



RESPIRATORY RESEARCH, INC.

1167 Raintree Drive Charlottesville, Virginia 22901 USA

www.respiratoryresearch.com (434) 825-7627 fax (+1) 512 233-2281 info@respiratoryresearch.com

## EBC H<sub>2</sub>O<sub>2</sub> References

Reference Type: Journal Article

Record Number: 45

Author: Baldwin, S. R.; Simon, R. H.; Grum, C. M.; Ketai, L. H.; Boxer, L. A.; Devall, L. J.

Year: 1986

Title: Oxidant activity in expired breath of patients with adult respiratory distress syndrome

Journal: Lancet

Volume: 1

Issue: 8471

Pages: 11-4

Label: 86090980

Keywords: \*Breath Tests

Human

Hydrogen Peroxide/\*analysis

Leukocyte Count

Muramidase/blood

Neutrophils/enzymology

Oxygen/analysis

Respiration, Artificial

Respiratory Distress Syndrome, Adult/blood/\*metabolism/therapy

Support, Non-U.S. Gov't

Support, U.S. Gov't, P.H.S.

Abstract: Hydrogen peroxide levels were measured in the breath condensate of 43 patients receiving mechanical ventilation. In 16 patients the mean breath condensate peroxide level was 1.68 +/- 0.35 mumol/l on the day they met diagnostic criteria for adult respiratory distress syndrome (ARDS). The peak breath condensate peroxide level in the 27 patients in whom ARDS did not develop was significantly lower (0.34 +/- 0.08 mumol/l). Plasma lysozyme, a measure of in-vivo neutrophil turnover, was significantly higher in ARDS than in non-ARDS patients (9.2 +/- 2.2 U/ml v 3.4 +/- 1.1 U/ml). These findings support the hypothesis that neutrophil activation and oxidant production are involved in the pathogenesis of ARDS.

Reference Type: Journal Article

Record Number: 38

Author: Sznajder, J. I.; Fraiman, A.; Hall, J. B.; Sanders, W.; Schmidt, G.; Crawford, G.; Nahum, A.; Factor, P.; Wood, L. D.

Year: 1989

Title: Increased hydrogen peroxide in the expired breath of patients with acute hypoxemic respiratory failure

Journal: Chest

Volume: 96

Issue: 3

Pages: 606-12

Label: 89356052

Keywords: Breath Tests

Human

Hydrogen Peroxide/\*analysis

Intensive Care Units

Respiration, Artificial

Respiratory Distress Syndrome, Adult/etiology/\*metabolism

Respiratory Insufficiency/etiology/\*metabolism

Spectrophotometry

Support, Non-U.S. Gov't

Support, U.S. Gov't, P.H.S.

## Surgical Procedures, Operative

**Abstract:** Acute hypoxemic respiratory failure (AHRF) can result from diverse lung insults. Toxic oxygen metabolites have been implicated in this clinical condition and in animal models of pulmonary edema. Hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>), an oxygen metabolite, mediates tissue injury. We measured H<sub>2</sub>O<sub>2</sub> levels by a spectrophotometric technique in the breath condensate of 68 mechanically ventilated patients; 13 patients with normal lungs undergoing elective surgery had no such detectable levels of H<sub>2</sub>O<sub>2</sub>. Fifty-five patients in the ICU meeting criteria for the adult respiratory distress syndrome (ARDS) had a higher concentration of H<sub>2</sub>O<sub>2</sub> in the expired breath condensate than ICU patients without pulmonary infiltrates (2.34 +/- 1.15 vs 0.99 +/- 0.72 mumol/L, p less than 0.005). This marker had a sensitivity of 87.5 percent and a specificity of 81.3 percent in separating the two patient populations. Patients with AHRF and focal pulmonary infiltrates who did not meet criteria for ARDS also had higher concentrations of H<sub>2</sub>O<sub>2</sub> (2.45 +/- 1.55 mumol/L) than patients without pulmonary infiltrates (p less than 0.001). No difference was observed between the expired H<sub>2</sub>O<sub>2</sub> concentrations of patients with ARDS or patients with focal pulmonary infiltrates. Patients with brain injury or sepsis tended to have higher levels of H<sub>2</sub>O<sub>2</sub> regardless of lung pathology. Increased levels of H<sub>2</sub>O<sub>2</sub> are detected in the expired breath of ICU patients with focal lung infiltrates and in ARDS patients, which is consistent with the hypothesis that oxygen metabolites participate in the pathogenesis of ARDS and other forms of AHRF.

Reference Type: Journal Article

Record Number: 34

Author: Wilson, W. C.; Swetland, J. F.; Benumof, J. L.; Laborde, P.; Taylor, R.

Year: 1992

Title: General anesthesia and exhaled breath hydrogen peroxide

Journal: Anesthesiology

Volume: 76

Issue: 5

Pages: 703-10

Label: 92246318

Keywords: \*Anesthesia, General

Anesthesia, Inhalation

Anesthesia, Intravenous

Breath Tests

Cardiopulmonary Bypass

Comparative Study

Human

Hydrogen Peroxide/\*analysis

\*Isoflurane

\*Nitrous Oxide

Random Allocation

Respiratory Distress Syndrome, Adult/metabolism/surgery

Spectrophotometry

Support, Non-U.S. Gov't

**Abstract:** To study the role of free radical formation on the impairment of pulmonary function seen with general anesthesia, we measured the hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) concentration in the Exhaled Breath Condensate of 27 patients. Patients were divided into three study groups: a healthy patient group (group 1, n = 15) consisting of ASA physical status 1 and 2 patients undergoing elective noncardiothoracic surgery; a specific anesthetic event group (group 2, n = 6) composed of patients undergoing cardiopulmonary bypass (CPB); and a positive control group (group 3, n = 6) consisting of patients with the adult respiratory distress syndrome (ARDS). The Exhaled Breath Condensate was collected by diverting exhaled breath through a glass condensation coil submerged in an ice/salt water bath. The Exhaled Breath Condensate samples were then assayed using a spectrophotometric method. In group 1, samples were collected before and after the induction of general anesthesia with intravenous drugs, and before and after the administration of the inhalational anesthetics isoflurane (1.5%) (n = 7) or N<sub>2</sub>O (70%) (n = 8). In group 2, samples were collected pre- and post-CPB, and in group 3, when specific diagnostic criteria for ARDS were met. There was no significantly detectable H<sub>2</sub>O<sub>2</sub> (not significantly different from zero) in any of the samples from the group 1 patients. Similarly, group 2 patients had exhaled breath H<sub>2</sub>O<sub>2</sub> concentrations near zero except for one patient who was positive for the lupus anticoagulant. Group 3 patients had a mean (+/- SE) exhaled breath H<sub>2</sub>O<sub>2</sub> concentration of 0.55 (+/- 0.08) microM, which was significantly greater than zero (P less than 0.001). (ABSTRACT TRUNCATED AT 250 WORDS)

Reference Type: Journal Article

Record Number: 29

Author: Dohlman, A. W.; Black, H. R.; Royall, J. A.

Year: 1993

Title: Expired breath hydrogen peroxide is a marker of acute airway inflammation in pediatric patients with asthma

Journal: Am Rev Respir Dis

Volume: 148

Issue: 4 Pt 1

Pages: 955-60

Label: 94028337

Keywords: Acute Disease

Adolescence

Asthma/\*physiopathology

Biological Markers/analysis

Breath Tests/methods

Bronchitis/\*physiopathology

Child

Comparative Study

Female

Human

Hydrogen Peroxide/\*analysis

Male

Respiratory Function Tests/statistics & numerical data

Support, Non-U.S. Gov't

Support, U.S. Gov't, P.H.S.

Abstract: Airway inflammation is important in the development and progression of many pulmonary disorders, including asthma. We hypothesized that the hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) concentration in expired breath may be a marker of airway inflammation. Expired breath condensate was collected by cooling and the H<sub>2</sub>O<sub>2</sub> concentration was measured fluorimetrically. Thirty-five samples were collected from 22 pediatric patients with asthma who were 7 to 18 yr of age and from 11 healthy, nonasthmatic controls. Asthmatic subjects were determined to be well or sick (acute disease of the upper or lower respiratory tract) by clinical examination. Pulmonary function tests were determined to be abnormal if there was a > 15% reduction in FEV<sub>1</sub> or > 20% reduction in FEF<sub>25-75</sub> compared with baseline values. Expired breath H<sub>2</sub>O<sub>2</sub> was elevated in asthmatic subjects compared with controls (0.81 +/- 0.70 versus 0.25 +/- 0.27  $\mu$ mol/L). The difference was primarily due to elevation of H<sub>2</sub>O<sub>2</sub> in sick asthmatic subjects, whose expired breath H<sub>2</sub>O<sub>2</sub> level of 1.5 +/- 0.5 (n = 10) was different from that of well asthmatics (0.54 +/- 0.56, n = 25). There was a high correlation between expired breath H<sub>2</sub>O<sub>2</sub> and clinical status. Elevation of expired H<sub>2</sub>O<sub>2</sub> occurred with either acute upper or lower respiratory tract disease. There was no statistically significant correlation between expired breath H<sub>2</sub>O<sub>2</sub> level and pulmonary function test results. We conclude that elevation of H<sub>2</sub>O<sub>2</sub> in the expired breath condensate is a simple, noninvasive method that can be used as a biochemical marker of airway inflammation.

Reference Type: Journal Article

Record Number: 31

Author: Kietzmann, D.; Kahl, R.; Muller, M.; Burchardi, H.; Kettler, D.

Year: 1993

Title: Hydrogen peroxide in expired breath condensate of patients with acute respiratory failure and with ARDS

Journal: Intensive Care Med

Volume: 19

Issue: 2

Pages: 78-81

Label: 93253194

Keywords: Adolescence

Adult

Aged

Blood Gas Analysis

\*Breath Tests/instrumentation/methods

Female

Human

Hydrogen Peroxide/\*analysis  
 Intensive Care Units  
 Lung Compliance  
 Male  
 Middle Age  
 Predictive Value of Tests  
 Prognosis  
 Pulmonary Gas Exchange  
 Respiration, Artificial  
 Respiratory Distress Syndrome, Adult/\*diagnosis/therapy  
 Respiratory Insufficiency/\*diagnosis/therapy  
 Risk Factors  
 Support, Non-U.S. Gov't  
 Survival Rate  
 Tidal Volume

Abstract: OBJECTIVE: Measurement of hydrogen peroxide concentrations in breath condensate of mechanically ventilated patients with ARDS and with risk factors for developing ARDS. DESIGN: Open study in intensive care patients. SETTING: Intensive care units of the Clinics of the University of Gottingen, a primary care center. PATIENTS: 10 post-operatively ventilated patients as a control group and 26 patients with acute respiratory failure, 7 of them with ARDS, 12 with polytrauma, 4 with pneumonia, 3 with cardiogenic or nephrogenic pulmonary edema. INTERVENTIONS: None. MEASUREMENTS: Breath condensate was collected by a special cold trap and was analysed for H<sub>2</sub>O<sub>2</sub> by a chemiluminescence method. Daily measurements were performed for 4.2 +/- 2.6 days (mean +/- SD) as soon as possible after manifestation of respiratory failure. RESULTS: Patients with acute respiratory failure exhibited higher H<sub>2</sub>O<sub>2</sub> concentrations than control patients (median 95 nmol/l, range 76-144 nmol/l), with the highest median value found in the ARDS group (552 nmol/l, range 154-893). After clinical improvement, H<sub>2</sub>O<sub>2</sub> concentrations decreased to the range of the control group. CONCLUSION: Since high concentrations of H<sub>2</sub>O<sub>2</sub> in breath condensate were only found in patients with ARDS or with risk factors for ARDS, the results add to the existing evidence that reactive oxygen species are associated with some acute lung diseases. Notes: Using Smart Source Parsing

Reference Type: Journal Article

Record Number: 24

Author: Dekhuijzen, P. N.; Aben, K. K.; Dekker, I.; Aarts, L. P.; Wielders, P. L.; van Herwaarden, C. L.; Bast, A. Year: 1996

Title: Increased exhalation of hydrogen peroxide in patients with stable and unstable chronic obstructive pulmonary disease

Journal: Am J Respir Crit Care Med Volume: 154

Issue: 3 Pt 1

Pages: 813-6

Label: 96406509

Keywords: Aged

Aged, 80 and over

Breath Tests

Comparative Study

Female

Forced Expiratory Volume

Human

Hydrogen Peroxide/analysis/\*metabolism

Lung Diseases, Obstructive/classification/\*metabolism/physiopathology

Male

Middle Age

Pulmonary Gas Exchange

Reference Values

Severity of Illness Index

Abstract: An imbalance between oxidative stress and antioxidative capacity is thought to play an important role in the development and progression of chronic obstructive pulmonary disease (COPD). To assess the lung oxidative status in patients with COPD, we studied whether exhaled hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) is increased in breath condensate of patients with stable COPD (n = 12, mean FEV1 51% pred) and in patients with exacerbated COPD (n = 19, actual FEV1 36% pred) compared with a healthy control group (n = 10, FEV1 108% pred). Expired breath condensate during 15 min of tidal breathing was collected

by cooling. The concentration of H<sub>2</sub>O<sub>2</sub> was measured spectrophotometrically by means of horse radish peroxidase-catalyzed oxidation of tetramethylbenzidine. Concentrations of H<sub>2</sub>O<sub>2</sub> (mean +/- SEM) were significantly elevated at 0.205 +/- 0.054 microM in patients with stable COPD compared with 0.029 +/- 0.012 microM in the control group (p 0.05) and were further increased to 0.600 +/- 0.075 microM in patients with acutely exacerbated COPD (p 0.001 compared with patients with stable COPD). Patients with pulmonary infiltrates on chest radiograph showed similar values compared with patients without obvious infiltrates. These findings demonstrate that patients with stable COPD exhibit increased oxidant production in the airways and that oxidant production increases further during exacerbations.

Reference Type: Journal Article

Record Number: 26

Author: Nowak, D.; Antczak, A.; Krol, M.; Pietras, T.; Shariati, B.; Bialasiewicz, P.; Jeczowski, K.; Kula, P. Year: 1996

Title: Increased content of hydrogen peroxide in the expired breath of cigarette smokers

Journal: Eur Respir J

Volume: 9

Issue: 4

Pages: 652-7

Label: 96326841

Keywords: Adult

\*Breath Tests

Comparative Study

Cotinine/analysis/urine

Female

Human

Hydrogen Peroxide/\*analysis

Male

Middle Age

Smoking/\*metabolism

Support, Non-U.S. Gov't

Abstract: Cigarette smoking causes an influx of mononuclear phagocytes and polymorphonuclear leucocytes into the lower airways. These cells have altered oxygen metabolism and release more H<sub>2</sub>O<sub>2</sub> than phagocytes from nonsmokers. In this study, we intended to determine whether asymptomatic cigarette smokers exhale more H<sub>2</sub>O<sub>2</sub> than healthy nonsmokers. The content of H<sub>2</sub>O<sub>2</sub> in the expired condensate of 27 nonsmokers and 33 cigarette smokers was measured spectrofluorimetrically (homovanillic acid method). The mean H<sub>2</sub>O<sub>2</sub> level in the expired breath condensate of all cigarette smokers was about fivefold higher than that found in the whole nonsmoker group (0.24 +/- 0.32 versus 0.05 +/- 0.11 nM). However, only 16 smokers (49%) and 6 nonsmokers (22%) had detectable levels of H<sub>2</sub>O<sub>2</sub> in expired breath that reached values 0.49 +/- 0.28 and 0.23 +/- 0.10 nM, respectively. Although the cigarette smoking status was similar for both male and female smokers, females expired 2.5 fold less H<sub>2</sub>O<sub>2</sub> than males (0.15 +/- 0.24 (n = 21) versus 0.38 +/- 0.39 (n = 12) nM. No correlation was found between expired H<sub>2</sub>O<sub>2</sub> levels and cigarette smoking status expressed as the daily cigarette consumption, cumulative cigarette consumption and urinary cotinine concentration. It is suggested that in some smokers, expressed H<sub>2</sub>O<sub>2</sub> can be a noninvasive marker of oxidant overload in the lower airways related to cigarette smoking.

Reference Type: Journal Article

Record Number: 19

Author: Antczak, A.; Nowak, D.; Shariati, B.; Krol, M.; Piasecka, G.; Kurmanowska, Z. Year: 1997

Title: Increased hydrogen peroxide and thiobarbituric acid-reactive products in expired breath condensate of asthmatic patients

Journal: Eur Respir J

Volume: 10

Issue: 6

Pages: 1235-41

Label: 97336127

Keywords: Adult

Asthma/\*metabolism/physiopathology

\*Breath Tests

Female

Forced Expiratory Volume

Human  
Hydrogen Peroxide/\*analysis  
Male

Peak Expiratory Flow Rate  
Support, Non-U.S. Gov't

Thiobarbituric Acid Reactive Substances/\*analysis

Abstract: Symptoms of bronchial asthma are a manifestation of airway inflammation. Circulatory leucocytes (predominantly eosinophils, mast cells and neutrophils), release inflammatory mediators, including reactive oxygen species, i.e. superoxide anion which is dismutated to hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>). Neutrophils from asthmatics generate greater amounts of these species than those of healthy subjects. Some of the H<sub>2</sub>O<sub>2</sub> and thiobarbituric acid-reactive products (TBARs) can evaporate from alveolar lining fluid, and could be expired from the airways of asthmatics. In this study, therefore, we determined whether asthmatic patients exhale more H<sub>2</sub>O<sub>2</sub> and TBARs than healthy subjects. We examined 10 healthy subjects as a control group and 21 asthmatic subjects. In asthmatic subjects, forced expiratory volume in one second (FEV<sub>1</sub>), was 68+/-9% of predicted value, peak expiratory flow rate (PEFR) was 65+/- 8% pred, and bronchial reversibility was 34+/-5% of prebronchodilated FEV<sub>1</sub>. The mean H<sub>2</sub>O<sub>2</sub> level measured spectrofluorimetrically in the expired breath condensate of asthmatic subjects was 26 fold higher than that in healthy controls (0.26+/-0.29 vs 0.01+/-0.03 nM; p0.05). The concentration of TBARs in breath condensate was also higher in asthmatic patients compared with nonasthmatics (0.073+/-0.071 vs 0.004+/-0.009 nM; p0.05). There was a significant correlation between H<sub>2</sub>O<sub>2</sub> level and concentration of TBARs in asthmatic patients (r=0.74; p0.01). There was also a strong inverse correlation between H<sub>2</sub>O<sub>2</sub> content of all asthmatics and FEV<sub>1</sub>% pred (r=-0.63; p0.005) and PEFR% pred (r=-0.52; p0.05). We conclude that there are elevated levels of hydrogen peroxide and thiobarbituric acid-reactive products in expired breath condensate of asthmatic patients, and that measurement of these substances in the expired breath condensate could be a simple, noninvasive method that could be used as a biochemical marker of airway inflammation.

Reference Type: Journal Article

Record Number: 22

Author: Jobsis, Q.; Raatgeep, H. C.; Hermans, P. W.; de Jongste, J. C.

