Material and methods This study comprised 406 individuals, with 717 samples, who were identified before onset of symptoms of RA (median 7.4 years IQR 3.3–12.6 years), as donors to the Medical Biobank of Northern Sweden. 204 of them were also sampled at the time of diagnose, and have been analysed together with 1305 population controls from the Medical Biobank for concentrations of antibodies towards thirteen different citrullinated peptides in plasma; fibrinogen 36–50, fibrinogen 72, fibrinogen 74, fibrinogen α 36–50, fibrinogen α 621–635, fibrinogen β 60–74, fibrinogen 573, fibrinogen 591, α-enolase 1, collagen Type II C1 arginine and citrulline and U1, CCP-1, vimentin 2–17, vimentin 60–75 using the microarray based ImmunoCAP ISAC system (Phadia Diagnostics, Uppsala, Sweden). All samples were also analysed for anti-CCP2 antibodies with ELISA (Euro-Diagnostics). Cutoff levels were set with 98% specificity.

Results The three antibodies with highest sensitivity for predicting RA was anti-CCP2 (33.8%), fibrinogen 36–52 (24.3%) and α enolase 1 (24.1%) counting ever being positive in all prepatient samples. On individual and group level, the concentrations of the citrullinated antibodies increased significantly the closer to onset of symptoms the samples were collected. The number of positive samples also increased the closer to disease onset. The predating time for the antibodies to appear (with concentrations above cut-off) varied significantly between them.

Conclusion Citrullinated antibodies and antibodies against native collagen appeared many years before onset of symptoms and at different time points. The concentrations increased gradually with few exceptions until onset of symptoms and there was an epitope spreading. Citrullination was an important preceding process for disease development maybe initiated by an earlier non-citrullinated antibody stimulation.

9 ANTIBODIES AGAINST NATIVE COLLAGEN AND CITRULLINATED PROTEINS PRECEDE THE DEVELOPMENT OF RHEUMATOID ARTHRITIS WITH A CONSECUTIVE PATTERN

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10.1136/annrheumdis-2011-201231.9

Background and objective Presence of antibodies against cyclic citrullinated peptides (anti-CCP2) has been demonstrated to precede the development of rheumatoid arthritis (RA) by several years. The RR for developing subsequent RA was increased by the combination of HLA- shared epitopes (SE) and also presence of PTPN22 T variant. The underlying process of why RA-patients develop antibodies against certain citrullinated peptides is largely unknown and here the authors have investigated antibody concentration against thirteen citrullinated proteins, besides anti-CCP2, to elucidate their predictive value in the prepatient phase of RA together with information about HLA-SE, and cigarette smoking.

Ann Rheum Dis: first published as 10.1136/annrheumdis-2011-201231.9 on 22 February 2012. Downloaded from http://ard.bmj.com/ on April 20, 2024 by guest. Protected by copyright.