increasing RF titre with pack years smoked.[7] Yet although the development of rheumatoid joint erosions, nodules, and disability was significantly increased by cigarette smoking, he found that this was independent of RF production.

We suspect that cigarette smoking and RF are strongly interlinked, but other mechanisms, as suggested by Masi, may also be at work. For example, cigarette smoke contains numerous oxidising agents that can inactivate α_1-proteinase inhibitor (α_1-PI),[8] the natural inhibitor of neutrophil elastase (NE), a serine proteinase that can degrade articular cartilage.[9] Cigarette smoke can also prime neutrophils to degranulate and discharge NE,[10] activate macrophages to produce matrix metalloproteinases,[11] up regulate production of interleukin 1β and interleukin 8[12] and down regulate interleukin 1 receptor antagonist,[13] and interleukin 10.[14] Furthermore, cigarette smoking induces disease processes in a specific dose dependent fashion (independent of current smoking status), such as pulmonary emphysema, in which there is increased neutrophil priming, increased oxidised α_1-PI and α_1-PI-NE complexes (indicative of increased NE activity).[8] Therefore a heavy smoker may have an otherwise benign short lived inflammatory arthritis modified by the mechanisms outlined above and develop RA.

Whether RA increases or decreases cigarette consumption remains uncertain. Our controls had a pack year total estimated at entry to the study and not at the time of their disease onset. We are, however, unaware of any data to suggest that RA increases cigarette consumption. Indeed, a study by Harrison *et al* observed that 18% of all smokers with polyarthritis stopped smoking within three years of disease onset as opposed to <1% of non-smoking patients who started smoking during this period.[15]

Other important questions remain unanswered. For example, does increased cumulative cigarette consumption increase RA susceptibility independently of RF production? (Data presented here by Masi *et al* only consider cigarette consumption at one time point.) If so, do these subjects have an increased prevalence of circulating levels of α_1-PI-NE complexes, high levels of oxidised and inactivated α_1-PI complexes, and therefore pulmonary emphysema?

We welcome the heightened interest in the relationship between smoking and RA and look forward to the establishment of new studies designed to answer some of the interesting questions raised by recent studies.

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Rheumatoid arthritis associated with ulcerative colitis

I was interested to read the letter on "Rheumatoid arthritis associated with ulcerative colitis" by Boyer *et al* published recently in the *Annals*,[1] and would like to make the following comments. Studies in patients with established Crohn's disease (CD) have generally supported the predominance of Th1 responses.[2 3] In ulcerative colitis, although enhanced humoral immunity has been described, evidence for classical Th2 predominance remains to be demonstrated. On the other hand, it has been shown that interleukin 15 is overexpressed in the inflamed mucosa of patients with inflammatory bowel disease at the level of macrophages.[4] Similar findings have been reported in patients with rheumatoid arthritis (RA).[5]

As shown in this case, it is sometimes quite difficult to distinguish by clinical manifestations alone between two diseases which start almost at the same time. However, the presence of a positive rheumatoid factor and DR1 genotype are arguments for RA. The existence of polymorphisms affecting other genes may take place in such type of arthritis.[6]

Results obtained with anti-tumour necrosis factor monoclonal antibody to prevent mucosal inflammation in CD,[7] suggest that such an approach may also be of interest in this unusual situation.

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Authors' reply

We thank Dr Mosquera-Martinez for his letter and are happy that our report has stimulated active discussion and suggestions.[1] Indeed, control of disease was difficult even when combining methotrexate 15 mg/week IM, salazopyrine 3 g/day, and prednisone 10 mg/day. The patient still had active arthritis affecting wrists and hands with an erythrocyte sedimentation rate (ESR) of 47 mm/1st h. Furthermore, she also had active colitis, and current treatment prevented surgery for colon anastomosis.

Accordingly, infliximab was started following the now classical rheumatoid arthritis protocol.[2] Seven months later, steroids could be stopped. Surgery for permanent colon anastomosis could then be performed with success and with no healing delays. When last seen in July 2001, she showed major improvement, with no pain at night and no morning stiffness. She had gained weight and had no sign of active colitis. The ESR was 26 mm/1st h and C reactive protein <4 mg/l.

Such follow up extends the concept of common mechanisms between rheumatoid arthritis and ulcerative colitis. Both diseases appear to depend, at least in part, on the contribution of tumour necrosis factor α.

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