Year: 1997

Title: Hydrogen peroxide in exhaled air is increased in stable asthmatic children

Journal: Eur Respir J

Volume: 10

Issue: 3

Pages: 519-21

Label: 97225708

Keywords: Adult

Anti-Asthmatic Agents/therapeutic use

Anti-Inflammatory Agents, Steroidal/therapeutic use

Asthma/\*diagnosis/drug therapy/physiopathology

Breath Tests

Case-Control Studies

Child

Comparative Study

Cross-Sectional Studies

Female

Human

Hydrogen Peroxide/\*analysis

Male

Support, Non-U.S. Gov't

Abstract: Exhaled air condensate provides a noninvasive means of obtaining samples from the lower respiratory tract. Hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) in exhaled air has been proposed as a marker of airway inflammation. We hypothesized that in stable asthmatic children the H<sub>2</sub>O<sub>2</sub> concentration in exhaled air condensate may be elevated as a result of airway inflammation. In a cross-sectional study, 66 allergic asthmatic children (of whom, 41 were treated with inhaled steroids) and 21 healthy controls exhaled through a cold trap. The resulting condensate was examined fluorimetrically for the presence of H<sub>2</sub>O<sub>2</sub>. All subjects were clinically stable, nonsmokers, without infection. The median H<sub>2</sub>O<sub>2</sub> level in the exhaled air condensate of the asthmatic patients was significantly higher than in healthy controls (0.60 and 0.15 micromol, respectively; p0.05), largely because of high values in the stable asthmatic children who did not use anti-inflammatory treatment (0.8 micromol; p0.01 compared to controls). We conclude that hydrogen

peroxide is elevated in exhaled air condensate of children with stable asthma, and may reflect airway inflammation.

Reference Type: Journal Article

Record Number: 15

Author: Jobsis, Q.; Raatgeep, H. C.; Schellekens, S. L.; Hop, W. C.; Hermans, P. W.; de Jongste, J. C. Year: 1998

Title: Hydrogen peroxide in exhaled air of healthy children: reference values

Journal: Eur Respir J

Volume: 12

Issue: 2

Pages: 483-5

Label: 98394789

Keywords: \*Breath Tests

Child

Female

Human

Hydrogen Peroxide/\*analysis

Male

Reference Values

Reproducibility of Results

Respiratory Function Tests

Support, Non-U.S. Gov't

Abstract: An increased content of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>), a marker of inflammation, has been described in the condensate of exhaled air from adults and children with inflammatory lung disorders, including asthma. However, the normal range of [H<sub>2</sub>O<sub>2</sub>] in the exhaled air condensate from healthy children has not been established. Therefore, the aim of this study was to determine the reference range of exhaled [H<sub>2</sub>O<sub>2</sub>] in healthy school-aged children. Ninety-three healthy nonsmoking children (48 female and 45 male, mean age 10 yrs, range 8-13 yrs), with a negative history for allergy, eczema or respiratory disease and with a normal lung function, participated. Exhaled air condensate was examined fluorimetrically for the presence of H<sub>2</sub>O<sub>2</sub>. In addition, the reproducibility of [H<sub>2</sub>O<sub>2</sub>] within subjects and between days and the stability of [H<sub>2</sub>O<sub>2</sub>] during storage at -20 degrees C were assessed. The median [H<sub>2</sub>O<sub>2</sub>] in the exhaled air condensate of all children was 0.13 microM, with a 2.5-97.5% reference range of 0.01-0.48 microM. No significant difference existed between males and females. There was no correlation between exhaled [H<sub>2</sub>O<sub>2</sub>] and age or lung function. Repeated [H<sub>2</sub>O<sub>2</sub>] measurements on 2 consecutive days showed satisfactory within-subject reproducibility and [H<sub>2</sub>O<sub>2</sub>] in stored samples remained stable for at least 1 month at -20 degrees C. In conclusion, this study provides reference data for exhaled hydrogen peroxide in a large group of healthy children. The observed levels were lower than those reported previously for healthy adults and were independent of age, sex and lung function.

Reference Type: Journal Article

Record Number: 14

Author: Loukides, S.; Horvath, I.; Wodehouse, T.; Cole, P. J.; Barnes, P. J. Year: 1998

Title: Elevated levels of expired breath hydrogen peroxide in bronchiectasis

Journal: Am J Respir Crit Care Med

Volume: 158

Issue: 3

Pages: 991-4

Label: 98402685

Keywords: Administration, Inhalation

Adult

Androstadienes/administration & dosage/therapeutic use

Bronchiectasis/\*metabolism/pathology/physiopathology

Bronchitis/metabolism/pathology/physiopathology

Case-Control Studies

Comparative Study

Disease Progression

Eosinophils/metabolism

Female

Forced Expiratory Volume/physiology

Glucocorticoids, Topical/administration & dosage/therapeutic use

Human

Hydrogen Peroxide/\*analysis

Lung/physiopathology

Macrophages, Alveolar/metabolism

Male

Middle Age

Neutrophils/metabolism

Oxidative Stress/physiology

Reactive Oxygen Species/metabolism

\*Respiration

Respiratory Burst/physiology

Abstract: Airway inflammation is important in the development and progression of many lung diseases, including bronchiectasis. Activation of inflammatory cells such as neutrophils, eosinophils, and macrophages induces a respiratory burst resulting in the production of reactive oxygen species such as hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>). We have measured exhaled H<sub>2</sub>O<sub>2</sub> in patients with documented bronchiectasis and investigated whether the concentration of H<sub>2</sub>O<sub>2</sub> is related to the disease severity, as defined by lung function. We also investigated whether the concentrations of expired H<sub>2</sub>O<sub>2</sub> were different in bronchiectatic patients who received inhaled corticosteroids compared with steroid-naïve patients. In 37 patients with bronchiectasis (mean age, 45 +/- 2.5 yr; FEV<sub>1</sub>, 59 +/- 3% pred), mean H<sub>2</sub>O<sub>2</sub> concentration in Exhaled Breath Condensate was significantly elevated as compared with the values in 25 age-matched (mean age, 42 +/- 2 yr) normal subjects (0.87 +/- 0.01 versus 0.26 +/- 0.04 microM, p 0.05). We conclude that H<sub>2</sub>O<sub>2</sub> is elevated in exhaled air condensate of patients with bronchiectasis and is correlated with disease severity. Measurement of H<sub>2</sub>O<sub>2</sub> may be used as a simple noninvasive method to monitor airway inflammation and oxidative stress.

URL: <http://www.ncbi.nlm.nih.gov/cgi-bin/Entrez/referer?http://www.ajrccm.org/cgi/content/full/158/3/991>

Reference Type: Journal Article

Record Number: 12

Author: Nowak, D.; Kasielski, M.; Pietras, T.; Bialasiewicz, P.; Antczak, A.

Year: 1998

Title: Cigarette smoking does not increase hydrogen peroxide levels in expired breath condensate of patients with stable COPD

Journal: Monaldi Arch Chest

Dis Volume: 53

Issue: 3

Pages: 268-73

Label: 99001988

Keywords: Breath Tests

Case-Control Studies

Female

Human

Hydrogen Peroxide/\*metabolism

Lung Diseases, Obstructive/complications/diagnosis/\*metabolism

Male

Middle Age

Oxidants/\*metabolism

Smoking/\*adverse effects

Abstract: Cigarette smoking is the most common factor responsible for the development of chronic obstructive pulmonary disease (COPD) leading to oxidant overload in the lower airways because of the presence of oxidants in cigarette smoke and recruitment and activation of pulmonary phagocytes. In this study we intended to determine whether: 1) patients with stable COPD have higher H<sub>2</sub>O<sub>2</sub> levels in expired breath condensate than healthy nonsmoking subjects and 2) whether cigarette smoking increases H<sub>2</sub>O<sub>2</sub> exhalation in patients with stable COPD. The H<sub>2</sub>O<sub>2</sub> content of the expired breath condensate of 17 healthy nonsmoking subjects and 38 patients (10 current smokers, 17 exsmokers and 11 who have never smoked) with stable COPD (forced expiratory volume in one second (FEV<sub>1</sub>) 63.3 +/- 15.5% of predicted value) was measured spectrofluorimetrically (homovanillic acid method). The mean H<sub>2</sub>O<sub>2</sub> concentration in the expired breath condensate of COPD subjects was 10- times higher than that found in healthy controls (0.55 +/- 0.69 microM versus 0.05 +/- 0.07 microM, p 0.005). There were no significant differences between H<sub>2</sub>O<sub>2</sub> levels found in current smokers with COPD (0.44 +/- 0.56 microM) and COPD subjects who have never smoked (0.49 +/- 0.70 microM). No correlation was found between expired H<sub>2</sub>O<sub>2</sub> and daily cigarette consumption or cumulative

cigarette consumption in current smokers or exsmokers with COPD. These findings demonstrate that subjects with stable chronic obstructive pulmonary disease exhibit increased H<sub>2</sub>O<sub>2</sub> generation in the airways and that cigarette smoking does not increase H<sub>2</sub>O<sub>2</sub> production.

Reference Type: Journal Article

Record Number: 111

Author: Antczak, A.; Nowak, D.; Bialasiewicz, P.; Kasielski, M.

Year: 1999

Title: Hydrogen peroxide in expired air condensate correlates positively with early steps of peripheral neutrophil activation in asthmatic patients

Journal: Arch Immunol Ther Exp

Volume: 47

Issue: 2

Pages: 119-26

Label: 99218890

Keywords: Adult

Asthma/blood/\*immunology/\*metabolism

Breath Tests

Calcium/metabolism

Female

Human

Hydrogen Peroxide/analysis/\*metabolism

Male

Middle Age

N-Formylmethionine Leucyl-Phenylalanine/pharmacology

Neutrophil Activation/\*immunology

Neutrophils/drug effects/immunology

Pulmonary Alveoli/metabolism

Reactive Oxygen Species/metabolism

Abstract: We have found an increased H<sub>2</sub>O<sub>2</sub> level in expired air of asthmatic patients. Neutrophils from these subjects generated higher amounts of superoxide radicals after challenge with phorbol esters than those from healthy subjects which may result from an increased activity of NADPH-oxidase. The enhanced Ca<sup>2+</sup> mobilisation in neutrophils from asthmatics could be responsible for increased production and subsequent elevated H<sub>2</sub>O<sub>2</sub> concentration in expired breath condensate. In this study we wished to determine whether neutrophils of asthmatic patients have enhanced [Ca<sup>2+</sup>]<sub>i</sub> response after N-formyl-methionyl-leucyl-phenylalanine--fMLP challenge as compared with cells from healthy donors, and if so, does it correlate with H<sub>2</sub>O<sub>2</sub> levels in expired air. We examined 21 patients, 10 healthy individuals as a control group (mean age 34.3 +/- 5.5, 6 males and 4 females) and 11 asthmatic subjects (mean age 38.2 +/- 7.2, 7 males and 4 females). The rise of [Ca<sup>2+</sup>]<sub>i</sub> as an early event of neutrophil activation, was measured spectrofluorimetrically with Fura-2-AM. The mean H<sub>2</sub>O<sub>2</sub> level, measured spectrofluorimetrically in the expired breath of asthmatics, was 20-fold higher than that in healthy control (0.18 +/- 0.20 vs. 0.01 +/- 0.04 microM, p < 0.05). [Ca<sup>2+</sup>]<sub>i</sub> increase after challenge by fMLP (delta [Ca<sup>2+</sup>]<sub>i</sub>) was much higher in asthmatics than in control group (205.0 +/- 44 vs. 113.0 +/- 22 nM, p < 0.05, respectively). A strong correlation was observed between H<sub>2</sub>O<sub>2</sub> and delta [Ca<sup>2+</sup>]<sub>i</sub> and maximal velocity of increase in [Ca<sup>2+</sup>]<sub>i</sub> in asthmatics (r = 0.87, p < 0.01 and r = 0.64, p < 0.05). We conclude that elevated H<sub>2</sub>O<sub>2</sub> level in the expired breath condensate of asthmatics can be generated by activated neutrophils in the course of mucosal inflammation observed in bronchial asthma. Notes: Using Smart Source Parsing

Reference Type: Journal Article

Record Number: 106

Author: Heard, S. O.; Longtine, K.; Toth, I.; Puyana, J. C.; Potenza, B.; Smyrniotis, N.

Year: 1999

Title: The influence of liposome-encapsulated prostaglandin E1 on hydrogen peroxide concentrations in the exhaled breath of patients with the acute respiratory distress syndrome

Journal: Anesth Analg

Volume: 89

Issue: 2

Pages: 353-7.

Label: 99368620  
Keywords: Adult  
Alprostadil/\*administration & dosage  
\*Breath Tests  
Drug Carriers  
Female  
Human  
Hydrogen Peroxide/\*analysis  
Infusions, Intravenous  
Leukocyte Count  
Liposomes  
Male  
Middle Age  
Respiratory Distress Syndrome, Adult/blood/\*metabolism/therapy  
Support, Non-U.S. Gov't

Abstract: Hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) levels are increased in the exhaled breath of patients with the acute respiratory distress syndrome (ARDS). Because liposome-encapsulated prostaglandin E1 (PGE1) downregulates the CD11/CD18 receptor of the neutrophil, thereby limiting endothelial adhesion, the use of this drug should decrease the excretion of H<sub>2</sub>O<sub>2</sub> in the expiratory condensate of patients with ARDS. Patients > 11 yr of age with ARDS (diffuse, patchy infiltrates by chest radiograph; Pao<sub>2</sub>/fraction of inspired oxygen [P/F] ratio < or = 200 mm Hg; pulmonary capillary wedge pressure < or = 18 mm Hg; and the requirement for mechanical ventilation) were randomized to receive placebo (n = 14) or escalating doses (0.15-3.6 micrograms/kg) of liposomal PGE1 (n = 14) every 6 h for up to 7 days. Condensate was collected every morning from the expiratory tubing that was submerged in an ice saltwater bath (-5 degrees C). H<sub>2</sub>O<sub>2</sub> levels were measured by using a horseradish peroxidase assay. Other data collected included white blood cell count and P/F ratios. There was no significant difference in the concentration of H<sub>2</sub>O<sub>2</sub> in the expiratory condensate between the liposomal PGE1 group and the control group either before (0.99 +/- 0.52 vs 0.93 +/- 0.48 mumol/L) or during treatment (1.04 +/- 0.45 vs 0.76 +/- 0.25 mumol/L). Liposomal PGE1 treatment improved the P/F ratio and decreased the white blood cell count over time. Despite its ability to downregulate the CD11/CD18 neutrophil receptor, liposomal PGE1 did not reduce exhaled H<sub>2</sub>O<sub>2</sub> excretion. Implications: White blood cells (WBC) are thought to be part of the cause of the acute respiratory distress syndrome, a lung disease. WBC in the lung produce hydrogen peroxide, which is exhaled. Liposomal PGE1 inhibits WBC function but was found to have no effect in decreasing exhaled hydrogen peroxide in patients with the acute respiratory distress syndrome.

Reference Type: Journal Article  
Record Number: 94  
Author: Ho, L. P.; Faccenda, J.; Innes, J. A.; Greening, A. P.  
Year: 1999  
Title: Expired hydrogen peroxide in breath condensate of cystic fibrosis patients  
Journal: Eur Respir J  
Volume: 13  
Issue: 1  
Pages: 103-6.  
Label: 20294321  
Keywords: Adult  
Breath Tests  
Cystic Fibrosis/\*metabolism  
Female  
Human  
Hydrogen Peroxide/\*metabolism  
Male  
Support, Non-U.S. Gov't

Abstract: Stimulated inflammatory cells release large amounts of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>). Breath condensate H<sub>2</sub>O<sub>2</sub> has been shown to be elevated in stable asthmatic children, chronic obstructive pulmonary disease and intubated adult respiratory distress syndrome. In cystic fibrosis airways, where neutrophilic inflammation dominates, it is postulated that H<sub>2</sub>O<sub>2</sub> in breath condensate would be elevated and may be used as a marker of airways inflammation. Expired breath condensate was collected from 16 clinically stable cystic fibrosis (CF) patients (mean age 25.3 yrs, mean forced expiratory volume in one second (FEV<sub>1</sub>) 50.2%) and 14

normal subjects (mean age 29.9 yrs). Total plasma leukocyte, neutrophil, monocyte and eosinophil counts and lung function were also measured on the day of collection. A method of breath condensate collection excluding the confounding factors of nasal air and saliva contamination was validated and used and H<sub>2</sub>O<sub>2</sub> measured fluorometrically using an optimized assay. The median level of H<sub>2</sub>O<sub>2</sub> concentration in breath condensate of CF patients was lower than that in normal subjects (0.064 versus 0.089 microM), but this did not reach statistical significance (p = 0.20, Mann-Whitney rank sum test). Within the CF group, there was no correlation between H<sub>2</sub>O<sub>2</sub> concentration and lung function. Expired breath condensate H<sub>2</sub>O<sub>2</sub> is not elevated in patients with cystic fibrosis, and is thus not a suitable marker of airways inflammation in these patients. Possible explanations include physical barriers to its detection caused by viscous airways secretions, reaction with other reactive species or increased antioxidant activity caused by trapping of positively charged antioxidants in negatively charged airways secretions.

Reference Type: Journal Article

Record Number: 97

Author: Mumby, S.; Block, R.; Petros, A. J.; Gutteridge, J. M.

Year: 1999

Title: Hydrogen peroxide and catalase are inversely related in adult patients undergoing cardiopulmonary bypass: implications for antioxidant protection

Journal: Redox Rep

Volume: 4

Issue: 1-2

Pages: 49-52

Label: 20178654

Keywords: Adult

\*Cardiopulmonary Bypass

Catalase/\*metabolism

Glutathione/metabolism

Human

Hydrogen Peroxide/\*metabolism

Oxidative Stress

Support, Non-U.S. Gov't

Abstract: Adult patients undergoing cardiopulmonary bypass (CPB) surgery are subjected to increased oxidative stress and show a spectrum of lung injury. Increased levels of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) are often seen during episodes of oxidative stress, such as the use of high F<sub>i</sub>O<sub>2</sub>s, and this molecule plays a key role in the formation of highly damaging oxidants such as the hydroxyl radical. Oxidative damage to plasma proteins was assessed by measuring free thiol groups, and antioxidant protection against H<sub>2</sub>O<sub>2</sub> by measuring catalase activity. CPB patients (n = 39) receiving either 100% or 50% oxygen at the end of bypass were studied by measuring levels of H<sub>2</sub>O<sub>2</sub> in breath condensate and levels of catalase in their plasma, and comparing these to pre-bypass levels. Post-bypass, all CPB patients exhaled significantly lower levels of H<sub>2</sub>O<sub>2</sub> (P < 0.0001) at a time when they had significantly increased activity (0.809 +/- 0.11 versus 1.688 +/- 0.18 U/mg protein) of catalase in their plasma. There were no significant differences in these parameters between the 100% and 50% oxygen groups. At a time when oxidative stress is greatest, there appears to be a corresponding plasma increase in the antioxidant catalase. Whether this change is fortuitous or a response to oxidative stress is at present under consideration. Notes: Using Smart Source Parsing

Reference Type: Journal Article

Record Number: 105

Author: Nowak, D.; Kasielski, M.; Antczak, A.; Pietras, T.; Bialasiewicz, P.

Year: 1999

Title: Increased content of thiobarbituric acid-reactive substances and hydrogen peroxide in the expired breath condensate of patients with stable chronic obstructive pulmonary disease: no significant effect of cigarette smoking

Journal: Respir Med

Volume: 93

Issue: 6

Pages: 389-96.

