoms, role of triggers, personal or family history, measurement of lung function and PEF monitoring. Pharmacological treatment of type 1 brittle asthma in addition to the high doses of inhaled and/or oral steroids and bronchodilators includes subcutaneous injections of beta2 agonist and inhalation of long acting beta2 agonist. The treatment of patients with type 2 brittle asthma includes exclusion of allergen exposure, identification of triggers, self management and management of acute attacks.

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Valerio G.,  
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In: *Respiratory Physiology  
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**THE I.V. INFUSION OF MANNITOL DECREASES AIRWAY RESPONSIVENESS TO METHACHOLINE IN ASTHMA.**

Bronchial asthma and chronic obstructive pulmonary disease (COPD) are characterized by airway inflammation and oedema. The oedema of the airway wall may contribute to airway narrowing and hyperresponsiveness by increasing airway wall thickness, by altering airway compliance, or by impairing the transmission of the lung elastic recoil to the airway smooth muscle (ASM). We hypothesized that the i.v. infusion of mannitol, an osmotic diuretic, would reduce the water content of the airway wall in asthma and COPD, thus decreasing airway responsiveness to methacholine (MCh). In eight asthmatic and in six COPD patients, airway responsiveness to MCh, lung volumes and lung mechanics were measured before and after infusion of mannitol. In the asthmatics, mannitol decreased airway responsiveness to MCh and lung elastic recoil. In the COPD patients, no differences were recorded after mannitol infusion. These data suggest that the airway wall oedema, in asthma, has an impact on airway responsiveness to MCh. The differential effect of mannitol in asthma versus COPD, may relate to the specific pathologic features of the diseases.

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In: *Current Medical  
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**COMMENTS ON: EFFECTS OF CLARITHROMYCIN IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS.**

Letter to the editor.

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Balbi B.,  
Ambrosino N.In: *Respiratory Medicine*;  
2007; 101; 1961-1970.

## SEVEN-YEAR TIME COURSE OF LUNG FUNCTION, SYMPTOMS, HEALTH-RELATED QUALITY OF LIFE, AND EXERCISE TOLERANCE IN COPD PATIENTS UNDERGOING PULMONARY REHABILITATION PROGRAMS.

*Aim:* To evaluate the long-term course of outcome indexes in patients with chronic obstructive pulmonary disease (COPD) undergoing repeated pulmonary rehabilitation programs (PRP).*Design:* Prospective, observational study.*Setting:* Pulmonary Rehabilitation Center.*Patients:* Forty-eight COPD patients (M 33, age 59.6±8.9 years, forced expiratory volume in 1 s (FEV<sub>1</sub>) 58±16% predicted, DLCO 71±17% predicted.) undergoing 5 Day-Hospital based PRPs in a period of 7.2±0.8 years.*Measurements:* Lung function, exercise capacity (incremental cycle ergometry, test-6-minute walking test (6MWD)), dyspnoea (Baseline-BDI and Transitional-TDI Dyspnoea Index and Medical Research Council score-MRC), health-related quality of life (HRQL) (St. George Respiratory Questionnaire (SGRQ), and the derived BODE index were assessed pre and post each PRP.*Results:* During follow-up, patients showed a 18±22 (mean±SEM) ml/year FEV<sub>1</sub> decline (95%CI: -24.4 to 11.6; p<0.001). Exercise tolerance and BDI remained stable over time whereas SGRQ improved (DeltaSGRQ total score: -9.6±14%, p<0.001). BODE index significantly worsened (from 1.27±1.14 to 1.98±1.64; p<0.001), being this change mainly attributable to worsening in FEV<sub>1</sub>. Each PRP elicited significant improvement in exercise capacity, dyspnoea, SGRQ and BODE score. Post-PRP improvements in 6MWD, MRC and TDI were higher after the first three than after the last two PRPs (p<0.001), whereas the greatest gain in SGRQ was observed after PRP1 and then it was lower (p<0.03) but stable in the following periods of observation.*Conclusion:* Despite progressive loss in effectiveness of repeated PRP, COPD patients undergoing those programs do not show any significant worsening in exercise tolerance, dyspnoea and HRQL along a period of 7 years.

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Nava S.In: *Respiratory Medicine*;  
2007; 101; 8: 1702-1707.

## EFFECT OF SLEEP ON PATIENT/VENTILATOR ASYNCHRONY IN PATIENTS UNDERGOING CHRONIC NON-INVASIVE MECHANICAL VENTILATION.

*Background:* Patients who require home non-invasive ventilation (NIV) during sleep normally have the ventilation settings adjusted empirically during daytime wakefulness. However, patient-ventilator asynchrony may occur during sleep. To detect the incidence of ineffective efforts (IE) during the sleep compared to wakefulness, we studied 48 patients already enrolled in a long-term home NIV programme. *Methods:* We evaluated arterial blood gases, breathing pattern during spontaneous breathing (SB) and ventilation during wakefulness. In addition, we assessed the breathing pattern and oxygen gas exchange during night-time NIV.*Results:* Daytime NIV significantly improved blood gases compared to SB (PaO<sub>2</sub> NIV 10.2 ± 1.95 kPa vs PaO<sub>2</sub> SB 8 ± 1.37, p < 0.001; PaCO<sub>2</sub> NIV 5.75 ± 1.08 kPa, vs PaCO<sub>2</sub> SB 6.5 ± 1.25, p < 0.001). The IE index was higher during sleep compared to wakefulness (48 ± 39.5 events/h versus 0 ± 0). The IE index was correlated with the time spent with SaO<sub>2</sub> < 90% (r = 0.39, p < 0.01), but not with ventilator parameters, underlying disease, ventilation mode or type of mask. Eight patients had an IE index >100 events/h; these patients had a faster respiratory rate, required a higher level of inspiratory assistance and had poor gas exchange during sleep.*Conclusions:* We conclude that IE to breathe are common during nocturnal NIV and that they may be associated with desaturations even in patients who are considered compliant and effectively treated.

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This review intends to summarize all articles published in Intensive Care Medicine in 2006 grouped by specific topics.

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This review intends to summarize all articles published in Intensive Care Medicine in 2006 grouped by specific topics.

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2: 90-96.

## RECENT ADVANCES ON THE ROLE OF CHEMOKINES/CHEMOKINE RECEPTORS IN THE PATHOGENESIS OF IDIOPATHIC PULMONARY FIBROSIS.

Idiopathic pulmonary fibrosis (IPF) is a progressive and irreversible lung disease characterized by fibrosis in the lung parenchyma and collagen deposition leading to respiratory failure. Different etiopathogenic hypothesis have been formulated during the last years and many studies recently published demonstrated that in most of processes suggested for the onset and the development of IPF, chemokines and their receptors are involved. Dysregulated expression of chemokines and their receptors during inflammatory processes might also alter the equilibrium between angiostatic and angiogenic processes leading to neovascularization in the lung tissue. Studies on chemokines /chemokine receptors could shed light on the mechanisms involved in IPF and draw new therapeutic strategies to block the progression of the disease.

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Bernard A.In: *Chest*; 2007; 131;  
1: 172-179.

## UTEROGLOBIN-RELATED PROTEIN 1 AND CLARA CELL PROTEIN IN INDUCED SPUTUM OF PATIENTS WITH ASTHMA AND RHINITIS.

*Rationale:* Uteroglobin-related protein 1 (UGRP1) and Clara cell protein (CC16), members of the secretoglobulin family, increasingly appear to play a role in airway inflammatory response.

*Objective:* To explore levels of UGRP1 and CC16 in induced sputum of patients with asthma and rhinitis. *Methods:* Induced-sputum samples of patients with asthma or rhinitis (n = 32 each; atopic asthma, n = 24; atopic rhinitis, n = 20) and from 19 nonsmoking nonatopic control subjects were analyzed for cytology and levels of UGRP1, CC16, and albumin.

*Measurements and Main Results:* Sputum UGRP1 increased in both asthma and rhinitis, most strikingly so in asthma, in which changes were most significant in atopic individuals. By contrast, sputum CC16 did not change significantly in either condition, although it was positively correlated with UGRP1 in patients and control subjects. Changes in sputum UGRP1 in atopic asthma were not linked to permeability changes reflected by increased albumin levels but correlated positively with sputum macrophages and negatively with eosinophils. The observed differences in UGRP1 and CC16 may be linked to different cell populations being responsible for their secretion; UGRP1 is mainly secreted in larger conducting airways, whereas CC16 is mainly secreted by the nasal and peripheral airways epithelium.

*Conclusions:* The increase in UGRP1 but not of CC16 in asthma and rhinitis suggests that UGRP1 may play a role in these inflammatory diseases.

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PAVIADevlin J.W.,  
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Hill N.S.In: *Critical Care  
Medicine*; 2007; 21.

## SURVEY OF SEDATION PRACTICES DURING NONINVASIVE POSITIVE-PRESSURE VENTILATION TO TREAT ACUTE RESPIRATORY FAILURE.

*Objectives:* Noninvasive positive-pressure ventilation (NPPV) is increasingly used in patients with acute respiratory failure, but few data exist regarding current sedation practices during NPPV. We sought to characterize current practices and attitudes regarding sedation during NPPV.

*Design:* Cross-sectional Web-based survey.

*Setting:* Medical institutions.

*Participants:* Physician members of the American College of Chest Physician's Critical Care Network (n = 2,656) and the European Respiratory Society's Assembly of Critical Care (n = 339).

*Interventions:* Survey.

*Measurements and Main Results:* Of the 790 of 2,985 (27%) of physicians who responded, 15%, 6%, and 28% never used sedation, analgesia, or hand restraints any of the time for NPPV patients, respectively, and the large majority reported using these interventions in < or = 25% of patients. Sedation, analgesia, and hand restraints were more commonly used by North Americans than Europeans (41% vs. 24% for sedation, 48% vs. 35% for analgesia, and 27% vs. 16% for hand restraints, all p < .01) and critical care vs. noncritical care physicians (42% vs. 24% for sedation and 50% vs. 34% for analgesia, all p < .01). A benzodiazepine alone was the most preferred (33%), followed by an opioid alone (29%). Europeans were less likely to use a benzodiazepine alone (25% vs. 39%, p < .001) but more likely to use an opioid alone (37% vs. 26%, p < .009). Sedation was usually administered as an intermittent intravenous bolus, outside of a protocol, and was assessed by nurses using clinical end points rather than a sedation scale.

*Conclusions:* Most physicians infrequently use sedation and analgesic therapy for NPPV to treat acute respiratory failure, but practices vary widely within and between specialties and geographic regions.

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## NONINVASIVE VENTILATION IN ACUTE RESPIRATORY FAILURE.

**Background:** Noninvasive ventilation has assumed an important role in the management of respiratory failure in critical care units, but it must be used selectively depending on the patient's diagnosis and clinical characteristics.

**Data:** We review the strong evidence supporting the use of noninvasive ventilation for acute respiratory failure to prevent intubation in patients with chronic obstructive pulmonary disease exacerbations or acute cardiogenic pulmonary edema, and in immunocompromised patients, as well as to facilitate extubation in patients with chronic obstructive pulmonary disease who require initial intubation. Weaker evidence supports consideration of noninvasive ventilation for chronic obstructive pulmonary disease patients with postoperative or postextubation respiratory failure; patients with acute respiratory failure due to asthma exacerbations, pneumonia, acute lung injury, or acute respiratory distress syndrome; during bronchoscopy; or as a means of preoxygenation before intubation in critically ill patients with severe hypoxemia.

**Conclusion:** Noninvasive ventilation has assumed an important role in managing patients with acute respiratory failure. Patients should be monitored closely for signs of noninvasive ventilation failure and promptly intubated before a crisis develops. The application of noninvasive ventilation by a trained and experienced intensive care unit team, with careful patient selection, should optimize patient outcomes.

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## RISK OF WHEEZING ASSOCIATED WITH HOUSE-DUST MITE ALLERGENS AND INDOOR AIR QUALITY AMONG THREE-YEAR-OLD CHILDREN. KRAKÓW INNER CITY STUDY.

The aim of the study was to describe the distribution of house-dust mite (HDM) allergens in homes of three-year-old children and to test the hypothesis whether the content of HDM allergens exceeding 2 mug/g of dust may be regarded as a risk level possibly affecting respiratory health in early childhood.

**Materials and Methods:** House-dust samples were collected in 275 dwellings from mattresses, children's bedrooms and kitchen floors. In the laboratory, dust samples were analyzed for Der f 1 and Der p 1 using monoclonal antibody enzyme-linked immunosorbent assays (ELISA). At the time of the house-dust collection, mothers were interviewed on the household characteristics and their children's respiratory health. Respiratory outcome variables included wheezing or whistling in the chest irrespective of respiratory infections. The number of the wheezing episodes and their duration in days over the last 6 months were recorded in the questionnaire. In the multivariate Poisson regression analysis on the association between the occurrence of wheezing and exposure, a set of potential confounders, such as child's gender, maternal education, maternal allergy, older siblings, presence of moulds, house dampness, and environmental tobacco smoke (ETS) was taken into account.

**Results:** The adjusted incidence rate ratios (IRR) of wheezing ascribed to a higher HDM level ( $> 2.0$  mug/g dust) were 1.84 (95% CI: 1.45-2.34) for duration of wheezing and 1.56 (95% CI: 0.88-2.75) for episodes. Of the confounders taken into consideration, the presence of moulds had the strongest impact on the risk of wheezing (IRR = 4.24; 95% CI: 3.08-5.84).

**Conclusion:** The data support the view that exposure to a higher level of HDM allergens increases the burden of respiratory diseases in the early childhood and the effect is independent of maternal atopy, ETS, and moulds in homes.

**513****Rivista recensita su Index Medicus e/o Science Citation Index**Istituto di  
PAVIA*Mulqueeny Q.,  
Ceriana P.,  
Carlucci A.,  
Fanfulla F.,  
Delmastro M.,  
Nava S.**In: Intensive Care  
Medicine; 2007; 33;  
11: 2014-2018.***AUTOMATIC DETECTION OF INEFFECTIVE TRIGGERING AND DOUBLE TRIGGERING DURING MECHANICAL VENTILATION.**

*Objective:* Imperfect patient-ventilator interaction is common during assisted ventilation, and the detection of clinically relevant mismatching requires visual monitoring of the ventilator screen. We have assessed the feasibility, sensitivity and specificity of an algorithm embedded in a ventilator system that is able to automatically detect the occurrence of ineffective triggering and double triggering in real time.

*Design:* Prospective study.

*Setting:* Respiratory intensive care unit.

*Methods:* Twenty patients undergoing pressure-support ventilation, either non-invasively (NIV, n=10) or conventionally ventilated (n=10), were studied.

*Measurements:* The detection of ineffective triggering and double triggering from the algorithm was compared by two operators with the "real" occurrence of the phenomena as assessed using the transdiaphragmatic pressure (Pdi).

*Results:* Seven of the 20 patients exhibited gross mismatching, while in the remaining patients patient-ventilator mismatching was artificially induced using a pressure control, with a low respiratory rate. Ineffective triggering and double triggering were identified by the operators in 507 and 19 of the 3343 analyzed breaths, respectively. False positives were significantly more frequent in the NIV group than with conventional ventilation. The algorithm had an overall sensitivity of 91% and specificity of 97%. Specificity was statistically higher in the conventional ventilated group than with NIV (99% vs. 95%, p<0.05).

*Conclusions:* We have demonstrated the feasibility and efficacy of a new algorithm to detect the occurrence of impaired patient-ventilator interaction during mechanical ventilation in real time. This software may help the clinician in the identification of this problem, which has been shown to have important clinical consequences.

**514****Rivista recensita su Index Medicus e/o Science Citation Index**Istituto di  
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Sturani C.,  
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European Respiratory  
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making in end stage  
lung disease.**In: European Respiratory  
Journal; 2007; 30;  
1: 156-164.***END-OF-LIFE DECISION-MAKING IN RESPIRATORY INTERMEDIATE CARE UNITS: A EUROPEAN SURVEY.**

A survey was performed on behalf of the European Respiratory Society to assess end-of-life practices in patients admitted to European respiratory intermediate care units and high dependency units over a 6-month period. A 33-item questionnaire was sent by e-mail to physicians throughout Europe and the response rate was 28 (29.5%) out of 95. A total of 6,008 patients were admitted and an end-of-life decision was taken in 1,292 (21.5%). The mortality rate in these patients was 68% (884 out of 1,292). The patients received similar proportions of withholding of treatment (298 (23%) out of 1,292), do-not-resuscitate or do-not-intubate orders (442 (34%) out of 1,292) and noninvasive mechanical ventilation as the ceiling of ventilatory care (402 (31%) out of 1,292). Withdrawal of therapy was employed in 149 (11%) out of 1,292 patients and euthanasia in one. Do-not-intubate/do-not-resuscitate orders were more frequently used in North compared with South Europe. All of the 473 competent patients directly participated in the decision, whereas, in 722 (56%) out of 1,292 cases, decision-making was reported to be shared with the nurses. In European respiratory intermediate care units and high dependency units, an end-of-life decision is taken for 21.5% of patients admitted. Withholding of treatment, do-not-intubate/do-not-resuscitate orders and noninvasive mechanical ventilation as the ventilatory care ceiling are the most common procedures. Competent patients are often involved, together with nurses.

**515****Rivista recensita su Index Medicus e/o Science Citation Index**Istituto di  
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Nava S.

*In: Jama; Feb. 21;  
297 (7): 697.  
Author Reply 698-9.***PREOPERATIVE INSPIRATORY MUSCLE TRAINING AND POSTOPERATIVE COMPLICATIONS (AUTHOR REPLAY).**

Letter to editor.

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In: *Intensive Care  
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## NON-INVASIVE VENTILATION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS: HELMET VERSUS FACIAL MASK.

*Rationale:* The helmet is a new interface with the potential of increasing the success rate of non-invasive ventilation by improving tolerance.

*Objectives:* To perform a physiological comparison between the helmet and the conventional facial mask in delivering non-invasive ventilation in hypercapnic patients with chronic obstructive pulmonary disease.

*Methods:* Prospective, controlled, randomized study with cross-over design. In 10 patients we evaluated gas exchange, inspiratory effort, patient-ventilator synchrony and patient tolerance after 30 min of non-invasive ventilation delivered either by helmet or facial mask; both trials were preceded by periods of spontaneous unassisted breathing.

*Measurements:* Arterial blood gases, inspiratory effort, duration of diaphragm contraction and ventilator assistance, effort-to-support delays (at the beginning and at the end of inspiration), number of ineffective efforts, and patient comfort.

*Main Results:* Non-invasive ventilation improved gas exchange ( $p < 0.05$ ) and inspiratory effort ( $p < 0.01$ ) with both interfaces. The helmet, however, was less efficient than the mask in reducing inspiratory effort ( $p < 0.05$ ) and worsened the patient-ventilator synchrony, as indicated by the longer delays to trigger on ( $p < 0.05$ ) and cycle off ( $p < 0.05$ ) the mechanical assistance and by the number of ineffective efforts ( $p < 0.005$ ). Patient comfort was no different with the two interfaces.

*Conclusions:* Helmet and facial mask were equally tolerated and both were effective in ameliorating gas exchange and decreasing inspiratory effort. The helmet, however, was less efficient in decreasing inspiratory effort and worsened the patient-ventilator interaction.

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Scala R.,  
Nava S.,  
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Hill N.S.

In: *Intensive Care  
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Dec., 33 (12): 2101-8.

## NONINVASIVE VERSUS CONVENTIONAL VENTILATION TO TREAT HYPERCAPNIC ENCEPHALOPATHY IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE.

*Objective:* We recently reported a high success rate using noninvasive positive pressure ventilation (NPPV) to treat COPD exacerbations with hypercapnic encephalopathy. This study compared the hospital outcomes of NPPV vs. conventional mechanical ventilation (CMV) in COPD exacerbations with moderate to severe hypercapnic encephalopathy, defined by a Kelly score of 3 or higher.

*Design and Setting:* A 3-year prospective matched case-control study in a respiratory semi-intensive care unit (RSICU) and intensive care unit (ICU).

*Patients and Participants:* From 103 consecutive patients the study included 20 undergoing NPPV and 20 CMV, matched for age, simplified acute physiology score II, and baseline arterial blood gases.

*Measurements and Results:* ABG significantly improved in both groups after 2 h. The rate of complications was lower in the NPPV group than in the CMV group due to fewer cases of nosocomial pneumonia and sepsis. In-hospital mortality, 1-year mortality, and tracheostomy rates were similar in the two groups. Fewer patients remained on ventilation after 30 days in NPPV group. The NPPV group showed a shorter duration of ventilation.

*Conclusions:* In COPD exacerbations with moderate to severe hypercapnic encephalopathy, the use of NPPV performed by an experienced team compared to CMV leads to similar short and long-term survivals with a reduced nosocomial infection rate and duration of ventilation.

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In: *Chest*; 2007;  
Mar.; 131 (3): 711-7.

## INSPIRATORY MUSCLE UNLOADING BY NEURALLY ADJUSTED VENTILATORY ASSIST DURING MAXIMAL INSPIRATORY EFFORTS IN HEALTHY SUBJECTS.

*Background:* Neurally adjusted ventilatory assist (NAVA) is a mode of mechanical ventilation in which the ventilator is controlled by the electrical activity of the diaphragm (EAdi). During maximal inspirations, the pressure delivered can theoretically reach extreme levels that may cause harm to the lungs. The aims of this study were to evaluate whether NAVA could efficiently unload the respiratory muscles during maximal inspiratory efforts, and if a high level of NAVA would suppress EAdi without increasing lung-distending pressures.

*Method:* In awake healthy subjects ( $n = 9$ ), NAVA was applied at increasing levels in a stepwise fashion during quiet breathing and maximal inspirations. EAdi and airway pressure (Paw), esophageal pressure (Pes), and gastric pressure, flow, and volume were measured.



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*Results:* During maximal inspirations with a high NAVA level, peak Paw was  $37.1 \pm 11.0$  cm H<sub>2</sub>O (mean  $\pm$  SD). This reduced Pes deflections from  $-14.2 \pm 2.7$  to  $2.3 \pm 2.3$  cm H<sub>2</sub>O ( $p < 0.001$ ) and EAdi to  $43 \pm 7\%$  ( $p < 0.001$ ), compared to maximal inspirations with no assist. At high NAVA levels, inspiratory capacity showed a modest increase of  $11 \pm 11\%$  ( $p = 0.024$ ).

*Conclusion:* In healthy subjects, NAVA can safely and efficiently unload the respiratory muscles during maximal inspiratory maneuvers, without failing to cycle-off ventilatory assist and without causing excessive lung distention. Despite maximal unloading of the diaphragm at high levels of NAVA, EAdi is still present and able to control the ventilator.

