RHEUMATOID ARTHRITIS

Nicotine exacerbates arthritis

“In the collagen-induced arthritis mouse model, administration of nicotine exacerbated inflammatory arthritis”

Nicotine can induce neutrophil extracellular trap (NET) formation (a process known as NETosis), according to new research published in *Rheumatology*, providing a mechanism through which use of nicotine-containing products could contribute to rheumatoid arthritis (RA). “This work supports the hypothesis that smoking and nicotine use might drive immune activation, including the generation of autoantigens through NETosis, which could be involved in the transition from preclinical autoimmunity to clinical RA,” states corresponding author Jeremy Sokolove.

Previous studies have suggested that NETosis contributes to RA pathogenesis through the release of autoantigens in the context of circulating autoantibodies. As smoking is a

known risk factor for RA, Sokolove’s group set out to investigate the effects of nicotine on NETosis using neutrophils from healthy individuals. “One of the most interesting findings of the study was increased spontaneous and phorbol 12-myristate 13-acetate (PMA)-induced NETosis in neutrophils derived from current smokers compared with non-smokers,” says Sokolove. Furthermore, *ex vivo* treatment with nicotine induced NETosis in neutrophils from non-smokers in a dose-dependent manner.

Investigating the underlying mechanism, the researchers demonstrated the involvement of nicotinic acetylcholine receptors (nAChRs), which were expressed on neutrophils from healthy non-smokers. Stimulation of these receptors using an agonist specific

for the $\alpha 7$ subunit of nAChR induced NETosis, whereas nicotine-induced NETosis was attenuated when the neutrophils were pretreated with an $\alpha 7$ -nAChR antagonist. In the collagen-induced arthritis mouse model, administration of nicotine exacerbated inflammatory arthritis, with nicotine-treated mice exhibiting both increased clinical scores and high plasma levels of NET-associated myeloperoxidase–DNA complexes (markers for NETosis).

“The most significant finding of this study is the implication that even tobacco-free nicotine-containing products, such as e-cigarettes, have the potential to exacerbate arthritis, as well as a variety of other inflammatory conditions, by priming or driving neutrophil activation,” explains Sokolove. “Future work will include epidemiological confirmation that these tobacco-free nicotine-containing products are associated with increased severity or exacerbation of RA and related inflammatory disease activity.”

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