Label: 99394086

Keywords: Antioxidants/\*adverse effects/metabolism

Biological Markers/analysis

Breath Tests

Female  
Forced Expiratory Volume  
Human  
Hydrogen Peroxide/\*metabolism  
Lung Diseases, Obstructive/etiology/\*metabolism  
Male  
Middle Age  
Smoking/adverse effects/\*metabolism  
Thiobarbituric Acid Reactive Substances/\*metabolism

Abstract: The imbalance between oxidants and antioxidants is known to play an important role in the pathogenesis of chronic obstructive pulmonary disease (COPD). Cigarette smoking is the most frequent factor responsible for development of COPD by leading to oxidant overload in the lower airways, due to presence of its own oxidants and to recruitment and activation of pulmonary phagocytes. We aimed to determine whether (1) patients with stable COPD have higher thiobarbituric acid-reactive substances (TBARs, an end-product of lipid peroxidation) and H<sub>2</sub>O<sub>2</sub> levels in expired breath condensate than healthy subjects who have never smoked; (2) COPD subjects who are current smokers exhale more TBARs and H<sub>2</sub>O<sub>2</sub> than COPD ex-smokers and those who have never smoked; and (3) concentration of TBARs correlates with H<sub>2</sub>O<sub>2</sub> levels in the breath condensate of COPD patients. The TBAR and H<sub>2</sub>O<sub>2</sub> content in expired breath condensate of 17 healthy nonsmoking subjects and 44 patients (11 current smokers, 20 ex-smokers and 13 who had never smoked) with stable COPD [forced expiratory volume in 1 s (FEV<sub>1</sub>) 63.3 +/- 16.3% and FEV<sub>1</sub> reversibility 5.2 +/- 4.3% predicted value] was measured spectrofluorimetrically by the thiobarbituric acid and homovanillic acid methods, respectively. The mean concentrations of TBARs and H<sub>2</sub>O<sub>2</sub> in the expired breath condensate of COPD subjects were 12 (0.48-0.86 microM vs. 0.04 +/- 0.14 microM; P < 0.05) and 10 times (0.48 +/- 0.67 microM vs. 0.05 +/- 0.07 microM; P < 0.005) higher than in healthy controls. Current smokers with COPD did not exhale more H<sub>2</sub>O<sub>2</sub> than COPD ex-smokers and those who had never smoked. TBARs levels shared only a tendency to be higher in the breath condensate of smoking COPD subjects than in that of ex-smokers (0.92 +/- 1.49 microM vs. 0.35 +/- 0.44 microM) and of COPD subjects who had never smoked (0.92 +/- 1.49 microM vs. 0.30 +/- 0.53 microM). No correlation was found between TBAR and H<sub>2</sub>O<sub>2</sub> levels in the whole COPD group. These variables did not correlate with cigarette smoking status and the time from smoking cessation. Subjects with stable COPD exhibit increased lipid peroxidation and H<sub>2</sub>O<sub>2</sub> generation in the airways. Current cigarette smoking does not distinguish COPD subjects with respect to TBARs and H<sub>2</sub>O<sub>2</sub> exhalation.

Reference Type: Journal Article

Record Number: 91

Author: Antczak, A.; Kurmanowska, Z.; Kasielski, M.; Nowak, D.

Year: 2000

Title: Inhaled glucocorticosteroids decrease hydrogen peroxide level in expired air condensate in asthmatic patients

Journal: Respir Med

Volume: 94

Issue: 5

Pages: 416-21.

Label: 20324554

Keywords: Administration, Inhalation

Adult

Asthma/\*drug therapy/physiopathology

Beclomethasone/\*administration & dosage

Double-Blind Method

Female

Forced Expiratory Volume/physiology

Glucocorticoids, Synthetic/\*administration & dosage

Human

Hydrogen Peroxide/\*analysis

Male

Abstract: H<sub>2</sub>O<sub>2</sub> is elevated in the exhaled air condensate in several inflammatory disorders of the lung, including bronchial asthma, and thus may reflect inflammatory processes in the airways. Exhaled H<sub>2</sub>O<sub>2</sub> may be used to guide the anti-inflammatory treatment of patients with asthma. Therefore in this study we analysed the effect of inhaled glucocorticosteroid beclomethasone for 4 weeks on H<sub>2</sub>O<sub>2</sub> level in the exhaled air condensate. Seventeen asthmatics and 10 healthy subjects were included to the study. Eleven patients were given inhaled beclomethasone and six were given placebo (3M Health Care). In all patients pulmonary function tests

were performed. H<sub>2</sub>O<sub>2</sub> in the expired air condensate was measured spectrofluorimetrically (homovanillic acid method). Inhaled beclomethasone significantly decreased H<sub>2</sub>O<sub>2</sub> in the expired air condensate in the active-treatment group, with a fall from baseline on day 1 which remained on day 43 (follow-up) ( $P < 0.05$ ). Exhaled H<sub>2</sub>O<sub>2</sub> in the active-treatment group was significantly lower than that in placebo group ( $P < 0.05$ ). A negative correlation between H<sub>2</sub>O<sub>2</sub> and forced expiratory volume in 1 sec (FEV<sub>1</sub>) on day 29 was observed. The decrease in exhaled H<sub>2</sub>O<sub>2</sub> in the active-treatment group was accompanied by an improvement in pulmonary function tests results. Inhaled glucocorticoids reduce the level of H<sub>2</sub>O<sub>2</sub> in the expired air condensate of asthmatic patients over a 4-week period and this may reflect their anti-inflammatory activity in lung diseases.

Reference Type: Journal Article

Record Number: 58

Author: De Benedetto, F.; Aceto, A.; Dragani, B.; Spacone, A.; Formisano, S.; Cocco, R.; Sanguinetti, C. M.

Year: 2000

Title: Validation of a new technique to assess exhaled hydrogen peroxide: results from normals and COPD patients

Journal: Monaldi Arch Chest Dis

Volume: 55

Issue: 3

Pages: 185-8.

Label: 20404463

Keywords: Adult

Aged

Aged, 80 and over

\*Breath Tests

Evaluation Studies

Female

Human

Hydrogen Peroxide/\*analysis

Lung Diseases, Obstructive/\*diagnosis/therapy

Male

Middle Age

Abstract: Chronic airways inflammation in chronic obstructive pulmonary disease (COPD) induces the activation of several cell types with delivery of proteases and reactive oxygen species (ROS). Assessing oxidant content in the exhaled air of COPD patients has proven useful in monitoring airway inflammation. The present study was designed to confirm the usefulness of exhaled hydrogen peroxide concentration determination in COPD patients using a new technique which allows longer storage of the expired air condensate before the H<sub>2</sub>O<sub>2</sub> assay. The technique was applied in 13 healthy nonsmoking subjects (six male, age range 22-40 yrs) and in seven patients (five male, age range 58-81 yrs) with mild or moderate COPD. Subjects breathed into a one-valve mouthpiece, and the exhaled air was directed into a vial kept at 0 degree C. After approximately 15 min of quiet breathing, 1 mL of expired air condensate was collected. An aliquot, 450 microL, of this sample was immediately added to an equal volume of a reaction mixture containing 2 mM 3,5,3',5'-tetramethylbenzidine and 40 microL of enzyme stock solution (0.5 mg.mL<sup>-1</sup>). After 15 min, 45 microL sulphuric acid was added (1 N final concentration), resulting in a reaction mixture pH of 1.0. After a further 10-min incubation, H<sub>2</sub>O<sub>2</sub> concentration determination was performed spectrophotometrically at 450 nm. This solution, as well as the H<sub>2</sub>O<sub>2</sub> assay, was stable for  $\geq 24$  h if the sample was kept in the dark and at 4 degrees C. There was high stability on repeated measures, with a coefficient of variation equal to zero. The mean  $\pm$  SD H<sub>2</sub>O<sub>2</sub> level in exhaled air from normal subjects was 0.12  $\pm$  0.09 microM, whereas it was significantly increased in COPD patients (0.50  $\pm$  0.11 microM;  $p = 0.0001$  compared to healthy subjects). In three healthy control subjects, a normal H<sub>2</sub>O<sub>2</sub> level in expired air increased to 0.70-0.80 microM during an acute upper respiratory tract infection. This new technique of hydrogen peroxide assay in expired air condensate greatly minimizes the inaccuracy deriving from the instability of hydrogen peroxide. The preliminary results obtained using this technique provide direct evidence for increased reactive oxygen species production in the airways of stable chronic obstructive pulmonary disease patients. However, the specificity of the procedure could be reduced by the interference of upper respiratory tract infections.

Reference Type: Journal Article

Record Number: 84

Author: Gibson, P. G.; Henry, R. L.; Thomas, P.

Year: 2000

Title: Noninvasive assessment of airway inflammation in children: induced sputum, exhaled nitric oxide, and breath condensate

Journal: Eur Respir J

Volume: 16  
Issue: 5  
Pages: 1008-15.  
Label: 21026461  
Keywords: \*Breath Tests  
Bronchitis/\*diagnosis  
Child, Preschool  
Human  
\*Nitric Oxide  
\*Respiration  
Sputum/\*cytology

Abstract: Noninvasive markers of airway inflammation are needed for use in research and clinical practice in childhood asthma. Induced sputum and exhaled nitric oxide are well established as direct markers of inflammation for use in asthma research. Sputum can be induced from children of >6 yrs using inhalation of hypertonic saline, and, if appropriate, can be combined with an assessment of airway responsiveness to hypertonic saline. The success rate of sputum induction in children is 68-100%. Most studies have processed sputum using the plug selection method, and show that the dominant cell in sputum from normal children is the macrophage, and that the upper normal limit for sputum eosinophils in children is 2.5%. The inflammatory response in childhood asthma is characterized by elevated numbers of sputum eosinophils, and eosinophil cationic protein concentration, as well as increased nitric oxide and hydrogen peroxide levels in exhaled breath. Sputum eosinophils correlate with objective markers of disease severity in steroid-naive children with asthma, and in severe asthma. Inflammatory marker levels are lower in children using glucocorticosteroids. Induced sputum and exhaled gases are important markers of inflammation in childhood asthma. The clinical utility of these markers warrants further study.

Reference Type: Journal Article

Record Number: 55

Author: Guatura, S. B.; Martinez, J. A.; Santos Bueno, P. C.; Santos, M. L.

Year: 2000

Title: Increased exhalation of hydrogen peroxide in healthy subjects following cigarette consumption

Journal: Sao Paulo Med J

Volume: 118

Issue: 4

Pages: 93-8.

Label: 20347629

Keywords: Adult

Breath Tests

Female

Forced Expiratory Volume

Human

Hydrogen Peroxide/analysis/\*metabolism

Lung Diseases, Obstructive/etiology

Male

Middle Age

Oxidants/analysis/\*metabolism

Oxidative Stress

Prospective Studies

Smoking/\*adverse effects

Spirometry

Abstract: CONTEXT: Increased hydrogen peroxide has been described in the expired breath condensate (H<sub>2</sub>O<sub>2</sub>-E) of several lung conditions, such as acute respiratory distress syndrome, chronic obstructive pulmonary disease and asthma. This technique has been advocated as being a simple method for documenting airway inflammation. OBJECTIVE: To evaluate H<sub>2</sub>O<sub>2</sub>-E in healthy cigarette smokers, and to determine the acute effects of the consumption of one cigarette on H<sub>2</sub>O<sub>2</sub>-E levels. TYPE OF STUDY: Prospective, controlled trial. SETTING: A pulmonary function laboratory in a University Hospital. PARTICIPANTS: Two groups of healthy volunteers: individuals who had never smoked (NS; n=10; 4 men; age = 30.6 +/- 6.2 years) and current cigarette smokers (S; n=12; 7 men; age = 38.7 +/- 9.8). None of the volunteers had respiratory symptoms and all showed normal spirometric tests. INTERVENTION: Expired air was collected from all volunteers through a face mask and a plastic collecting system leading into a

flask with dry ice and pure ethanol. Samples from the group S were collected twice, before and half an hour after the combustion of one cigarette. MAIN MEASUREMENTS: Expired hydrogen peroxide using the Gallati and Pracht method. RESULTS: The S and NS groups showed comparable levels of H<sub>2</sub>O<sub>2</sub>-E at basal conditions [NS = 0.74 microM (DP 0.24) vs. S = 0.75 microM (DP 0.31)]. The smokers showed a significant increase in H<sub>2</sub>O<sub>2</sub>-E levels half an hour after the consumption of only one cigarette [0.75 microM (DP 0.31) vs. 0.95 microM (DP 0.22)]. CONCLUSION: The present results are consistent with the concept that smokers increase oxidative stress with elevated production of reactive oxygen species, contributing to the development of smoking-related disorders. URL: [http://www.scielo.br/scielo.php?script=sci\\_arttext&pid=S1516-31802000000400004&lng=en&nrm=iso](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1516-31802000000400004&lng=en&nrm=iso)

Reference Type: Journal Article

Record Number: 88

Author: Jobsis, Q.; Raatgeep, H. C.; Schellekens, S. L.; Kroesbergen, A.; Hop, W. C.; de Jongste, J. C.

Year: 2000

Title: Hydrogen peroxide and nitric oxide in exhaled air of children with cystic fibrosis during antibiotic treatment

Journal: Eur Respir J

Volume: 16

Issue: 1

Pages: 95-100.

Label: 20386212

Keywords: Acute Disease

Antibiotics/\*therapeutic use

\*Breath Tests

Child

Cystic Fibrosis/complications/metabolism/\*pathology

Female

Forced Expiratory Volume

Human

Hydrogen Peroxide/\*analysis

Male

Nitric Oxide/\*analysis

Respiratory Tract Infections/complications/drug therapy

Support, Non-U.S. Gov't

Abstract: Cystic fibrosis (CF) patients characteristically have severe chronic airway inflammation associated with bacterial infection. A noninvasive marker of airway inflammation could be a useful guide to treatment of CF lung disease. The aim of this study was to assess whether measurement of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) and nitric oxide (NO) in exhaled air can serve to monitor the effect of treatment with antibiotics in CF-children with acute infective pulmonary exacerbations. Sixteen CF-patients (mean age 12.3 yrs) with exacerbation of their lung infection were treated with intravenous antibiotics in an uncontrolled study. During treatment, H<sub>2</sub>O<sub>2</sub> in exhaled air condensate was measured twice a week. In addition, serial NO measurements were performed in nine patients. During antibiotic treatment the median H<sub>2</sub>O<sub>2</sub> concentration in exhaled air condensate decreased significantly from 0.28 microM (range 0.07-1.20 microM) to 0.16 microM (range 0.05-0.24 microM, p=0.002) and the mean forced expiratory volume in one second significantly increased from 55% predicted to 75% pred (p=0.001). In individual subjects, changes of H<sub>2</sub>O<sub>2</sub> and FEV<sub>1</sub> between pairs of serial measurements correlated weakly (p=0.08). Data on exhaled NO were inconclusive; exhaled NO did not change systematically during treatment. It is concluded that cystic fibrosis patients with an acute pulmonary exacerbation have abnormally high concentrations of hydrogen peroxide, but not of nitric oxide, in exhaled air, which decrease during intravenous antibiotic treatment. Further controlled studies should establish if exhaled hydrogen peroxide, may serve as a noninvasive parameter of airway inflammation to guide antibiotic treatment in cystic fibrosis lung disease.

Reference Type: Journal Article

Record Number: 96

Author: Lases, E. C.; Durkens, V. A.; Gerritsen, W. B.; Haas, F. J.

Year: 2000

Title: Oxidative stress after lung resection therapy: A pilot study

Journal: Chest

Volume: 117

Issue: 4

Pages: 999-1003.

Label: 20231583  
Keywords: Aged  
Biological Markers  
Breath Tests  
Chromatography, High Pressure Liquid  
Comparative Study  
Female  
Human  
Hydrogen Peroxide/\*metabolism  
Lung Neoplasms/\*metabolism/surgery  
Male  
Malondialdehyde/\*urine  
Middle Age  
\*Oxidative Stress  
Pilot Projects  
Pneumonectomy/\*adverse effects  
Prognosis  
Prospective Studies  
Pulmonary Edema/\*metabolism/surgery  
Spectrophotometry

Abstract: STUDY OBJECTIVES: To investigate whether oxidative stress occurs following lobectomy and pneumonectomy and to evaluate whether markers of oxidative stress might be of value in the assessment of the diagnosis, course, and prognosis of postoperative complications. DESIGN: A prospective study. SETTING: A specialized thoracic surgical unit in a large referral hospital. PATIENTS: Twenty-eight patients with lung carcinoma undergoing thoracotomy. MEASUREMENTS: Exhaled H<sub>2</sub>O<sub>2</sub> concentrations in breath condensate were measured by spectrophotometry, while malondialdehyde (MDA) levels in urine samples collected every 24 h were measured by reversed-phase, ion-pair high-performance liquid chromatography using ultraviolet detection. RESULTS: Our results show increased H<sub>2</sub>O<sub>2</sub> and MDA levels in lobectomy patients compared with pneumonectomy patients. A strong correlation was found between the levels of H<sub>2</sub>O<sub>2</sub> and MDA. CONCLUSION: The present data support the hypothesis that oxidative stress may occur following pulmonary resection.

Reference Type: Journal Article  
Record Number: 63  
Author: Schleiss, M. B.; Holz, O.; Behnke, M.; Richter, K.; Magnussen, H.; Jorres, R. A.  
Year: 2000  
Title: The concentration of hydrogen peroxide in exhaled air depends on expiratory flow rate  
Journal: Eur Respir J  
Volume: 16  
Issue: 6  
Pages: 1115-8.  
Label: 21187463  
Keywords: Adult  
\*Breath Tests  
Female  
Forced Expiratory Flow Rates/\*physiology  
Forced Expiratory Volume/physiology  
Human  
Hydrogen Peroxide/\*analysis  
Lung Diseases, Obstructive/diagnosis/physiopathology  
Male  
Pulmonary Ventilation/physiology  
Reference Values  
Support, Non-U.S. Gov't

Abstract: Hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) is known to be detectable in exhaled air. The present study aimed to determine whether the concentration of exhaled H<sub>2</sub>O<sub>2</sub> depends on expiratory flow rate in order to make inferences on the site of its production within the lung. Breath condensate was collected in cooled Teflon tubes, at three different expiratory flow rates, in 15 healthy or mild

asthmatic subjects. Tests were repeated 2-5 times to assess reproducibility. Mean $\pm$ SEM concentrations of H<sub>2</sub>O<sub>2</sub> at flow rates of 140, 69 and 48 mL.s(-1) were 0.12 $\pm$ 0.02, 0.19 $\pm$ 0.02 and 0.32 $\pm$ 0.03 microM, respectively. These values differed significantly from each other (p<0.001). For comparison, average coefficients of variability within repeated measurements at each of the three flow rates were 68, 62 and 82%, respectively. These data demonstrate that the concentration of exhaled hydrogen peroxide depends on expiratory flow rate. Since flow dependence is an indicator of production within the airways, this result suggests that, to a large extent, the exhaled hydrogen peroxide originates within the airways. However, even under strictly controlled conditions, a high degree of variability persists, which may limit the usefulness of exhaled hydrogen peroxide as a marker of airway inflammation.

Reference Type: Journal Article

Record Number: 217

Author: Antczak, A.; Gorski, P.

Year: 2001

Title: Endogenous Airway Acidification And Oxidant Overload In Infectious Exacerbation of COPD.

Journal: Am J Respir Crit Care Med

Volume: 163

Issue: 5

Pages: 725A

Abstract: Oxidant/antioxidant imbalance plays a pivotal role in chronic obstructive pulmonary disease (COPD). In this study we hypothesised that levels of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) and pH of exhaled air condensate are impaired in infectious exacerbation of COPD and that they normalise during therapy. We measured H<sub>2</sub>O<sub>2</sub> (spectrofluorimetrically - homovanillic acid method) and pH (Corning pH microelectrode, Corning, N.Y., USA) in exhaled air condensate in 10 COPD patients with infectious exacerbation (mean age 62 $\pm$ 10 yr., 7 male) on 1st, 3rd, and 6th days of antibiotic treatment (cephalosporins or macrolides). There was a significant fall in H<sub>2</sub>O<sub>2</sub> concentration on 3rd and 6th day of therapy compared to baseline (0.54 $\pm$ 0.1 and 0.36 $\pm$ 0.1 vs. 0.81 $\pm$ 0.14 mM, p<0.001, p<0.001, respectively). This was accompanied by 1 log order lower air condensate pH on 1st day compared to that on the 6th (6.25 $\pm$ 0.46 vs. 7.46 $\pm$ 0.1, p<0.001, respectively) with lowered pH on day 3 (6.75 $\pm$ 0.40, p<0.01). No correlation between H<sub>2</sub>O<sub>2</sub> and pH of the exhaled air condensate was observed. We conclude that an oxidant overload in the airways can be observed in exacerbation of COPD and that this normalises during antibiotic treatment. We speculate that endogenous airway acidification may have a pathophysiological role in COPD.