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Tuggey J.M.,  
Delmastro M.,  
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In: *Respiratory Medicine*;  
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**THE EFFECT OF MOUTH LEAK AND HUMIDIFICATION DURING NASAL NON-INVASIVE VENTILATION.**

*Background:* Poor mask fit and mouth leak are associated with nasal symptoms and poor sleep quality in patients receiving domiciliary non-invasive ventilation (NIV) through a nasal mask. Normal subjects receiving continuous positive airways pressure demonstrate increased nasal resistance following periods of mouth leak. This study explores the effect of mouth leak during pressure-targeted nasal NIV, and whether this results in increased nasal resistance and consequently a reduction in effective ventilatory support.

*Methods:* A randomised crossover study of 16 normal subjects was performed on separate days. Comparison was made of the effect of 5 min of mouth leak during daytime nasal NIV with and without heated humidification. Expired tidal volume (V(T)), nasal resistance (R(N)), and patient comfort were measured.

*Results:* Mean change (Delta) in V(T) and R(N) were significantly less following mouth leak with heated humidification compared to the without (DeltaV(T)  $-36 \pm 65$  ml vs.  $-88 \pm 50$  ml,  $p < 0.001$ ; DeltaR(N)  $+0.9 \pm 0.4$  vs.  $+2.0 \pm 0.7$  cm H<sub>2</sub>O l s<sup>-1</sup>,  $p < 0.001$ ). Baseline comfort was worse without humidification ( $5.3 \pm 0.4$  vs.  $6.2 \pm 0.4$ ,  $p < 0.01$ ), and only deteriorated following mouth leak without humidification.

*Conclusions:* In normal subjects, heated humidification during nasal NIV attenuates the adverse effects of mouth leak on effective tidal volume, nasal resistance and improves overall comfort. Heated humidification should be considered as part of an approach to patients who are troubled with nasal symptoms, once leak has been minimised.

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Balzano G.,  
Fuschillo S.,  
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Gaudiosi C.,  
Mancini A.,  
Caputi M.

In: *Monaldi Archives  
for Chest Disease*; 2007;  
67; 3: 135-141.

**PERSISTENT AIRWAY INFLAMMATION AND HIGH EXACERBATION RATE IN ASTHMA THAT STARTS AT MENOPAUSE.**

*Background and Aims:* Asthma that begins around the time of menopause is frequently characterized by marked clinical severity and poor response to treatment.

We sought to assess the clinical characteristics, bronchial responsiveness, perception of induced bronchoconstriction, and airway inflammation in women with menopausal asthma, as compared to women of similar age with pre-existing asthma.

*Methods:* Nine women with pre-existing asthma were selected for clinical severity (symptoms, lung function and medication requirements) similar to that in 11 women with menopausal asthma. Antiasthmatic treatment in all the study patients included high dose inhaled (with or without oral) corticosteroids.

*Results:* The women with menopausal asthma demonstrated less atopy, more chronic recurrent sinusitis, similar airway responsiveness, and similar perception of induced bronchoconstriction, but a significantly higher sputum eosinophil count ( $19.5$  ( $10.8$  versus  $3.3$  ( $4.3\%$ ;  $P < .001$ )) and a higher severe exacerbation rate during the 1-year follow-up period ( $5.09$  ( $4.85$  versus  $0.78$  ( $0.97$ ;  $P < .05$ )). Sputum eosinophil count and severe asthma exacerbation rate correlated well in both groups considered as a whole ( $r = 0.65$ ;  $P < .005$ ).

*Conclusion:* The eosinophilic airway inflammation present in women with menopausal asthma is poorly responsive to anti-inflammatory treatment with corticosteroids and predisposes to frequent severe exacerbations. Airway inflammation should be monitored in women with menopausal asthma.

**521****Rivista recensita su Index Medicus e/o Science Citation Index**Istituto di  
TRADATEChetta A.,  
Zanini A.,  
Torre O.,  
Olivieri D.*In: Inflammation Allergy  
Drug Targets; 2007;  
6; 1: 41-45.***VASCULAR REMODELLING AND ANGIOGENESIS IN ASTHMA: MORPHOLOGICAL ASPECTS AND PHARMACOLOGICAL MODULATION.**

Tissue remodelling can affect the entire bronchial wall, including the vascular component of the mucosa, in bronchial asthma. The bronchial mucosa is more vascularized in asthmatic patients than in healthy subjects, showing an increase in the number and dimension of vessels and vascular area. In addition, vascular changes can contribute to obstructing the airway flow in asthma.

Vascular Endothelial Growth Factor, a mediator derived from endothelial cells, but also from most inflammatory cells in asthma, plays a primary role in vascular remodelling and angiogenesis. Studies on lung biopsies showed that anti-asthma drugs can decrease to varying degrees the vascular component of airway remodelling in asthma. Among asthma medications, inhaled corticosteroids effectively reverse all aspects of vascular remodelling such as vasodilatation, increased vascular permeability and angiogenesis. A better knowledge of angiogenetic mechanisms in asthma will support the selection of specific medications acting on this aspect of airway remodelling.

The aim of this review is to analyze the morphological aspects of the vascular component in airway remodelling in asthma, as well as its pharmacological modulation.

**522****Rivista recensita su Index Medicus e/o Science Citation Index**Istituto di  
TRADATEChetta A.,  
Zanini A.,  
Olivieri D.*In: Pulmonary  
Pharmacology  
Therapeutics;  
2007; 20; 1: 1-8.***THERAPEUTIC APPROACH TO VASCULAR REMODELING IN ASTHMA.**

Bronchial asthma can be characterized by some significant changes in airway blood vessels, which may contribute to airway remodeling. Despite the clinical and functional consequences of bronchial microvascular remodeling in asthma, up to now, little data has been published on the therapeutic approach to this phenomenon. Corticosteroids are the only anti-asthma drugs that act positively on the three aspects of bronchial vascular remodeling: angiogenesis, dilatation and permeability. Modest positive effects of treatments with 2-agonists and leukotrienes receptor antagonists on bronchial microcirculatory changes have been reported. In the future, agents that specifically inhibit angiogenesis could represent a novel approach for positively acting on bronchial microvascular changes in chronic inflammatory airway diseases, such as chronic bronchitis and asthma.

**523****Rivista recensita su Index Medicus e/o Science Citation Index**Istituto di  
TRADATEChiang C.-Y.,  
Enarson D.A.,  
Hassmiller K.,  
Fanning A.,  
Gupta P.,  
Ray C.,  
Migliori G.B.  
*as a member of the  
Steering committee.**In: The International  
Journal of Tuberculosis  
and Lung Disease; 2007;  
11; 10: 1049-1061.***TOBACCO AND TUBERCULOSIS: A QUALITATIVE SYSTEMATIC REVIEW AND META-ANALYSIS.**

*Objectives:* To assess the strength of evidence in published articles for an association between smoking and passive exposure to tobacco smoke and various manifestations and outcomes of tuberculosis (TB). Clinicians and public health workers working to fight TB may not see a role for themselves in tobacco control because the association between tobacco and TB has not been widely accepted. A qualitative review and meta-analysis was therefore undertaken.

*Methods:* Reference lists, PubMed, the database of the International Union Against Tuberculosis and Lung Disease and Google Scholar were searched for a final inclusion of 42 articles in English containing 53 outcomes for data extraction. A quality score was attributed to each study to classify the strength of evidence according to each TB outcome. A meta-analysis was then performed on results from included studies.

*Results:* Despite the limitations in the data available, the evidence was rated as strong for an association between smoking and TB disease, moderate for the association between second-hand smoke exposure and



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TB disease and between smoking and retreatment TB disease, and limited for the association between smoking and tuberculous infection and between smoking and TB mortality.

There was insufficient evidence to support an association of smoking and delay, default, slower smear conversion, greater severity of disease or drug-resistant TB or of second-hand tobacco smoke exposure and infection.

*Conclusions:* The association between smoking and TB disease appears to be causal. Smoking can have an important impact on many aspects of TB. Clinicians can confidently advise patients that quitting smoking and avoiding exposure to others' tobacco smoke are important measures in TB control.

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*Fattorini L.,  
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*In: Annali Istituto  
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2007; 43; 4: 317-319.*

**EXTENSIVELY DRUG-RESISTANT (XDR) TUBERCULOSIS: AN OLD AND NEW THREAT.**

Tuberculosis remains a worldwide emergency (8 million new cases per year, 2 million deaths annually) mostly affecting poor countries. To this old, persistent threat, a new emergency is adding further challenges, i.e., the multidrug-resistant TB, of which TB in its extreme and highly lethal form, is called XDR TB (extensively drug-resistant tuberculosis). How to fight XDR TB is a high research and public health priority.

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*Matteelli A.,  
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Centis R.,  
Girardi E.,  
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*In: Expert Review  
of anti-infective therapy;  
2007; 5; 5: 857-871.*

**MULTIDRUG-RESISTANT AND EXTENSIVELY DRUG-RESISTANT MYCOBACTERIUM TUBERCULOSIS: EPIDEMIOLOGY AND CONTROL.**

The emergence of multidrug-resistant (MDR)-TB and, more recently, of extensively drug-resistant (XDR)-TB is a real threat to achieve TB control and elimination. Over 400,000 new cases of MDR-TB occur each year and, although their number is currently unknown, XDR cases are recognized in every setting where there has been the capacity to detect them. The long-term vision for the full control of MDR-TB requires the scaling-up of culture and drug-susceptibility testing capacity, which is very limited in disease-endemic countries, and the expanded use of high-technology assays for rapid determination of resistance. MDR cases are treatable and well designed regimens, largely based on second-line anti-TB drugs, can considerably improve cure rates. However, treatment regimens need to be markedly improved through the introduction of less toxic and more powerful drugs, thus reducing duration of treatment and tolerability. This is of utmost importance for XDR-TB cases. The prevalence of MDR-TB and XDR-TB are inversely correlated with the quality of TB control and the proper use of second-line anti-TB drugs. Adherence to proper standards of care and control is imperative and a top priority of all TB control efforts. However, the risk of an uncontrollable epidemic of MDR- and XDR-TB is real considering current levels of financing and commitment to care.

**526****Rivista recensita su Index Medicus e/o Science Citation Index**Istituto di  
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In: *European Respiratory  
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**CLINICAL AND OPERATIONAL VALUE OF THE EXTENSIVELY DRUG-RESISTANT TUBERCULOSIS DEFINITION.**

Currently, no information is available on the effect of resistance/susceptibility to first-line drugs different from isoniazid and rifampicin in determining the outcome of extensively drug-resistant tuberculosis (XDR-TB) patients, and whether being XDR-TB is a more accurate indicator of poor clinical outcome than being resistant to all first-line anti-tuberculosis (TB) drugs. To investigate this issue, a large series of multidrug-resistant TB (MDR-TB) and XDR-TB cases diagnosed in Estonia, Germany, Italy and the Russian Federation during the period 1999-2006 were analysed. Drug-susceptibility testing for first- and second-line anti-TB drugs, quality assurance and treatment delivery was performed according to World Health Organization recommendations in all study sites. Out of 4,583 culture-positive TB cases analysed, 361 (7.9%) were MDR and 64 (1.4%) were XDR. XDR-TB cases had a relative risk (RR) of 1.58 to have an unfavourable outcome compared with MDR-TB cases resistant to all first-line drugs (isoniazid, rifampicin ethambutol, streptomycin and, when tested, pyrazinamide), and an RR of 2.61 compared with "other" MDR-TB cases (those susceptible to at least one first-line anti-TB drug among ethambutol, pyrazinamide and streptomycin, regardless of resistance to the second-line drugs not defining XDR-TB). The emergence of extensively drug-resistant tuberculosis confirms that problems in tuberculosis management are still present in Europe. While waiting for new tools which will facilitate management of extensively drug-resistant tuberculosis, accessibility to quality diagnostic and treatment services should be urgently ensured and adequate public health policies should be rapidly implemented to prevent further development of drug resistance.

**527****Rivista recensita su Index Medicus e/o Science Citation Index**Istituto di  
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Migliori G.B.,  
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In: *European Respiratory  
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2: 194-198.

**RIPPED FROM THE HEADLINES: HOW CAN WE HARNESS COMMUNICATIONS TO CONTROL TB?**

Tuberculosis, the "white plague," still causes more than 9 million illnesses and claims more than 1.6 million lives annually, 125 years after Robert Koch discovered the tubercle bacillus and 63 years since the discovery of streptomycin, the first anti-TB drug. Even with this tremendous toll, little attention has been paid to TB by the media or the general public, contributing to a lack of political will and public action to solve this global health emergency. With the recent rekindling of media and popular interest in the emerging threat of extensively drug resistant TB (XDR-TB), the health community has a critical opportunity to leverage more coordinated and purposeful communications as an important weapon in the fight against TB. Data gathered through a population-based cross-sectional study performed in Italy by DOXA, a major Institute of Research Statistics and Analysis of Public Opinion, on request of StopTB Italia Onlus during February - March 2007 are a starting point for developing a communications strategy and key messages to improve Europe's response to the TB epidemic.

**528****Rivista recensita su Index Medicus e/o Science Citation Index**Istituto di  
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In: *Eurosurveillance*;  
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**FIRST TUBERCULOSIS CASES IN ITALY RESISTANT TO ALL TESTED DRUGS.**

Extensively Drug Resistant Tuberculosis (XDR-TB) is a very serious form of TB against which our treatment weapons have lost the majority of, if not all, their power [1-5]. The term XDR-TB appeared for the first time only in March 2006, to describe a form of disease caused by strains of *Mycobacterium tuberculosis* which were resistant not only to isoniazid and rifampicin (i.e., the definition of multidrug-resistant TB, MDR-TB), but also to at least three of the six classes of second-line anti-TB drugs (aminoglycosides, polypeptides, fluoroquinolones, thioamides, cycloserine and para-aminosalicylic acid) [1]. The definition was modified in October 2006 to define cases that are resistant to at least rifampicin and isoniazid, in addition to any fluoroquinolone, and to at least of the three following injectable drugs used to treat TB: capreomycin, kanamycin and amikacin [2]. Available evidence shows that 10 out of 21 countries that had at least one notified case of XDR-TB as of March 2007, are in, or bordering, Europe [3]. Recently, the term "XXDR" was proposed [3] to define "extremely drug resistant" TB, i.e. the cases being resistant to all first- and second-line drugs with a proven activity against *M. tuberculosis*.

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**CLINICAL AND OPERATIONAL VALUE OF THE EXTENSIVELY DRUG-RESISTANT TUBERCULOSIS DEFINITION.**

Currently, no information is available on the effect of resistance/susceptibility to first-line drugs different from isoniazid and rifampicin in determining the outcome of extensively drug-resistant tuberculosis (XDR-TB) patients, and whether being XDR-TB is a more accurate indicator of poor clinical outcome than being resistant to all first-line anti-tuberculosis (TB) drugs.

To investigate this issue, a large series of multidrug-resistant TB (MDR-TB) and XDR-TB cases diagnosed in Estonia, Germany, Italy and the Russian Federation during the period 1999-2006 were analysed. Drug-susceptibility testing for first- and second-line anti-TB drugs, quality assurance and treatment delivery was performed according to World Health Organization recommendations in all study sites.

Out of 4,583 culture-positive TB cases analysed, 361 (7.9%) were MDR and 64 (1.4%) were XDR. XDR-TB cases had a relative risk (RR) of 1.58 to have an unfavourable outcome compared with MDR-TB cases resistant to all first-line drugs (isoniazid, rifampicin, ethambutol, streptomycin and, when tested, pyrazinamide), and a RR of 2.61 compared with "other" MDR-TB cases (those susceptible to at least one first-line anti-TB drug among ethambutol, pyrazinamide and streptomycin, regardless of resistance to the second-line drugs not defining XDR-TB).

The emergence of extensively drug-resistant tuberculosis confirms that problems in tuberculosis management are still present in Europe. While waiting for new tools which will facilitate management of extensively drug-resistant tuberculosis, accessibility to quality diagnostic and treatment services should be urgently ensured and adequate public health policies should be rapidly implemented to prevent further development of drug resistance.

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*In: European Respiratory  
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3: 423-427.*

**125 YEARS AFTER ROBERT KOCH'S DISCOVERY OF THE TUBERCLE BACILLUS: THE NEW XDR-TB THREAT. IS "SCIENCE" ENOUGH TO TACKLE THE EPIDEMIC?**

The year 2006 will be remembered for the appearance of extensively drug-resistant TB (XDR-TB), a very serious form of TB against which our armamentarium has virtually lost all its most powerful ammunitions. The term XDR-TB was used for the first time in March 2006, in a report jointly published by the US Centers for Disease Control and Prevention (CDC) and WHO to describe a disease caused by strains of *Mycobacterium tuberculosis* which were resistant, not only to isoniazid and rifampicin (i.e., MDR-TB), but also to at least three of the six classes of second-line anti-TB drugs (aminoglycosides, polypeptides, fluoroquinolones, thioamides, cycloserine and para-aminosalicylic acid). As the definition is dependent on difficult-to-perform drug susceptibility testing (DST) and as some forms of drug-resistance are less treatable than others, it was eventually modified at a meeting of the WHO XDR-TB Task Force that took place on 10-11 October 2006 in Geneva. Thus, XDR-TB is now defined as resistance to at least rifampicin and isoniazid (which is the definition of MDR-TB), in addition to any fluoroquinolone, and to at least one of the three following injectable drugs used in anti-TB treatment: capreomycin, kanamycin and amikacin.

The aim of this paper is to describe XDR-TB, focusing on the mechanism determining its selection and spread, the implications and challenges that XDR-TB poses to TB control, and the possible approaches to tackle it.

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*In: Emerging Infectious  
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## EXTENSIVELY DRUG-RESISTANT TUBERCULOSIS, ITALY AND GERMANY.

Twenty-three countries have reported >1 case of extensively drug-resistant tuberculosis (XDR TB) (1); however, information about XDR TB is still incomplete. In particular, the response of XDR TB to treatment in countries with low incidence is not known. We compared mortality rates from XDR TB with those from multidrug-resistant (MDR) TB.

We analyzed data from all culture-confirmed TB cases diagnosed during 2003–2006 by the TB clinical reference centers in Italy (Sondalo, Milan, Rome) and Germany (Borstel, Grosshansdorf, Bad-Lippspringe) and reviewed original clinical records. Drug susceptibility testing for first- and second-line anti-TB drugs was performed according to World Health Organization (WHO) recommendations by quality-assured laboratories and retested at WHO Supranational Reference Laboratories (Rome/Milan; Borstel) (2–4).

XDR TB was defined as resistance to at least rifampin and isoniazid (MDR TB definition) in addition to any fluoroquinolone and >1 of 3 injectable anti-TB drugs (capreomycin, kanamycin, amikacin) (3). Characteristics of MDR TB and XDR TB cases were compared by 2 test (categorical variables), Student t test (admission days), and Kaplan-Maier curve (sputum smear, culture conversion), where appropriate. Of 2,888 culture-positive TB cases analyzed (Italy 2,140, Germany 748), 126 (4.4%) were MDR (Italy 83, Germany 43) and 11 (0.4%) were XDR (Italy 8, Germany 3). We estimate that the TB cases analyzed represent 24% of culture-positive cases reported in Italy (69.7% of MDR) and 4.2% of those reported in Germany (12.6% of MDR). XDR TB was diagnosed in each year of the study. All 11 XDR TB patients were receiving retreatment, and of the 126 MDR TB patients, 74 (58.7%) were receiving retreatment. All XDR TB patients were HIV seronegative; and of 109 MDR TB patients tested for HIV, 10 (9.2%) were HIV seropositive. Details about previous treatment regimens, drug resistance, and duration of treatment of XDR TB patients are summarized in the Appendix Table. XDR TB patients were significantly more likely than MDR TB patients to be resistant to all first-line drugs (8/11 vs. 36/126,  $p < 0.005$ ); 2 of these patients were resistant to all tested drugs (Appendix Table).

In Germany, nonnationals accounted for 95.3% (41/43) of MDR TB cases and 100% (3 of 3) of XDR TB cases (all from the former Soviet Union); in Italy, they accounted for 72.3% (60/83) and 50% (4/8), respectively ( $p < 0.001$ ). Of 126 patients with MDR, 8 (6.3%) died, 45 (35.7%) were treated successfully, 67 (53.2%) were still receiving treatment (after achieving bacteriologic conversion, radiologic and clinical improvement, or both), and 6 defaulted (4.8%). Of 11 patients with XDR, 4 (36.4%) died and 7 (63.6%) were still receiving treatment. Compared with MDR TB patients, XDR TB patients had a 5-fold higher risk for death (relative risk 5.45; 95% confidence interval 1.95–15.27;  $p < 0.01$ ) and required longer hospitalization (mean  $\pm$  SD 241.2  $\pm$  177.0 vs. 99.1  $\pm$  85.9 days;  $p < 0.001$ ) and longer treatment durations (30.3  $\pm$  29.4 vs. 15.0  $\pm$  23.8 months;  $p < 0.05$ ). Smear and culture conversions were observed for 4 XDR TB patients compared with 102 MDR TB patients (smear median 110 vs. 41 days; culture median 97.5 vs. 58 days, respectively); time to smear and culture conversion significantly differed between the 2 groups ( $p < 0.01$ ). A higher percentage of XDR TB than MDR TB patients had received previous anti-TB treatment (100% [11/11] vs. 59% [74/126], respectively,  $p < 0.01$ ) and were >45 years of age (64% [7/11] and 23% [29/126], respectively,  $p < 0.01$ ). Radiologic patterns of the thorax did not differ between XDR TB and MDR TB patients. In the overall sample, the only variable significantly associated with death (other than XDR TB status) was immigrant status ( $p < 0.01$ ). The association between XDR TB status and risk for death remained significant after stratification by immigrant status ( $p < 0.05$ ).

Our findings suggest that mismanagement of TB cases plays a major role in emergence of the problem in Europe (along with suboptimal infection control in congregate settings) (5), while in high HIV-prevalence settings (e.g., South Africa) XDR TB was mainly observed in patients never treated previously (6). Mortality rates among MDR TB patients treated in reference centers (6.3%) were lower than the rate observed in a previous study in general hospitals in Italy (8.7%) (5), although a proportion of our MDR TB patients are still completing treatment. This difference in rates is probably due to better management of MDR in the reference centers. Because of the high proportion of XDR TB patients still receiving treatment, further follow-up is necessary to assess potential for cure. The clinical relevance of resistance to all first-line drugs or other factors (e.g., delayed or inadequate treatment, suboptimal observation of drug intake) as major determinants of death needs further evaluation. The appearance of XDR TB in western Europe confirms that poor management and poor infection control in congregate settings exist and that new rapid diagnostic tests and new drugs are urgently needed.

