Sputum autoantibodies in patients with established rheumatoid arthritis and subjects at risk of future clinically apparent disease.

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**Abstract**

**OBJECTIVE:** To evaluate the generation of rheumatoid arthritis (RA)-related autoantibodies in the lung.

**METHODS:** Simultaneous collection of serum and induced sputum was performed in 21 healthy controls, 49 at-risk subjects without inflammatory arthritis but at risk of RA due to family history or seropositivity for anti-citrullinated protein antibodies, and 14 subjects with early RA. Samples were tested for anti-cyclic citrullinated peptide 2 (anti-CCP2), anti-CCP3, anti-CCP3.1, rheumatoid factor isotypes IgM, IgG, and IgA, and total IgM, IgG, and IgA.

**RESULTS:** One or more autoantibodies were present in sputum of 39% of at-risk seronegative subjects, 65% of at-risk seropositive subjects, and 86% of subjects with early RA. In at-risk seronegative subjects, the rate of anti-CCP3.1 positivity and the median number of autoantibodies were elevated in sputum versus serum. In subjects with early RA, the rate of positivity for several individual autoantibodies and the median number of autoantibodies were higher in serum than in sputum. Results in at-risk seropositive subjects were intermediate between these groups. In at-risk subjects with autoantibody positivity in sputum, the ratios of autoantibody to total Ig were higher in sputum than in serum, suggesting that these autoantibodies are generated or sequestered in the lung.

**CONCLUSION:** RA-related autoantibodies are detectable in sputum in subjects at risk of RA and in subjects with early RA. In a subset of at-risk subjects, the presence of sputum autoantibodies in the absence of seropositivity, and the increased autoantibody-to-total Ig ratios in sputum, suggest that the lung may be a site of autoantibody generation in the early development of RA. These findings suggest an important role of the lung in the pathogenesis of RA.

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