[\*\*] Thematic Poster Session (Abstract Page: 725) Session: 8:15 am-4:45 pm, OXIDANTS/ANTIOXIDANTS

Reference Type: Journal Article

Record Number: 66

Author: Emelyanov, A.; Fedoseev, G.; Abulimity, A.; Rudinski, K.; Fedoulov, A.; Karabanov, A.; Barnes, P. J.

Year: 2001

Title: Elevated concentrations of exhaled hydrogen peroxide in asthmatic patients

Journal: Chest

Volume: 120

Issue: 4

Pages: 1136-9.

Label: 21475390

Abstract: BACKGROUND: Airway inflammation is important in the development and progression of asthma. Activation of inflammatory cells induces a respiratory burst resulting in the production of reactive oxygen species, such as H<sub>2</sub>O<sub>2</sub>. The aim of this study was to measure the concentration of H<sub>2</sub>O<sub>2</sub> in exhaled breath condensate and its correlation with airway obstruction, airway hyperresponsiveness, and concentration of eosinophil cationic protein (ECP) in serum in 70 steroid-naive, atopic patients with unstable asthma (20 men; age range, 18 to 62 years) and 17 normal subjects (7 men; age range, 19 to 34 years). METHODS: Exhaled H<sub>2</sub>O<sub>2</sub> was measured using a colorimetric assay, and the concentration of ECP in serum was measured using radioimmunoassay. Airway hyperresponsiveness was expressed as the provocative concentration of inhaled histamine causing a 20% fall in FEV<sub>1</sub> (PC<sub>20</sub>). RESULTS: In patients with asthma, the mean H<sub>2</sub>O<sub>2</sub> concentration was significantly elevated compared to values in normal subjects: 0.127  $\pm$  0.083 mol/L vs 0.024  $\pm$  0.016 mol/L (p < 0.001). There was a significant correlation among H<sub>2</sub>O<sub>2</sub> concentration, FEV<sub>1</sub>, PC<sub>20</sub>, and ECP in serum. CONCLUSION: We conclude that exhaled H<sub>2</sub>O<sub>2</sub> is significantly elevated in asthmatic patients. This is correlated with disease severity and indirect markers of airway inflammation. Measurement of exhaled H<sub>2</sub>O<sub>2</sub> may be useful to assess airway inflammation and oxidative stress in asthmatic patients.

Reference Type: Journal Article

Record Number: 67

Author: Ferreira, I. M.; Hazari, M. S.; Gutierrez, C.; Zamel, N.; Chapman, K. R.

Year: 2001

Title: Exhaled nitric oxide and hydrogen peroxide in patients with chronic obstructive pulmonary disease. Effects of inhaled beclomethasone

Journal: Am J Respir Crit Care Med

Volume: 164

Issue: 6

Pages: 1012-5.

Label: 21471714

Abstract: There is controversy about the role of inhaled corticosteroids in chronic obstructive pulmonary disease (COPD). Although they appear to have little impact on airways obstruction or its progression, their use may reduce the frequency and/or severity of exacerbations in a subset of patients. We undertook the following study to determine the impact of inhaled corticosteroid on two noninvasive markers of airways inflammation. We assigned 20 stable nonsmoking patients with COPD in random, double-blind crossover fashion to two 2-wk treatment periods with inhaled beclomethasone 500 µg twice daily or matching placebo, followed by a 2-wk washout period. We measured exhaled nitric oxide (ENO), breath condensate H<sub>2</sub>O<sub>2</sub>, and flow volume spirometry at weekly intervals. Median baseline ENO was 26.2 (19.3 to 54.8) ppb and fell significantly following 1 and 2 wk of beclomethasone (-10.6 ppb, *p* = 0.002, and -6.3 ppb, *p* = 0.013, respectively) but was unchanged by placebo inhalation. Breath condensate H<sub>2</sub>O<sub>2</sub> levels did not change significantly with inhaled beclomethasone or placebo. Although there were no significant changes in FEV<sub>1</sub> with BDP therapy, there was a moderate inverse correlation between changes in ENO and changes in FEV<sub>1</sub> (*r* -0.50). We conclude that inhaled beclomethasone reduces ENO levels in stable nonsmoking patients with COPD, a finding compatible with an antiinflammatory mechanism of action.

Reference Type: Journal Article

Record Number: 70

Author: Ganas, K.; Loukides, S.; Papatheodorou, G.; Panagou, P.; Kalogeropoulos, N.

Year: 2001

Title: Total nitrite/nitrate in expired breath condensate of patients with asthma

Journal: Respir Med

Volume: 95

Issue: 8

Pages: 649-54.

Label: 21421794

Keywords: Adrenergic beta-Antagonists/therapeutic use

Adult

Asthma/drug therapy/\*metabolism

Biological Markers/analysis

Breath Tests

Case-Control Studies

Glucocorticoids, Topical/therapeutic use

Human

Hydrogen Peroxide/analysis

Nitrates/\*analysis

Nitrites/\*analysis

Oxidative Stress

Smoking

Abstract: Production of nitric oxide (NO) is generally increased during inflammatory diseases including asthma. The eventual fate of NO is oxidation to nitrite (NO<sub>2</sub>) and nitrate (NO<sub>3</sub>), both of which are end-products of NO metabolism. Hydrogen Peroxide (H<sub>2</sub>O<sub>2</sub>) is increased in Exhaled Breath Condensate of asthmatic subjects and may be used as a non-invasive marker of oxidative stress. NO has in some cases been shown to attenuate oxidant-induced lung injury. Total NO<sub>2</sub>/NO<sub>3</sub> concentration and H<sub>2</sub>O<sub>2</sub> levels were measured in expired breath condensate in 50 clinically stable asthmatics [all males, all atopics, mean age 22 (3) SD yrs, forced expiratory volume in 1 sec (FEV<sub>1</sub>) 91 (10)% predicted, PD<sub>20</sub> to histamine 0.262 (0.16) mg 20 on inhaled steroids, 20 smokers, all steroid-naïve] and in 10 normal, non-atopic subjects [all males, age 23 (4) yrs, FEV<sub>1</sub> 101 (14)% predicted, PD<sub>20</sub> to histamine 1.3 (0.55) mg]. NO<sub>2</sub>/NO<sub>3</sub> levels were significantly higher in patients with asthma than in normal subjects (1.08, 95% CI 0.86-1.3 µM vs. 0.6; 95% CI 0.46-0.8, *P* < 0.001). Patients who were on inhaled steroids had significantly lower values compared to steroid-naïve (0.71, 95% CI 0.55-0.87 µM vs. 1.33, 95% CI 1-1.65 µM, *P* < 0.001). Similar results were observed between smokers

and non-smokers (1.11, 95% CI 0.74-1.47 microM vs. 1.77, 95% CI 1.1-2.4 microM,  $P < 0.0001$ ). There was a significant positive correlation between NO<sub>2</sub>/NO<sub>3</sub> levels and H<sub>2</sub>O<sub>2</sub> concentration in expired breath condensate ( $r = 0.48$ ,  $P < 0.0001$ ). No correlation was observed between NO<sub>2</sub>/NO<sub>3</sub> levels, airway obstruction and bronchial hyper-reactivity as assessed by PD20 to histamine. Total NO<sub>2</sub>/NO<sub>3</sub> levels in expired breath condensate are raised in patients with stable asthma and are significantly related to oxidative stress as assessed by H<sub>2</sub>O<sub>2</sub> concentration. Measurement of expired breath NO<sub>2</sub>/NO<sub>3</sub> and H<sub>2</sub>O<sub>2</sub> levels may be clinically useful in the management of oxidation and inflammation mediated lung injury.

Reference Type: Journal Article

Record Number: 71

Author: Horvath, I.; MacNee, W.; Kelly, F. J.; Dekhuijzen, P. N.; Phillips, M.; Doring, G.; Choi, A. M.; Yamaya, M.; Bach, F. H.; Willis, D.; Donnelly, L. E.; Chung, K. F.; Barnes, P. J.

Year: 2001

Title: "Haemoxygenase-1 induction and exhaled markers of oxidative stress in lung diseases", summary of the ERS Research Seminar in Budapest, Hungary, September, 1999

Journal: Eur Respir J

Volume: 18

Issue: 2

Pages: 420-30.

Label: 21419983

Abstract: In recent years, there has been increasing interest in noninvasive monitoring of airway inflammation and oxidative stress. Several volatile and nonvolatile substances can be measured in exhaled breath and have been suggested as potential biomarkers of these events. Exhaled gases, including carbon monoxide (CO), alkanes (ethane, pentane), and substances measured in breath condensate, such as hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) and isoprostanes were all suggested as potential markers of oxidative stress in the lung. A European Respiratory Society (ERS) International Research Seminar entitled "Haemoxygenase-1 induction and exhaled markers of oxidative stress in lung diseases" was organized by the Airway Regulation and Provocation Group of the Clinical Allergy and Immunology Assembly in Budapest, Hungary in September, 1999 to integrate the latest knowledge on these issues and accelerate further improvement in this area. During this 2-day event several issues were raised about: the use and standardization of measurements in exhaled breath; problems of measuring expired H<sub>2</sub>O<sub>2</sub> and other mediators in breath condensate; role and regulation of haemoxygenase (HO)-1 in the lung; and conditions and factors influencing exhaled CO. This report is a summary of the main presentations at the seminar, together with the current areas of research in this rapidly expanding field.

Reference Type: Journal Article

Record Number: 193

Author: Jobsis, R. Q.; Schellekens, S. L.; Fakkkel-Kroesbergen, A.; Raatgeep, R. H.; de Jongste, J. C.

Year: 2001

Title: Hydrogen peroxide in breath condensate during a common cold

Journal: Mediators Inflamm

Volume: 10

Issue: 6

Pages: 351-4.

Accession Number: 11817678

Abstract: BACKGROUND: Hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) in exhaled air condensate is elevated in inflammatory disorders of the lower respiratory tract. It is unknown whether viral colds contribute to exhaled H<sub>2</sub>O<sub>2</sub>. AIM: To assess exhaled H<sub>2</sub>O<sub>2</sub> during and after a common cold. METHODS: We examined H<sub>2</sub>O<sub>2</sub> in the breath condensate of 20 normal subjects with acute symptoms of a common cold and after recovery 2 weeks later and, similarly, in 10 subjects without infection. H<sub>2</sub>O<sub>2</sub> was measured with a fluorimetric assay. RESULTS: At the time of infection exhaled H<sub>2</sub>O<sub>2</sub> (median, ranges) was 0.20 microM (0.03-1.2 microM), and this decreased to 0.09 microM ( $< 0.01$ -0.40 microM) after recovery ( $p = 0.006$ ). There was no significant difference in lung function (forced vital capacity and forced expiratory volume in 1 sec) during and after colds. In the controls, exhaled H<sub>2</sub>O<sub>2</sub> did not change over a 2-week period. CONCLUSIONS: H<sub>2</sub>O<sub>2</sub> in exhaled air condensate is elevated during a common cold, and returns to normal within 2 weeks of recovery in healthy subjects. Hence, symptomatic upper respiratory tract infection may act as a confounder in studies of H<sub>2</sub>O<sub>2</sub> as a marker of chronic lower airway inflammation. URL: <http://www.ncbi.nlm.nih.gov/htbin-post/Entrez/query?db=m&form=6&dopt=r&uid=11817678> Author Address: Department of Paediatrics, Division of Paediatric Respiratory Medicine, Erasmus University Medical Center/Sophia Children's Hospital, Rotterdam, The Netherlands.

Reference Type: Journal Article

Record Number: 76

Author: Kasielski, M.; Nowak, D.

Year: 2001

Title: Long-term administration of N-acetylcysteine decreases hydrogen peroxide exhalation in subjects with chronic obstructive pulmonary disease

Journal: Respir Med

Volume: 95

Issue: 6

Pages: 448-56.

Label: 21314332

Keywords: Acetylcysteine/\*therapeutic use

Adult

Aged

Analysis of Variance

Breath Tests

Double-Blind Method

Female

Free Radical Scavengers/\*therapeutic use

Human

Hydrogen Peroxide/\*metabolism

Lipid Peroxidation/drug effects

Lung Diseases, Obstructive/\*drug therapy/metabolism

Male

Middle Age

Spectrometry, Fluorescence

Statistics, Nonparametric

Support, Non-U.S. Gov't

Thiobarbituric Acid Reactive Substances/analysis

Treatment Outcome

**Abstract:** Patients with chronic obstructive pulmonary disease (COPD) exhale more hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) and lipid peroxidation products than healthy subjects. This may reflect oxidative stress in the airways that plays important role in the development and progression of COPD. N-acetylcysteine (NAC), a mucolytic drug, possesses antioxidant properties as it is a precursor of reduced glutathione that together with glutathione peroxidase may decompose H<sub>2</sub>O<sub>2</sub> and lipid peroxides. We aimed to determine the effect of NAC, 600 mg effervescent tablets (Fluimucil), once a day for 12 months, and placebo on the concentration of H<sub>2</sub>O<sub>2</sub> and thiobarbituric acid reactive substances (TBARs) in expired breath condensate and serum levels of two lipid peroxidation products (TBARs, lipid peroxides) in patients with COPD. The study was performed as a double-blind, double-dummy comparison between active drug and placebo in two parallel groups. Forty-four outpatients with stable COPD (22 in the NAC group and 22 in the placebo group) completed the study. Specimens of expired breath condensate and serum were collected at the randomization visit and then every 3 months over 1 year. The concentration of TBARs and H<sub>2</sub>O<sub>2</sub> in expired breath condensate was measured spectrofluorimetrically by the thiobarbituric acid and homovanillic acid methods, respectively. Serum levels of lipid peroxides were determined spectrophotometrically after extraction with butanol and pyridine. Initially, H<sub>2</sub>O<sub>2</sub> exhalation did not differ between the placebo and NAC groups up to 6 months of treatment. After this the significant differences were observed. After 9 and 12 months of treatment NAC group exhaled 2.3-fold (0.17±0.33 microM vs. 0.41±0.26 microM, P<0.04) [median 0.01 microM, quartile range (qr)=0.22 vs. median 0.15 microM, qr =0.43] and 2.6-fold (0.15±0.23 microM vs. 0.40±0.25 microM, P<0.05) median = 0.00 microM, qr = 0.23 vs. median = 0.36 microM, qr = 0.51] less H<sub>2</sub>O<sub>2</sub> than placebo receivers, respectively. No significant effect of NAC administration on TBARs exhalation and serum levels of TBARs and lipid peroxides were noted over the whole treatment period. Also no significant associations between exhaled H<sub>2</sub>O<sub>2</sub> and concentrations of lipid peroxidation products were noted in both treatment groups at any time-point. These results indicate that long-term oral administration of NAC attenuates H<sub>2</sub>O<sub>2</sub> formation in the airways of COPD subjects and prove anti-oxidant action of drug. However, further studies are necessary to estimate the clinical significance of this finding.

Reference Type: Journal Article

Record Number: 184

Author: Loukides, S.; Papatheodorou, G.; Ganas, K.; Kostikas, K.; Psathakis, K.; Panagou, P.

Year: 2001

Title: Endogenous airway acidification in expired breath condensate of patients with inflammatory airway diseases

Journal: Am J Respir Crit Care Med

Volume: 163

Issue: 5

Pages: A723

Abstract: Endogenous Airway Acidification In Expired Breath Condensate Of Patients With Inflammatory Airway Diseases, Athens, Greece. Tuesday, May 22, 2001, 8:15 AM, Area J (Hall D, Lower Level), Moscone Center Endogenous airway acidification as assessed by pH in expired breath condensate is implicated in asthma pathophysiology (Hunt et al AJRCCM 2000). Aim of our study was to evaluate pH in expired breath condensate in inflammatory airway diseases and to find out whether its levels might contribute to oxidative stress as assessed by hydrogen peroxide and 8-isoprostane, to nitric oxide metabolism as assessed by total nitrate/nitrite and finally to inflammatory process as assessed by differential cell counts in induced sputum. 20 patients with bronchial asthma (10 with severe disease FEV1  $60 \pm 10$  %pred), 10 with bronchiectasis, 10 with COPD, and 10 normal subjects were studied. Our results showed that both COPD and bronchiectasis patients had significantly lower values compared to asthmatics and normal subjects ( $7.16 \pm 0.17$ SD,  $7.12 \pm 0.1$ ,  $7.41 \pm 0.26$ ,  $7.58 \pm 0.1$ ,  $p < 0.0001$ ). Further analysis showed that severe asthmatics had significantly lower values compared to mild ( $7.55 \pm 0.18$  vs  $7.26 \pm 0.26$ ,  $p = 0.0003$ ). We additionally showed that the above values of pH were related to sputum neutrophilia and consequently to oxidative stress. However in patients with severe asthma there was a significant correlation between pH and total nitrate/nitrite. We conclude that airway acidification in inflammatory airway diseases is related to sputum neutrophilia and therefore to oxidative stress and might reflect the inflammatory process in diseases, which are neutrophil dependent.

[\*\*] Thematic Poster Session (Abstract Page: 723) Session: 8:15 am-4:45 pm, OXIDANTS/ANTIOXIDANTS

Reference Type: Journal Article

Record Number: 83

Author: Nowak, D.; Kalucka, S.; Bialasiewicz, P.; Krol, M.

Year: 2001

Title: Exhalation of H<sub>2</sub>O<sub>2</sub> and thiobarbituric acid reactive substances (TBARs) by healthy subjects

Journal: Free Radic Biol Med

Volume: 30

Issue: 2

Pages: 178-86.