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In: *Respiratory Medicine*;  
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## DOTS IMPLEMENTATION IN A POST-WAR, UNITED NATIONS ADMINISTERED TERRITORY: LESSONS FROM KOSOVO.

*Setting:* The WHO-recommended strategy of tuberculosis control (DOTS Strategy) has been shown to be effective in reducing tuberculosis incidence in a variety of countries/ settings. Little evidence exists on the implementation, and effectiveness of DOTS in a transitional, post-war setting.

*Objective:* To describe the process of establishing a National Tuberculosis Control Program (NTP) and implementing DOTS throughout Kosovo, and the outcomes achieved by this international collaboration in a post-war transitional setting during 1999-2005.

*Methods:* In 1999, as part of the re-organization of health services, a DOTS-based NTP was established and operationalized through a collaboration of several international partners in Kosovo. Five key steps supported these activities.

*Results:* Kosovo has reached the World Health Assembly targets, having achieved 75% case detection rate (sputum smear-positive cases) and 93% treatment success rate. During 2000-2005, new smear-positive tuberculosis case notifications decreased by 44.5% (median annual decrease for all cases: 7.6%).

*Conclusions:* Kosovo's success story is a collaborative tale, each partner involved playing a unique role in supporting NTP activities. The Kosovo example provides yet another setting in which DOTS implementation has resulted in successful patient outcomes. The international TB control community would be well-served by formal guidelines for implementing DOTS and the new STOP TB Strategy in these settings.

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In: *Respiratory Medicine*;  
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## CHANGES IN SPUTUM COMPOSITION DURING 15 MIN OF SPUTUM INDUCTION IN HEALTHY SUBJECTS AND PATIENTS WITH ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE.

The use of sputum induction by inhalation of hypertonic saline to study the cellular and biochemical composition of the airways allows noninvasive sampling of the airways content and identification of markers of airways inflammation.

*Objective:* The present study aimed to identify possible changes in the cellular composition of induced sputum between samples obtained sequentially (three periods of 5 min each) during one sputum induction. Moreover, difference between these samples and the mixed one (mixture of samples obtained after 5, 10 and 15 min of induction) was investigated.

*Methods:* Forty-six subjects (10 healthy volunteers, 12 patients with chronic obstructive pulmonary disease (COPD) and 24 patients with asthma) (mean age  $53.0 \pm 14.0$  yr, forced expiratory volume in one second (FEV<sub>1</sub>)  $71.8 \pm 19.0\%$  pred) produced sputum after three consecutive 5 min periods of hypertonic (4.5%) saline inhalation. Stained cytopspins from the three periods separately and from the mixed sample were produced and analyzed.

*Results:* The mean percentage of neutrophils, eosinophils, lymphocytes and epithelial cells did not change significantly in samples obtained consecutively after 5, 10 and 15 min of the induction procedure. There was no significant difference in the cellular composition of samples obtained after 5, 10 and 15 min of induction and the cellular composition of the mixed sample ( $P=0.06$ ).

*Conclusion:* The separate analysis of induced sputum from three consecutive sampling and the mixed sample did not demonstrate significant changes in their cellular composition. Fifteen minutes induction procedure with the fixed concentration of hypertonic saline and processing of the mixed sample can be recommended for clinical settings and clinical trials.

Keywords: Asthma; Chronic obstructive pulmonary disease; Induced sputum.

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Spanevello A.In: *Annals of Allergy,  
Asthma & Immunology*;  
2007; 99; 3: 232-235.**VALIDITY AND REPRODUCIBILITY OF MORPHOLOGIC ANALYSIS OF NASAL SECRETIONS OBTAINED USING ULTRASONIC NEBULIZATION OF HYPERTONIC SOLUTION.***Background:* Collection of nasal secretions is important for the evaluation of upper airways inflammation in many nasal disorders.*Objective:* To study the validity and reproducibility of nasal secretion cellularity induced by nebulization of hypertonic solution in patients with allergic rhinitis (AR), patients with nonallergic rhinitis with eosinophilia syndrome (NARES), and control subjects.*Methods:* Sixty-eight individuals (29 with AR [mean  $\pm$  SD age, 33.3  $\pm$  16.9 years], 23 with NARES [mean  $\pm$  SD age, 46.4  $\pm$  16.6 years], and 16 controls [mean  $\pm$  SD age, 42.1  $\pm$  15.1 years]) underwent ultrasonic nebulization of hypertonic (4.5%) saline solution on 2 different occasions to study the validity and reproducibility of total and differential cell counts of nasal secretions.*Results:* The mean  $\pm$  SD percentage of eosinophils was significantly higher in samples from patients with AR (20.8%  $\pm$  23.1%) and NARES (18.7%  $\pm$  22.8%) than in samples from controls (0.6%  $\pm$  0.6%;  $P < .001$  for both). There was a significant correlation between 2 samples of nasal secretions obtained on 2 different occasions for percentages of macrophages, neutrophils, eosinophils, and epithelial cells.*Conclusions:* The analysis of nasal secretions obtained using ultrasonic nebulization of hypertonic solution can distinguish patients with AR and NARES from controls. The reproducibility of this technique is good for macrophages, neutrophils, eosinophils, and epithelial cells. This method could be used to detect nasal airway inflammation in clinical settings.**535****Rivista recensita su Index Medicus e/o Science Citation Index**Istituto di  
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and Clinical Immunology*;  
2007; 120; 2: 329-333.**CHYMASE-POSITIVE MAST CELLS PLAY A ROLE IN THE VASCULAR COMPONENT OF AIRWAY REMODELLING IN ASTHMA.***Background:* There is increasing evidence to support a role for total mast cells in the vascular component of airway remodeling in asthma. On the contrary, up to now, no study has addressed the role of chymase-positive mast cells (MCTC) in microvasculature changes.*Objective:* To assess the role of MCTC in the vascular component of airway remodeling in asthma.*Methods:* We recruited 8 mild to moderate asthmatic patients and 8 healthy volunteers, as a control group. Fiberoptic bronchoscopy with endobronchial biopsy specimens was successfully performed in all subjects. Immunostaining was performed for quantification of vessels, VEGF+ cells, total mast cells (MCTOT) and MCTC.*Results:* As compared to healthy subjects, endobronchial biopsies from asthmatic patients showed an increased number of MCTOT and MCTC and VEGF+ cells ( $p < 0.05$ ). In asthmatic patients, the number of vessels and the vascular area were also higher than in healthy subjects ( $p < 0.05$ ). Additionally, in asthmatic patients the number of MCTC was significantly related to the vascular area ( $r_s = 0.74$ ,  $p < 0.01$ ) and to the number of VEGF+ cells ( $r_s = 0.78$ ,  $p < 0.01$ ). Moreover, a colocalization study revealed that MCTC were a relevant cellular source of VEGF. Finally, a 6-wks treatment with inhaled Fluticasone Propionate was able to reduce MCTC.*Conclusion:* MCTC can play a role in the vascular component of airway remodeling in asthma, possibly through induction of VEGF.*Clinical implications:* Specific targeting of MCTC may be a tool for treating vascular remodeling in asthma.**536****Rivista recensita su Index Medicus e/o Science Citation Index**Istituto di  
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Balbi B.

In: *Giornale Italiano  
di Medicina del Lavoro  
ed Ergonomia*; 2007;  
29; 1: 62-64.**LA VALUTAZIONE DEL PAZIENTE CON INSUFFICIENZA RESPIRATORIA.**

L'Insufficienza Respiratoria (IR) è una condizione clinica caratterizzata dalla inadeguatezza dell'apparato respiratorio a compiere il proprio ruolo fisiologico, e fondamentalmente a scambiare i gas respiratori, ossigeno (O<sub>2</sub>) ed anidride carbonica (CO<sub>2</sub>), con l'aria esterna all'organismo. In quest'ottica quindi l'IR è una condizione che viene riconosciuta e diagnosticata a mezzo di una determinazione emogasanalitica arteriosa, volta a misurare le pressioni parziali dell'O<sub>2</sub> (PaO<sub>2</sub>) e della CO<sub>2</sub> (PaCO<sub>2</sub>) nel sangue arterioso. Se tali pressioni risultano al di sotto di una certa soglia per l'O<sub>2</sub> od al di sopra per la CO<sub>2</sub> viene posta la diagnosi di IR. L'IR



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con diminuzione della PaO<sub>2</sub> senza incremento della PaCO<sub>2</sub> si definisce IR ipossiémica o semplice, mentre la IR con diminuzione della PaO<sub>2</sub> ed associato incremento della PaCO<sub>2</sub> si definisce IR ipossiémica/ipercapnica o globale. I meccanismi fisiopatologici che causano o concausano l'IR sono molteplici. In primo luogo possiamo distinguere il deficit di "pompa", inteso come la incapacità della complessa struttura formata dalla gabbia toracica e dai muscoli respiratori che sovrintendono ai movimenti respiratori, ed all'opposto il deficit del parenchima polmonare, inteso come la conseguenza delle alterazioni strutturali avvenute nelle strutture alveolo-capillari e delle vie aeree nelle diverse malattie respiratorie. Oltre a questa differenza fondamentale nella patogenesi dell'IR, è possibile ulteriormente identificare quattro meccanismi fisiopatologici della IR:

- 1) ipoventilazione alveolare;
- 2) alterazioni della diffusione alveolo-capillare;
- 3) shunt destro-sinistro;
- 4) alterazioni del rapporto ventilazione/perfusione.

Tutti questi meccanismi fisiopatologici possono coesistere anche nella medesima patologia. Nella BPCO, ad esempio, possono essere presenti sia le alterazioni del parenchima (distruzione dei setti alveolari) sia le alterazioni della pompa muscolare (esaurimento funzionale dei muscoli respiratori); similmente, nei pazienti con BPCO l'ipoventilazione alveolare, le alterazioni della diffusione, lo shunt destro-sinistro e le alterazioni del rapporto ventilazione/perfusione cooperano nella genesi della IR, in maniera diversa da caso a caso. Quindi i diversi meccanismi vanno intesi come coesistenti e non mutualmente esclusivi nella gran maggioranza dei casi delle patologie respiratorie.

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**BRONCHOALVEOLAR LAVAGE, SPUTUM AND EXHALED CLINICALLY RELEVANT INFLAMMATORY MARKERS: VALUES IN HEALTHY ADULTS.**

Bronchoalveolar lavage (BAL), induced sputum (IS) and the recently introduced exhaled biomarkers, nitric oxide (NO) and exhaled breath condensate (EBC), are biological tools applied with the aim of being an aid in the diagnostic process of various respiratory diseases. One pre-requisite to give value to their results is to have reliable reference data in normal subjects. This review will focus on the literature data that specifically addressed the issue of normal reference values in the four methodologies. Only the literature on inflammatory parameters in adult subjects has been reviewed. The data shows the differences in the way these problems have been approached for each methodology, in the amount and type of the normal data collected and ultimately in the availability and reliability of normal data in different adult populations. This analysis demonstrates that the issue of normal reference values for each methodology is still not completely covered, more evidently for the new, non-invasive exhaled biomarkers.

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**PATIENT-VENTILATOR INTERACTION AND SLEEP IN MECHANICALLY VENTILATED PATIENTS: PRESSURE SUPPORT VERSUS PROPORTIONAL ASSIST VENTILATION.**

*Objectives:* To understand the role of patient-ventilator asynchrony in the etiology of sleep disruption and determine whether optimizing patient-ventilator interactions by using proportional assist ventilation improves sleep.

*Design:* Randomized crossover clinical trial.

*Setting:* A tertiary university medical-surgical intensive care unit.

*Patients:* Thirteen patients during weaning from mechanical ventilation.

*Interventions:* Patients were randomized to receive pressure support ventilation or proportional assist ventilation on the first night and then crossed over to the alternative mode for the second night. Polysomnography and measurement of light, noise, esophageal pressure, airway pressure, and flow were performed from 10 pm to 8 am. Ventilator settings (pressure level during pressure support ventilation and resistive and elastic proportionality factors during proportional assist ventilation) were set to obtain a 50% reduction of the inspiratory work (pressure time product per minute) performed during a spontaneous breathing trial.



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*Measurements and Main Results:* Arousals per hour of sleep time during pressure support ventilation were 16 (range 2-74) and 9 (range 1-41) during proportional assist ventilation ( $p = .02$ ). Overall sleep quality was significantly improved on proportional assist ventilation ( $p < .05$ ) due to the combined effect of fewer arousals per hour, fewer awakenings per hour (3.5 [0-24] vs. 5.5 [1-24]), and greater rapid eye movement (9% [0-31] vs. 4% [0-23]), and slow wave (3% [0-16] vs. 1% [0-10]) sleep. Tidal volume and minute ventilation were lower on proportional assist ventilation, allowing for a greater increase in  $Paco_2$  during the night. Patient-ventilator asynchronies per hour were lower with proportional assist ventilation than with pressure support ventilation ( $24 \pm 15$  vs.  $53 \pm 59$ ;  $p = .02$ ) and correlated with the number of arousals per hour ( $R = .65$ ,  $p = .0001$ ). *Conclusions:* Patient ventilator discordance causes sleep disruption. Proportional assist ventilation seems more efficacious than pressure support ventilation in matching ventilatory requirements with ventilator assistance, therefore resulting in fewer patient-ventilator asynchronies and better quality of sleep.

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*In: Monaldi Archives  
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**DEGREE OF CONTROL OF PHYSICIAN-DIAGNOSED ASTHMA AND COPD IN ITALY.**

*Background:* It is important for the Italian National Health Service to obtain data on the degree of control of asthma and chronic obstructive pulmonary disease (COPD) in the general population in Italy in order for balanced planning of future investments in these diseases to be made. Currently, precise estimates of these parameters are not available in literature.

*Objectives:* In collaboration with the Italian Academy of General Practitioners (SIMG; www.simg.it) we have investigated the degree of control of physician-diagnosed asthma and COPD in Italy.

*Methods:* A standardised questionnaire on asthma and COPD has been self-administered to a sample of 1937 Italian family physicians (representing around 5% of all the Italian doctors involved in general practice) chosen to cover all the Italian counties.

*Results:* We have collected questionnaire data from 19,917 patients with asthma and COPD followed in their practice and 12,438 (62.4%) were correctly filled in enabling evaluation. We selected the number of emergency room visits, hospitalisations and intensive care unit admissions for asthma and COPD in the last 12 months as objective measures of the degree of asthma and COPD morbidity in these patients. The figures were respectively 12.4% (emergency room visits), 17.3% (hospitalisations) and 1.2% (intensive care unit admissions) of all patients with physician-diagnosed asthma and COPD.

*Conclusions:* This data suggests that in Italy the morbidity of asthma and COPD remains high; representing a significant burden for the Italian National Health Service. There is a clear necessity for further studies to investigate the causes of this incomplete control.

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**EFFICACY OF PULMONARY REHABILITATION IN CHRONIC RESPIRATORY FAILURE (CRF) DUE TO CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD): THE MAUGERI STUDY.**

While the effectiveness of pulmonary rehabilitation (PR) in chronic obstructive pulmonary disease (COPD) is well established, its effectiveness in the most severe category of COPD, i.e. patients with chronic respiratory failure (CRF), is less well known.

*Objective:* To verify the effects of PR in patients with CRF, and compare the level of improvement with PR in these patients to that of COPDs not affected by CRF.

*Methods:* A multi-centre study was carried out on COPD patients with versus without CRF. The PR program included educational support, exercise training, and nutritional and psychological counselling. Lung function, arterial gases, walk test (6MWT), dyspnoea (MRC; BDI/TDI), and quality of life (MRF28; SGRQ) were evaluated.

*Results:* Thousand forty seven consecutive COPD inpatients (327 with CRF) were evaluated. In patients with CRF all parameters improved after PR (0.001). Mean changes:  $FEV_1$ , 112 ml;  $PaO_2$ , 3.0 mmHg;  $PaCO_2$ , 3.3 mmHg; 6MWT, 48 m; MRC, 0.85 units; MRF28 total score, 11.5 units. These changes were similar to those observed in patients without CRF.

*Conclusions:* This study, featuring the largest cohort so far reported in the literature, shows that PR is equally effective in the more severe COPD patients, i.e. those with CRF, and supports the prescription of PR also in these patients. *Keywords:* Chronic obstructive pulmonary disease; Chronic respiratory failure; Pulmonary rehabilitation; Quality of life.

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Abatangelo G.In: *Clinical and  
Experimental Allergy*;  
2007; 37; 872-879.MATRIX METALLOPROTEASE IN VERNAL KERATOCONJUNCTIVITIS,  
NASAL POLYPS AND ALLERGIC ASTHMA.

**Background:** Allergic conditions in different organs share many similarities in their inflammatory response. Vernal keratoconjunctivitis (VKC), asthma and nasal polyps exhibit several similar, but site-specific mucosal structural changes. The aim of the study was to investigate whether matrix metalloproteases contribute to different tissue remodelling aspects in different organs.

**Methods:** Mucosal biopsies were obtained from conjunctiva of healthy donors, tarsal conjunctiva of vernal patients, bronchi of non-asthmatic subjects, bronchi of mild stable asthmatic patients, nasal mucosa of non-allergic donors and nasal polyps of allergic patients. Distribution of metalloprotease-1, -3, -9, -13, tissue inhibitor of metalloproteases-1, collagens I and III and the presence of eosinophils and CD4+ cells were evaluated by immunohistochemistry.

**Results:** Collagens were highly diffuse in the giant papillae of VKC and in nasal polyps, and yet less increased in the subepithelium of asthmatic patients. Immunostaining for metalloprotease-1, -3, -9 and -13 was significantly higher in VKC compared with normal conjunctiva. Metalloprotease-9 staining was higher in the stroma of polyps vs. normal nasal mucosa, and only metalloprotease-13 was significantly more expressed in asthmatic vs. nonasthmatic subjects. Metalloprotease-9 immunostaining was more intense in vernal compared with other tissues. In all pathological tissues, metalloprotease-9-positive staining was in association with eosinophils and CD4+ cells.

**Conclusions:** Expression of metalloproteases may play an important role in inducing the structural changes seen in VKC, nasal polyps and asthma. Tissue remodelling and gelatinase immunoeexpression was more dramatic in giant papillae of vernal patients compared with other tissue sites of chronic allergic inflammation.

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13: 1-8.MAUGERI RESPIRATORY FAILURE QUESTIONNAIRE REDUCED FORM: A METHOD  
FOR IMPROVING THE QUESTIONNAIRE USING THE RASCH MODEL.

**Purpose:** The Maugeri Respiratory Failure questionnaire (MRF-28) is the first instrument specifically developed for use with chronic respiratory failure (CRF) patients. The 28 items were selected using classical test theory. The purpose of the current analysis was to further refine the questionnaire using item response theory, specifically, the Rasch model analysis.

**Methods:** Three hundred and seventeen CRF patients (mean aged 66.7 yrs; Male 219, Female 98) completed the MRF-28 health status measure. Data were collected through the self-report questionnaire and analyzed using 1-parameter logistic models by means of RUMM software.

**Results:** The 28-item questionnaire has good psychometric properties in terms of discriminant power because the Person Separation Index is 0.896. However, the item-trait interaction was not good as shown by the total-item Chi-square ( $c2112 = 182.7, p < 0.001$ ). Removing two items that did not fit the Rasch model well, produced a minor improvement in Person Separation Index to 0.899 and the item-trait interaction improved ( $c2104 = 127.1, p = NS$ ). In the preliminary analysis we identified 21 patients who were outliers; when they were excluded the distribution of the residuals, according to the Kolmogorov-Smirnov statistics, was normal and factor analysis of the item residuals showed that the components had similar eigenvalues and no strong correlation with items. These results suggest that the MRF-26 is a unidimensional measure of health-related quality of life impairment for chronic respiratory failure patients.

**Conclusions:** A combination of classical psychometric tests and Rasch analysis produced an instrument of moderate size that covers a wide range of effects of CRF and has interval scaling properties.

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In: *Monaldi Archives  
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67; 142-147.

## HOME MECHANICAL VENTILATION PATIENTS: A RETROSPECTIVE SURVEY TO IDENTIFY LEVEL OF BURDEN IN REAL LIFE.

*Background and Aim:* Home care for patients under home mechanical ventilation (HMV) may cause dramatic physical and economic burden in addition to the burden of time on family/caregivers and health care service (HCS) with difficult resource allocation decision-making.

Our aims were: 1. To identify conditions causing major care burden in managing HMV patients according to family and payer's perspectives related to characteristics of the disease, dependency and accessibility; and 2. To find, if any, differences among diseases.

*Methods:* A questionnaire was sent to eight pulmonary centres to identify factors connected with the greater care burden. Retrospective data of 792 patients still alive and in HMV was reviewed.

*Results:* Compared to neuromuscular disorders (NM) and chest wall deformities, the COPD group have presented a statistically greater number of hospitalisations/yr ( $1.37 \pm 0.77$ ), greater length of stay ( $13 \pm 10$  days), higher number of outpatient visits/yr ( $2.55 \pm 1.73$ ) or emergency room accesses/yr ( $0.74 \pm 1.08$ ). Patients with NM diseases need more home care. The prevalence of one, two and three among five selected burden criteria (needs of MV > 12 hrs/day, tracheotomy, high dependency, distance from hospital, frequent hospitalisations) was respectively 19%, 30% and 33% of the cases; the NM was the group most represented.

*Conclusions:* In HMV patients: 1. underlying disease, level of their dependency, hours spent under MV, presence of tracheotomy, home distance from hospital, hospital accesses are the causes of major care burden; and 2. as a novelty we have demonstrated that more than fifty percent of them present two or three contemporaneous criteria selected as care burden, being NM and COPD patients the most representative group necessitating of family's and HCS's care respectively.

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Vitacca M.,  
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29; 1: 65-71.

## LO SVEZZAMENTO DALLA VENTILAZIONE MECCANICA: PROTOCOLLI DELICATI.

Lo svezzamento dalla ventilazione meccanica rappresenta quel delicato momento in cui si cerca di riportare il paziente all'autonomia respiratoria ovvero alla capacità di sostenere il respiro spontaneo senza supporto esterno (anche con miscela arricchita di ossigeno). Il successo dello svezzamento viene di norma decretato dopo almeno 24/48 ore di respiro spontaneo senza segni di intolleranza da parte del paziente.

I protocolli di svezzamento sono delle nozioni e opinioni mediche riconosciute scientificamente raccolte in un piano di cura o algoritmo che serve per indirizzare le azioni o le decisioni terapeutiche da intraprendere in relazione alla valutazione di variabili misurabili sul paziente.

