Figure 1 Dependency of the post-test probability of axial spondyloarthritis (SpA) on the resulting likelihood ratio (LR) product for an assumed pretest probability of 5% (according to Underwood and Dawes²). This probability curve is meant to be applied in patients with chronic back pain suspected to have axial SpA.

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Examining the exhaled levels of hydrogen peroxide in rheumatoid arthritis: a pilot study

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Previous studies have assessed airway inflammation in rheumatoid arthritis by using bronchoalveolar lavage (BAL).^{1,2} To widen the scope of the study, a biomarker that is less invasive and less expensive is necessary. Recent studies have shown that exhaled breath condensate (EBC), a measure that is minimally invasive and substantially less expensive than BAL, can be used to assess inflammation in the lower respiratory tract.^{3,4} To assess the utility of this measure, we compared the levels of EBC hydrogen peroxide (H₂O₂) in patients with rheumatoid arthritis with values in controls.

Patients with rheumatoid arthritis (n = 22) meeting the disease classification criteria⁵ and controls (n = 23) were studied. As smoking influences EBC measures of inflammation,⁶ we assessed smoking status (current smoker v non-smoker), excluding subjects self-reporting a diagnosis of chronic lung disease or those taking inhaled drugs indicative of such a diagnosis.

Specimens were collected by using EcoScreen (Erich Jaeger, Hoechberg, Germany), which uses a portable unit

that freezes exhaled air and permits the participants to breathe normally from room air. Levels of H₂O₂ were measured by using an assay with a 0.1 µM/ml detection threshold, a measure based on the H₂O₂-dependent oxidation of homovanillic acid to a highly fluorescent dimmer.⁷ Group comparisons of H₂O₂ values were carried out using analysis of variation, adjusting for age. Levels of H₂O₂ in all patients with rheumatoid arthritis were compared with those in all controls, subsequently stratifying analyses by smoking status. H₂O₂ values falling below the assay sensitivity were given the default value of 0.1 µmol/ml.

Table 1 shows the characteristics of patients with rheumatoid arthritis (n = 22) and controls (n = 23). Patients with rheumatoid arthritis had higher levels of EBC H₂O₂ (0.302 µmol/ml (standard deviation (SD) 0.202) v 0.202 µmol/ml (SD 0.159); p = 0.05) than controls. Differences in levels of exhaled H₂O₂ were most pronounced

Abbreviations: BAL, bronchoalveolar lavage; EBC, exhaled breath condensate; H₂O₂, hydrogen peroxide

Table 1 Characteristics of patients with rheumatoid arthritis (n = 22) and controls (n = 23)

Patient characteristics*	Patients with RA	Controls
Age (years), mean (SD)	57.8 (11.9)	48.2 (13.1)
Female sex	16 (73)	17 (74)
Caucasian race or ethnicity	20 (91)	18 (86)
Current smoker	10 (45)	8 (35)
RF positive	13 (87)	—
DMARD use	22 (100)	—
Methotrexate	16 (73)	—
Etanercept	3 (14)	—
Hydroxychloroquine	15 (68)	—
Sulfasalazine	8 (36)	—
Minocycline	8 (36)	—
Other	3 (14)	—
NSAID use	13 (59)	—
Prednisone use	15 (68)	—

*DMARD, disease-modifying antirheumatic drug; —, not measured in the healthy controls; NSAID, non-steroidal anti-inflammatory drug; RA, rheumatoid arthritis; RF, rheumatoid factor.

Values are expressed as n (%), unless otherwise indicated.

Race or ethnicity data are missing for two controls. RF status is unknown for seven patients with rheumatoid arthritis.

Figure 1 Values of exhaled hydrogen peroxide (H₂O₂) (μmol/ml) are shown for non-smoking controls (n = 15) and patients with rheumatoid arthritis (RA; n = 12). Bars show mean H₂O₂ values.

among non-smokers (fig 1). Non-smokers with rheumatoid arthritis had substantially higher values of exhaled H₂O₂ (0.291 μmol/ml (SD 0.107) v 0.149 μmol/ml (SD 0.123); p = 0.001) than controls. By contrast, there was no demonstrable difference in exhaled H₂O₂ when comparing smokers with rheumatoid arthritis with control smokers (0.314 μmol/ml (SD 0.287) v 0.301 μmol/ml (SD 0.180); p = 0.73).

In this pilot study, patients with rheumatoid arthritis had increased levels of exhaled H₂O₂ compared with controls, suggesting that EBC H₂O₂ is a potentially useful biomarker. Results from this study must be interpreted with caution. Several unmeasured factors may have contributed to the increased levels of H₂O₂. For instance, it is possible that methotrexate, a known pulmonary toxin, may confound the association of rheumatoid arthritis with increased EBC H₂O₂. In the absence of other measures of pulmonary status (ie, radiographs, spirometry), it is possible that subjects were misclassified in terms of airways disease, important because chronic lung disease affects H₂O₂ values.

In addition to controlling for possible circadian changes in expression of H₂O₂,⁸ future studies will need to incorporate methods aimed at more precisely exploring the relationship of EBC levels of H₂O₂ with measures of disease activity (ie, joint counts and acute-phase reactants), the evolution of

extra-articular disease features (ie, interstitial lung disease) and the use of disease-modifying treatments.

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