Label: 21100476

Keywords: Adult

Age Factors

Albuterol/administration & dosage/pharmacology

Body Mass Index

Bronchodilator Agents/pharmacology

Circadian Rhythm/drug effects

Exercise/physiology

Female

Human

Hydrogen Peroxide/\*metabolism

Ipratropium/administration & dosage/pharmacology

Male

Pulmonary Ventilation/drug effects

Regression Analysis

\*Respiration/drug effects

Sex Factors

Smoking/adverse effects

Spirometry

Thiobarbituric Acid Reactive Substances/\*metabolism

Abstract: Enhanced exhalation of H<sub>2</sub>O<sub>2</sub> and TBARs have been reported in various inflammatory lung diseases. This may reflect activated phagocytes influx and free radical generation in the airways. However, to apply these compounds as markers of oxidative stress it is necessary to understand factors influencing their exhalation in healthy subjects. We investigated the concentration of H<sub>2</sub>O<sub>2</sub> and TBARs in expired breath condensate (EBC) of 58 healthy volunteers. EBC was collected seven times every 4 h during 24 h and three times every 7 d during 2 consecutive weeks. The H<sub>2</sub>O<sub>2</sub> exhalation revealed diurnal variation with two-peak values

0.45 +/- 0.29 microM and 0.43 +/- 0.22 microM at 12:00 and 24:00 h. The lowest concentrations, 0.26 +/- 0.13 microM and 0.25 +/- 0.26 microM, were found at 20:00 and 8:00 h. Cigarette smokers exhaled about 2.4 times more H<sub>2</sub>O<sub>2</sub> than never smoked subjects. Moreover, in contrast to nonsmokers, cigarette smokers' H<sub>2</sub>O<sub>2</sub> exhalation was stable over 2 week observation. The mean H<sub>2</sub>O<sub>2</sub> concentration estimated over the whole 2 week period was higher in subjects above 40 years regardless of smoking habit, and it positively correlated with age in never smoked subjects (p <.004). Smoking of one cigarette caused 1.8-fold rise in H<sub>2</sub>O<sub>2</sub> exhalation (p <.01). The baseline H<sub>2</sub>O<sub>2</sub> levels correlated with cumulative cigarette consumption (p <.05) and MEF 25% of predicted (p <.05). Neither moderate exercise nor one puff of salbutamol nor ipratropium influenced significantly the concentration of H<sub>2</sub>O<sub>2</sub> and TBARs in EBC. Only 4 of 120 EBC specimens from never smoked subjects revealed detectable levels of TBARs. Cigarette smokers exhaled more TBARs (p <.05) than never smoked volunteers. Our results indicate that healthy never smoked subjects exhale H<sub>2</sub>O<sub>2</sub> with diurnal variation and significant changes over 2 week observation. Cigarette smoking enhanced H<sub>2</sub>O<sub>2</sub> generation in the airways. These results could be useful for planning studies with exhaled H<sub>2</sub>O<sub>2</sub> as a marker of airway inflammation. Occasional detection of TBARs in EBC of never smoked persons may be a result of sufficient antioxidant activity in the airways that protects tissues from peroxidative damage.

Reference Type: Journal Article

Record Number: 72

Author: Zappacosta, B.; Persichilli, S.; Mormile, F.; Minucci, A.; Russo, A.; Giardina, B.; De Sole, P.

Year: 2001

Title: A fast chemiluminescent method for H<sub>2</sub>O<sub>2</sub> measurement in exhaled breath condensate

Journal: Clin Chim Acta

Volume: 310

Issue: 2

Pages: 187-91.

Label: 21389208

Keywords: Adult

\*Chemiluminescence

Human

Hydrogen Peroxide/\*analysis

Middle Age

Pulmonary Alveoli/metabolism

Reference Values

\*Respiration

Sensitivity and Specificity

Smoking/metabolism

Abstract: BACKGROUND: Breath condensate can give useful information on volatile compounds produced at alveolar level.

Actual concentration of H<sub>2</sub>O<sub>2</sub> in breath condensate is dependent on its production at alveolar level and on the efficacy of the detoxifying systems, catalase, glutathione peroxidase, etc. METHODS: In the present paper, a simple chemiluminescent method for the determination of the H<sub>2</sub>O<sub>2</sub> collected in exhaled breath is shown and data of both smokers and nonsmokers volunteers are presented. RESULTS: The chemiluminescent response is linear up to 100 micromol/l H<sub>2</sub>O<sub>2</sub>. The analytical sensitivity is about 0.01 micromol/l. Most of the nonsmokers have a H<sub>2</sub>O<sub>2</sub> content lower than 0.05 micromol/l, while smokers have a content ranging from 0.1 to 0.6 micromol/l.

Reference Type: Journal Article

Record Number: 257

Author: Antczak, A.; Gorski, P.

Year: 2002

Title: Markers of pulmonary diseases in Exhaled Breath Condensate

Journal: Int J Occup Med Environ Health

Volume: 15

Issue: 4

Pages: 317-23

Accession Number: 12608619

Keywords: Adult

Biological Markers/\*analysis

\*Breath Tests

Child  
Human  
Lung Diseases/\*diagnosis  
Oxidative Stress  
Poland

Abstract: Exhaled Breath Condensate has been more and more extensively used as a novel and non-invasive method to study airway inflammation. It is simple to perform, very well tolerated by patients and no adverse events have been reported so far. Serial measurements can be made with no harmful effects on patients, which is of extreme value in occupational medicine. Exhaled breath condensate has been obtained from both adult and children patients suffering from various pulmonary diseases such as asthma, cystic fibrosis, chronic obstructive pulmonary disease, and interstitial lung diseases. Several markers and mediators are detectable in breath condensate: hydrogen peroxide, thiobarbituric acid-reactive substances, isoprostanes, prostaglandins and leukotrienes. Nitric oxide-related markers have also been studied in the condensate. There is increasing body of evidence that changes in condensate markers reflect local abnormalities of airway lining fluid.

Notes: 1232-1087

Journal Article

Review

Review, Tutorial

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=12608619](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12608619)

Author Address: Department of Pneumology and Allergology, Medical University, Lodz, Poland.

Reference Type: Journal Article

Record Number: 244

Author: Kharitonov, S. A.; Barnes, P. J.

Year: 2002

Title: Biomarkers of some pulmonary diseases in exhaled breath

Journal: Biomarkers

Volume: 7

Issue: 1

Pages: 1-32

Date: Jan-Feb

Accession Number: 12101782

Keywords: Ammonia/analysis

Asthma/diagnosis

Biological Markers

Breath Tests/\*methods

Carbon Monoxide/analysis

Cystic Fibrosis/diagnosis

Human

Hydrogen Peroxide/analysis

Lipid Peroxidation

Lung Diseases/\*diagnosis

Nitric Oxide/analysis

Pulmonary Disease, Chronic Obstructive/diagnosis

Abstract: Analysis of various biomarkers in exhaled breath allows completely non-invasive monitoring of inflammation and oxidative stress in the respiratory tract in inflammatory lung diseases, including asthma, chronic obstructive pulmonary disease (COPD), cystic fibrosis (CF), bronchiectasis and interstitial lung diseases. The technique is simple to perform, may be repeated frequently, and can be applied to children, including neonates, and patients with severe disease in whom more invasive procedures are not possible. Several volatile chemicals can be measured in the breath (nitric oxide, carbon monoxide, ammonia), and many non-volatile molecules (mediators, oxidation and nitration products, proteins) may be measured in Exhaled Breath Condensate. Exhaled breath analysis may be used to quantify inflammation and oxidative stress in the respiratory tract, in differential diagnosis of airway disease and in the monitoring of therapy. Most progress has been made with exhaled nitric oxide (NO), which is increased in atopic asthma, is correlated with other inflammatory indices and is reduced by treatment with corticosteroids and antileukotrienes, but not (beta 2-agonists. In contrast, exhaled NO is normal in COPD, reduced in CF and diagnostically low in primary ciliary dyskinesia. Exhaled carbon monoxide (CO) is increased in asthma, COPD and CF. Increased concentrations of 8-isoprostane, hydrogen peroxide, nitrite and 3-nitrotyrosine are found in Exhaled Breath Condensate in

inflammatory lung diseases. Furthermore, increased levels of lipid mediators are found in these diseases, with a differential pattern depending on the nature of the disease process. In the future it is likely that smaller and more sensitive analyzers will extend the discriminatory value of exhaled breath analysis and that these techniques may be available to diagnose and monitor respiratory diseases in the general practice and home setting.

Notes: 1354-750x

Journal Article

Review

Review, Tutorial

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=12101782](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12101782)

Author Address: Department of Thoracic Medicine, National Heart and Lung Institute, Faculty of Medicine, Imperial College, Royal Brompton Hospital, London, UK. s.kharitonov@ic.ac.uk

Reference Type: Journal Article

Record Number: 214

Author: Latzin, P.; Griese, M.

Year: 2002

Title: Exhaled hydrogen peroxide, nitrite and nitric oxide in healthy children: decrease of hydrogen peroxide by atmospheric nitric oxide

Journal: European Journal of Medical Research

Volume: 7

Issue: 8

Pages: 353-8

Abstract: Hydrogen peroxide (H subset 2O subset 2) and nitrite (NO subset 2-) in Exhaled Breath Condensate have recently been suggested as non-invasive markers of airway inflammation. The goal of this study was to clarify the role of factors that may potentially influence the measurement of H subset 2O subset 2 and nitrite and to look for possible correlations among these inflammatory markers. - H subset 2O subset 2 and nitrite values were assessed fluorometrically in breath condensate of 102 healthy children (age 4-18 years) and a detailed status of atopy (including history, lung function and skin prick test) was taken in all children. To find out the role of atmospheric nitric oxide, eNO and envNO were measured via chemiluminescence in association with the sampling of the breath condensate. - Median (interquartile range) H subset 2O subset 2 was 0.51 (0.26 - 0.74) mgrg;M and nitrite was 3.3 (2.7 4.1) mgrg;M. A significant negative correlation between H subset 2O subset 2 and envNO was observed ( $r = -0.50$ ;  $p < 0.0001$ ). ENO was independent of envNO at our envNO range up to 56 ppb. No further correlation was found. - The inflammatory markers in Exhaled Breath Condensate H subset 2O subset 2, nitrite and eNO are not interrelated to each other in healthy children. Whereas eNO was not dependent on envNO values, high envNO values must be taken into account when measuring H subset 2O subset 2 in exhaled breath condensate.

Notes: English

0949-2321

Reference Type: Journal Article

Record Number: 258

Author: Latzin, P.; Griese, M.

Year: 2002

Title: Exhaled hydrogen peroxide, nitrite and nitric oxide in healthy children: decrease of hydrogen peroxide by atmospheric nitric oxide

Journal: Eur J

Med Res Volume: 7

Issue: 8

Pages: 353-8

Date: Aug 30

Accession Number: 12204843

Keywords: Adolescent

Biological Markers

Breath Tests

Child

Female

Hay Fever/\*diagnosis/metabolism

Human  
Hydrogen Peroxide/\*metabolism  
Lung Diseases/diagnosis/metabolism  
Male  
Multivariate Analysis  
Nitric Oxide/\*metabolism  
Nitrites/\*metabolism  
Respiratory Function Tests

Abstract: Hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) and nitrite (NO<sub>2</sub><sup>-</sup>) in Exhaled Breath Condensate have recently been suggested as non-invasive markers of airway inflammation. The goal of this study was to clarify the role of factors that may potentially influence the measurement of H<sub>2</sub>O<sub>2</sub> and nitrite and to look for possible correlations among these inflammatory markers. H<sub>2</sub>O<sub>2</sub> and nitrite values were assessed fluorometrically in breath condensate of 102 healthy children (age 4-18 years) and a detailed status of atopy (including history, lung function and skin prick test) was taken in all children. To find out the role of atmospheric nitric oxide, eNO and envNO were measured via chemiluminescence in association with the sampling of the breath condensate. Median (interquartile range) H<sub>2</sub>O<sub>2</sub> was 0.51 (0.26 - 0.74) microM and nitrite was 3.3 (2.7 4.1) microM. A significant negative correlation between H<sub>2</sub>O<sub>2</sub> and envNO was observed (r = -0.50; p < 0.0001). ENO was independent of envNO at our envNO range up to 56 ppb. No further correlation was found. The inflammatory markers in Exhaled Breath Condensate H<sub>2</sub>O<sub>2</sub>, nitrite and eNO are not interrelated to each other in healthy children. Whereas eNO was not dependent on envNO values, high envNO values must be taken into account when measuring H<sub>2</sub>O<sub>2</sub> in Exhaled Breath Condensate.

Notes: 0949-2321 Journal Article

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=12204843](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12204843)

Author Address: Children's Hospital, Ludwig Maximilians-University of Munich, Germany.

Reference Type: Journal Article

Record Number: 205

Author: Loukides, S.; Bouros, D.; Papatheodorou, G.; Panagou, P.; Sifakas, N. M.

Year: 2002

Title: The relationships among hydrogen peroxide in expired breath condensate, airway inflammation, and asthma severity

Journal: Chest

Volume: 121

Issue: 2

Pages: 338-46.

Accession Number: 11834641

Keywords: Asthma/pathology/\*physiopathology

Blood Proteins/analysis

\*Breath Tests

Eosinophils/metabolism/pathology

Human

Hydrogen Peroxide/\*analysis

Inflammation

Neutrophils/metabolism/pathology

Severity of Illness Index

Sputum/cytology

Abstract: STUDY OBJECTIVE: To investigate which cells are the main source of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) production in stable patients with asthma and the associations among H<sub>2</sub>O<sub>2</sub> levels, airway inflammation, and disease severity. SETTING: Inpatient respiratory unit and outpatient clinic in tertiary-care hospital. PATIENTS: Fifty stable asthmatic patients with disease severity ranging from mild to moderate. METHODS: H<sub>2</sub>O<sub>2</sub> was measured in expired breath condensate and was correlated with variables expressing both asthma severity (ie, FEV<sub>1</sub> percent predicted, peak expiratory flow rate [PEFR] variability, symptom score, and histamine airways responsiveness) and airway inflammation (ie, differential cell counts from induced sputum and levels of eosinophil cationic protein [ECP]). RESULTS: The mean (95% confidence interval [CI]) concentration of H<sub>2</sub>O<sub>2</sub> was significantly elevated in patients with asthma compared to that in control subjects (mean, 0.67 microM [95% CI, 0.56 to 0.77 microM] vs 0.2 microM [95% CI, 0.16 to 0.24 microM]; p < 0.0001). The difference was primarily due to the elevation of H<sub>2</sub>O<sub>2</sub> in patients with moderate asthma whose expired breath H<sub>2</sub>O<sub>2</sub> level of 0.95 microM (95% CI, 0.76 to 1.12 microM) was significantly higher from that of patients with mild-persistent and mild-intermittent asthma (mean, 0.59 microM [95% CI, 0.47 to 0.7 microM] and 0.27 [95% CI, 0.23 to 0.32 microM], respectively; p < 0.0001). H<sub>2</sub>O<sub>2</sub> concentration was positively related to sputum eosinophilia

as well as to ECP concentration. A similar correlation was found between H<sub>2</sub>O<sub>2</sub> and neutrophils in patients with moderate asthma. A positive correlation was observed between H<sub>2</sub>O<sub>2</sub> level, symptom score, and PEF variability. H<sub>2</sub>O<sub>2</sub> level was negatively related to FEV<sub>1</sub> percent predicted. Further analysis showed that only patients with moderate asthma who were not receiving inhaled steroids were found to have a strong relationship with the variables tested. CONCLUSIONS: Eosinophils are the predominate cells that generate H<sub>2</sub>O<sub>2</sub> in all forms of the disease, while neutrophils might be responsible for the highest levels that are observed in the more severe forms of the disease. The role of H<sub>2</sub>O<sub>2</sub> concentration in predicting the severity of the disease as well as in the inflammatory process is limited and depends on the use of inhaled steroid therapy and the classification of the severity of the disease.

URL: <http://www.ncbi.nlm.nih.gov/htbin-post/Entrez/query?db=m&form=6&dopt=r&uid=11834641>

<http://www.chestjournal.org/cgi/content/full/121/2/338>

<http://www.chestjournal.org/cgi/content/abstract/121/2/338>

Author Address: Department of Pneumonology and Clinical Research Unit, Athens Army General Hospital, Athens, Greece. [ssat@hol.gr](mailto:ssat@hol.gr)

Reference Type: Journal Article

Record Number: 200

Author: van Beurden, W. J.; Harff, G. A.; Dekhuijzen, P. N.; van den Bosch, M. J.; Creemers, J. P.; Smeenk, F. W.

Year: 2002

Title: An efficient and reproducible method for measuring hydrogen peroxide in Exhaled Breath Condensate

Journal: Respir Med

Volume: 96

Issue: 3

Pages: 197-203.

Accession Number: 11908513

Keywords: Aged

Breath Tests/instrumentation/\*methods

Cryopreservation

Female

Human

Hydrogen Peroxide/\*analysis

Male

Middle Age

Pulmonary Disease, Chronic Obstructive/\*diagnosis

Reproducibility of Results

Sensitivity and Specificity

Support, Non-U.S. Gov't

Abstract: We investigated the sensitivity and reproducibility of a test procedure for measuring hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) in Exhaled Breath Condensate and the effect of storage of the condensate on the H<sub>2</sub>O<sub>2</sub> concentration, and compared the results to previous studies. Twenty stable COPD patients breathed into our collecting device twice for a period of 10 min. The total exhaled air volume (EAV) and condensate volume were measured both times and the H<sub>2</sub>O<sub>2</sub> concentration of the condensate was determined fluorimetrically. The concentration was measured again after freezing the reaction product at -70 degrees C for a period of 10, 20 and 40 days. We collected 2-5 ml condensate in 10 min. The EAV and condensate volumes were strongly correlated. There was no significant difference between the mean H<sub>2</sub>O<sub>2</sub> concentration of the first and second test. We obtained a detect on limit for the H<sub>2</sub>O<sub>2</sub> concentration of 0.02 micromol(-1). The H<sub>2</sub>O<sub>2</sub> concentration appeared to remain stable for a period up to 40 days of freezing. Compared to previous studies we developed a more efficient breath condensate collecting device and obtained a lower H<sub>2</sub>O<sub>2</sub> detection limit. The measurement of exhaled H<sub>2</sub>O<sub>2</sub> was reproducible. In addition, storage of the samples up to 40 days showed no changes in H<sub>2</sub>O<sub>2</sub> concentration.

URL: <http://www.ncbi.nlm.nih.gov/htbin-post/Entrez/query?db=m&form=6&dopt=r&uid=11908513>

Author Address: Department of Pulmonology, Catharina Hospital, Eindhoven, The Netherlands. [w.beurden@researchlab-long.demon.nl](mailto:w.beurden@researchlab-long.demon.nl)

Reference Type: Journal Article

Record Number: 246

Author: Van Beurden, W. J.; Dekhuijzen, P. N.; Harff, G. A.; Smeenk, F. W.

Year: 2002

Title: Variability of Exhaled Hydrogen Peroxide in Stable COPD Patients and Matched Healthy Controls

Journal: Respiration

Volume: 69

Issue: 3

Pages: 211-6

Accession Number: 12097763

Abstract: Background: Because inflammation induces oxidative stress, exhaled hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>), which is a marker of oxidative stress, may be used as a non-invasive marker of airway inflammation in chronic obstructive pulmonary disease (COPD). There are no data on the circadian variability of exhaled H<sub>2</sub>O<sub>2</sub> in COPD patients. Objective: The aim of this study was to investigate the variability of the H<sub>2</sub>O<sub>2</sub> concentration in breath condensate of stable COPD patients and of matched healthy control subjects. Methods: We included 20 patients with stable mild COPD (forced expiratory volume in 1 s approximately 70% of predicted) and 20 healthy subjects, matched for age, sex and pack-years, all smokers or ex-smokers. Breath condensate was collected and its H<sub>2</sub>O<sub>2</sub> concentration determined fluorometrically three times on day 0 (9 and 12 a.m., and 3 p.m.) and once on days 1, 2, 3, 8 and 21. Results: The mean H<sub>2</sub>O<sub>2</sub> concentration increased significantly during the day in both the patient and control groups ( $p = 0.02$  and  $p < 0.01$ , respectively). Over a longer period up to 21 days, the mean concentration did not change in both groups. There was no significant difference between patients and controls. The mean coefficient of variation over 21 days was 45% in the patient group and 43% in the control group ( $p = 0.8$ ). Conclusions: The exhaled H<sub>2</sub>O<sub>2</sub> concentration increased significantly during the day in both stable COPD patients and controls. Over a period of 3 weeks, the mean H<sub>2</sub>O<sub>2</sub> concentration did not change and the variability within the subjects was similar in both groups.

Notes: 0025-7931

Journal Article

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=12097763](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12097763)

Author Address: Department of Pulmonology, Catharina Hospital Eindhoven, The Netherlands.