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In: *American Journal  
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## THE SERPINE2 GENE IS ASSOCIATED WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN TWO LARGE POPULATIONS.

*Rationale:* Chronic obstructive pulmonary disease (COPD) is a complex disease influenced by multiple genes and environmental factors. A region on chromosome 2q has been shown to be linked to COPD. A positional candidate gene from the chromosome 2q region SERPENTINE2 (Serpin peptidase inhibitor, clade E [nexin, plasminogen activator inhibitor type 1], member 2), was previously evaluated as a susceptibility gene for COPD in two association studies, but the results were contradictory.

*Objectives:* To identify the relationship between SERPENTINE2 polymorphisms and COPD-related phenotypes using family-based and case-control association studies.

*Methods:* In the present study, we genotyped 25 single nucleotide polymorphisms (SNPs) from SERPENTINE2 and analyzed qualitative and quantitative COPD phenotypes in 635 pedigrees with 1,910 individuals and an independent case-control population that included 973 COPD cases and 956 control subjects. The family data were analyzed using family-based association test. The case-control data were analyzed using logistic regression and linear models.

*Measurement and Main Results:* Six SNP2 demonstrated significant associations with COPD phenotypes in the family-based association analysis. ( $0.0016 < \text{or} = p < \text{or} = 0.042$ ). Five of these SNP2 demonstrated replicated associations in the case-control analysis ( $0.021 < \text{or} = p < \text{or} = 0.031$ ). In addition, the results of haplotype analyses supported the results from single SNP analyses.

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## Comunicazione scientifica recensita su Index Medicus e/o Science Citation Index

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In: *European Respiratory  
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Suppl. 51: 728S.

## PATHOPHYSIOLOGY AND RISK PREDICTORS OF PROLONGED MECHANICAL VENTILATION IN POST-CARDIAC SURGERY PATIENTS WITH DIAPHRAGM PARALYSIS.

Diaphragm paralysis is a post-cardiac surgery complication (DPpcs) often associated with ventilatory failure requiring prolonged invasive mechanical ventilation (MV). We aimed to assess the pathophysiological causes underlying MV need, and to detect MV risk predictors. We studied 20 DPpcs patients (age  $64 \pm 20$  yrs), 13 requiring (MV group,  $29 \pm 11$  days) and 7 liberated from (S group) MV.

We measured the breathing pattern (f, VT, f/VT), respiratory mechanics (C<sub>dyn,L</sub>, RL<sub>insp</sub>, PEEP<sub>i,dyn</sub>), drive (P<sub>0.1</sub>), effective inspiratory impedance (P<sub>0.1</sub>/VT/TI), and maximal inspiratory pressures (MIP, Pesmax and P<sub>d</sub>max). *Results:* mean $\pm$ SD. Statistics: unpaired t test, significance =  $p < 0.05$ . Linear regression: correlation between variables. High f/VT indicated ventilatory failure (MV =  $122.8 \pm 47.3$ , S =  $30.4 \pm 16.7$ ,  $p = 0.0001$ ). P<sub>0.1</sub> and P<sub>0.1</sub>/VT/TI were higher in the MV compared to S group (P<sub>0.1</sub> =  $4.0 \pm 2.4$  vs  $1.8 \pm 0.7$  cm H<sub>2</sub>O; P<sub>0.1</sub>/VT/TI =  $12.6 \pm 7.4$  vs  $4.5 \pm 1.5$  cm H<sub>2</sub>O/l/s, respectively,  $p < 0.05$ ). Inspiratory workload was higher in the MV compared to S group (C<sub>dyn,L</sub> =  $0.08 \pm 0.05$  vs  $0.16 \pm 0.09$  l/cm H<sub>2</sub>O; RL<sub>insp</sub> =  $7.8 \pm 3.8$  vs  $3.9 \pm 2.4$  cm H<sub>2</sub>O/l/s; PEEP<sub>i,dyn</sub>, NS). Maximal inspiratory pressures were reduced, but not significantly different between groups (e.g. MIP =  $35.2 \pm 16.4$  and  $42.6 \pm 11.2$  cm H<sub>2</sub>O, MV vs S, respectively). Finally, f/VT was correlated with C<sub>dyn,L</sub> ( $p = 0.049$ ), and P<sub>0.1</sub>/VT/TI ( $p = 0.013$ ), but not with maximal inspiratory pressures. We conclude that DPpcs patients risk prolonged MV only when impaired diaphragmatic force is associated with increased inspiratory workload. Thus, respiratory mechanics assessment before cardiac surgery could identify DPpcs patients at risk of prolonged MV.

*Conclusion:* These data provide further support for SERPENTINE2 as a COPD susceptibility gene.

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Suppl. 51: 313S.

## BREATHING PATTERN AND NEUROMUSCULAR DRIVE ARE CORRELATED WITH THE CLINICAL OUTCOME OF PATIENTS WITH POST-CARDIAC SURGERY DIAPHRAGM PARALYSIS.

Diaphragm paralysis is a post-cardiac surgery complication (DPpcs) often associated with prolonged mechanical ventilation (MV), and long hospital stay. We aimed to assess predictors of MV duration (primary endpoint), and hospital length of stay (HLS, secondary endpoint). We studied 18 DPpcs patients (age  $63 \pm 7$  yrs), 12 requiring (MV group) and 6 liberated from (S group) MV. We measured the breathing pattern (f, VT, f/VT), neuromuscular drive (P<sub>0.1</sub>), effective inspiratory impedance (P<sub>0.1</sub>/VT/TI), and maximal inspiratory pressure (MIP). Analysis: linear and stepwise regressions.

*Results:* MV duration was significantly correlated with f/VT (MV duration =  $-4.4 + 43 * f/VT$ ; R<sub>2</sub> = 0.60;  $p = 0.0002$ ), P<sub>0.1</sub> (MV duration =  $12.2 + 7.6 * P_{0.1}$ ; R<sub>2</sub> = 0.29;  $p = 0.02$ ), and the effective inspiratory impedance (MV duration =  $8.2 + 2.9 * P_{0.1}/VT/TI$ ; R<sub>2</sub> = 0.43;  $p = 0.003$ ). f/VT was the first and sole variable included in the stepwise regression (MV duration vs 3 independents, R<sub>2</sub> = 0.60). Hospital length of stay. HLS was significantly correlated with f/VT (HLS =  $23.8 + 0.4 * f/VT$ ; R<sub>2</sub> = 0.37;  $p = 0.008$ ), P<sub>0.1</sub> (HLS =  $25.1 + 11.9 * P_{0.1}$ ; R<sub>2</sub> = 0.46;  $p = 0.002$ ), and the effective inspiratory impedance (HLS =  $37.7 + 2.6 * P_{0.1}/VT/TI$ ; R<sub>2</sub> = 0.23;  $p = 0.043$ ). P<sub>0.1</sub> was the first variable included in the stepwise regression (HLS vs 3 independents, R<sub>2</sub> = 0.46). Both f/VT and P<sub>0.1</sub>/VT/TI were also included, increasing the R<sub>2</sub> to 0.75. No relationship was found between the endpoints and the inspiratory muscle force. We conclude that quite simple, non-invasive respiratory indexes could be useful in the evaluation of DPpcs patients' clinical outcome.

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In: *European Respiratory  
Journal*; 2007; 30;  
Suppl. 51: 766S.

## MAUGERI RESPIRATORY FAILURE QUESTIONNAIRE REDUCED FORM (MRF26): A METHOD FOR IMPROVING THE QUESTIONNAIRE USING THE RASCH MODEL.

The Maugeri Respiratory Failure (MRF28) is the first questionnaire specifically developed to be used in patients with chronic respiratory failure. The 28 items were selected by formal and classical statistical analyses that included factorial analysis (Eur Respir J 1999; 13: 1293-1300).

*Aim of the Study:* To verify if the MRF28 psychometric characteristics improve after a re-evaluation using item response theory with Rasch model analysis.

*Method:* Three hundred and seventeen CRF patients (mean age 66.7 yrs; Male 219, Female 98) filled out the MRF28 health status measure. Data were collected through the self-report questionnaire and analyzed using simple logistic models by means of RUMM software.



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**Results:** The 28-item questionnaire has good psychometric properties when reliability only is considered; the Person Separation Index is 0.896. Nevertheless, item-trait interaction was not good as shown by the total-item Chi-square ( $\chi^2_{2112}=182.7, p<0.001$ ). Removing two items identified by the Rasch analysis as misfitting, produces a minor improvement in Person Separation Index to 0.899 but the resulting 26-item scale (MRF26) now shows good item-trait interaction ( $\chi^2_{2104}=127.1, p=n.s.$ ), showing that these 26 items correspond to one unidimensional construct.

**Conclusion:** The Rasch model, compared with the methods available through traditional test theory, appears to provide more information to help make decisions about the development of a valid and reliable measuring instrument. These results support the plausibility of using the MRF26 as a unidimensional measure of health-related quality of life impairment in chronic respiratory failure patients.

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In: *European Respiratory Journal*; 2007; 30; Suppl. 51: 137S.

## SIMILARITIES AND DISCREPANCIES IN OXIDATIVE AND NITROSATIVE STRESS IN SEVERE COPD AND POST-INFARCTION CHRONIC HEART FAILURE.

Myeloperoxidase (MPO) is capable to generate HClO and 3-chlorotyrosine (3-CT) as end-product of oxidative stress and protein nitration, the end stage of nitrosative stress, is also possible via activation of MPO. Increased oxidative and nitrosative stress has been implicated in the pathogenesis of COPD and has also been reported in Chronic Heart Failure (CHF). However, a relationship between oxidative and nitrosative stress has not been investigated and compared in these disease states. We quantified MPO, Nitrotyrosine (NT) and 3-CT by immunohistochemistry and semiquantitative scoring in bronchial biopsies (BB) from 12 severe stable COPD patients ( $34\pm 8$  post-bronchodilator FEV<sub>1</sub>% pred.) and in heart tissue (HT) from 4 patients with post infarction CHF, receiving heart transplantation. Scored values in the BB and HT were (median (range)): 2 (1-3) and 0.75 (0.5-2) for MPO; 1.5 (1.25-3) and 1 (0.5-2) for NT, 2.5 (1.5-3) and 2 (1-2.5) for 3-CT, respectively. This positivity was differently distributed: in the HT capillary vessels and heart muscle were frequently immunostained for NT and more extensively for 3-CT. In the BB an extracellular pattern of immuno-positivity was present for NT and more extensively, for 3-CT. In contrast, in both BB and HT, inflammatory cells were similarly stained for NT and more frequently, for 3-CT. These data show that in severe COPD and severe CHF, end-products of oxidative and nitrosative stress accumulate in damaged tissues, although with a different pattern distribution.

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In: *European Respiratory Journal*; 2007; 30; Suppl. 51: 136S.

## INCREASED NEUTROPHIL ADHESION IN BRONCHIAL BIOPSIES FROM PATIENTS WITH SEVERE COPD.

Increased neutrophil presence has been reported in COPD, particularly in bronchial biopsies from severe patients. CXC and CC chemokines are thought to play a role in neutrophil chemoattraction and activation. Furthermore, increased tissutal neutrophilia may be related to increased adhesion to submucosal collagens. We investigated the immunorexpression of CXCL7(NAP-2), CCL5(RANTES), CD44 and CD11b in bronchial biopsies from subjects with severe stable COPD ( $n=13; 33\pm 9$  post-bronchodilator FEV<sub>1</sub>% pred.), mild/moderate stable COPD ( $n=12; 72\pm 12$  post-bronchodilator FEV<sub>1</sub>% pred.), and from control smokers ( $n=12; 106\pm 12$  FEV<sub>1</sub>% pred.) and control non smokers ( $n=11; 115\pm 14$  FEV<sub>1</sub>% pred.). Immunopositivity was quantified as number of immunopositive cells/mm<sup>2</sup> in the submucosa. Severe COPD and mild/moderate COPD had higher CXCL7 immunopositivity in the submucosa (median(range): 38(0-83) and 74(0-129), respectively) compared to control non smokers (14(0-32),  $p<0.05$ ) but did not differ from control smokers (24(0-136)). Severe COPD also had higher CCL5 immunopositivity in the submucosa (281(75-839) compared to control non smokers (77(26-203),  $p<0.05$ ). No significant differences were observed in the total cell count of CD44 and CD11b receptors in the four groups examined. Double staining of neutrophils coexpressing CD44 and CD11b showed increased percentages of CD44+Neu+ and CD11b+Neu+ cells in severe COPD (48(39-54) and 47(38-52), respectively) compared to control smokers (13(9-20) and 17(10-21), respectively,  $p<0.025$ ). These data show that increased presence of chemotactic factors for neutrophils and increased neutrophil adhesiveness may play a role in sustaining neutrophilia in patients with severe COPD.

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In: *Intensive Care  
Medicine*; 2007; 33;  
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## COMPARISON OF AUTOMATIC TUBE COMPENSATION (ATC) WITH PRESSURE SUPPORT VENTILATION (PSV) DURING SPONTANEOUS BREATHING TRIALS.

*Introduction:* PSV and ATC have been alternatively used during spontaneous breathing trials performed to predict the outcome of disconnection from the ventilator and eventually of extubation. At variance with other ventilatory modes, ATC has been claimed to work as an "electronic extubation" device, having the possibility to simulate spontaneous breathing without the endotracheal tube. Data about the hypothetical superiority of ATC are still conflicting. The aim of the present study was to assess the accuracy of the compensation provided by PSV and ATC relative to the endotracheal tube-related resistive pressure dissipation.

*Methods:* 11 patients were studied during a period of spontaneous unassisted breathing on T-tube, as well as during application of both CPAP plus PSV 5 cm H<sub>2</sub>O (PSV) and CPAP plus ATC (ATC). During both PSV and ATC, CPAP was set at 5 cm H<sub>2</sub>O. All the ventilator modes were maintained for 20 to 30 minutes and treatments were randomized. Ventilator settings remained constant during the protocol including a fractional inspired oxygen concentration that ensured arterial oxygen saturation more than 90%. We measured the breathing pattern, the inspiratory muscle effort (PTP) and the difference between theoretical pressure required to overcome the tube resistive properties (Paw<sub>teor</sub>) and the actual pressure (Paw<sub>act</sub>) delivered by the ventilator on both PSV and ATC. STATISTICS: data: mean ± SD; ATC vs PSV: paired t test and Bland & Altman analysis.

*Results:* Breathing pattern was similar in all the conditions tested. The overall absolute difference between Paw<sub>teor</sub> and Paw<sub>act</sub> during PSV and ATC was 2.8 ± 2.7 cm H<sub>2</sub>O and 0.9 ± 0.8 cm H<sub>2</sub>O respectively, p = 0.02. Moreover, this difference was negative (i.e. Paw<sub>teor</sub> < Paw<sub>act</sub>) in 5 out of 11 patients during PSV, where it was always positive, and negligible during ATC.

*Conclusion:* ATC seems more suited to provide an "electronic extubation" as compared to fixed levels of PSV during SBT trials. This might improve the specificity and the sensitivity of the SBT test used to predict weaning and extubation outcome.

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## Comunicazione scientifica recensita su Index Medicus e/o Science Citation Index

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In: *European Respiratory  
Journal*; 2007; 30;  
Suppl. 51: 138S.

## EXPRESSION OF BRADYKININ B2 RECEPTOR (B2R) AND VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) IN ASTHMA AND COPD.

Submucosal angiogenesis is part of airway remodeling in patients with asthma and COPD. Bradykinin, a proinflammatory peptide involved in acute asthma, is also able to release the proangiogenic factor VEGF by different resident cells in the airways. We investigated bronchial vascularity (expressed as CD31+ endothelial cells), VEGF and B2R expression in bronchial biopsies from subjects with mild intermittent asthma (n=9; FEV<sub>1</sub>% pred 91±7), with COPD (I-II stage GOLD; n=18; FEV<sub>1</sub>% pred 66±3) and from control non smokers (n=11; FEV<sub>1</sub>% pred 115±4). The aforementioned molecules were analysed using frozen bronchial biopsies by immunohistochemistry. Immunopositivity was quantified as number of immunopositive cells/mm<sup>2</sup> in the submucosa. Asthmatics showed a higher B2R immunopositivity in the submucosa (median(range): 107(32-226) compared to COPD (76(0-609)) and control non smokers (73(0-396)) without reaching statistical significance. No significant difference was observed in the total cell count of CD31 in the three groups examined. Asthmatics showed a higher VEGF immunopositivity in the submucosa (88(0-183) compared to COPD (44(0-145) p>0.05) and control non smokers (32(0-97), p<0.04). In asthmatics, B2R+ cells and VEGF+ cells did not correlate. We conclude that overexpression of VEGF, in conjunction with a tendency of B2R upregulation, in mild asthmatics suggests a possible role of VEGF in pathogenesis of mild asthma without pathological evidences of neoangiogenesis.

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Foschino Barbaro M.P.In: *European Respiratory  
Journal - Abstracts*  
17<sup>th</sup> ERS Annual Congress;  
2007; 51: 586S.**SYSTEMIC AND AIRWAYS INFLAMMATION IN HEALTHY SUBJECTS AND COPD PATIENTS OF DIFFERENT AGES.**

*Background:* Increased systemic inflammatory activity accompanies ageing. However, few data are available on airways inflammation in elderly. A great interest has recently been generated for the study of airways inflammation by non invasive methods such as breath condensate and induced sputum.

*Aim:* The aim of this study was to investigate systemic and airways inflammation in healthy and COPD subjects of different ages. Furthermore we studied possible correlations between inflammation and respiratory function.

*Material and Methods:* We enrolled 28 healthy subjects and 28 mild COPD patients divided in 2 groups of different ages (group1 <65 years, group2 >65 years). Serum fibrinogen and C-reactive protein (CRP), exhaled nitric oxide (NO), pH of breath condensate and cell counts in induced sputum were measured.

*Results:* We found an increase of systemic and airways inflammatory markers from group 1 to group 2 either in healthy subjects (CRP mg/l: 0.8±0.6 vs 3.9±4.3; fibrinogen mg/dl: 250±6.3 vs 330±48; exhaled pH 7.7±0.3 vs 7.4±0.2; sputum neutrophil count % .33±8.8 vs 57±7.7) or in COPD patients (CRP mg/dl: 5.2±5.5 vs 5.5±6.5; fibrinogen mg/dl: 293±52 vs 300±15; exhaled pH 7.5±0.7 vs 7.2±0.3; sputum neutrophil count % 61±8.9 vs 65±11.6). A negative correlation was observed between systemic inflammation and lung function in healthy and COPD subjects.

*Conclusion:* Findings suggest that ageing is accompanied by a physiological increase of systemic and airways inflammation.

**554****Comunicazione scientifica recensita su Index Medicus e/o Science Citation Index**Istituto di  
CASSANO MURGECarpagnano G.E.,  
Spanevello A.,  
Curci C.,  
Cagnazzo M.G.,  
Foschino Barbaro M.P.In: *European Respiratory  
Journal - Abstracts*  
17<sup>th</sup> ERS Annual Congress;  
2007; 51: 535S.**3P MICROSATELLITE EVALUATION IN NSCLC EXHALED BREATH CONDENSATE: VALIDATION STUDY.**

Microsatellite alteration (MA) in the 3p chromosome has been considered to have a pivotal role in lung carcinogenesis. Our previous results confirmed this hypothesis and evidenced the possibility to analyze MA in the exhaled breath condensate from NSCLC patients. For the first time we provided evidence that EBC-DNA is highly sensitive in detecting microsatellite alteration (MA) from NSCLC and healthy subjects. In order to validate this data, we considered 18 patients affected from NSCLC and 17 healthy subjects (false positive), in which EBC and tumour tissue DNA have been investigated for 5 MA (D3S2338, D3S1266, D3S1300, D3S1304, D3S1289) located in 3p chromosome.

84% (75/90) of the analyses resulted in informative microsatellites. Loss of heterozygosity (LOH) was found in 23% (21/90), where as microsatellite instability (MI) in 20% (18/90) of the informative loci in EBC-DNA and its related tissue-DNA of NSCLC patients. However, we identified only 5% (5/90) of LOH and 4% (4/90) of MI in WB-DNA. EBC-DNA and tissue-DNA provided a similar spectrum of informative loci in all the patients (100% of agreement in terms of capability to individualize informative loci). All MAs found in tissue-DNA were also evident in EBC-DNA. These data demonstrated the EBC is highly specific in the identification of MA of 3p and underlined the possibility to use EBC-DNA, collected in a very simple and non invasive way, to study genetic biomarkers associated to early prediction and prognosis of NSCLC.

**555****Comunicazione scientifica recensita su Index Medicus e/o Science Citation Index**Istituto di  
CASSANO MURGECarpagnano G.E.,  
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Foschino Barbaro M.P.In: *European Respiratory  
Journal - Abstracts*  
17<sup>th</sup> ERS Annual Congress;  
2007; 51: 535S.**MICROSATELLITE ALTERATIONS OF 6 P AND 14 P IN THE EXHALED BREATH CONDENSATE OF ASTHMATIC SUBJECTS.**

*Introduction:* The use of DNA microsatellites has become popular in the analysis of complex genetic disorders such as asthma. Alterations of microsatellites of 6 p and 14 p have been recently described in the induced sputum of asthmatic subjects.

*Study objectives:* The aim of this study was to investigate microsatellite alterations in the exhaled breath condensate (EBC) of atopic and asthmatic subjects. In total 5 highly polymorphic microsatellite markers located on chromosome 6 p and 14 p were investigated.

*Patients and Methods:* We studied 30 patients with diagnosis of asthma, 10 atopic patients and 10 healthy control subjects. Exhaled breath condensate (EBC) and blood were collected from all subjects. DNA was extracted from EBC and blood. Microsatellite instability and LOH were analyzed by polymerase chain



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reaction using a panel of 5 microsatellite DNAMarkers spanning chromosome 6 p and 14 p and the alleles were sized with ABIPrism310 (Applied Biosystem, Foster City, USA).

**Results:** None of healthy individuals showed any genetic alteration in EBC and WB DNA. In asthmatic subjects the results showed 75% LOH (90/120 of informative loci) and 25% MI (30/120). The atopic subjects enrolled exhibited 66% LOH (25/38) and 3 4% MI (13/38).

**Conclusion:** This study demonstrated for the first time the presence of microsatellites alterations of 6 p and 14 p in DNA of EBC and supported the hypothesis that it is possible used the exhaled breath condensate for the study of genetic alterations characteristics of asthma.

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## Comunicazione scientifica recensita su Index Medicus e/o Science Citation Index

Istituto di  
CASSANO MURGE

Carratù P.,  
Scoditti C.,  
Carpagnano G.E.,  
Maniscalco M.,  
Seccia M. T.,  
Di Gioia G.,  
Pierucci P.,  
Spanevello A.,  
Foschino Barbaro M.P.,  
Resta O.

