vitro stimulation of EC with CSE results in neo-angiogenesis ($p<0.01$) and induces disassembly of EC F-actin cytoskeleton where filopodia protrusion and membrane ruffling occur with increasing CSE. In vitro exposure of RA synovial explants and PBMCs to 1–10% CSE had no effect on cytokine secretion. No effect was observed on EC proliferation.

Conclusion Our results suggest that smoking interferes with normal vascular function and induces monocyte chemotaxis which together may conspire to prompt egress of immune cells to the synovium in RA and PsA and so result in synovitis. These findings may explain the gene environment interaction between smoking and the shared epitope that results in RA and may explain why smokers have more persistent disease than non-smokers.

A23 SMOKING INTERFERES WITH THERAPY OF RA AND PSA, INDUCES CHEMOTAXIS AND IMPAIRS VASCULAR FUNCTION IN RA

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10.1136/ard.2010.149096.23

Background Smoking tobacco confers a >40 RR of developing rheumatoid arthritis (RA). We investigated the clinical effect of cigarette's in vivo on the therapy of RA and psoriatic arthritis (PsA) and on the function of the vascular and immune compartments both in vivo in active RA/PsA patients and in vitro.

Materials and methods A prospective longitudinal database of RA/PsA anti TNFα treated patients was compiled (n=708). Patients with inflammatory arthritis (RA/PsA) were grouped as ever smokers (n=435, current and ex-smokers) and never smokers (n=273). Synovial tissue biopsies, synovial fluid and peripheral blood mononuclear cells (PBMCs) were obtained from patients with active RA/PsA at arthroscopy (n=19). Clinical measures of disease activity were obtained and serum cytokine profiles (Ang2, IL1β, IFNγ, TNFα, IL6, MIP1α) were quantified by multiarray and specific ELISA. Whole tissue synovial explants, PBMCs and endothelial cells (EC) were exposed to range 1–10% cigarette smoke extract (CSE) for 24hrs. Cell proliferation was assessed by a crystal violet assay. EC tube formation was assessed using matrigel angiogenic assays. Cytoskeletal rearrangement was assessed using immunofluorescent staining for filamentous actin (F-actin). Monocyte migration was assessed using an invasion and migration assay.

Results 60% of patients in our database are ever smokers (63% in subanalysis). Ever smokers have a 1.5 RR of failing at least one anti TNFα and DMARD agent compared to never smokers. Current smokers have on average 1 more swollen and tender joint at 12 months compared to never smokers. Ever smokers have higher serum levels of MIP1α ($p<0.05$, $r=.586$) in vivo and CSE induces monocyte migration in vitro in a dose dependent manner. Ever smokers express less Ang 2 in their serum ($p<0.05$, $r= -0.414$) and synovial fluid. In