Reference Type: Journal Article

Record Number: 318

Author: Cheah, F. C.; Darlow, B. A.; Winterbourn, C. C.

Year: 2003

Title: Problems associated with collecting breath condensate for the measurement of exhaled hydrogen peroxide from neonates on respiratory support

Journal: Biol Neonate

Volume: 84

Issue: 4

Pages: 338-41

Accession Number: 14593246

Abstract: We developed a bedside method for collecting Exhaled Breath Condensate (EBC) from neonates who were ventilated or receiving nasal continuous positive airway pressure (CPAP) and analyzed their EBC for hydrogen peroxide levels. A sufficient volume for analysis could be collected over 25-40 min from neonates on the ventilator and nasal CPAP (medians 5.3 and 2.7 ml, respectively). There was no significant difference between hydrogen peroxide levels from neonates on a ventilator or CPAP (median 0.28 vs. 0.38 microM,  $p = 0.06$ ) and these were no different from a background with the ventilator or CPAP system alone (median for each 0.31 microM). The dilution of breath condensate by humidified gases plus the existence of background hydrogen peroxide resulted in this collecting setup being insufficiently sensitive to use for the detection of exhaled hydrogen peroxide in infants who were ventilated or on nasal CPAP.

Notes: 0006-3126

Journal Article

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=14593246](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14593246)

Author Address: Free Radical Research Group, Department of Pathology, Christchurch School of Medicine and Health Sciences, University of Otago, Christchurch, New Zealand. fookchoe.cheah@chmeds.ac.nz

Reference Type: Journal Article

Record Number: 322

Author: Kostikas, K.; Papatheodorou, G.; Psathakis, K.; Panagou, P.; Loukides, S.

Year: 2003

Title: Oxidative stress in expired breath condensate of patients with COPD

Journal: Chest

Volume: 124

Issue: 4

Pages: 1373-80

Date: Oct

Accession Number: 14555568

Keywords: Adult

Aged

Androstadienes/therapeutic use

Anti-Inflammatory Agents/therapeutic use

Breath Tests

Bronchodilator Agents/therapeutic use

Exhalation

Human

Male

Middle Aged

\*Oxidative Stress

Pulmonary Disease, Chronic Obstructive/drug therapy/immunology/\*metabolism

Theophylline/therapeutic use

**Abstract:** **OBJECTIVE:** To evaluate the levels of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) and 8-isoprostane in the expired breath condensate (EBC) of patients with COPD, and to assess the relationship between the above markers of oxidative stress and parameters expressing inflammatory process and disease severity. **SETTING:** Inpatient respiratory unit and outpatient clinic in tertiary care hospital. **DESIGN:** Cross-sectional study. **PATIENTS:** Thirty stable COPD patients (all smokers) with disease severity ranging from mild to severe. Ten subjects who were smokers with stage 0 disease (ie, at risk for COPD; mean [± SD] FEV<sub>1</sub>, 88 ± 5% predicted) were studied as a control group. **METHODS:** H<sub>2</sub>O<sub>2</sub> and 8-isoprostane levels were measured in EBC, and the values were correlated with variables expressing COPD severity (ie, FEV<sub>1</sub> percent predicted, dyspnea severity score (ie, Medical Research Council scale) and airway inflammation (ie, differential cell counts from induced sputum). **RESULTS:** The mean concentration of H<sub>2</sub>O<sub>2</sub> was significantly elevated in COPD patients compared to control subjects (mean, 0.66 micromol/L [95% confidence interval (CI), 0.54 to 0.68 micromol/L] vs 0.31 micromol/L [95% CI, 0.26 to 0.35 micromol/L], respectively; p < 0.0001). The difference was primarily due to the elevation of H<sub>2</sub>O<sub>2</sub> in patients with severe and moderate COPD, whose expired breath H<sub>2</sub>O<sub>2</sub> levels were significantly higher than those of patients with mild disease (mean, 0.96 micromol/L [95% CI, 0.79 to 1.13 micromol/L], 0.68 micromol/L [95% CI, 0.55 to 0.81 micromol/L], and 0.33 micromol/L [95% CI, 0.24 to 0.43 micromol/L], respectively, p < 0.0001). The mean concentration of 8-isoprostane was significantly elevated in patients with COPD compared to that of the control group (47 pg/mL [95% CI, 41 to 53 pg/mL] vs 29 pg/mL [95% CI, 25 to 33 pg/mL], respectively; p < 0.0001) but did not differ significantly among the different stages of the disease (p = 0.43). Repeatability and stability data within measurements showed that H<sub>2</sub>O<sub>2</sub> has a better repeatability and stability than 8-isoprostane. Furthermore, we observed significant correlations of H<sub>2</sub>O<sub>2</sub> with FEV<sub>1</sub>, neutrophil count, and dyspnea score. Those correlations existed only in patients with moderate and severe disease. No correlations were found between levels of 8-isoprostane and the above parameters. **CONCLUSIONS:** We conclude that levels of H<sub>2</sub>O<sub>2</sub> and 8-isoprostane are elevated in the EBC of patients with COPD, but that H<sub>2</sub>O<sub>2</sub> seems to be a more repeatable and a more sensitive index of the inflammatory process and the severity of the disease.

**Notes:** 0012-3692 Journal Article

**URL:** [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=14555568](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14555568)

**Author Address:** Pneumology and Clinical Research Department, Athens Army General Hospital, Athens, Greece.

**Reference Type:** Journal Article

**Record Number:** 316

**Author:** Latzin, P.; Beck, J.; Bartenstein, A.; Griese, M.

**Year:** 2003

**Title:** Comparison of Exhaled Breath Condensate from nasal and oral collection

**Journal:** Eur J Med Res

**Volume:** 8

**Issue:** 11

**Pages:** 505-10

**Date:** Nov 12

**Accession Number:** 14644706

**Abstract:** **BACKGROUND:** Analysis of Exhaled Breath Condensate may provide new insights into pulmonary inflammatory

processes. A new collection method via suction of nasally expired air especially suitable for younger children was presented recently. Here we compare this nasal suction method with the more widely used oral collection method regarding the amount of condensate collected as well as the concentrations of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>), nitrite and nitrate, respectively. MATERIALS AND METHODS: Exhaled Breath Condensate was collected from 11 healthy adults for the measurements of the amount of condensate and H<sub>2</sub>O<sub>2</sub> concentration and from 17 children for the measurements of nitrite and nitrate. Condensate was collected via nasal suction and oral exhalation from each subject. RESULTS: Overall, no differences between both collection methods were found for all variables assessed except the concentration of H<sub>2</sub>O<sub>2</sub>, whereas the latter closely correlated (Spearman  $r = 0.88$ ,  $p = 0.0007$ ) between both collection methods. No correlation was found for the amount of condensate collected and the concentration of nitrite and nitrate. The Bland-Altman limits of agreement scattered over a wide range with clinical impact, proving significant differences between both collection methods for all variables measured. CONCLUSIONS: Although nasal and oral collection method proved again suitable for the collection of Exhaled Breath Condensate, the variability of the results obtained precludes the interchangeable usage of the inflammatory markers assessed here.

Notes: 0949-2321 Journal Article

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=14644706](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14644706)

Author Address: CF-Ambulanz, Lindwurmstrasse 4, D-80337 Munich, Germany.

Reference Type: Journal Article

Record Number: 285

Author: Luczynska, M.; Szkudlarek, U.; Dziankowska-Bartkowiak, B.; Waszczykowska, E.; Kasielski, M.; Sysa-Jedrzejowska, A.; Nowak, D.

Year: 2003

Title: Elevated exhalation of hydrogen peroxide in patients with systemic sclerosis

Journal: Eur J Clin Invest

Volume: 33

Issue: 3

Pages: 274-9

Date: Mar

Accession Number: 12641548

Keywords: Breath Tests/methods

Female

Human

Hydrogen Peroxide/analysis/\*metabolism

Male

Middle Age

Reactive Oxygen Species/metabolism

Scleroderma, Systemic/\*metabolism

Support, Non-U.S. Gov't

Abstract: BACKGROUND: Systemic sclerosis is accompanied by an influx of activated phagocytes into distal airways. These cells release H<sub>2</sub>O<sub>2</sub>, which may evaporate from the airways surface and be detected in expired breath condensate. We tested whether patients with systemic sclerosis exhale more H<sub>2</sub>O<sub>2</sub> than healthy subjects and whether breath condensate H<sub>2</sub>O<sub>2</sub> levels correlate with some clinical parameters. MATERIAL AND METHODS: H<sub>2</sub>O<sub>2</sub> was measured fluorimetrically in the expired breath condensate of 27 patients (22 women, five men, mean age 49 +/- 13.1 years) with systemic sclerosis and 27 age- and sex- matched healthy controls. RESULTS: Exhaled H<sub>2</sub>O<sub>2</sub> levels were 3.5-fold higher (0.88 +/- 0.62 microM vs. 0.25 +/- 0.17 microM,  $P < 0.001$ ) in the patients with systemic sclerosis than in the controls. Treatment with cyclophosphamide and/or prednisone (29 +/- 50 months, range 3-168 months) did not significantly decrease H<sub>2</sub>O<sub>2</sub> exhalation (0.78 +/- 0.50 microM,  $n = 10$  vs. 0.94 +/- 0.67 microM,  $n = 17$ ,  $P > 0.05$ ). No significant difference was found between patients with limited and diffuse scleroderma (1.03 +/- 0.69 microM,  $n = 17$  vs. 0.63 +/- 0.41 microM,  $n = 10$ ,  $P > 0.05$ ). H<sub>2</sub>O<sub>2</sub> levels correlated with disease duration ( $r = 0.38$ ,  $P < 0.05$ ) and time from the first Raynaud's episode ( $r = 0.44$ ,  $P < 0.05$ ). CONCLUSIONS: Patients with systemic sclerosis exhale more H<sub>2</sub>O<sub>2</sub> than healthy controls, suggesting involvement of reactive oxygen species in disease processes. Lack of significant intergroups differences in H<sub>2</sub>O<sub>2</sub> levels may have resulted from the small number of patients analyzed.

Notes: 0014-2972 Journal Article

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=12641548](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12641548)

Author Address: Department of Experimental and Clinical Physiology, Institute of Physiology and Biochemistry, Medical University of Lodz, Lodz, Poland.

Reference Type: Journal Article

Record Number: 293

Author: Moloney, E. D.; Mumby, S. E.; Gajdocsi, R.; Cranshaw, J. H.; Kharitonov, S. A.; Quinlan, G. J.; Griffiths, M. J.

Year: 2003

Title: Exhaled Breath Condensate detects markers of pulmonary inflammation after cardio-thoracic surgery

Journal: Am J Respir Crit Care Med

Date: Oct 9

Accession Number: 14551168

Abstract: Cardiac surgery using cardio-pulmonary by-pass and, to a greater extent lung resection, cause acute lung injury that is usually sub-clinical. Analysis of mediators in Exhaled Breath Condensate is a promising means of monitoring inflammation in a variety of airway diseases but the contribution of the airway lining fluid from the lower respiratory tract is uncertain. We compared the analysis of markers of lung injury in Exhaled Breath Condensate and broncho-alveolar lavage, in endo-tracheally intubated patients before and after coronary artery bypass graft surgery with cardio-pulmonary bypass and lobectomy. The neutrophil count and leukotriene B4 concentration in broncho-alveolar lavage fluid rose after coronary artery bypass graft surgery ( $p < 0.05$ ), but there was no significant change in leukotriene B4, hydrogen peroxide, or hydrogen ion concentrations in Exhaled Breath Condensate. By contrast, after lobectomy, the concentration in Exhaled Breath Condensate of leukotriene B4, hydrogen peroxide and hydrogen ions rose significantly ( $p < 0.05$ ). Exhaled breath condensate is a safe, non-invasive method of sampling the milieu of the distal lung and is sufficiently sensitive to detect markers of inflammation and oxidative stress in patients after lobectomy, but not after the milder insult associated with cardiac surgery.

Notes: 1073-449x Journal article

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=14551168](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14551168)

Author Address: Unit of Critical Care, Imperial College London at the National Heart and Lung Institute, London, United Kingdom.

Reference Type: Journal Article

Record Number: 221

Author: Sandrini, A.; Ferreira, I. M.; Jardim, J. R.; Zamel, N.; Chapman, K. R.

Year: 2003

Title: Effect of nasal triamcinolone acetonide on lower airway inflammatory markers in patients with allergic rhinitis

Journal: J Allergy Clin Immunol

Volume: 111

Issue: 2

Pages: 313-320

Date: Feb

Accession Number: 12589351

Abstract: BACKGROUND: Allergic rhinitis (AR) and asthma are commonly associated, and similar underlying inflammatory processes link both diseases. AR, even in the absence of asthma, is associated with increased levels of exhaled nitric oxide (ENO) and hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) in Exhaled Breath Condensate, 2 noninvasive markers of lower airway inflammation. OBJECTIVE: We sought to evaluate the effect of treatment with the nasal steroid triamcinolone acetonide on ENO and exhaled H<sub>2</sub>O<sub>2</sub> in subjects with AR. METHODS: We allocated 23 subjects in a randomized, double-blind, parallel-controlled fashion to 4-week treatment with triamcinolone acetonide (220 µg/d) or matching placebo. RESULTS: ENO levels were greater in the subgroup with concomitant asthma (16/23 subjects) and decreased significantly with triamcinolone acetonide treatment in this subgroup of patients in comparison with patients receiving placebo. Breath condensate levels of H<sub>2</sub>O<sub>2</sub> were higher in patients with AR without asthma than in those with asthma but decreased significantly with triamcinolone acetonide treatment in both subgroups. No changes were observed in bronchial hyperresponsiveness, nasal and asthma symptoms, or peak expiratory flow with active treatment or placebo. CONCLUSION: We conclude that treatment of AR with triamcinolone acetonide results in decrease of 2 noninvasive markers of lower airway inflammation, ENO and H<sub>2</sub>O<sub>2</sub>, supporting that upper and lower airway inflammation should be seen as a continuum in subjects with AR with and without asthma. ENO might be a more specific marker of the lower airway inflammation present in asthma.

Notes: 0091-6749 Journal article

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=12589351](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12589351)

Author Address: Asthma and Airway Centre of the Toronto Western Hospital, University Health Network, Division of Respiratory Medicine, University of Toronto, Toronto.

Reference Type: Journal Article

Record Number: 286

Author: Sandrini, A.; Ferreira, I. M.; Jardim, J. R.; Zamel, N.; Chapman, K. R.

Year: 2003

Title: Effect of nasal triamcinolone acetonide on lower airway inflammatory markers in patients with allergic rhinitis

Journal: J Allergy Clin Immunol

Volume: 111

Issue: 2

Pages: 313-20

Date: Feb

Accession Number: 12589351

Keywords: Administration, Intranasal

Adolescent

Adult

Aged

Asthma/complications

Biological Markers

Bronchial Hyperreactivity/drug therapy

Double-Blind Method

Female

Forced Expiratory Volume

Hay Fever/complications/\*drug therapy/physiopathology

Human

Hydrogen Peroxide/metabolism

Inflammation Mediators/metabolism

Male

Middle Age

Nitric Oxide/metabolism

Respiration

Rhinitis, Allergic, Perennial/complications/\*drug therapy/physiopathology

Support, Non-U.S. Gov't

Triamcinolone Acetonide/\*administration & dosage

Abstract: BACKGROUND: Allergic rhinitis (AR) and asthma are commonly associated, and similar underlying inflammatory processes link both diseases. AR, even in the absence of asthma, is associated with increased levels of exhaled nitric oxide (ENO) and hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) in Exhaled Breath Condensate, 2 noninvasive markers of lower airway inflammation. OBJECTIVE: We sought to evaluate the effect of treatment with the nasal steroid triamcinolone acetonide on ENO and exhaled H<sub>2</sub>O<sub>2</sub> in subjects with AR. METHODS: We allocated 23 subjects in a randomized, double-blind, parallel-controlled fashion to 4-week treatment with triamcinolone acetonide (220 microg/d) or matching placebo. RESULTS: ENO levels were greater in the subgroup with concomitant asthma (16/23 subjects) and decreased significantly with triamcinolone acetonide treatment in this subgroup of patients in comparison with patients receiving placebo. Breath condensate levels of H<sub>2</sub>O<sub>2</sub> were higher in patients with AR without asthma than in those with asthma but decreased significantly with triamcinolone acetonide treatment in both subgroups. No changes were observed in bronchial hyperresponsiveness, nasal and asthma symptoms, or peak expiratory flow with active treatment or placebo. CONCLUSION: We conclude that treatment of AR with triamcinolone acetonide results in decrease of 2 noninvasive markers of lower airway inflammation, ENO and H<sub>2</sub>O<sub>2</sub>, supporting that upper and lower airway inflammation should be seen as a continuum in subjects with AR with and without asthma. ENO might be a more specific marker of the lower airway inflammation present in asthma.

Notes: 0091-6749 Clinical Trial

Journal Article

Randomized Controlled Trial

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=12589351](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12589351)

Author Address: Asthma and Airway Centre of the Toronto Western Hospital, University Health Network, Division of Respiratory Medicine, University of Toronto, 399 Bathurst Street, Toronto, Ontario M5T 2S8, Canada.

Reference Type: Journal Article

Record Number: 323

Author: Sandrini, A.; Ferreira, I. M.; Gutierrez, C.; Jardim, J. R.; Zamel, N.; Chapman, K. R.

Year: 2003

Title: Effect of montelukast on exhaled nitric oxide and nonvolatile markers of inflammation in mild asthma

Journal: Chest  
Volume: 124  
Issue: 4  
Pages: 1334-40  
Date: Oct  
Accession Number: 14555563  
Keywords: Acetates/\*pharmacology  
Adult  
Anti-Asthmatic Agents/\*pharmacology  
Asthma/complications/\*drug therapy/\*metabolism  
Biological Markers/analysis  
Breath Tests  
Cross-Over Studies  
Cysteine/\*analysis  
Double-Blind Method  
Exhalation  
Female  
Forced Expiratory Volume/drug effects  
Human  
Hydrogen Peroxide/\*analysis  
Inflammation Mediators/\*analysis  
Leukotrienes/\*analysis  
Male  
Nitric Oxide/\*analysis  
Peak Expiratory Flow Rate/drug effects  
Pneumonia/etiology/\*metabolism  
Quinolines/\*pharmacology  
Severity of Illness Index  
Support, Non-U.S. Gov't

**Abstract:** STUDY OBJECTIVES: Leukotriene receptor antagonists appear to exert anti-inflammatory activity in asthma. We undertook the present study to evaluate the effect of montelukast on levels of exhaled nitric oxide (ENO) and two inflammatory markers, hydrogen peroxide (H(2)O(2)), and cysteinyl leukotrienes (cys-LTs), in the Exhaled Breath Condensate of subjects with mild asthma. PATIENTS: Twenty stable subjects with mild asthma (15 women and 5 men; mean [+/- SD] age, 34.8 +/- 12.6 years) were included in the study. INTERVENTION: A 1-week run-in period was followed by 2 weeks of treatment (with montelukast or placebo) that was administered in randomized, double-blind, crossover fashion. One week of washout followed each treatment arm. RESULTS: Montelukast significantly reduced the levels of ENO from baseline (median, 52.5 parts per billion [ppb]; 25th to 75th percentile, 37.8 to 101.8 ppb) during the entire treatment period (ie, day 1 to day 14), with the effect measurable as early as day 1 (median, 45.9 ppb; 25th to 75th percentile, 29.3 to 92.5 ppb) and with the maximal effect being observed on day 7 (median, 35.7 ppb; 25th to 75th percentile, 27.6 to 66.6 ppb). The levels of ENO did not change significantly with placebo therapy. Montelukast improved symptom score and reduced peak expiratory flow (PEF) variability. Changes in PEF variability correlated positively with changes in ENO (r = 0.46; p = 0.04). No significant changes in FEV(1) or concentration of H(2)O(2) in the Exhaled Breath Condensate were observed. Levels of cys-LTs were undetectable in the exhaled breath condensate. CONCLUSIONS: We concluded that montelukast reduces the levels of ENO in patients with mild asthma, a finding that is compatible with an anti-inflammatory effect of montelukast, and that ENO appears to be more sensitive in detecting this effect than FEV(1) and H(2)O(2) levels in the Exhaled Breath Condensate.