In: *European Respiratory Journal - Abstracts 17<sup>th</sup> ERS Annual Congress; 2007; 51: 55S.*

## EXHALED CONDENSATE OF ENDOTHELIN-1 AND EXHALED NITRIC OXIDE ARE INCREASED IN COPD PATIENTS WITH SECONDARY PULMONARY HYPERTENSION.

**Background:** Pulmonary hypertension (PH) is frequently observed in patients with advanced COPD and is considered as predictor of poor outcome. Hypoxia and imbalance between vascular mediators, such as endothelin-1(ET) and nitric oxide (NO), have been implicated in the pathogenesis of PH associated to COPD.

**Aim:** To evaluate ET serum levels, ET in the exhaled breath condensate (EBC), and exhaled NO (FENO) in COPD with or without PH, and in primary pulmonary hypertension (PPH) patients, in order to investigate the clinical role of these two mediators in PH secondary to COPD.

**Methods:** We enrolled 52 (44 Males, mean age 64±7) consecutive patients: 36 with COPD, 12 with PH (mean PAPS 58.43±12 mmHg) secondary to COPD, and 4 with PPH (mean PAPS 82±14 mmHg) currently treated with bosentan. 15 healthy (9 Males, mean age 65±9) non smoking subjects were the control group. ET was detected by ELISA in venous and arterial blood and in the EBC. FENO was analyzed by chemiluminescence.

**Results:** Increased levels of ET in both arterial and venous blood ( $p<0.0001$ ) and in the EBC was found in COPD with PH as compared to COPD without PH ( $p<0.0001$ ). Increased ET in the EBC of COPD with PH as compared to PPH patients treated with bosentan ( $p<0.0001$ ) was also observed. FENO was higher in COPD with or without PH, compared to patients with PPH ( $p<0.0001$ ).

**Conclusions:** ET in the EBC of patients with PH secondary to COPD could be a useful marker of early detection and of disease progression.

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CASSANO MURGE

Dragonieri S.,  
Annema J.T.,  
Schot R.,  
Resta O.,  
Spanevello A.,  
Serk P.J.

In: *Proceedings of the American Thoracic Society; 2007; A330.*

## AN ELECTRONIC NOSE IN THE DETECTION OF LUNG CANCER.

**Rationale:** Exhaled breath contains thousands of gaseous volatile organic compounds (VOCs) that may be used as non-invasive markers of lung disease. Electronic nose systems allow VOCs analysis by composite nano-sensor arrays with learning algorithms. It has been shown that an electronic nose can distinguish the VOCs pattern in exhaled breath of lung cancer (LC) patients from healthy controls (Machado et al. AJRCCM 2005).

**HYPOTHESIS:** An electronic nose can discriminate patients with LC from healthy controls and COPD patients by analyzing the VOCs profile in exhaled breath.

**Methods:** 10 (ex)smoking patients with confirmed NSCLC (age 6.4 9.0, FEV<sub>1</sub> 84.3 21.7), 10 healthy never-smoking subjects (age 57.3 7.1, FEV<sub>1</sub> 107.9 14.6) and 10 (ex)smoking patients with COPD (age 61.4 5.5, FEV<sub>1</sub> 70.0 14.8) participated in a cross-sectional study. The experiments in LC and controls were done in duplicate. After 5 minutes tidal breathing through a non-rebreathing valve with inspiratory VOC-filter, the subjects performed a single vital capacity manoeuvre to collect dried exhaled air into a Tedlar bag (exp resist 20 cmH<sub>2</sub>O). The bag was connected to the electronic nose (Cyranose 320) within 10 min, with VOC-filtered room air as baseline. The smellprints were analyzed by online principal component analysis and canonical discriminant analysis.

**Results:** Smellprints from LC patients clustered distinctly from those of healthy subjects in both duplicate measurements (cross validation value [CVV]: 90% and 80% respectively; M-distance: 3.10 and 2.00). LC patients could also be discriminated from COPD patients (CVV: 85% M-distance: 3.83).

**Conclusion:** VOC analysis of exhaled breath discriminates patients with lung cancer from healthy controls as well as COPD patients.

**Implication:** The electronic nose may qualify as a screening tool for lung cancer in the future.

**558****Comunicazione scientifica recensita su Index Medicus e/o Science Citation Index**Istituto di  
CASSANO MURGEDragonieri S.,  
Arets H.G.,  
Schot R.,  
Carratu P.,  
Spanevello A.,  
Resta O.,  
Hoekstra M.O.,  
Sterk P.J.In: *European Respiratory Journal - Abstracts 17<sup>th</sup> ERS Annual Congress; 2007; 51: 61S.***AN ELECTRONIC NOSE IN THE DIAGNOSTIC ASSESSMENT OF ASTHMA IN PEDIATRIC PATIENTS.**

**Rationale:** Exhaled breath contains a mixture of thousands of volatile organic compounds (VOCs). Electronic nose systems allow real-time recognition of VOCs by composite nano-sensor arrays combined with powerful learning algorithms. We showed that an electronic nose can discriminate patients with asthma from controls (Dragonieri et al. submitted). We postulated that this discrimination can be replicated in pediatric patients.

**Methods:** 10 Children with asthma defined by episodic symptoms and airway hyperresponsiveness (age: 11.7±4 yr, FEV<sub>1</sub>: 89.2±11.3% pred), and 10 control subjects (age: 13.8±0.6, FEV<sub>1</sub>: 104.7±12.9) participated in a cross-sectional study. After 5 min tidal breathing through a mouthpiece connected to a 2-way non-rebreathing valve with inspiratory VOC-filter, the subjects performed a single deep inspiration followed by an expiratory vital capacity manoeuvre (expflow 0.1 0.2 l/s) into a 10 l Tedlar bag. After 10 min the electronic nose (Cyrano 320) was connected to the bag followed by 1 min sampling of expired air. VOC-filtered room air was used as baseline. The smellprints of the exhaled breath samples were analysed by principal component analysis (PCA) and canonical discriminant analysis (CDA).

**Results:** In the PCA the asthmatics clustered distinctly from the controls. Using CDA the asthmatics could be discriminated from the controls (correct cross validation: 75%) with Mahalanobis distance 1.78.

**Conclusion:** An electronic nose can discriminate exhaled breath of children with asthma from controls, but the distinction is less sharp than in adults. These findings warrant diagnostic validation in newly presented children with asthma.

**559****Comunicazione scientifica recensita su Index Medicus e/o Science Citation Index**Istituto di  
MONTESCANOBaldi S.,  
Pinna G.D.,  
Mombiaruzzo P.,  
Biglieri M.,  
De Martini A.,  
Palange P.In: *European Respiratory Journal; 2007; 30; 51: 771S-771S.***INDEPENDENT CONTRIBUTION OF C-REACTIVE PROTEIN AND OXYGEN STATUS OF ARTERIAL BLOOD TO TISSUE HYPOXIA IN STABLE COPD PATIENTS.**

**Aim:** To investigate the relationship between systemic inflammation and tissue hypoxia in COPD, by exploring the association between C-Reactive Protein (CRP) levels and physiological variables reflecting tissue hypoxia, such as oxygen extraction tension (PaO<sub>2</sub>x).

**Materials and Methods:** In 44 stable COPD (FEV<sub>1</sub> 48±21% pred.) patients we measured, while breathing room air, blood CRP lung function testing, BODE index, resting arterial acid-base and oxygen status. Oxygen tension at half saturation (P50), and PaO<sub>2</sub>x were calculated along the shape of oxygen binding curve (̄). Multiple linear regression analysis was performed by using an R2 square selection method to identify those variables that correlate with PaO<sub>2</sub>x.

**Results:** Median (IQR) CRP mg/L was 4.3 (3.0-8.4). PaO<sub>2</sub> was closely related to blood CRP (r=0.72, p<0.0001), and fairly to BODE index (r=-0.30, p<0.05). Multiple linear regression analysis indicated that blood CRP, P50, haemoglobin (Hb) and PaO<sub>2</sub> were the strongest independent determinants of PaO<sub>2</sub>x (R2 0.80, p<0.0001). Hence, blood CRP, P50, Hb and BODE index also enabled a robust prediction of PaO<sub>2</sub>x (R2 0.77, p<0.0001).

**Conclusions:** These findings indicate that systemic inflammation together with variables of the oxygen triad, i.e. PaO<sub>2</sub>, oxygen binding capacity, and affinity, independently contribute to tissue hypoxia. They also emphasize the need of an integrate approach in the management of stable COPD.

**560****Comunicazione scientifica recensita su Index Medicus e/o Science Citation Index**Istituto di  
PAVIANava S.,  
Esquinas A.,  
Ferrer M.,  
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Scala R.,  
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Naldi M.,  
Cuomo A.M.In: *European Respiratory Journal; 2007.***MULTICENTER RANDOMIZED STUDY OF THE USE OF NON-INVASIVE VENTILATION IN END STAGE SOLID CANCER PATIENTS WITH RESPIRATORY FAILURE AND DISTRESS.**

In this multicenter randomised trial we have evaluated the feasibility, and clinical efficacy of NIV as a palliative tool, on relieving dyspnea and reducing the need for morphine, in end-stage solid cancer patients. 76 patients with a Mc Crabe index>3, and with acute respiratory failure (PaO<sub>2</sub>/FiO<sub>2</sub><250) and respiratory distress (dyspnea>3 Borg and/or a breathing frequency>30 b/min) were randomized to receive NIV (n. 38) or O<sub>2</sub> (n. 38). A total of 111 patients met the inclusion criteria, 23 refused "a priori" the enrolment, 9 after they had the NIV technique explained and 3 withdrew after a brief NIV trial. Only 13/38 (34%) and 12/38 (32%) of the patients for NIV and O<sub>2</sub> group, respectively survived the acute episode. Three and six month mortality rate was 91% and 96%, respectively. NIV and O<sub>2</sub> were equally effective in reducing dyspnea at 1, 3 and 24 hours (NIV=6.4+3 admission vs 5.2+3 at 1h, 3.8+2 at 3h and 3.6+3 at 24 hrs (all p<0.001) and



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O<sub>2</sub>=6.9+3 vs 6.2+3, 5.3+3 and 4.3+2, respectively (p<0.01). Respiratory rate showed a significantly faster rate of reduction in the NIV group at 1 hour vs O<sub>2</sub> group (p<0.05). The average use of morphine on the first 24 hours was significantly lower in the NIV patients (10.2+10.2 mg vs 18.0+11.1 mg p<0.05), while other sedatives were evenly distributed among the patients. In conclusion both NIV and O<sub>2</sub> may be useful in acutely reducing dyspnea in a selected population of end-stage solid cancer patients with respiratory failure and distress. These results are achieved with lower doses of morphine in the NIV group.

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## Comunicazione scientifica recensita su Index Medicus e/o Science Citation Index

Istituto di  
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Pignatti P.,  
Balestrino A.,  
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Moretto D.,  
Corrasi M.,  
Alinovi R.,  
Delmastro M.,  
Vogelmeier C.,  
Nava S.,  
Moscato G.,  
Balbi B.

In: *European Respiratory Journal*; 2007; 30; 768.

## CHRONIC CARE IN TRACHEOSTOMISED PATIENTS: THE ROLE OF ANALYSIS OF TRACHEAL ASPIRATES SAMPLES.

Tracheostomised patients represent a challenge for their clinical management in which the issue of infection/colonisation is very important. We studied 38 patients (13 COPD, 6 neurological (N) and 19 with miscellaneous (M) diagnosis); 8/38 patients were ventilated. The average time elapsed from tracheotomy and tracheal aspirate (TA) analysis was 53 days. 18 patients were treated with corticosteroids, 11 had received antibiotics before the collection of TA. TA were analysed for microbiology, cell differential counts, levels of defensins (hBD-2 and LL37), of matrix metalloproteinase 9 (MMP-9); the data were correlated with the clinical parameters. We found 21/34 *Pseudomonas aeruginosa* (P.A.)+ samples, 61.5% among COPD; 68.7% in M and 40.0% in N group. hBD-2 and LL-37 were detectable in all samples and no change was associated with steroid and antibiotic treatments. Patients with a P.A.+ TA tended to have higher hBD2 levels, hBD-2 levels negatively correlated with the TA % of eosinophils (r=-0.44, p=0.03), LL-37 levels were associated with the amount of neutrophils in TA (r=0.51, p=0.01), and MMP9 levels were negatively associated with LL-37 (r=-0.91, p=0.000000). Considering all the patients enrolled, there was a weak correlation between the percentage of neutrophils in TA and the degree of hypercapnia (r=0.33, p<0.05). Furthermore, in patients with COPD as underlying diagnosis, there was a negative correlation between MMP9 levels in TA and the degree of hypoxemia (r=-0.64, p=0.02). No other correlations with clinical and physiological parameters were found. TA represents a useful tool to study the host-bacteria interaction as a model of colonisation and infection in the airways.

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Istituto di  
TRADATE

Bothamley G.,  
Solovic I.,  
Migliori G.B.,  
Lange C.,  
on behalf of TB-NET.

In: *European Respiratory Journal*; Abstract Book ERS 17<sup>th</sup> Annual Congress; 2007; 518S.

## ACTIVE CASE-FINDING OF TUBERCULOSIS IN EUROPE.

Active case-finding of tuberculosis is an important but variable part of tuberculosis control in Europe. We wanted to know what was consistent and what varied in active case-finding among the different countries. A standard questionnaire (3 sections: who should be screened, what screening methods and nature of preventive treatment) was circulated to representatives of all European countries. Twenty-eight representatives from 39 countries replied (93% of EU27 population and 68% of non-EU Europe). Countries were equally divided between those who screened contacts of all or just pulmonary TB. Two-thirds screened immigrants. Most countries (>two-thirds) would screen HIV+ individuals, prisoners and inpatient contacts. All used the tuberculin skin test and or chest x-rays; less than half would ask for symptoms; 16 would examine sputum if cough was present for >3 weeks. Countries with a higher incidence of TB were more likely to screen with a chest x-ray. There was substantial disagreement as to what constituted a positive tuberculin skin test, unexplained by BCG policy or age of subject. If a chest x-ray were abnormal, 75% would request sputum examination. All countries used 6-9 months isoniazid, six would also use 3 months rifampicin and isoniazid and four 4 months rifampicin. Estimated uptake of chemoprophylaxis was 60% of those eligible. Follow-up with serial chest x-rays was accepted in 11 countries as an alternative to chemoprophylaxis. Screening could be limited to those in whom a positive finding would result in action. Symptoms and sputum smear examination could be more widely used. The definition of latent tuberculosis infection was variable.

**563****Comunicazione scientifica recensita su Index Medicus e/o Science Citation Index***Istituto di  
TRADATE**Migliori G.B.,  
De Iaco G.,  
Besozzi G.,  
Centis R.,  
Cirillo D.M.**In: Euro Surveillance  
2007; 12 (5): E070517.1.***FIRST TUBERCULOSIS CASES IN ITALY RESISTANT TO ALL TESTED DRUGS.**

A study from Italy and Germany has recently demonstrated that the occurrence of XDR-TB, as currently defined, has both a clinical value (predicting poor outcome) and an operational implication (underlying the loss of first-line drugs coupled with key second-line ones). The study reports on the first two cases that were resistant to all drugs tested. The cases have some similarities: both of them were young females, born in Italy and belonging to middle class families. Both of them were diagnosed and initially treated in non-specialised TB facilities where they received three different treatment courses for over 30 days before being admitted as MDR-TB to the reference hospital in Sondalo with a very severe clinical picture (extended bilateral cavities). Both died in 2003, before 50 years of age, after a long, unsuccessful treatment with all the available drugs without achieving bacteriological conversion.

II XDR- and about 50% of MDR-TB cases as reported in the study mentioned above were previously treated for TB in the past. This finding, coupled with the unlucky story of the two cases mentioned above, suggests the major role played by mismanagement of TB cases and sub-optimal infection control in determining the emergence of the problem. Furthermore, the finding that immigration is significantly associated with the XDR-TB status (multivariate analysis, Italy-Germany study) needs to be underlined. Improvement of policies and practices is necessary if we want to reach TB elimination in Europe.

**564****Comunicazione scientifica recensita su Index Medicus e/o Science Citation Index***Istituto di  
TRADATE**Migliori G.B.,  
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Raviglione M.C.,  
and SMIRA/TBNET  
Study Group.**In: European Respiratory  
Journal; Abstract Book  
ERS 17<sup>th</sup> Annual Congress;  
2007; 216S.***RISK OF MORTALITY OF EXTENSIVELY DRUG-RESISTANT TUBERCULOSIS (XDR-TB) IN ITALY AND GERMANY.**

The response to treatment of XDR-TB (resistance to at least rifampin and isoniazid, in addition to any fluoroquinolone, and at least one of the three injectable anti-TB drugs: capreomycin, kanamycin, amikacin) in low TB incidence countries is unknown. We compared the mortality of XDR-TB with that of multidrug-resistant (MDR)-TB at TB-reference centres in Italy and Germany.

Original clinical records from all culture confirmed TB cases diagnosed between 2003 and 2006 by the TB clinical reference centres (Italy: Sondalo, Milan, Rome; Germany: Borstel, Grosshansdorf, Bad-Lippspringe) were analyzed. Drug susceptibility testing for first- and second-line anti-TB drugs was performed according to WHO recommendations by quality assured laboratories.

Out of 2,888 culture-positive TB cases, 126 (4.4%) were MDR and 11 (0.4%) XDR. XDR-TB cases had a six-fold increase in the risk of death (RR5.73; 95% Confidence Intervals 2.04-16.04;  $P<0.01$ ). XDR-TB cases were significantly more likely to be resistant to all first-line drugs (8/11 vs 36/126,  $P<0.005$ ), and required longer hospitalization (241.2177.0 vs. 99.185.9 days;  $P<0.001$ ) and treatment duration (30.329.4 vs. 15.023.8 months;  $P<0.05$ ), than MDR-TB cases. Bacteriological conversion was observed in 4/11 XDR- vs 102/126 MDR-TB cases (median: smear: 110 vs. 41 days; culture: 97.5 vs. 58 days, respectively;  $P<0.01$ ).

The presence of XDR-TB in Western Europe suggests that poor management of TB still exists and that without rapid improvement of policies and practices, as well as development of new rapid diagnostics and drugs, it will not be possible to achieve TB elimination in Europe.

**565****Comunicazione scientifica recensita su Index Medicus e/o Science Citation Index**Istituto di  
TRADATEPiana F.,  
Baldan R.,  
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Ferrese M.,  
Cirillo D.M.In: *European Respiratory  
Journal; Abstract Book  
ERS 17<sup>th</sup> Annual  
Congress; 2007; 282S.***COMPARISON OF EFFECTOR T-CELL RESPONSES IN PATIENTS WITH ACTIVE TB DISEASE COMPARED TO LATENT TB INFECTION.**

A T-cell based assay (T-SPOT.TB, OxfordImmunitec, Abingdon, UK) is available for the diagnosis of active tuberculosis (TB) and latent TB infection (LTBI). Previous studies showed its higher sensitivity in detecting active TB disease and LTBI than Mantoux test (TST). In some active TB cases, diagnosis is difficult and based on the ex-juvantibus criterion. In these cases, it is difficult to assess if T-SPOT.TB positivity is due to active TB or LTBI. The aim of the study is to investigate if the number of spots differs in patients with active TB from those with LTBI.

We enrolled 73 patients with high suspicion of active TB. They underwent radiological, histological and microbiological examination and a TST. We also recruited 561 contacts of infectious TB cases who underwent TST to detect LTBI and, if positive, radiological examination to rule out active TB. All participants received a T-SPOT.TB test. In 34 cases, active TB was culture-confirmed, in 39 diagnosis was based on clinical and radiological findings consistent with TB, and in 17 (20.5%) on the ex-juvantibus criterion.

We compared the spot counts in patients with active TB with those with LTBI and positive T-SPOT.TB tests. On average, counts were significantly lower among people with LTBI, but the ROC curve showed a weak ability to discriminate between active and latent TB on the basis of spot count alone. Although average spot counts are higher in active TB, due to the extent of the overlap between the two distributions, the test is not able to reliably distinguish between the two conditions based on a single cut-off value.

**566****Comunicazione scientifica recensita su Index Medicus e/o Science Citation Index**Istituto di  
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Patesio A.,  
Balbi B.In: *Giornale Italiano  
di Medicina del Lavoro  
ed Ergonomia; 2007;  
29; 1: 126-127.***LA RIABILITAZIONE RESPIRATORIA DEI PAZIENTI AFFETTI DA PARALISI DIAFRAMMATICA: STUDIO PILOTA DI UN NUOVO APPROCCIO BASATO SULL'IMPIEGO DEI MUSCOLI ESPIRATORI.**

**Razionale:** La paralisi diaframmatica (e.g. post-cardiochirurgica) è causa riconosciuta di insufficienza respiratoria e di dipendenza dalla ventilazione meccanica (AJRCCM 2000; 161: 1115-7). Lesioni della funzione diaframmatica più lievi possono comunque determinare dispnea e limitazione all'esercizio fisico. Dato che l'attivazione fasica dei muscoli espiratori (EM) si è dimostrata efficace nell'evitare la fatica diaframmatica in condizioni sperimentali di stress meccanico del diaframma (ARRD 1988; 137: 1401-5), abbiamo ipotizzato che sia possibile ridurre la dispnea ed aumentare la tolleranza all'esercizio in pazienti sintomatici colpiti da paralisi diaframmatica mediante un programma di riabilitazione composto di tre procedure (rieducazione respiratoria, rieducazione posturale e riallenamento allo sforzo), comprendente sedute specifiche volte ad acquisire un automatismo comportamentale del controllo del respiro che include la contrazione volontaria dei muscoli espiratori durante l'espirazione ed il loro rilasciamento ad inizio inspirazione (EM breathing).

**Metodi:** Sono stati reclutati 6 pazienti (età 59.2±9.8 anni) con paralisi diaframmatica mono- (n. 5) o bilaterale per essere sottoposti al programma riabilitativo sopra descritto della durata di 4 settimane comprendente 2 sedute giornaliere di 60 min mirate ad includere l'attività dei muscoli espiratori nel pattern respiratorio abituale dei pazienti stessi. Sono state misurate la capacità vitale (VC), il volume espiratorio massimo/s (FEV<sub>1</sub>), le pressioni inspiratorie massime (MIP), i gas arteriosi (ABG), la tolleranza all'esercizio fisico (6 min walking test, 6WT), lo stato di benessere (Saint George respiratory Questionnaire, SGRQ), il livello di dispnea basale (baseline dyspnea index, BDI) e le sue variazioni (transition dyspnoea index, TDI) prima (iniziale = I) e dopo (finale = F) il ciclo di riabilitazione.