Notes: 0012-3692

Clinical Trial

Journal Article

Randomized Controlled Trial

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=14555563](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14555563)

Author Address: Asthma & Airway Centre of the Toronto Western Hospital, Division of Respiratory Medicine, University Health Network, University of Toronto, Toronto, ON, Canada.

Reference Type: Journal Article

Record Number: 278

Author: Szkudlarek, U.; Maria, L.; Kasielski, M.; Kaucka, S.; Nowak, D.

Year: 2003

Title: Exhaled hydrogen peroxide correlates with the release of reactive oxygen species by blood phagocytes in healthy subjects

Journal: Respir Med

Volume: 97

Issue: 6

Pages: 718-25

Date: Jun

Accession Number: 12814160

Keywords: Adult

Breath Tests

Female

Human

Hydrogen Peroxide/\*analysis

Luminescence

Male

Phagocytes/\*metabolism

Reactive Oxygen Species/blood/\*metabolism

Support, Non-U.S. Gov't

Thiobarbituric Acid Reactive Substances/analysis

Abstract: Various cells including polymorphonuclear leukocytes, alveolar macrophages and type-II pneumocytes may be a source of exhaled hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) in airways of humans. H<sub>2</sub>O<sub>2</sub> can convert into hydroxyl radicals leading to peroxidative damage of airways structures and formation of volatile thiobarbituric acid-reactive substances (TBARs). We tested whether exhalation of H<sub>2</sub>O<sub>2</sub> and TBARs by healthy subjects depends on reactive oxygen species generation from blood phagocytes. The expired breath condensate (EBC) and blood specimens were collected from 41 healthy, never smoked subjects (mean age 20.7 +/- 0.8 years, 18 men, 23 women) and then the EBC concentration of H<sub>2</sub>O<sub>2</sub> and TBARs and 2 x 10<sup>-5</sup> M fMLP-provoked whole blood chemiluminescence response was measured. The mean concentration of H<sub>2</sub>O<sub>2</sub> and TBARs in EBC was 0.28 +/- 0.17 and 0.04 +/- 0.13 microM with ratio of positive readings reaching 36/41 and 4/41, respectively. The chemiluminescence response to n-formyl-methionyl-leuyl-phenylalanine stimulation was obtained in all cases and the following parameters were estimated: basal chemiluminescence (bCl); peak chemiluminescence (pCl); absolute light emission (aCl); and peaktime. H<sub>2</sub>O<sub>2</sub> levels in EBC positively correlated (Spearman test) with bCl (r=0.41, P<0.01), pCl (r=0.47, P<0.01), aCl (r=0.49, P<0.001), peaktime (r=0.52, P<0.001) in the whole group and with bCl (r=0.56, P<0.01), pCl (r=0.67, P<0.01), aCl (r=0.66, P<0.01) in men and with aCl (r=0.41, P<0.05) and peaktime (r=0.48, P<0.05) in women. No association between exhaled TBARs and blood phagocytes activity was found. These results indicate that H<sub>2</sub>O<sub>2</sub> exhalation in healthy never smoked subjects depends on ability of blood phagocytes to generate reactive oxygen species.

Notes: 0954-6111

Journal Article

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=12814160](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12814160)

Author Address: Department of Experimental and Clinical Physiology, Institute of Physiology and Biochemistry, Medical University of Lodz, Mazowiecka str 6/8, 92-215 Lodz, Poland.

Reference Type: Journal Article

Record Number: 256

Author: Uczynska, L.; Szkudlarek, U.; Dziaukowska-Bartkowiak, B.; Waszczykowska, E.; Kasielski, M.; Sysa-Jedrzejowska, A.; Nowak, D.

Year: 2003

Title: Elevated exhalation of hydrogen peroxide in patients with systemic sclerosis

Journal: Eur J Clin Invest

Volume: 33

Issue: 3

Pages: 274-9

Date: Mar

Accession Number: 12641548

Abstract: BACKGROUND: Systemic sclerosis is accompanied by an influx of activated phagocytes into distal airways. These cells release H<sub>2</sub>O<sub>2</sub>, which may evaporate from the airways surface and be detected in expired breath condensate. We tested whether patients with systemic sclerosis exhale more H<sub>2</sub>O<sub>2</sub> than healthy subjects and whether breath condensate H<sub>2</sub>O<sub>2</sub> levels correlate

with some clinical parameters. MATERIAL AND METHODS: H<sub>2</sub>O<sub>2</sub> was measured fluorimetrically in the expired breath condensate of 27 patients (22 women, five men, mean age 49 +/- 13.1 years) with systemic sclerosis and 27 age- and sex- matched healthy controls. RESULTS: Exhaled H<sub>2</sub>O<sub>2</sub> levels were 3.5-fold higher (0.88 +/- 0.62 micro M vs. 0.25 +/- 0.17 micro M, P < 0.001) in the patients with systemic sclerosis than in the controls. Treatment with cyclophosphamide and/or prednisone (29 +/- 50 months, range 3-168 months) did not significantly decrease H<sub>2</sub>O<sub>2</sub> exhalation (0.78 +/- 0.50 micro M, n= 10 vs. 0.94 +/- 0.67 micro M, n= 17, P > 0.05). No significant difference was found between patients with limited and diffuse scleroderma (1.03 +/- 0.69 micro M, n= 17 vs. 0.63 +/- 0.41 micro M, n= 10, P > 0.05). H<sub>2</sub>O<sub>2</sub> levels correlated with disease duration (r = 0.38, P < 0.05) and time from the first Raynaud's episode (r = 0.44, P < 0.05). CONCLUSIONS: Patients with systemic sclerosis exhale more H<sub>2</sub>O<sub>2</sub> than healthy controls, suggesting involvement of reactive oxygen species in disease processes. Lack of significant intergroups differences in H<sub>2</sub>O<sub>2</sub> levels may have resulted from the small number of patients analyzed.

Notes: 0014-2972

Journal Article

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=12641548](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12641548)

Author Address: Medical University of Lodz, Lodz, Poland.

Reference Type: Journal Article

Record Number: 270

Author: van Beurden, W. J.; Harff, G. A.; Dekhuijzen, P. N.; van der Poel-Smet, S. M.; Smeenk, F. W.

Year: 2003

Title: Effects of inhaled corticosteroids with different lung deposition on exhaled hydrogen peroxide in stable COPD patients

Journal: Respiration

Volume: 70

Issue: 3

Pages: 242-8

Date: May-Jun

Accession Number: 12915742

Abstract: BACKGROUND: The effects of inhaled corticosteroids (ICS) on markers of oxidative stress in patients with stable COPD are unclear. OBJECTIVES: The aim was to investigate the effect of ICS on exhaled H<sub>2</sub>O<sub>2</sub> in stable COPD patients and to compare ICS with different lung deposition. METHODS: Forty-one stable patients with moderate COPD (FEV<sub>1</sub> approximately 60% predicted) were randomized to sequence 1; first HFA-134a beclomethasone dipropionate (HFA-BDP, an ICS with more peripheral deposition) 400 microg b.i.d., then fluticasone propionate (FP, an ICS with more central deposition) 375 microg b.i.d. (n = 20) or sequence 2; first FP, then HFA-BDP (n = 21). Both 4-week treatment periods were preceded by a 4-week washout period. After each period, the concentration of H<sub>2</sub>O<sub>2</sub> in Exhaled Breath Condensate was measured. RESULTS: The H<sub>2</sub>O<sub>2</sub> concentration decreased significantly after the first treatment period in both sequence 1 and 2 (p < 0.05, p = 0.01, respectively). In neither sequence was there a return to baseline values after the second washout, indicating a carry-over effect. The concentrations remained low in both sequences during the second treatment period. CONCLUSIONS: Both ICS appeared to reduce exhaled H<sub>2</sub>O<sub>2</sub> in stable COPD patients. However, this study showed no difference between ICS with different deposition patterns, which in part may be due to the carry-over effect.

Notes: 0025-7931

Journal Article

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=12915742](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12915742)

Author Address: Department of Pulmonology, Catharina Hospital Eindhoven, The Netherlands. wendy.beurden@wanadoo.nl

Reference Type: Journal Article

Record Number: 315

Author: van Beurden, W. J.; van den Bosch, M. J.; Janssen, W. C.; Smeenk, F. W.; Dekhuijzen, P. N.; Harff, G. A.

Year: 2003

Title: Fluorimetric analysis of hydrogen peroxide with automated measurement

Journal: Clin Lab

Volume: 49

Issue: 11-12

Pages: 637-43

Accession Number: 14651334

Abstract: In the pathophysiology of chronic obstructive pulmonary disease (COPD) oxidative stress plays an important role, which can be determined by measuring hydrogen peroxide. Hydrogen peroxide can be measured fluorimetrically in Exhaled Breath

Condensate (EBC), however, not standardized. The objective of this study was to investigate the sensitivity and reproducibility of measuring the hydrogen peroxide concentration in EBC of COPD patients using an automated flow injection device with varying flow rates and measurements. METHODS: 10 microl p-hydroxyphenylacetic acid (1.0 mmol/l) and 10 microl horseradish peroxidase (15 mU/l) were manually added to several hydrogen peroxide containing solutions and EBC of patients suffering from COPD. The fluorescence of the reaction product was measured with an automated sampler, flow injection and scanning fluorescence detector, excitation wave 295 nm, emission wave 405 nm, at different flow rates. The degree of fluorescence was expressed as either the area under the curve or the peak value. RESULTS: A flow rate of 1 ml/min gave the best results. There were no significant differences in calibration curves or detection limits using area under the curve or peak value (respectively 0.007 and 0.005 micromol/l) (flow rate 1.0 ml/min). The mean volume of EBC was 2.8 ml, the mean hydrogen peroxide concentration in the patient group was 0.2 micromol/l and the standard deviation of duplication 0.009 micromol/. CONCLUSIONS: The low detection limit may be explained by using flow injection, because it measures the fluorescence over a period of time. It is important to choose an appropriate flow rate. There is no difference in the detection limit between measuring the fluorescence as area under the curve or as peak value.

Notes: 1433-6510

Journal Article

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=14651334](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14651334)

Author Address: Department of Pulmonary Diseases, Catharina Hospital Eindhoven, The Netherlands. wendy.beurdenvan@wanado.o.nl

Reference Type: Journal Article

Record Number: 365

Author: van Beurden, W. J.; Smeenk, F. W.; Harff, G. A.; Dekhuijzen, P. N.

Year: 2003

Title: Markers of inflammation and oxidative stress during lower respiratory tract infections in COPD patients

Journal: Monaldi Arch Chest Dis

Volume: 59

Issue: 4

Pages: 273-80

Date: Oct-Dec

Accession Number: 15148836

Keywords: Administration, Inhalation

Adrenal Cortex Hormones/therapeutic use

Aged

Aged, 80 and over

Analysis of Variance

Blood Chemical Analysis

Comparative Study

Disease Progression

Female

Hospitalization

Human

Inflammation Mediators/\*analysis

Male

Middle Aged

Oxidative Stress/\*physiology

Pneumonia/complications/\*diagnosis

Probability

Prognosis

Pulmonary Disease, Chronic Obstructive/complications/\*diagnosis/drug therapy

Respiratory Function Tests

Risk Assessment

Sampling Studies

Sensitivity and Specificity

Severity of Illness Index

## Spirometry

## Statistics, Nonparametric

**Abstract:** BACKGROUND: Lower respiratory tract infections (LRTI) occur frequently in patients with Chronic Obstructive Pulmonary Disease (COPD), and are a major cause of morbidity, mortality and health care utilization. The aim of this study was to investigate if non- or less invasive markers of inflammation and oxidative stress can predict the course of the infections. METHODS: Twenty-five COPD patients who were admitted to hospital with a LRTI were included. Within 24 hours after admittance, spirometry (FEV<sub>1</sub>, FVC, MEF50), measurement of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) in Exhaled Breath Condensate (EBC), symptom scores and analyses of ESR, CRP, ECP, and MPO in serum were performed. All patients were treated with intravenous dexamethasone, nebulised salbutamol/ ipratropium and, if needed, antibiotics. The tests were repeated at day 2, 3, 7 and 30. RESULTS: Complete data of the first four visits were collected in 19 patients. The H<sub>2</sub>O<sub>2</sub> concentration and spirometry parameters did not change significantly during the study period. CRP, ESR and MPO levels decreased significantly during treatment, while the other serum inflammatory parameters did not change. There were no significant correlations between H<sub>2</sub>O<sub>2</sub> concentration, spirometry and serum inflammatory parameters. CONCLUSIONS: In conclusion, this study showed no significant changes in H<sub>2</sub>O<sub>2</sub> concentration in EBC, or spirometry during treatment of a LRTI in COPD patients. In contrast, several serum inflammatory markers did decrease during hospitalization, thus providing a simple tool to monitor exacerbations.

Notes: 1122-0643

## Journal Article

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=15148836](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15148836)

Author Address: Department of Pulmonology, Catharina Hospital, Eindhoven, The Netherlands. wendy.beurdenvan@wanadoo.nl

Reference Type: Journal Article

Record Number: 342

Author: Vass, G.; Huszar, E.; Barat, E.; Horvath, I.

Year: 2003

Title: [Exhaled Breath Condensate and its analysis--a new method in pulmonology]

Journal: Orv Hetil

Volume: 144

Issue: 51

Pages: 2517-24

Date: Dec 21

Accession Number: 14974158

Keywords: Asthma/diagnosis/metabolism

Biological Markers/analysis

Breath Tests/\*methods

Bronchiectasis/diagnosis/metabolism

Cystic Fibrosis/diagnosis/metabolism

English Abstract

F2-Isoprostanes/analysis

Human

Hydrogen Peroxide/analysis

Oxidative Stress

Pulmonary Disease, Chronic Obstructive/diagnosis/metabolism

Respiratory Distress Syndrome, Adult/diagnosis/metabolism

Respiratory Tract Diseases/\*diagnosis/\*metabolism

Smoking/metabolism

**Abstract:** In the middle of the nineties a new, non-invasive method for investigation of the lung aroused the interest of many researchers: the exhaled breath condensate. It shows the extent of the interest that in the last five years more than 80 original articles have been published in this theme. Many substances are found in the expired breath which are detectable in the liquid that we obtain by cooling (= condensing) the exhaled breath. The advantages of this method are that it is non-invasive, convenient, it could be performed with mechanically ventilated patients as well as with children. The most studied substance is the hydrogen-peroxide, which is the marker of oxidative stress, and its level in condensate is elevated in numerous inflammatory diseases. 8-isoprostane was also studied a lot, which is another marker of oxidative stress. Numerous substances could be even measured in condensate, so the decay-product of nitric-oxide (nitrite, nitrate, nitrotyrosine), further nitrosothiol, adenosine, ammonia, different ions, leukotrienes, cytokines; recently even other feature of condensate is examined, such as its pH. The different mediators could help us to know better the diseases, support the diagnosis, follow the treatment or the disease. In this

study the authors attempt to present the most important knowledge till now.

Notes: 0030-6002

Journal Article

Review

Review, Tutorial

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=14974158](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14974158)

Author Address: Orszagos Koranyi Tbc es Pulmonologiai Intezet, Korelettani Osztaly, Budapest. vassgeza@koranyi.hu

Reference Type: Journal Article

Record Number: 280

Author: Wilhelm, J.; Vankova, M.; Maxova, H.; Siskova, A.

Year: 2003

Title: Hydrogen peroxide production by alveolar macrophages is increased and its concentration is elevated in the breath of rats exposed to hypoxia: relationship to lung lipid peroxidation

Journal: *Physiol Res*

Volume: 52

Issue: 3

Pages: 327-32

Accession Number: 12790764

Abstract: Hypoxic exposure triggers a generation of reactive oxygen species that initiate free radical damage to the lung. Hydrogen peroxide is the product of alveolar macrophages detectable in the expired breath. We evaluated the significance of breath H<sub>2</sub>O<sub>2</sub> concentration for the assessment of lung damage after hypoxic exposure and during posthypoxic period. Adult male rats were exposed to normobaric hypoxia (10 % O<sub>2</sub>) for 3 hours or 5 days. Immediately after the hypoxic exposure and then after 7 days or 14 days of air breathing, H<sub>2</sub>O<sub>2</sub> was determined in the breath condensate and in isolated lung macrophages. Lipid peroxidation was measured in lung homogenates. Three-hour hypoxia did not cause immediate increase in the breath H<sub>2</sub>O<sub>2</sub>; 5-day hypoxia increased breath H<sub>2</sub>O<sub>2</sub> level to 458 %. After 7 days of subsequent air breathing H<sub>2</sub>O<sub>2</sub> was elevated in both groups exposed to hypoxia. Increased production of H<sub>2</sub>O<sub>2</sub> by macrophages was observed after 5 days of hypoxia and during the 7 days of subsequent air breathing. Lipid peroxidation increased in the periods of enhanced H<sub>2</sub>O<sub>2</sub> generation by macrophages. As the major increase (1040 %) in the breath H<sub>2</sub>O<sub>2</sub> concentration found 7 days after 3 hours of hypoxia was not accompanied by lipid peroxidation, it can be concluded that the breath H<sub>2</sub>O<sub>2</sub> is not a reliable indicator of lung oxidative damage.

Notes: 0862-8408

Journal Article

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=12790764](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12790764)

Author Address: Department of Medical Chemistry and Biochemistry, Second Faculty of Medicine, Charles University, Prague, Czech Republic. jiri.wilhelm@lfmotol.cuni.cz

Reference Type: Journal Article

Record Number: 328

Author: Deaton, C. M.; Marlin, D. J.; Smith, N. C.; Smith, K. C.; Newton, R. J.; Gower, S. M.; Cade, S. M.; Roberts, C. A.; Harris, P. A.; Schroter, R. C.; Kelly, F. J.

Year: 2004

Title: Breath condensate hydrogen peroxide correlates with both airway cytology and epithelial lining fluid ascorbic acid concentration in the horse

Journal: *Free Radic Res*

Volume: 38

Issue: 2

Pages: 201-8

Date: Feb

Accession Number: 15104214

Abstract: The relationship between hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) concentration in expired breath condensate (EBC) and cytology of the respiratory tract obtained from tracheal wash (TW) or bronchoalveolar lavage (BAL), and epithelial lining fluid (ELF) antioxidant status is unknown. To examine this we analysed the concentration of H<sub>2</sub>O<sub>2</sub> in breath condensate from healthy horses and horses affected by recurrent airway obstruction (RAO), a condition considered to be an animal model of human asthma. The degree of airway inflammation was determined by assessing TW inflammation as mucus, cell density and neutrophil scores, and by BAL cytology. ELF antioxidant status was determined by measurement of ascorbic acid, dehydroascorbate, reduced and

oxidised glutathione, uric acid and alpha-tocopherol concentrations. RAO-affected horses with marked airway inflammation had significantly higher concentrations of breath condensate H<sub>2</sub>O<sub>2</sub> than control horses and RAO-affected horses in the absence of inflammation (2.0 +/- 0.5 micromol/l, 0.4 +/- 0.2 micromol/l and 0.9 +/- 0.2 micromol/l H<sub>2</sub>O<sub>2</sub>, respectively;  $p < 0.0001$ ). The concentration of breath condensate H<sub>2</sub>O<sub>2</sub> was related inversely to the concentration of ascorbic acid in ELF ( $r = -0.80$ ;  $p < 0.0001$ ) and correlated positively with TW inflammation score ( $r = 0.76$ ,  $p < 0.0001$ ) and BAL neutrophil count ( $r = 0.80$ ,  $p < 0.0001$ ). We conclude that the concentration of H<sub>2</sub>O<sub>2</sub> in breath condensate influences the ELF ascorbic acid concentration and provides a non-invasive diagnostic indicator of the severity of neutrophilic airway inflammation.