I risultati sono espressi come media+SD. I valori dei parametri pre e post sono stati paragonati mediante il test del t di Student per dati appaiati. La significatività statistica è stata individuata per valori di p<0.05.

**Risultati:** Al termine del ciclo di riabilitazione i pazienti erano in grado di mantenere con facilità e senza disagio l'EM breathing sia a riposo (posizione seduta ed in piedi), sia durante esercizio fisico. Non si sono osservate variazioni significative di VC, FEV<sub>1</sub>, MIP e dei valori di ABG dopo riabilitazione.

Per contro, si è riscontrato un significativo miglioramento del 6WT (6WT-I: 306±133 m; 6WT-F: 388±97 m; p<0.05), dei punteggi delle categorie "sintomi" (differenza media: 7.5, p=0.06) ed "attività" (differenza media: 17.7, p=0.008) del questionario SGRQ e del TDI (p<0.05).

**Conclusioni:** Concludiamo che l'EM breathing si propone quale potenziale strumento riabilitativo mirato al miglioramento della tolleranza allo sforzo ed alla riduzione della dispnea nei pazienti con paralisi diaframmatica.

**567****Rivista non recensita**

Istituto di  
CASSANO MURGE

Aliani M.,  
Battista A.,  
Cuomo V.,  
Spanevello A.

In: *GiMT - Giornale  
Italiano delle Malattie  
del Torace*; 2007;  
1: 42-43.

### RIPRESA A TEMPO PIENO DELL'ATTIVITÀ LAVORATIVA E DELLE NORMALI ATTIVITÀ DI VITA QUOTIDIANA DOPO TRATTAMENTO CON OMALIZUMAB.

Viene presentato un caso d'asma allergico scarsamente controllata malgrado l'uso di antileucotrieni orali e di broncodilatatori e steroidi per via inalatoria, nel quale l'introduzione in terapia di Omalizumab risulta migliorativa in termini clinico-funzionali e di qualità di vita.

**568****Rivista non recensita**

Istituto di  
CASSANO MURGE

Aliani M.,  
Cirasino L.

In: *Pneumorama*; 2007;  
41: 23-28.

### DIAGNOSI FUNZIONALE D'ORGANO DELL'ASMA BRONCHIALE ALLERGICO.

La diagnosi di Asma Bronchiale si avvale di indagini cliniche, strumentali e di tipo biologico.  
INDAGINI CLINICHE: La diagnosi clinica di asma si pone in presenza di segni o sintomi che generalmente sono variabili, si possono presentare di giorno o di notte e il più delle volte in seguito a vari stimoli.  
Indagini strumentali: I test strumentali necessari per porre diagnosi di asma bronchiale si possono distinguere in:  
- misurazione della limitazione al flusso aereo (spirometria, monitoraggio del picco di flusso espiratorio (PEF);  
- reversibilità dimostrata della limitazione del flusso aereo dopo un trattamento con un broncodilatatore oppure dopo breve corso di terapia antiasmatica;  
- misura di iperesponsività bronchiale in assenza di limitazione di flusso d'aria.  
PROVE ALLERGologiche: Una valutazione allergologica corretta non può prescindere da una accurata anamnesi volta ad accertare i rapporti causali tra la comparsa dei sintomi e l'esposizione agli allergeni.

**569****Rivista non recensita**

Istituto di  
CASSANO MURGE

Esposito L.M.,  
Cuomo V.,  
Foschino Barbaro M.P.,  
Digilio V.S.,  
Carpagnano G.E.,  
Spanevello A.

In: *Ageing Lung*; 2007;  
4: 11-16.

### LA RIABILITAZIONE POLMONARE NEL PAZIENTE ANZIANO CON BRONCO-PNEUMOPATIA CRONICA OSTRUTTIVA.

La BPCO è una patologia comune negli anziani, spesso sottodiagnosticata e curata in ritardo, con una prevalenza che incrementa progressivamente con l'età. Al progredire della malattia è associato l'incremento della dispnea, della disabilità e delle frequenti ospedalizzazioni. La disabilità associata alla BPCO conduce il paziente ad un progressivo e rapido declino dell'autonomia funzionale globalmente intesa, infatti i soggetti BPCO anziani sono spesso limitati fisicamente e quindi destinati ad una progressiva immobilità a causa della dispnea dovuta prevalentemente ad una ridotta tolleranza allo sforzo, sintomi caratteristici della patologia respiratoria, che per questo rappresentano la 2ª causa di disabilità negli anziani. Il trattamento mirato a risolvere la broncoostruzione si è rivelato spesso inefficace. Recenti Linee Guida per la gestione della BPCO sottolineano l'importanza della Riabilitazione Polmonare come fondamentale in un approccio integrato multidisciplinare, comprendente componenti che vanno dall'allenamento all'esercizio fisico all'intervento psico-comportamentale; il suo impatto sulla storia naturale della malattia è supportato da forti evidenze scientifiche che ne documentano gli effetti benefici, in particolare sulla Qualità della Vita correlata alla salute in soggetti BPCO di tutte le età.

**570****Rivista non recensita**

Istituto di  
CASSANO MURGE

Sabato R.,  
Carpagnano G.E.,  
Spanevello A.,  
Depalo A.,  
Ventura I.,  
Turchiarelli V.,  
Foschino Barbaro M.P.

In: *Rassegna di Patologia  
dell'Apparato Respiratorio*;  
2007; 2: 89-97.

**VALUTAZIONE NON INVASIVA DELLA FLOGOSI NELLE VIE AEREE DI PAZIENTI CON SINDROME DELLE APNEE OSTRUTTIVE NOTTURNE.**

*Introduzione:* Nei pazienti affetti dalla Sindrome delle Apnee Ostruttive Notturne (OSAS), l'infiammazione delle vie aeree è stata attribuita al trauma cronico connesso con il susseguirsi degli episodi di ostruzione e successiva riapertura delle vie aeree superiori (VAS), associato all'instaurarsi di congestione ed edema dei tessuti molli di tali territori. Inoltre è stata avanzata l'ipotesi che la flogosi delle vie aeree giocherebbe un ruolo significativo nell'ambito dei meccanismi fisiopatologici alla base dell'instabilità delle VAS nell'OSAS.

*Scopo:* Abbiamo verificato, in un campione di soggetti OSAS, la presenza di infiammazione delle vie aeree con il dosaggio, nell'esalato, di uno specifico marcatore di flogosi bronchiale quale l'ossido nitrico (eNO) e con l'analisi della cellularità dell'escreato raccolto con la tecnica dell'espettorato indotto (EI).

*Materiali e Metodi.* In un campione di 12 soggetti affetti da OSAS moderato-severa con indice di apnea-ipopnea (AHI) >10/h e in 10 soggetti sani di controllo è stato dosato, al risveglio dal sonno notturno, l'eNO con analizzatore a chemoluminescenza; l'EI è stato ottenuto con soluzione ipertonica.

*Risultati:* I livelli di eNO negli OSAS erano più elevati rispetto al gruppo di controlli sani; la conta cellulare differenziale tra i due gruppi, ottenuta con l'EI, mostrava un aumento significativo dei neutrofili nelle vie aeree dei pazienti affetti da OSAS.

*Conclusioni:* Nel campione di soggetti OSAS da noi esaminato, si rileva la presenza di infiammazione delle vie aeree per l'aumento dell'eNO (marker di flogosi bronchiale) e per il contemporaneo aumento della quota dei neutrofili nella cellularità dell'EI.

**571****Rivista non recensita**

Istituto di  
PAVIA

Moscato G.,  
Preziosi D.

In: *Nuovo Collegamento*;  
2007; 3: 33-39.

**TERAPIA FARMACOLOGICA DELLE ALLERGIE.**

Nell'articolo vengono passati in rassegna i farmaci utili nelle più importanti patologie allergiche (rinite e congiuntivite, asma bronchiale, dermatite atopica, dermatite da contatto, orticaria).

Per ogni molecola vengono descritti il meccanismo d'azione, la posologia, le vie di somministrazione, gli effetti collaterali. Vengono illustrati gli schemi terapeutici più attuali proposti dalla Linee Guida internazionali per ogni patologia.

**572****Rivista non recensita**

Istituto di  
TELESE-CAMPOLI

Balzano G.

In: *Pneumorama*; 2007;  
46: 6-7.

**INFIAMMAZIONE SISTEMICA NELLA BPCO.**

Di recente l'attenzione dei ricercatori si è focalizzata sulle manifestazioni extrapolmonari della BPCO tanto che le linee guida GOLD 2006 le hanno incluso nella definizione della BPCO. Tra le manifestazioni extrapolmonari che possono associarsi alla BPCO - infiammazione sistemica, perdita di peso, aumentato rischio cardiovascolare, alterazioni neurologiche, ect. - l'infiammazione sistemica merita un posto di rilievo. L'autore sottolinea, riportando i dati di un recente follow-up della durata di 8 anni condotto su 1300 pazienti con BPCO, il ruolo della proteina C-reattiva (PCR) quale marker di infiammazione sistemica nella BPCO.

**573****Rivista non recensita***Istituto di  
TELESE-CAMPOLI**Balzano G.**In: Pneumorama; 2007;  
47: 6-7.***UN ALTRO TENTATIVO FALLITO NELLA TERAPIA DELLA BPCO.**

L'autore riporta i deludenti risultati circa l'utilizzo dell'infliximab, un anticorpo monoclonale rivolto contro il TNF-alfa, nella terapia della BPCO.

**574****Rivista non recensita***Istituto di  
TELESE-CAMPOLI**Balzano G.**In: Reading in  
Broncopneumologia;  
2007; 2: 1-6.***MORTALITÀ NELLA BPCO: RUOLO DELLE MALATTIE COESISTENTI E DEI CORTICOSTEROIDI PER VIA INALATORIA.**

La BPCO è stata a livello mondiale la sesta causa di morte nel 1990 e la quarta nel 2000 e si prevede che passerà al terzo posto nel 2020. Nei pazienti con BPCO la morte spesso è da mettere in relazione con le condizioni morbose extrapolmonari. Recentemente, soprattutto in pazienti con BPCO in fase avanzata, è stata enfatizzata la presenza di infiammazione sistemica accanto a quella polmonare. Numerosi dati suggeriscono il ruolo dell'infiammazione polmonare e/o sistemica nella genesi delle diverse condizioni morbose associate con la BPCO.

I corticosteroidi per via inalatoria sono risultati associati ad una riduzione di mortalità del 25%. Tale riduzione ha riguardato in larga misura la mortalità per cause cardiovascolari.

**575****Rivista non recensita***Istituto di  
TELESE-CAMPOLI**Balzano G.**In: Pneumorama; 2007;  
48: 6-8.***COMORBIDITÀ E CAUSE DI MORTE NELLA BPCO.**

Nei pazienti con BPCO le morti dovute a problemi respiratori costituiscono solo una minoranza nel totale delle cause di morte. Da uno studio dell'Organizzazione Mondiale della Sanità in pazienti BPCO è emerso che nella BPCO lieve e moderata le cause di morte predominanti sono le malattie cardiovascolari e il cancro, mentre, a mano a mano che la malattia diventa più grave, acquista un ruolo progressivamente maggiore l'insufficienza respiratoria.

L'autore si sofferma sulla importanza delle comorbidity nella storia naturale della BPCO e sui rapporti tra infiammazione sistemica nella BPCO e condizioni morbose ad essa associate quali malattie cardiovascolari, carcinomi, cachessia ect. ect.

**576****Rivista non recensita**

Istituto di  
TELESE-CAMPOLI

Balzano G.

In: *Pneumorama*; 2006;  
45: 6-8.

**ASMA GRAVE.**

L'autore si sofferma ad analizzare i motivi alla base dell'attuale interesse della comunità scientifica per l'asma grave.

Il primo motivo, di natura epidemiologico, è dato dal fatto che i pazienti con asma grave pur rappresentando il 10 per cento della popolazione asmatica assorbono circa il 50% e più dei costi totali sostenuti dalla società per l'asma.

Il secondo motivo è di tipo patogenetico. L'asma grave si caratterizza per la scarsa responsività alle terapie attuali. Al fine di studiare i meccanismi responsabili della refrattarietà alle terapie attuali nell'asma grave numerose informazioni di ordine clinico, funzionali e relative all'infiammazione delle vie aeree vengono raccolte a livello nazionale ed in collaborazioni internazionali al fine di individuare i diversi fenotipi di asma grave.

Il terzo motivo è riferito alla terapia. Nuovi farmaci agenti con meccanismo immunologico sono stati proposti per il trattamento dell'asma grave. Tra questi l'autore si sofferma sul ruolo dell'omalizumab un anticorpo monoclonale umanizzato rivolto contro le IgE.

**577****Rivista non recensita**

Istituto di  
TRADATE

Giovannelli F.,  
Neri M.

In: *Aria Ambiente  
e Salute*; 2006;  
Anno IX; 4: 4-7.

**INQUINAMENTO ATMOSFERICO: UNA REALTÀ DINAMICA.**

La qualità dell'aria attira, negli ultimi tempi, una attenzione sempre maggiore tanto che cercando di regolamentare la tipologia degli inquinanti atmosferici nei diversi Paesi, si va definendo un vero e proprio quadro epidemiologico legato dell'inquinamento.

L'aumentata prevalenza delle patologie respiratorie, specialmente nei paesi industrializzati, rende evidente l'importanza dell'intervento anche di fattori ambientali; è stata ormai dimostrata da tempo l'esistenza di una significativa correlazione tra mortalità, ricoveri ospedalieri e livello di inquinamento misurato nei giorni precedenti. Sono ormai noti gli effetti che quest'ultimo reca sulla funzionalità respiratoria inducendo un'aumentata responsività delle vie aeree ed ostruzione bronchiale, con conseguente incremento dell'utilizzo di farmaci, sia nei soggetti predisposti sia in quelli più vulnerabili come bambini ed anziani. In primo piano, com'è noto, ci sono i grandi centri abitati in cui l'alta concentrazione di sorgenti industriali e domestiche, nonché la frequente congestione veicolare conseguente a un incremento demografico molto spesso rapido e senza controllo, li colloca tra i principali produttori di sostanze inquinanti quali biossido di azoto (NO<sub>2</sub>), materiale particolato (PM) e anche, seppure in modo indiretto, ozono (O<sub>3</sub>). È interessante notare come nelle grandi città le modifiche degli impianti di riscaldamento centralizzate e il controllo obbligatorio delle emissioni dei motori, nonché l'introduzione delle marmitte catalitiche ha fatto in modo che la concentrazione di sostanze quali l'anidride solforosa e il monossido di carbonio si siano via via ridotte fino a diventare attualmente di trascurabile importanza, lasciando però il posto ad altri inquinanti quali quelli precedentemente citati.

La realtà, quindi, ci insegna come la lotta alla air pollution sia in continua evoluzione e ci pone di fronte ad una situazione estremamente mutevole e dinamica.

**578****Rivista non recensita**

Istituto di  
VERUNO

Corda L.,  
Balbi B.

In: *Multidisciplinary  
Respiratory Medicine*;  
2007; 2: 84-87.

**INDICATORI DI ATTIVITÀ PROTEASICA NEL DEFICIT DI ALFA1-ANTITRIPSINA.**

La teoria patogenetica denominata dello "squilibrio proteasi-antiproteasi" prevede che alla base dello sviluppo dell'enfisema polmonare vi sia un patologico sbilanciamento tra le ridotte difese antielastasiche del polmone e l'azione dell'elastasi leucocitaria poco efficacemente contrastata, con una conseguente marcata degradazione dell'elastina e delle altre componenti della matrice extracellulare del parenchima polmonare. Nel deficit di alfa-1 antitripsina viene meno la maggior difesa antielastastica a livello alveolare, essendo il suo ruolo preminente quello di circoscrivere la proteolisi durante i precessi infiammatori. Il dosaggio di marcatori diretti della degradazione dell'elastina come la desmosina e l'isodesmosina pare promettente per seguire l'evoluzione delle patologie polmonari verso l'enfisema, sebbene sia ancora necessario raggiungere una buona attendibilità metodologica e una rilevanza clinica correlata alla progressione del decadimento funzionale. Questi indici infatti riflettono a livello biochimico un'accelerata degradazione dell'elastina del parenchima polmonare che si verifica quando l'infiammazione è incrementata, fenomeno non facilmente quantificabile con parametri di funzionalità respiratoria o con i punteggi ottenibili con la TC, rappresentando così un marker complementare ai più tradizionali indici di evoluzione della patologia cronica ostruttiva.

**579****Rivista non recensita***Istituto di  
VERUNO**Vitacca M.,  
Scalvini S.,  
Spanevello A.,  
Balbi B.**In: Breathe; 2006; 3;  
2: 148-158.***TELEMEDICINE AND HOME-CARE: CONTROVERSIES AND OPPORTUNITIES.**

This review focuses on the prospects, and possible drawbacks, of a new innovative instrument of care known as "home telehealth", "telecare" or "telemedicine". The main results from utilising telemedicine in respiratory diseases (asthma and chronic obstructive pulmonary disease (COPD) as the illustrative conditions) are presented. A principal goal of telemedicine is to improve access to healthcare services. During this process, savings in time and travel costs should be achieved, thereby rationalising access to medical care. The field of telemedicine is relatively new and expanding. In order to establish evidence-based guidelines for the design and implementation of disease management plans that employ telemedicine, further research is required. Telemedicine is not simply "technology" but an innovative medical approach (based more on a dedicated healthcare team than on high-tech instruments) that will help the medical team to care for patients and their families. In the future, it is hoped that telemedicine will form a valuable part of the disease management process, because, when used intelligently, home telehealth should supplement conventional delivery techniques and not replace them.

**580****Libro in lingua inglese***Istituto di  
PAVIA**Nava S.,  
Carlucci A.**In: Non-invasive  
respiratory support.  
A practical handbook;  
2007; 123-132.***NON-INVASIVE VENTILATION AND POST-EXTUBATION RESPIRATORY FAILURE.**

We have solid evidences that NIV may be used in selected population of stable hypercapnic patients to shorten the length of invasive mechanical ventilation. The role of NIV in all the other conditions (i.e. hypoxic patients, post-surgical patients) still remains to be elucidated. Randomised controlled studies have also demonstrated that NIV may be even harmful to treat an "overt" episode of post-extubation respiratory failure, while promising results were obtained when NIV was used to prevent the occurrence of reintubation in the subset of patients considered at risk.

**581****Libro in lingua inglese***Istituto di  
VERUNO**Donner C.F.,  
Carone M.**In: Clinical Challenge  
COPD; 2007.***CLINICAL CHALLENGE-COPD.**

When the idea first came up with the publisher to produce Clinical Challenges in COPD (if I remember correctly it was during a European Respiratory Society congress in 2004) the target we agreed on was something quite different from the usual textbook format for publications in respiratory medicine. As you probably well know, the great majority of books on the subject of COPD have largely the same characteristics, with differences only in the level of depth and type of information given to the reader depending on whether the specific target is the general practitioner, pulmonary clinician or academic clinician. With this new venture, we hoped and planned to bring out a publication on COPD addressed to all clinicians dealing with pulmonary patients, in a format that we consider substantially innovative. We wanted to break away from the traditional idea of expounding a list of diseases or therapeutic approaches: even if well described in terms of aetiology, pathogenesis, diagnosis and treatment we would not have added anything new to the stock of literature already published in this field. We also did not want simply to provide a list of clinical cases. In this book, what we wished to do was integrate all these aspects in a new vision: starting from the description of a real clinical case – such as the clinician typically encounters in everyday clinical practice – the idea was to open up a panel discussion, as it were, on all aspects related to



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## Libro in lingua inglese

the diagnosis and treatment of the case of interest to the clinical specialist. In this way, we hoped to give the reader an updated state-of-the-art on specific issues of respiratory medicine relevant to clinical practice, presented in a novel, easy-to-read manner. We selected 21 topics which, while they do not represent all the aspects of COPD, cover all the real cases that the clinician may encounter in everyday clinical practice. All chapters present a similar structure:

- a background, to set the scene and give the general picture of the specific clinical problem;
- the case report, including history, basic diagnostic assessment, differential diagnosis, and treatment (pharmacological, rehabilitation and follow-up);
- a discussion, examining the different possible scenarios arising from the different assessment approaches; and
- a conclusion, summing up what has come out of the discussion and giving clear options for diagnosis, management and follow-up of the specific patient/disease.

The discussion, in particular, is in the style of a panel discussion: it looks at what would be the 4 or 5 questions most likely to come from the floor, debating these from the different possible angles. For this reason, where there were debatable perspectives, we sought to have two or more co-authors to enable interaction as though they were part of a panel of experts. The authors are outstanding authorities in their specific field, each with a long list high-level publications to their name. Notwithstanding their expert status, we asked them to write in a colloquial manner, as if they were talking from the floor. As such, we hope to offer here a distillation of the best knowledge available in the field, so as to provide clinicians with a useful tool to keep on their desk for rapid consultation in daily practice. We thank the 44 authors for the time and effort they have devoted to the task despite their heavy clinical and scientific commitments, and for their goodwill in following the editors' indications to produce an innovative book. We hope that that this publication will not only be useful reading but a job companion for all clinicians who, we are confident, will appreciate this new format.

## 582

## Capitolo di Libro in lingua inglese o francese

Istituto di  
CASSANO MURGE

Carpagnano G.E.,  
Carpagnano F.,  
Spanevello A.,  
Foschino Barbaro M.P.

In: *Oncologia Toracica*  
- *Mesotelioma Pleurico*  
*Maligno*; 2007; 79-83.

## NON INVASIVE STUDY OF MICROSATELLITE ALTERATIONS OF 3P I SUBJECTS WITH NON SMALL CELL LUNG CANCER.

It was estimated that about 10 to 20 genetic events are required for lung tumorigenesis (1). These genetic changes are triggered by smoking and persist for many years after smoking cessation (2). Cytogenetic analysis has established that genetic alterations on the short arm of chromosome 3 are among the most common abnormalities found in lung cancer (3, 4). The microsatellites alterations (MA) at chromosomal region 3p occur relatively early during the multistage development of NSCLC. These alterations could be considered a fingerprint of smoker subjects independently from tumor presence. Therefore they have been considered as a potential markers for the early detection of this cancer and screening of risk subjects (5). Several studies investigated microsatellite alterations in several biological samples of patients affected by lung cancer or at high risk to develop disease (5-9). However, collection of most of these samples requires invasive approaches, so limiting the possibility of their utilization in large scale prospective application. Our group has recently demonstrated the possibility to study genomic alterations in breath condensate (10) and, in particular, the feasibility of microsatellites alteration analysis (10). One of the most intriguing questions concerned the possibility that EBC-DNA could surrogate information on somatic DNA alterations peculiar of lung cancer. In fact, alterations in EBC-DNA have been reported as significantly more frequent than that in blood-DNA leading to the hypothesis that the detection of molecular abnormalities in EBC could identify patients at high risk of lung cancer and, as a consequence, candidate for further clinical examination (10). The aim of the present study was to investigate the possibility to detect MA in EBC-DNA of subjects (smokers and ex-smokers) surrogating genetic alterations present in paired lung tissue of healthy subjects and patients with NSCLC.

**583****Capitolo di Libro in lingua inglese o francese**Istituto di  
LUMEZZANEFoglio K,  
Ambrosino N.,  
Agati S.In: *Chronic Respiratory  
Disease*; 2007; 4;  
1: 59-60.**BOOK REVIEWS.**

La BPCO interessa il 6% della popolazione generale ed è una importante causa di morbidità e mortalità. Il riallenamento all'esercizio fisico, cardine della riabilitazione polmonare, determina miglioramento della dispnea, della capacità di esercizio e della qualità di vita nei pazienti BPCO a tutti gli stadi di malattia. Il problema più difficile è mantenere tali benefici. A lungo termine, riducendo i ricattizzazioni, i ricoveri e migliorando lo stato di dipendenza del paziente e la sua capacità di autogestione. Gli studi disponibili mostrano che i benefici della riabilitazione si riducono dopo 6-12 mesi dalla fine del trattamento, mentre meglio conservati appaiono i benefici nella qualità di vita che persistono fino a 2 anni dopo. La lunghezza del programma è un elemento spesso decisivo nel mantenimento dei benefici. Vari modelli di supervisione o self-management a domicilio sono stati presi in considerazione da diversi autori (programmi domiciliari, visita periodiche da parte di personale dello staff riabilitativo, telefonate a domicilio, utilizzo di presidi atti ad aumentare la compliance dei pazienti) ma non si è giunti a conclusioni univoche e definitive. Studi ulteriori sono necessari a chiarire l'impatto dei molti fattori potenzialmente influenzanti la durata dei benefici a breve termine di un programma riabilitativo. Fra questi la strutturazione del programma, i contenuti, la sede, il numero di ricattizzazioni, le comorbidità, i problemi di trasporto, la depressione o altri problemi personali che riguardano la vita del paziente non escluso il problema economico.

**584****Capitolo di Libro in lingua inglese o francese**Istituto di  
LUMEZZANEFoglio K,  
Ambrosino N.,  
Agati S.In: *Chronic Respiratory  
Disease*; 2007; 4;  
131-133.**MAINTAINING THE BENEFITS OF PULMONARY REHABILITATION FOR PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE: WHERE ARE WE NOW?**

La BPCO interessa il 6% della popolazione generale ed è una importante causa di morbidità e mortalità. Il riallenamento all'esercizio fisico, cardine della riabilitazione polmonare, determina miglioramento della dispnea, della capacità di esercizio e della qualità di vita nei pazienti BPCO a tutti gli stadi di malattia. Il problema più difficile è mantenere tali benefici. A lungo termine, riducendo i ricattizzazioni, i ricoveri e migliorando lo stato di dipendenza del paziente e la sua capacità di autogestione. Gli studi disponibili mostrano che i benefici della riabilitazione si riducono dopo 6-12 mesi dalla fine del trattamento, mentre meglio conservati appaiono i benefici nella qualità di vita che persistono fino a 2 anni dopo. La lunghezza del programma è un elemento spesso decisivo nel mantenimento dei benefici. Vari modelli di supervisione o self-management a domicilio sono stati presi in considerazione da diversi autori (programmi domiciliari, visita periodiche da parte di personale dello staff riabilitativo, telefonate a domicilio, utilizzo di presidi atti ad aumentare la compliance dei pazienti) ma non si è giunti a conclusioni univoche e definitive. Studi ulteriori sono necessari a chiarire l'impatto dei molti fattori potenzialmente influenzanti la durata dei benefici a breve termine di un programma riabilitativo. Fra questi la strutturazione del programma, i contenuti, la sede, il numero di ricattizzazioni, le comorbidità, i problemi di trasporto, la depressione o altri problemi personali che riguardano la vita del paziente non escluso il problema economico.

**585****Capitolo di Libro in lingua inglese o francese**Istituto di  
MONTECANO

Fanfulla F.

In: *Obstructive sleep  
apnea. Edit by Clete and  
Kushida*; 2007; 333-346.**OTHER RESPIRATORY CONDITIONS AND DISORDERS.**

The role that nocturnal desaturations play in the natural history of COPD is not well known. More attention has been paid to patients whose a wake arterial oxygen tension is above 60 mmHg, in other words patients with mild or absent daytime hypoxemia. It has been suggested that nocturnal desaturations occurring in patients without significant daytime hypoxemia could lead to permanent pulmonary hypertension, precipitating the development of cor pulmonale. The development of nocturnal desaturation in COPD patients has been attributed to several causes including changes in respiratory mechanics, worsening in ventilation (V/Q) mismatch increased air flow resistance, and progressive respiratory muscles weakness respiratory muscle activity and chest wall motion differ markedly in the various stages of sleep normally there is an increase in intercostal muscle activity during. In rem sleep, thus increasing the rib cage's contribution to spontaneous ventilation over that provided during wakefulness. The author describes the quality of sleep the most frequent polysomnographic findings in COPD patients are a decrease sleep time, reduction in remsleep, and more changes in sleep stage. Poor sleep quality may represent a factor in the development of chronic fatigue and reduced quality of life usually reported by patients with severe COPD. In the last part of the chapter the author describes the diagnostic approach and management of sleep disordered breathing in COPD patients and which is the optimal treatment of the underlying disease.

**586****Capitolo di Libro in lingua inglese o francese**Istituto di  
PAVIAIversen M.,  
Moscato G.In: Donner C.F.,  
Carone M. eds.,  
*Clinical Challenges  
in COPD. Clinical  
Publishing, Oxford 2007;*  
161-167.**A 58-YEAR-OLD WOMAN WITH COPD AND ACUTE FEVER AFTER VISITING RELATIVES IN THE COUNTRYSIDE-FARMER'S LUNG.**

We have described a case of acute allergic alveolitis after an accidental exposure to a high concentration of grain dust in a woman with pre-existing COPD and bronchiectasis and repeated episodes of pneumonia. Initially, the syndrome was misdiagnosed since both the patient and the family doctor considered the acute respiratory syndrome as another episode of pneumonia similar to those previously suffered by the patient, and antibiotics were therefore administered. When the doctor became aware of the acute environmental exposure, the suspicion of an environmentally related disorder promptly arose. According to the type of exposure and the respiratory and general symptoms, the main possible differential diagnoses could have been allergic alveolitis, ODS or NOx syndrome. The latter could be excluded due to the presence of high fever. The clinical course of symptoms, physical findings, radiological and lung and lung function studies and the rapid response to corticosteroid therapy eventually led to the diagnosis of allergic alveolitis. Follow-up visits demonstrated a disappearance of symptoms, but lung function and diffusion capacity with pre-existing impaired after 4 months.

This case clearly demonstrated that a patient with a pre-existing obstructive respiratory disease may develop another pulmonary disease with a different pathogenesis. A key element for differential diagnosis is the clinical history, which should be carefully taken in any patient, even if already well known for pre-existing disease. In this case, the family doctor did not ask the patient about the circumstance of onset of her symptoms and, as frequently happens, the patient did not report the acute exposure to dust until several days after the accident.

In the presence of acute respiratory and general symptoms after an accidental exposure to organic dusts, three main syndromes should be considered: Allergic alveolitis; ODS; NOx.

The main criteria for diagnosis of acute allergic alveolitis are known exposure to offending agents, compatible clinical history and chest radiographs compatible with diffuse bilateral infiltrates, although after the acute exposure the latter may briefly appear normal. In the case described above, another element favouring the diagnosis of allergic alveolitis could have been the previous exposure of the patient to mouldy materials during the period in which she had worked on the family farm. Moreover, during the period, in which it is likely that the sensitization to moulds had occurred, the patient had on several occasions experienced symptoms compatible with allergic alveolitis.

The main medical therapy for acute allergic alveolitis is corticosteroids. The usual starting dose is 0.5-1.0 mg/kg of prednisolone per day with tapering of the dose over 4-16 weeks. Such a regimen results in a rapid improvement of symptoms and of lung function. Corticosteroids therapy probably does not change the long-term prognosis of the disease.

Avoiding future exposure is an essential element in the management of the disease.

Primary prevention measures and the use of personal devices may allow the patient to continue their work in areas of potential high risk, but a close follow-up is essential to ensure that the patient is not showing any "new" symptoms.

The prognosis for allergic alveolitis is variable. With appropriate treatment and removal from exposure, recovery without lung impairment may occur. Some subjects, however, have progressive fibrosis and disability. The predictive factors for prognosis have not been clearly identified.

**587****Capitolo di Libro in lingua inglese o francese**Istituto di  
PAVIANava S.,  
Carlucci A.In: *Mechanical Ventilation:  
clinical applications and  
pathophysiology; 2007;*  
519-528.**WEANING THROUGH NONINVASIVE VENTILATION.**

In the majority of cases withdrawal of mechanical ventilation and extubation are possible immediately after resolution of underlying problems responsible for acute respiratory failure. However there is a group of ventilated patients, requiring a gradual and longer withdrawal of respiratory support. As reported in a Spanish survey, 41% of the total time of mechanical ventilation was devoted to weaning, with large differences between patients with different diseases, the process of discontinuation from mechanical ventilation being close to 50% or even pass this limit in patients affected by COPD, cardiac failure and neurological problems. Further, Epstein et al showed in a prospective cohort study of 289 patients who underwent a trial of extubation that weaning failure had a significant independent association with increased risk for death, prolonged ICU stay, and transfer to a long-term care or rehabilitation facility. Relevant differences in the weaning failure rate are reported in the literature, that could depend on the case mix and referrals of any individual ICU. In fact, as Brochard et al stated "the length of weaning is first explained by etiology of the diseases, with patients with COPD being the most difficult to separate from the ventilator".

**588****Capitolo di Libro in lingua inglese o francese***Istituto di  
VERUNO**Zanaboni S.,  
Appendini L.**In: Clinical Challenges  
in COPD; 2007; 192-198.***HEMIDIAPHRAGMATIC PARALYSIS AFTER CARDIAC SURGERY IN A 62-YEAR-OLD COPD PATIENT.**

Hemi-diaphragm paralysis is a condition that can precipitate ventilatory failure in post-cardiac surgery patients with impaired respiratory mechanics of whatever origin. Prompt diagnosis should be suspected in any of those patients whenever signs of respiratory distress occur. Respiratory mechanics assessment and respiratory muscle force generating capacity measurement are of help in the differential diagnosis of ventilatory failure in this subset of patients.

When hemi-diaphragmatic paralysis associated to COPD leads to ventilatory failure, the suggested therapeutic approach is mechanical ventilation in the PSV mode combined with CPAP set at a level close to the PEEPi measured in the patient. The physiological rationale of this combined ventilatory approach is that PSV assists the respiratory muscles in generating inspiratory flow and volume, whereas CPAP counterbalances the elastic threshold load induced by PEEPi itself. The choice of invasive vs noninvasive mechanical ventilation interface depends mainly on the severity of ventilatory failure and on the hours spent under mechanical ventilation during the day: full ventilator dependence suggests an invasive approach (tracheostomy), whereas the need of ventilatory assistance only during the night shifts the therapeutic choice to the noninvasive approach. Intermediate situations represent the "grey zone" in which it is hard to give standardized guidelines.

Finally, recovery from ventilator dependence in these patients rely on improvement of respiratory muscle function, of the respiratory workload or both. Surgical plication of the paretic hemi-diaphragm should be considered only as a late therapeutic option.

**589****Libro in italiano***Istituto di  
PAVIA**Ceriana P.,  
Springhetti I.**In: I Manuali della  
Fondazione Maugeri;  
2007; 3-42.***LA CANNULA TRACHEOTOMICA. ISTRUZIONI PER L'USO.**

Questo testo si propone come un manuale di utilizzo pratico e come una guida per la risoluzione dei dubbi e dei problemi che possono emergere quotidianamente da parte di tutte le figure di operatori sanitari addetti alla cura del paziente portatore di cannula tracheostomica.

**590****Capitolo di Libro in italiano***Istituto di  
MONTESCANO**Baldi S.,  
Fracchia C.,  
Oggionni T.,  
Harari S.,  
Solidoro P.**In: Valutazione funzionale  
in chirurgia toracica  
- Resezione oncologica  
- Trapianto polmonare  
- Chirurgia riduttiva.  
Edizioni Minerva; 2007;  
65-75.***CHIRURGIA RIDUTTIVA E TRAPIANTO POLMONARE.**

Le principali differenze tra la chirurgia riduttiva del polmone ed il trapianto sono legate alle diverse forme di BPCO (il trapianto utilizzabile in tutte le BPCO, mentre LVRS è indicata solo per il polmone enfisematoso con elevata iperinflazione) alla età (il trapianto è indicato fino a 60 o 65 anni, la LVRS è proponibile fino a 75 anni).

Gli autori descrivono in termini tecnici in che cosa consiste l'intervento di chirurgia riduttiva del polmone e vengono riportati i dati relativi all'outcome di questi pazienti che appartengono ad alcuni centri di chirurgia toracica a livello nazionale che hanno partecipato allo studio. nella seconda parte del capitolo si affronta il problema del trapianto polmonare partendo dalla selezione del ricevente alla scelta della procedura ed al termine del trapianto e concludendo con la gestione del paziente candidato al trapianto e poi trapiantato. vengono infine presentati, i dati relativi ai risultati della lurs e del trapianto.

**591****Capitolo di Libro in italiano**Istituto di  
MONTESCANOCallegari G.,  
Zanotti E.,  
Fracchia C.*In: Valutazione funzionale  
in chirurgia toracica.*- Resezione oncologica  
- Trapianto polmonare  
- Chirurgia riduttiva.Edizioni Minerva; 2007;  
27-35.**PREPARAZIONE DEL PAZIENTE CANDIDATO A CHIRURGIA TORACICA.**

Da molti decenni la riabilitazione respiratoria è parte integrante del trattamento medico e chirurgico di malattie respiratorie croniche. La riabilitazione respiratoria è potenzialmente utile prima di ogni intervento chirurgico ma è stata applicata e studiata, principalmente nella riduzione di volume polmonare, nella resezione polmonare e nel trapianto polmonare.

Nel capitolo gli autori analizzano in primo luogo l'importanza della valutazione funzionale del paziente prima di qualsiasi tipo d'intervento chirurgico. Si sottolinea inoltre il fondamentale ruolo della valutazione metabolico-nutrizionale e della terapia medica. L'ultima parte del capitolo è dedicata alla presentazione dei programmi di riabilitazione respiratoria con le raccomandazioni su cui si deve basare il percorso diagnostico e terapeutico del paziente pre e post chirurgico.

**592****Capitolo di Libro in italiano**Istituto di  
TRADATE

Zampogna E.

*In: Esame clinico  
e valutazione funzionale  
in riabilitazione respiratoria,  
ed. Masson; 2007;  
131-139.***LA VALUTAZIONE NUTRIZIONALE.**

La malnutrizione, intesa come stato di iponutrizione, è un evento piuttosto frequente nel corso delle malattie respiratorie croniche, in particolar modo nei pazienti affetti da enfisema polmonare. È per tale ragione che storicamente, la ricerca scientifica si è concentrata particolarmente su questa patologia respiratoria e conseguentemente, la conoscenza sull'iponutrizione deriva principalmente da studi condotti su pazienti affetti da Broncopneumopatia Cronica Ostruttiva (BPCO). Respirazione e nutrizione sono due funzioni interdipendenti, tanto che si stima, circa un terzo dei pazienti con BPCO, con il progredire della patologia, presenta uno stato di malnutrizione di grado da moderato a severo (Rochester, 1992), con incidenza maggiore nei soggetti enfisematosi piuttosto che bronchitici cronici (Openbrier, 1983). Tale presentazione potrebbe far pensare ad una relazione di causa effetto; in realtà è una correlazione significativa: il fenotipo sottopeso, pink puffer, è spesso associato ad un carattere enfisematoso.

I soggetti in condizione di sottopeso, rispetto ad individui normopeso con lo stesso grado di ostruzione, hanno un aumento dell'air-trapping, ridotta diffusione alveolo capillare e ridotta capacità di esercizio (Sahebjami, 1993;94). La malnutrizione è anche un fattore predittivo di ridotta possibilità di svezamento dalla ventilazione meccanica (Cook, 2001, MacIntyre, 2005). Infine uno stato nutrizionale inadeguato nei BPCO, in particolare la perdita di massa magra, è correlato ad elevata morbilità e mortalità (Wilson, 1989; Marquis, 2002).

In questo capitolo si cercherà dapprima di riassumere i complessi meccanismi che regolano il metabolismo energetico e successivamente si affronteranno le tecniche di valutazione oggi a disposizione (cliniche e di laboratorio) per il monitoraggio del metabolismo energetico e della composizione corporea.

**METABOLISMO ENERGETICO.** L'omeostasi del peso corporeo è regolata da complessi meccanismi fisiopatologici, ma grossolanamente dall'equilibrio tra dispendio energetico (Energy Expenditure, EE) ed introito alimentare (Energy Intake, EI).

**DISPENDIO ENERGETICO (ENERGY EXPENDITURE, EE).** L'EE quotidiano (24EE) consta di 3 componenti principali:

- tasso metabolico basale (Basal Metabolic Rate, BMR);
- effetto termico del cibo (Diet-Induced Energy Expenditure, DICE);
- costo energetico dell'attività fisica.

Nel soggetto BPCO si aggiunge un effetto termico addizionale, legato alla malattia e che può riflettersi su ciascuno dei precedenti tre elementi, come mostrato nella Tabella 1.

**Introito Energetico (Energy Intake, EI)**

L'aumentata spesa energetica (24EE) non è tuttavia sufficiente a spiegare, quando presente, il significativo calo ponderale nel paziente affetto da BPCO; deve pertanto configurarsi la contemporanea presenza di un ridotto introito energetico (EI). Numerose condizioni cliniche e comorbidità tipiche del paziente affetto da BPCO possono essere responsabili di un ridotto apporto calorico.

**LA MISURA DELLA COMPOSIZIONE CORPorea NEL PAZIENTE CON MALATTIA RESPIRATORIA CRONICA.** La valutazione nutrizionale-VN completa viene effettuata dal dietista, ma alcuni fattori possono essere valutati da altri membri del team. Il fisioterapista respiratorio non è quindi responsabile del processo valutativo, ma deve avere familiarità con esso e parteciparvi. La VN consiste in una raccolta della storia medica e "alimentare" del paziente, nella rilevazione delle misure antropometriche e nell'esecuzione di esami biochimici ed immunologici.

**593****Capitolo di Libro in italiano***Istituto di  
VERUNO**Carone M.,  
D'Arosca F.**In: Esame clinico  
e valutazione in  
riabilitazione respiratoria;  
2006; 210-218.***VALUTAZIONE DELLA QUALITÀ DI VITA (QOL).**

Negli anni recenti si è progressivamente sviluppato un interesse verso tutto ciò che riguarda la Qualità di Vita (QoL). In campo medico, l'interesse scientifico si è indirizzato verso quelle patologie che, per la loro gravità o per cronicità, non hanno effetti solo sulla funzionalità di un determinato organo ma anche sulle attività della vita quotidiana e sulla percezione di salute: in definitiva su quelle patologie che sembravano deteriorare maggiormente la QoL dei pazienti. In campo pneumologico, gli studi si sono concentrati soprattutto sulla BPCO. Questo è dovuto al fatto che è una patologia cronica ed "inguaribile": di conseguenza, l'efficacia del trattamento va vista come miglioramento del livello di malattia, piuttosto che come grado di curabilità reale. Il trattamento di questi pazienti dovrebbe allora essere indirizzato verso la prevenzione dei sintomi e delle riacutizzazioni, minimizzando l'effetto della patologia sullo stato di salute globale del paziente, in definitiva determinando il miglioramento obiettivamente della QoL, o quanto meno evitandone il peggioramento. Per di più, con l'aumento progressivo della vita media, oggi vediamo sempre più pazienti anziani i quali tendono ad essere affetti da più di una patologia e presentano gradi di malattia sempre più marcati. In particolare, quando il FEV<sub>1</sub> scende sotto il litro, vi è un rapido aumento dell'impatto della malattia sulla vita quotidiana del paziente e sul suo benessere, con una riduzione delle normali attività. Come conseguenza, nel tempo si è sempre più affermato il concetto di "riabilitazione" il cui scopo è essenzialmente quello di migliorare lo stato di salute dei pazienti. Da questo punto di vista, l'effetto della terapia sul benessere del paziente e sulla vita quotidiana rappresenta il più importante risultato soggettivo del trattamento. Tuttavia, le misurazioni normalmente utilizzate come indice di danno funzionale correlano scarsamente con la QoL e perciò forniscono un quadro incompleto dello stato di salute. È dunque chiaro che una stima globale della salute del paziente non può essere dedotta da altre misure. Un'adeguata valutazione della qualità della vita può essere ottenuta solo dal paziente stesso, attraverso l'utilizzo di questionari validi e affidabili.

**594****Comunicazione scientifica pubblicata su Rivista non recensita***Istituto di  
TRADATE**Matteelli A.,  
Migliori G.B.,  
Cirillo D.M.,  
Centis R.,  
Girardi E.,  
Raviglione M.C.**In: Expert Rev Anti Infect  
Ther; 2007; 5; 5: 857-871.***MULTIDRUG-RESISTANT AND EXTENSIVELY DRUG-RESISTANT MYCOBACTERIUM TUBERCULOSIS: EPIDEMIOLOGY AND CONTROL.**

The global tuberculosis (TB) epidemic has been complicated lately by the emergence of drug resistance. The emergence of multidrug-resistant TB (MDR-TB), and, more recently of extensively drug-resistant TB (XDR-TB) is considered a real threat to achieve TB control and elimination. Aim of the present review is: 1) to define MDR- and XDR-TB and to describe the mechanisms allowing selection of resistant mutants; 2) to review the available information on epidemiology, diagnosis and management of MDR- and XDR-TB, and 3) to discuss consensus strategies to control and care for MDR- and XDR-TB, and their cost-effectiveness. Finally, research priorities, funding opportunities and financial gaps will be discussed.