Notes: 1071-5762

Journal Article

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=15104214](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15104214)

Author Address: Centre for Equine Studies, Animal Health Trust, Lanwades Park, Kentford, Suffolk CB8 7UU, UK.

chris.deaton@aht.org.uk

Reference Type: Journal Article

Record Number: 359

Author: Majewska, E.; Kasielski, M.; Luczynski, R.; Bartosz, G.; Bialasiewicz, P.; Nowak, D.

Year: 2004

Title: Elevated exhalation of hydrogen peroxide and thiobarbituric acid reactive substances in patients with community acquired pneumonia

Journal: Respir

Med Volume: 98

Issue: 7

Pages: 669-76

Date: Jul

Accession Number: 15250234

Keywords: Adult

Aged

Biological Markers/analysis

Breath Tests/methods

C-Reactive Protein/metabolism

Community-Acquired Infections/metabolism

Female

Human

Hydrogen Peroxide/\*metabolism

Male

Middle Aged

Oxidative Stress

Pneumonia, Bacterial/drug therapy/\*metabolism

Support, Non-U.S. Gov't

Thiobarbituric Acid Reactive Substances/\*metabolism

Abstract: BACKGROUND: Bacterial pneumonia involves influx of activated phagocytes into distal airways. These cells release oxidants including H<sub>2</sub>O<sub>2</sub>, that may be exhaled or induce peroxidative damage to lung tissues with formation of thiobarbituric reactive substances (TBARs). STUDY OBJECTIVES: To determine whether concentrations of H<sub>2</sub>O<sub>2</sub> and TBARs in Exhaled Breath Condensate (EBC) is elevated and correlate with systemic response to pneumonia during 10 days of hospital treatment. DESIGN: The concentration of H<sub>2</sub>O<sub>2</sub> and TBARs was measured in EBC of 43 inpatients with community acquired pneumonia (CAP) and 20 healthy never smoked subjects over 10 days and were accompanied by monitoring of WBC count, serum concentration of C-reactive protein (CRP) and peroxy radical-trapping capacity. RESULTS: Patients with CAP exhaled 4.6-, 3.7-, 3.9-, 3.3-times more H<sub>2</sub>O<sub>2</sub> than healthy controls at 1st, 3rd, 5th and 10th day of treatment ( $P < 0.05$ ), respectively. EBC concentrations of TBARs were elevated at 1st and 3rd day. H<sub>2</sub>O<sub>2</sub> and TBARs levels decreased along with treatment course. Correlation ( $P < 0.05$ ) was found between H<sub>2</sub>O<sub>2</sub> levels and CRP and WBC count ( $r = 0.31$ ) at 1st day and between TBARs and CRP at 5th ( $r = 0.34$ ) and 10th day ( $r = 0.46$ ). The mean H<sub>2</sub>O<sub>2</sub> exhalation estimated over ten days of treatment correlated with pneumonic chest X-ray score ( $r = 0.42$ ), CRP levels ( $r = 0.46$ ) and WBC count ( $r = 0.33$ ) at admission ( $P < 0.05$ ). CONCLUSIONS: Pneumonia is accompanied by oxidative stress in airways that moderately correlates with intensity of systemic inflammatory response. Determination of H<sub>2</sub>O<sub>2</sub> in EBC may be helpful for non-invasive monitoring of oxidants production during lower respiratory tract infection.

Notes: 0954-6111

## Journal Article

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=15250234](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15250234)

Author Address: Department of Experimental and Clinical Physiology, Institute of Physiology and Biochemistry, Medical University of Lodz, Mazowiecka St. 6/8, 92-215 Lodz, Poland.

Reference Type: Journal Article

Record Number: 296

Author: Moloney, E. D.; Mumby, S. E.; Gajdocsi, R.; Cranshaw, J. H.; Kharitonov, S. A.; Quinlan, G. J.; Griffiths, M. J.

Year: 2004

Title: Exhaled Breath Condensate detects markers of pulmonary inflammation after cardiothoracic surgery

Journal: Am J Respir Crit Care Med

Volume: 169

Issue: 1

Pages: 64-9

Date: Jan 1

Accession Number: 14551168

Abstract: Cardiac surgery using cardiopulmonary by-pass and, to a greater extent, lung resection, causes acute lung injury that is usually subclinical. Analysis of mediators in Exhaled Breath Condensate is a promising means of monitoring inflammation in a variety of airway diseases but the contribution of the airway lining fluid from the lower respiratory tract is uncertain. We compared the analysis of markers of lung injury in Exhaled Breath Condensate and bronchoalveolar lavage in endotracheally intubated patients before and after coronary artery bypass graft surgery with cardiopulmonary bypass and lobectomy. The neutrophil count and leukotriene B4 concentration in bronchoalveolar lavage fluid rose after coronary artery bypass graft surgery ( $p < 0.05$ ), but there was no significant change in leukotriene B4, hydrogen peroxide, or hydrogen ion concentrations in Exhaled Breath Condensate. By contrast, after lobectomy, the concentration in Exhaled Breath Condensate of leukotriene B4, hydrogen peroxide and hydrogen ions rose significantly ( $p < 0.05$ ). Exhaled breath condensate is a safe, noninvasive method of sampling the milieu of the distal lung and is sufficiently sensitive to detect markers of inflammation and oxidative stress in patients after lobectomy, but not after the milder insult associated with cardiac surgery.

Notes: 1073-449x

Journal Article

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=14551168](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14551168)

Author Address: M.R.C.P., Adult Intensive Care Unit, Royal Brompton Hospital, Sydney Street, London SW3 6NP UK. m.griffiths@imperial.ac.uk

Reference Type: Journal Article

Record Number: 295

Author: Rysz, J.; Kasielski, M.; Apanasiewicz, J.; Krol, M.; Woznicki, A.; Luciak, M.; Nowak, D.

Year: 2004

Title: Increased hydrogen peroxide in the exhaled breath of uraemic patients unaffected by haemodialysis

Journal: Nephrol Dial Transplant

Volume: 19

Issue: 1

Pages: 158-163

Date: Jan

Accession Number: 14671051

Abstract: BACKGROUND: Uraemia is accompanied by conditions favouring the rise of H<sub>2</sub>O<sub>2</sub> activity in body fluids. This results from the increased release of H<sub>2</sub>O<sub>2</sub> by polymorphonuclear leukocytes and decreased plasma glutathione peroxidase activity. The purpose of this study was to determine if patients on chronic haemodialysis (HD) exhale more H<sub>2</sub>O<sub>2</sub> than healthy individuals, and if dialysis affects breath H<sub>2</sub>O<sub>2</sub> content. METHODS: We studied 29 chronic HD patients (mean age 49 +/- 11 years) and 40 healthy persons (mean age 44 +/- 9 years). H<sub>2</sub>O<sub>2</sub>, which is volatile, was measured fluorimetrically with the homovanillic acid method in the exhaled breath condensate (EBC) of the study cohort. EBC was collected immediately before and after the HD session and also at 20 and 60 min of HD treatment (n = 14) and once in controls. Peak expiratory flow (PEF), white blood cell (WBC) count, PaO<sub>2</sub> and circulatory cyclic guanosine monophosphate (cGMP), IL-6 and IL-8 concentrations were measured concomitantly. Finally, H<sub>2</sub>O<sub>2</sub> diffusion through the dialyser cuprophane membrane was determined in an in vitro experiment. RESULTS: At baseline, EBC H<sub>2</sub>O<sub>2</sub> concentration was 22 times higher in HD patients than in controls (2.92 +/- 4.64 vs 0.16 +/- 0.13 micro M, P < 0.001). Although the maximum decrease in PEF (431 +/- 52 vs 398 +/- 56 l/min, P < 0.01) and WBC count (6.72 +/- 1.02 vs 3.82

+/- 1.51 x 10<sup>3</sup>/micro I, P < 0.01) occurred at 20 min after the start of HD, no significant changes in breath H<sub>2</sub>O<sub>2</sub> levels were noted throughout the session. Plasma IL-6 and IL-8 levels remained unchanged whereas cGMP rose 1.3 times at 60 min (P < 0.01). In vitro, H<sub>2</sub>O<sub>2</sub> rapidly diffused through the cuprophane membrane. CONCLUSION: Chronic HD patients exhale more H<sub>2</sub>O<sub>2</sub> than healthy subjects. Although no change of breath H<sub>2</sub>O<sub>2</sub> concentration was observed during HD, as H<sub>2</sub>O<sub>2</sub> easily diffuses through the dialyser membrane, it is not possible to rule out that HD stimulates H<sub>2</sub>O<sub>2</sub> generation.

Notes: 0931-0509

Journal article

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=14671051](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14671051)

Author Address: Department of Internal Medicine and Dialysotherapy Medical University of Lodz, Lodz, Practical Clinical Training Centre, Medical University of Lodz, Lodz and Department of Experimental and Clinical Physiology, Institute of Physiology and Biochemistry, Medical University of Lodz, Lodz, Poland.

Reference Type: Journal Article

Record Number: 354

Author: Svensson, S.; Olin, A. C.; Larstad, M.; Ljungkvist, G.; Toren, K.

Year: 2004

Title: Determination of hydrogen peroxide in Exhaled Breath Condensate by flow injection analysis with fluorescence detection

Journal: J Chromatogr B Analyt Technol Biomed Life Sci

Volume: 809

Issue: 2

Pages: 199-203

Date: Oct 5

Accession Number: 15315765

Abstract: A method for the determination of hydrogen peroxide in exhaled breath condensate (EBC) by automated flow injection analysis (FIA) with fluorescence detection was developed and validated. In the enzymatic assay a fluorescent dimer of para-hydroxyphenyl acetic acid (HPAA) was formed by the redox coupling reaction between hydrogen peroxide and horseradish peroxidase (HRP). The calibration curve of hydrogen peroxide was linear over a range of 40-5000nM. The coefficient of variation (CV) for within-day precision was 1-3%; for between-day precision, it was 2-5% over the validated range. The assay requires a small sample aliquot (150microl) and no incubation time, and has an analytical runtime of <2min. It is therefore suitable for larger studies. The method was used to detect hydrogen peroxide in EBC of asthmatic patients and healthy volunteers. A statistically significant difference was found between patients with asthma (n = 19) and control subjects without asthma (n = 19), 780nM versus 480nM (P = 0.03).

Notes: 1570-0232

Journal Article

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=15315765](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15315765)

Author Address: Occupational and Environmental Medicine, Sahlgrenska University Hospital and Academy at Goteborg University, Sankt Sigfridsgatan 85, SE-41266 Goteborg, Sweden.

Reference Type: Journal Article

Record Number: 368

Author: Szkudlarek, U.; Zdziechowski, A.; Witkowski, K.; Kasielski, M.; Luczynska, M.; Luczynski, R.; Sarniak, A.; Nowak, D.

Year: 2004

Title: Effect of inhaled N-acetylcysteine on hydrogen peroxide exhalation in healthy subjects

Journal: Pulm Pharmacol Ther

Volume: 17

Issue: 3

Pages: 155-62

Accession Number: 15123225

Keywords: Acetylcysteine/administration & dosage/\*pharmacology

Administration, Inhalation

Adult

Antioxidants/administration & dosage/\*pharmacology

Breath Tests

Exhalation

Female

Human  
Hydrogen Peroxide/\*metabolism  
Male

Support, Non-U.S. Gov't

Abstract: N-acetylcysteine (NAC) has antioxidant properties and its oral administration decreased H<sub>2</sub>O<sub>2</sub> exhalation in patients with chronic obstructive pulmonary disease. In this study we tested whether inhaled NAC could suppress H<sub>2</sub>O<sub>2</sub> levels in Exhaled Breath Condensate (EBC) of eight healthy subjects that have never smoked (never-smokers). Original NAC solution (ACC vial, 300 mg NAC in 3 ml solvent), NAC-placebo (vehicle), sterile 0.9% NaCl or distilled water were nebulized via the pneumatic De Vilbiss nebulizer once daily every 7 days and H<sub>2</sub>O<sub>2</sub> and thiols exhalation was measured just before, 30 min and 3 h after the end of drug administration. Additional in vitro experiments were performed to evaluate NAC stability during nebulization, reactivity with H<sub>2</sub>O<sub>2</sub> and possible H<sub>2</sub>O<sub>2</sub> generation in aqueous NAC solutions. NAC almost completely abolished H<sub>2</sub>O<sub>2</sub> exhalation 30 min after inhalation (0.02±0.04 vs. 0.21±0.09 microM, p<0.001). However, 3 h later the H<sub>2</sub>O<sub>2</sub> levels raised 1.8-fold from baseline (p<0.01). Other inhaled solutions did not affect H<sub>2</sub>O<sub>2</sub> levels. Mean thiol concentration in EBC rose (p<0.05) after treatment with NAC and reached 1.03±0.48 microM at 3 h. Although, 25 and 50 mM NAC completely inhibited H<sub>2</sub>O<sub>2</sub>-peroxidase-luminol-dependent chemiluminescence, detectable amounts of H<sub>2</sub>O<sub>2</sub> were generated in NAC solutions. It was accompanied by moderate loss of -SH groups. Catalase and ascorbic acid prevented H<sub>2</sub>O<sub>2</sub> formation in NAC solutions. In conclusion inhaled NAC revealed biphasic effect on H<sub>2</sub>O<sub>2</sub> exhalation in healthy subjects, which depends on direct H<sub>2</sub>O<sub>2</sub> scavenging and H<sub>2</sub>O<sub>2</sub> generation related to drug oxidation. The net result of these processes may determine anti- or pro-oxidant action of inhaled NAC.

Notes: 1094-5539

Clinical Trial

Journal Article

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=15123225](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15123225)

Author Address: Department of Experimental and Clinical Physiology, Institute of Physiology and Biochemistry, Medical University of Lodz, Mazowiecka 6/8, 92-215 Lodz, Poland.

Reference Type: Journal Article

Record Number: 334

Author: Van Hoydonck, P. G.; Wuyts, W. A.; Vanaudenaerde, B. M.; Schouten, E. G.; Dupont, L. J.; Temme, E. H.

Year: 2004

Title: Quantitative analysis of 8-isoprostane and hydrogen peroxide in exhaled breath condensate

Journal: Eur Respir J

Volume: 23

Issue: 2

Pages: 189-92

Date: Feb

Accession Number: 14979489

Abstract: Exhaled Breath Condensate (EBC) provides a noninvasive means of sampling the lower respiratory tract. Collection of EBC might be useful in the assessment of airway oxidative stress in smokers. The aim of this study was to determine 8-isoprostane and hydrogen peroxide levels in EBC, and, in addition, to investigate the reproducibility of these measurements. EBC samples were collected from 12 healthy male smokers at three time points within 1 week. 8-isoprostane and H<sub>2</sub>O<sub>2</sub> were measured in nonconcentrated EBC using immunochemical and colorimetric assays, respectively. 8-isoprostane and H<sub>2</sub>O<sub>2</sub> were detected in only 36 and 47% of all EBC samples, respectively. It was not possible to calculate the within-subject variation in a reliable manner since only three of the 12 smokers exhibited detectable 8-isoprostane concentrations on all three occasions (mean 4.6 pg x mL<sup>-1</sup>; range 3.9-7.7 pg x mL<sup>-1</sup>), whereas H<sub>2</sub>O<sub>2</sub> could not be detected on all three occasions in any of the smokers. Spiking experiments revealed a recovery of 83.5-109.5% for 8-isoprostane and 69.9-129.0%, for H<sub>2</sub>O<sub>2</sub> in fresh EBC samples. It was concluded that levels of 8-isoprostane and hydrogen peroxide cannot be reproducibly assessed in Exhaled Breath Condensate from healthy smokers because of their low concentration and/or the lack of sensitivity of the available assays.

Notes: 0903-1936

Journal Article

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=14979489](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14979489)

Author Address: Dept of Public Health, Division of Nutritional Epidemiology, Catholic University of Leuven, Leuven, Belgium.

Reference Type: Journal Article

Record Number: 367

Author: Weissmann, N.; Vogels, H.; Schermuly, R. T.; Ghofrani, H. A.; Hanze, J.; Fink, L.; Rose, F.; Seeger, W.; Grimminger, F.

Year: 2004

Title: Measurement of exhaled hydrogen peroxide from rabbit lungs

Journal: Biol Chem

Volume: 385

Issue: 3-4

Pages: 259-64

Date: Mar-Apr

Accession Number: 15134339

Keywords: Animals

Comparative Study

Exhalation/\*physiology

Female

Hydrogen Peroxide/analysis/\*metabolism

Intubation, Intratracheal/methods

Lung/chemistry/\*metabolism

Male

Pulmonary Ventilation/physiology

Rabbits

Support, Non-U.S. Gov't

Abstract: Exhaled H<sub>2</sub>O<sub>2</sub> is considered an indicator of lung inflammatory and oxidative stress. Moreover, H<sub>2</sub>O<sub>2</sub> may be involved in signal transduction processes. It is not fully elucidated to what extent (i) H<sub>2</sub>O<sub>2</sub> escapes from the intravascular compartment, and (ii) pulmonary H<sub>2</sub>O<sub>2</sub> generation and nasopharyngeal H<sub>2</sub>O<sub>2</sub> generation contribute to exhaled H<sub>2</sub>O<sub>2</sub>. We investigated H<sub>2</sub>O<sub>2</sub> concentrations in breath condensate from isolated buffer-perfused and ventilated rabbit lungs, and from both intubated and spontaneously breathing rabbits with a horseradish peroxidase/2',7'-dichlorofluorescein assay. For the perfused lungs, a H<sub>2</sub>O<sub>2</sub> concentration of 58 +/- 19 nM was found. Addition of H<sub>2</sub>O<sub>2</sub> to the buffer fluid resulted in only minute appearance in the exhaled air (<0.001%). Levels of exhaled H<sub>2</sub>O<sub>2</sub> in intubated rabbits and perfused lungs were virtually identical. Nearly ten-fold higher levels were detected in spontaneously breathing rabbits. Decreasing the inspired oxygen concentration from 21% to 1% resulted in a tendency toward decreased H<sub>2</sub>O<sub>2</sub> exhalation in perfused lungs. In contrast, phorbol-12-myristate-13-acetate (PMA) prompted a approximately 4-fold increase in H<sub>2</sub>O<sub>2</sub> exhalation. We conclude that the horseradish peroxidase/2',7'-dichlorofluorescein assay is a feasible technique to measure H<sub>2</sub>O<sub>2</sub> in Exhaled Breath Condensate in rabbits. When collecting exhaled air via the tracheal tube, the signal represents pulmonary H<sub>2</sub>O<sub>2</sub> generation with the contribution of the remaining body being negligible.

Notes: 1431-6730

Journal Article

URL: [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=15134339](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15134339)

Author Address: Department of Internal Medicine, Justus-Liebig-University Giessen, Klinikstrasse 36, D-35392 Giessen, Germany.

Norbert.Weissmann@innere.med.uni-giessen.de