**595****Comunicazione scientifica pubblicata su Rivista non recensita***Istituto di  
TRADATE**Migliori G.B.,  
Besozzi G.,  
Codecasa L.R.,  
Raviglione M.C.**In: Rass Pat App Resp;  
2006; 21; 4-5: 179-180.***INTERNATIONAL STANDARDS FOR TUBERCULOSIS CARE: FINALMENTE IL DOCUMENTO UNIVERSALE CHE ASPETTAVAMO.**

Gli Standards sono un documento moderno, in grado di guidare il clinico alla diagnosi e terapia di infezione e malattia tubercolare, di indirizzare all'uso corretto dei nuovi test basati sul gamma-interferone e delle indagini invasive così come alla richiesta dei test batteriologici tradizionali. Gli Standards, inoltre, sottolineano le responsabilità di salute pubblica di chiunque gestisca un paziente con tubercolosi e, in particolare, la necessità di eseguire indagini presso i contatti e di notificare il caso nonché l'esito del trattamento. L'Italia e l'AIPO hanno avuto un ruolo importante nello sviluppo di questo documento a diversi livelli, dall'ideazione, alla stesura e revisione del documento, alla sua prima approvazione avvenuta nel corso della riunione del Comitato Esecutivo della Stop TB Partnership organizzato ad Assisi da Stop TB Italia nel Novembre 2005. Ecco il perché della pubblicazione del documento su questa rivista e della sua presentazione da parte di un Editoriale firmato dal Responsabile e dal Segretario del Gruppo di Studio AIPO TB, dal Responsabile del Gruppo di Studio TB dell'ERS e dal Direttore della Stop TB Department della WHO di Ginevra.

**596****Comunicazione scientifica pubblicata su Rivista non recensita***Istituto di  
TRADATE**Steering group members,  
Migliori G.B.  
as a member.**In: Rass Pat App Resp;  
2006; 21; 4-5: 197-226.***INTERNATIONAL STANDARDS FOR TUBERCULOSIS CARE: DIAGNOSIS, TREATMENT, PUBLIC HEALTH TUBERCULOSIS COALITION FOR TECHNICAL ASSISTANCE.**

The purpose of the International Standards for Tuberculosis Care (ISTC) is to describe a widely accepted level of care that all practitioners, public and private, should seek to achieve in managing patients who have, or are suspected of having, tuberculosis. The Standards are intended to facilitate the effective engagement of all care providers in delivering high-quality care for patients of all ages, including those with smear-positive, smear-negative, and extra-pulmonary tuberculosis, tuberculosis caused by drug-resistant *Mycobacterium tuberculosis* complex (*M. tuberculosis*) organisms, and tuberculosis combined with human immunodeficiency virus HIV infection. The basic principles of care for persons with, or suspected of having, tuberculosis are the same worldwide: a diagnosis should be established promptly and accurately; standardized treatment regimens of proven efficacy should be used, together with appropriate treatment support and supervision; the response to treatment should be monitored; and the essential public health responsibilities must be carried out. Prompt, accurate diagnosis and effective treatment are not only essential for good patient care—they are the key elements in the public health response to tuberculosis and the cornerstone of tuberculosis control. Thus, all providers who undertake evaluation and treatment of patients with tuberculosis must recognize that, not only are they delivering care to an individual, they are assuming an important public health function that entails a high level of responsibility to the community, as well as to the individual patient.

Although government program providers are not exempt from adherence to the Standards, non-program providers are the main target audience. It should be emphasized, however, that national and local tuberculosis control programs may need to develop policies and procedures that enable non-program providers to adhere to the Standards.

Such accommodations may be necessary, for example, to facilitate treatment supervision and contact investigations. In addition to healthcare providers and government tuberculosis programs, both patients and communities are part of the intended audience. Patients are increasingly aware of and expect that their care will measure up to a high standard. Having generally agreed-upon standards will empower patients to evaluate the quality of care they are being provided.

Good care for individuals with tuberculosis is also in the best interest of the community.

The Standards are intended to be complementary to local and national tuberculosis control policies that are consistent with world Health organization (WHO) recommendations.

They are not intended to replace local guidelines and were written to accommodate local differences in practice. They focus on the contribution that good clinical care of individual patients with or suspected of having tuberculosis makes to population-based tuberculosis control. A balanced approach emphasizing both individual patient care and public health principles of disease control is essential to reduce the suffering and economic losses from tuberculosis.

In addition, the ISTC serves as a companion document to the Patients' Charter for Tuberculosis Care developed in tandem with the Standards.

The Standards should be viewed as a living document that will be revised as technology, resources, and circumstances change. As written, the Standards are presented within a context of what is generally considered to be feasible now or in the near future.

The Standards are also intended to serve as a companion to and support for a Patients' Charter. This Charter specifies patients' rights and responsibilities and will serve as a set of standards from the point of view of the patient, defining what the patient should expect from the provider and what the provider should expect from the patient.

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## Comunicazione scientifica pubblicata su atti congressuali

Istituto di  
LUMEZZANEFiorenza D.,  
Polverino E.,  
Nava S.,  
Ceriana P.,  
Cini E.,  
Spada E.,  
Zanotti E.,  
Trianni L.,  
Barbano L.,  
Fracchia C.,  
Vitacca M.In: Congresso SMART  
2007.

## QUINDICI ANNI DI ATTIVITÀ IN CINQUE UNITÀ DI TERAPIA INTERMEDIA RESPIRATORIA DEDICATE ALLO SVEZZAMENTO DELLA VENTILAZIONE MECCANICA.

**Introduzione:** Negli ultimi quindici anni sono aumentati i pazienti che richiedono procedure per lo svezzamento prolungato dalla ventilazione meccanica. La percentuale di successo di svezzamento in specifiche unità dedicate è generalmente alto, ed è stato dimostrato che in pazienti selezionati, queste possono essere delle alternative meno costose di una Terapia Intensiva (TI), e che i pazienti sopravvissuti presentano una successiva accettabile qualità di vita.

**Scopi:** Valutare le variazioni delle diagnosi di ammissione e dei principali outcomes di pazienti ammessi in cinque Terapie Intensive Intermedie Respiratorie (UTIIR) dedicate allo svezzamento prolungato.

**Metodi:** Analisi retrospettiva di un periodo di 15 anni (1990-2005) utilizzando i registri amministrativi ospedalieri.

**Risultati:** Sono stati analizzati 3106 pazienti (2049, 66% dei casi, ammessi per svezzamento prolungato). Le caratteristiche principali dei pazienti e le diagnosi di ingresso sono descritte nella tabella (media±DS).

Età (anni)	76.0± 4.0
Maschi (%)	72
DIAGNOSI DI AMMISSIONE (% di casi)	
Broncopneumopatia Cronica Ostruttiva (BPCO)	67
Malattie cardiovascolari (MCV)	19
Malattie neurologiche e neuromuscolari (MNNM)	14
Comorbidità (n°)	2.5±0.2
Apache II score	13.3±0.9
Degenza media (giorni)	28.7±5.0
Mortalità intraospedaliera (%)	13
Successo svezzamento (%)	76
DESTINAZIONE ALLA DIMISSIONE (%)	
Domicilio	16
Reparto di Riabilitazione	72
Altri Reparti	8
RSA	4

Durante il periodo di osservazione, il numero di posti letto disponibili è progressivamente aumentato e la BPCO è rimasta la maggiore diagnosi di ingresso.

Il tasso di mortalità si è modificato durante i 15 anni nei gruppi di pazienti affetti da BPCO e MCV ( $p=0.024$  e  $p=0.013$  rispettivamente). Il tasso di successo per lo svezzamento si è ridotto da 86.6% a 66.0% (ANOVA  $p<0.01$ ).

Il tasso di mortalità, il successo di svezzamento e la possibilità di dimissione al domicilio sono risultati inversamente correlati alla riduzione del rapporto medico/paziente infermiere/paziente e fisioterapista/paziente.

La lunghezza del ricovero in TI generale prima dell'ammissione in UTIIR era inversamente correlata al successo di svezzamento ( $p=0.02$ ,  $r=-0.734$ ) e alla possibilità di dimissione al domicilio ( $p=0.01$ ,  $r=-0.786$ ).

Il successo di svezzamento era inversamente correlato al numero di comorbidità ( $p=0.045$ ,  $r=-0.523$ ).

**Conclusioni:** In quindici anni di attività di UTIIR dedicate allo svezzamento prolungato:

1. il fallimento dello svezzamento è peggiorato in conseguenza del ricovero di pazienti più severi e complicati;
2. la disponibilità di personale medico, infermieristico e fisioterapico sono risultati cruciali per la mortalità, il successo di svezzamento e la possibilità di dimissione al domicilio.

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## Comunicazione scientifica pubblicata su atti congressuali

Istituto di  
LUMEZZANE

Polverino E.,  
Nava S.,  
Ceriana P.,  
Clini E.,  
Spada E.,  
Zanotti E.,  
Trianni L.,  
Barbano L.,  
Fracchia C.,  
Balbi B.,  
Vitacca M.

In: ERS meeting 2007  
Stoccolma; 1599: 251S.

## FIFTEEN YRS REPORT FROM FIVE ITALIAN INTERMEDIATE INTENSIVE ACUTE CARE UNIT (ICU) DEDICATED TO WEANING.

We retrospectively analyzed the changes in the types of admission and patients outcome in 5 Italian ICUs dedicated to weaning programs over a 15 yrs period (1990-2005).  
Main patients' characteristics and clinical outcomes are presented in table (Mean SD).

Age, yrs	76±4
Admission diagnosis, % of cases	
COPD	67.6
Cardiovascular disease (CVD)	19.5
Neurological and neuromuscular disease (NNMD)	14.4
Weaning program, % of cases	66.11
Comorbidities, n	2.5 0.8
Apache II score	13.1
Mean hospital stay, days	29.5
In-hospital mortality, %	13.4
Weaning success, %	76.10
Discharge destination, %	
Home	16.5
Rehabilitation unit	72.4

3,106 patients (2049 admitted for difficult weaning) were analyzed. During the observational period beds were progressively augmented, with a percentage increase of NNMD admissions (ANOVA  $p < 0.05$ ), and COPD remained the main diagnosis of admission. The doctor to patients ratio significantly decreased over time (from 1:3 to 1:5,  $p = 0.001$ ) while the physiotherapist to patients ratio mild increased (from 1:6 to 1:4.5,  $p = 0.048$ ); no changes were registered in the morning shift for nurse to patients ratio (1:2.3) during the study period.

Previous ICU stay increased from 26 to 32 ( $p < 0.05$ ), the global weaning success decreased from 86.6 3.0% to 66.0 5.2% (ANOVA  $p < 0.01$ ) and, similarly, the percentage of home discharges significantly decreased from 21.8 ± 2.2% to 10.2 ± 1.9% ( $p < 0.001$ ) while proportionally augmented percentages of patients transferred to short stay acute hospitals ( $p = 0.005$ ), and rehabilitative units ( $p = 0.050$ ).

Mortality rate increased for COPD (from 7±2% to 13±2%;  $p = 0.024$ ) and CVD patients (from 9±2% to 14±2%;  $p = 0.013$ ), while N-NMD mortality rate (16±2%) was the highest over the entire study period and did not change over time.

Both weaning success and home discharge were negatively correlated with the number of comorbidities and the length of previous ICU stay and positively with the doctor to patients ratio ( $p < 0.01$ , each). The mortality rate of CVD patients was positively ( $p = 0.006$ ;  $r = 0.673$ ) correlated with the number of comorbidities.

By applying a linear regression model we found that doctors availability had a significant influence on global ( $p = 0.046$ ;  $t = -2.202$ ) and CVD ( $p = 0.002$ ;  $t = -3.836$ ) mortality rates, such as on weaning success ( $p = 0.002$ ;  $t = 3.918$ ) and home discharge ( $p = 0.005$ ;  $t = 3.379$ ).

The length of previous ICU stay showed to be negatively associated with weaning success ( $p = 0.012$ ;  $t = -3.022$ ) and home discharge ( $p = 0.004$ ;  $t = -3.509$ ). Finally, worst was the pre-morbidity life style score (PLS), lower was the weaning success rate ( $p = 0.039$ ;  $t = -2.347$ ).

In conclusion, in Intermediate Intensive Care Units:

1. clinical outcomes worsened over a long time;
2. worse clinical conditions before admission, a longer stay in general ICUs and a fewer medical staff availability appear to be independent, negative prognostic factors of major clinical outcomes.

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Medicina: Cura della  
Persona o Utopia"; 2007.

## LA TELEMEDICINA RESPIRATORIA COME AIUTO PER PAZIENTI TERMINALI VENTILATI AL DOMICILIO.

**Introduzione:** Le ultime fasi della vita di pazienti con IRC e ventilazione meccanica (VM) espongono l'équipe sanitaria, il paziente e i familiari a condividere gravi scelte cliniche di fine vita.

Scopo del presente studio è stato quello di analizzare l'impatto che un anno di assistenza in Telemedicina (TM) ha avuto sul paziente, sulla famiglia e sul gruppo sanitario di assistenza riguardo a trattamento del dolore e dei sintomi, adeguato senso di controllo della malattia, sollievo delle dipendenze, scelte di fine vita, problemi tecnici legati alla VM.

**Metodi:** Il programma di TM consisteva in chiamate telefoniche programmate e non, cartella informatizzata, saturimetro istantaneo o a trend, call-center informatizzato, assistenza infermieristica telefonica specializzata 5 gg/settimana, consulenza telefonica di un pneumologo 24H/24.

**Risultati:** All'interno del gruppo di 118 pazienti ( $61 \pm 18$  anni) arruolati in TM, 21 (18%) morirono dopo  $6 \pm 3$  mesi di follow up. La principale diagnosi del gruppo preso nel suo complesso era la BPCO (61%) mentre i 21 pazienti deceduti erano affetti da: BPCO (57%), sclerosi laterale amiotrofica (SLA) (24%), portatori di malattia restrittiva (5%), portatori di malattie neuromuscolari (14%).

I pazienti deceduti, se confrontati con quelli sopravvissuti, presentavano una età superiore ( $71 \pm 9$  vs  $59 \pm 18$ ), un più alto numero di ospedalizzazioni/mese ( $0.32 \pm 0.30$  vs  $0.08 \pm 0.11$ ), di accessi/mese in PS ( $0.28 \pm 0.32$  vs  $0.02 \pm 0.04$ ), di gravi riacutizzazioni domiciliari ( $0.40 \pm 0.42$  vs  $0.16 \pm 0.23$ ), di urgenti chiamate al MMG ( $0.22 \pm 0.34$  vs  $0.04 \pm 0.08$ ). Per i pazienti deceduti se confrontati con i sopravvissuti, gli infermieri tutor hanno eseguito un maggior numero di chiamate telefoniche programmate ( $3.37 \pm 2$  vs  $2.30 \pm 1.40$ ) e hanno ricevuto un maggior numero di contatti richiesti dal paziente ( $1.51 \pm 2.3$  vs  $0.7 \pm 0.7$ ). I consigli dati dalla nostra équipe riguardavano il buon uso dell'accesso in ospedale, l'aiuto nelle fasi terminali o nel peggioramento di fine vita comprese le manovre di rianimazione cardiorespiratoria qualora fossero state necessarie. Nei pazienti deceduti, il team della TM ha eseguito le seguenti azioni (espresse come numero volta/paziente): consulti con il MMG ( $1.04 \pm 0.75$ /pt), cambiamenti farmacologici ( $3.5 \pm 4$ /pt), condivisione di prescrizione di sedativi o morfina come terapia palliativa ( $1.0 \pm 1.2$ /pt), soluzione di problemi legati al ventilatore meccanico ( $0.7 \pm 0.8$ /pt), soluzione di problemi clinici generali ( $18 \pm 12$ /pt), second opinion pneumologica ( $3.5 \pm 4.3$ /pt), monitoraggio saturimetrico ( $12 \pm 9$ /pt), discussione e conforto su gravità della patologia ( $2.1 \pm 1.3$ /pt), coordinamento con gli infermieri domiciliari ( $2.1 \pm 2.3$ /pt). Il 90% dei pazienti deceduti non avevano lasciato direttive anticipate mentre un 43% non aveva mai discusso con i parenti riguardo alle loro decisioni di fine vita. La maggior parte dei caregiver hanno apprezzato la disponibilità e competenza dello staff, la rapidità delle informazioni dimostrato dalla piena soddisfazione segnalata nell'88% dei casi. I benefici psicologici furono percepiti nel 96% dei casi.

**Discussione:** Un programma di TM per pazienti terminali o in condizione di fine vita con IRC e VM domiciliare è fattibile se condotto da una unità pneumologica riabilitativa di 3° livello qualora il personale infermieristico sia ben motivato e sia disponibile un call center con solida struttura informatizzata.

**Conclusioni:** Nel periodo di fine vita di pazienti con IRC, un programma di telemedicina può:

1. migliorare la comunicazione tra lo staff sanitario e le famiglie;
2. migliorare le modalità di informazione e presa di coscienza della gravità della malattia;
3. migliorare la dignità e il livello di assistenza;
4. razionalizzare le necessità assistenziali ospedaliere e del servizio sanitario nazionale.

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Moscato G.

In: Atti Congresso  
SIAIC; Palermo,  
26-29 Settembre 2007;  
11-14.

## LA TOSSE CRONICA DAL PUNTO DI VISTA ALLERGOLOGICO.

La tosse rappresenta uno dei sintomi che più frequentemente porta un soggetto, a consultare il medico. I dati della letteratura indicano una frequenza nella popolazione generale variabile da 5 a 40% in base alle caratteristiche ambientali, all'età della popolazione e all'abitudine al fumo. La tosse cronica, ossia di durata superiore a 8 settimane, costituisce un problema clinico, diagnostico e conseguentemente terapeutico rilevante. Le cause più frequenti di tosse conica sono rappresentate da: asma ("cough variant asthma"), bronchite cronica, infezione delle alte e basse vie respiratorie, reflusso gastro-esofageo, gocciolamento retrorinale ("post-nasal drip") e bronchite eosinofila.

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339-340.IL TEST DI ATTIVAZIONE DEI BASOFILI IN SOGGETTI SOTTOPOSTI A ITS  
PER VELENO DI IMENOTTERI. DATI PRELIMINARI.

**Razionale:** L'immunoterapia specifica (ITS) per gli imenotteri viene in genere praticata per un numero elevato di anni e i valori di IgE e IgG specifici non sono indicativi per la sospensione dell'ITS. Scopo dello studio è quello di valutare l'utilità del test in vitro di attivazione dei basofili per definire la reattività dei soggetti dopo ITS al veleno di imenotteri.

**Materiali e Metodi:** Abbiamo arruolato nello studio 20 soggetti sottoposti ad ITS per veleno di imenotteri da almeno 1 anno (età media 42.5 anni, range 15-75). Il sangue dei soggetti è stato incubato in vitro con l'allergene utilizzato per l'ITS e l'espressione del CD63, marker di attivazione/degranulazione dei basofili è stata valutata al citofluorimetro. I risultati sono stati espressi come: %CD63 dopo attivazione - %CD63 dopo incubazione con tampone e come indice di stimolazione (%CD63 dopo attivazione - %CD63 dopo incubazione con tampone).

**Risultati:** 16/20 soggetti avevano ricevuto ITS per *Vespula*, 3/20 per *Polistes*, 1/20 per *Apis*. Il tempo medio trascorso dall'inizio dell'ITS era  $5.3 \pm 2.0$  anni. Al momento dello studio le IgE specifiche per il veleno di cui i soggetti stavano facendo l'ITS erano  $5.5 \pm 6.7$  KU/l mentre le IgE totali  $93.4 \pm 51.5$  KU/l. La media della percentuale di CD63 sui basofili, dopo attivazione con veleno di imenotteri per cui i soggetti erano sottoposti ad ITS, era  $57.3 \pm 32.7\%$ . L'indice di stimolazione era  $21.1 \pm 23.4$ . Solo 2/20 soggetti non presentavano più alcuna reattività in vitro al veleno dell'imenottero per cui stavano facendo ITS (*Vespula* da 7 e da 9 anni), pur mantenendo livelli dosabili di IgE specifiche (2.16 KU/l e 3.24 KU/l rispettivamente). Nessuna correlazione è stata evidenziata tra l'espressione del CD63 dopo attivazione e gli anni di terapia con ITS o i livelli di IgE totali e specifiche. Nessuna differenza nell'espressione del CD63 e nell'indice di stimolazione è stata evidenziata tra i soggetti che dopo l'inizio dell'ITS hanno subito nuovamente punture di imenotteri (n=17) e quelli che non sono più stati punti (n=3).

**Conclusioni:** Il test di attivazione dei basofili, potrebbe essere utilizzato per valutare la reattività residua dei soggetti sottoposti ad ITS prima della sospensione della terapia, evidenziando la presenza di IgE specifiche per il veleno degli imenotteri legate ai basofili e fornendo un dato aggiuntivo rispetto alle IgE specifiche nel siero.

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4<sup>th</sup> Congress of  
International Union  
Against Tuberculosis  
and Lung Diseases,  
Europe Region;  
Riga, Latvia,  
27-30 Giugno 2007; 34.RISK FACTORS FOR MULTIDRUG RESISTANT TUBERCULOSIS (MDR-TB):  
A 10-YEAR SURVEY IN BRESCIA, ITALY.

**Background:** Multidrug resistant tuberculosis (MDR-TB) is a current concern worldwide, and patients with MDR-TB migrating from Eastern Europe are a threat for TB control in some western European countries.

**Objective:** to assess the risk factors associated with MDR-TB in a general hospital in northern Italy.

**Methods:** a retrospective study was done including all patients with culture-positive TB diagnosed at Spedali Civili, Brescia, from 1994 to 2003. Drug susceptibility testing for first line TB drugs was performed. The association of MDR-TB with age, sex, country of origin, HIV status and year of diagnosis was determined.

**Results:** 824 cases of culture-positive TB were included in the analysis. Seventeen cases (2.1%) were MDR-TB; the percentage among new TB cases was 1% (7/679). In the univariate analyses, being Italian (OR=4.72; 95% C.I. 1.35 - 16.67; p<0.01) and previously treated for TB (OR= 16.0; 95% C.I. 5.36 - 47.73; p<0.005) were associated with a higher risk of MDR-TB. Among foreign-born patients, only 3 (17.6%) cases of MDR-TB were identified (1 patient from Brazil, 1 from China and 1 from Lithuania).

**Conclusions:** Up to 2003 in our setting MDR-TB was an unusual event limited to previously treated Italian patients. The increasing immigration flow from Eastern Europe has the potential to modify the trend and continuous monitoring is warranted.