

Short reports

Plasma nicotine concentration and the white blood cell count in smokers

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The peripheral blood total white cell count is 20–25% higher in smokers than in non-smokers (for review see ref 1). Smoking probably causes the increase in white cell count. Thus the count is higher in those who smoke and inhale more,² while a change in cigarette consumption is associated with a corresponding change in white cell count, and giving up smoking with a reduction in the count.³ Despite this evidence, the way in which smoking raises the white cell count is unknown. This study was conducted to determine if the white cell count in smokers is related to the concentration of nicotine in plasma or of carbon monoxide in end expired air.

Methods

Twenty two healthy young men of European extraction employed in the hospital were studied. None took any medication or had abnormal spirometric values. Twelve were regular cigarette smokers (median age 22 years) and 10 were lifelong non-smokers (median age 23.5 years). All gave written consent to be studied, and the ethics committee approved the study.

The subjects were studied between 2.35 and 4.40 pm. Exercise beforehand was prohibited but smokers were allowed to smoke as usual, except during the half hour before the samples of blood and expired air were taken, when all the subjects remained seated quietly. Samples of end expired air were obtained after a 20 second breath hold following maximal inspiration, and end expired carbon monoxide concentration was measured at once with an Ecolyzer 2000 series analyser (Energetics Science). A peripheral venous blood sample was taken immediately after the breath sample. The white cell count was measured with an ELT-800 automated whole blood analyser (Ortho Diagnostic Systems Inc), and plasma nicotine concentration by gas chromatography (smokers only). Correlation was determined with Spearman's rank coefficient, and a *p* value of <0.05 was regarded as significant.

Results

In smokers the median (range) duration of smoking was 6 (3–19) years, and usual daily consumption 18 (3–25) cigarettes. The number of cigarettes consumed on the test day was 7 (0–8), and the time between smoking the last cigarette and providing the breath and blood samples was 1.0 (0.6–14) hours.

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The median (range) plasma nicotine concentration was 11.2 (0.1–36.8) ng/ml in the smokers, and that of end expired carbon monoxide concentration 25 (6–42) ppm in the smokers and 4.0 (3.5–4.5) ppm in the non-smokers. Plasma nicotine and end expired carbon monoxide concentrations were significantly correlated in smokers ($r_s = 0.91$, $p < 0.001$). The mean (SD) white cell count was $7.37 (1.39) \times 10^9/l$ in the smokers and $6.73 (1.17) \times 10^9/l$ in the non-smokers. The white cell count was significantly related to the plasma nicotine concentration in smokers ($r_s = 0.58$, $p < 0.05$), but not to cigarette consumption on the test day or on usual days, or to end expired carbon monoxide concentration in smokers or non-smokers.

Discussion

This study discloses a significant relationship between the peripheral blood total white cell count in smokers and the plasma concentration of an individual constituent of cigarette smoke, nicotine. This relationship was present after excluding other external influences, and it accounts for about a third of the variance in the white cell count. The subjects were studied after a half hour rest during which smoking was forbidden, to allow breath and blood samples to be taken when carbon monoxide and nicotine concentrations were not changing rapidly just after a cigarette had been smoked.^{4,5} The findings do not, however, distinguish whether nicotine itself raises the white cell count, or whether it acts as a marker for other cigarette smoke constituents. An increased intake of one constituent is likely to be accompanied by an increased intake of others; yet, while there was a close correlation between the concentrations of nicotine and end expired carbon monoxide, only the nicotine concentration was significantly related to the white cell count. This may be because it is a better index of smoke exposure, though others have found end expired carbon monoxide satisfactory.⁶ Our results differ from those of Vanuxem *et al.*,⁷ who did not measure plasma nicotine concentrations but found that the white cell count in smokers was related to the carboxyhaemoglobin concentration.

The differential white cell count is almost identical in smokers and non-smokers.¹ Considering the variation in life cycle of the different types of leucocyte, it is difficult to conceive how a single smoke constituent might increase their numbers commensurately; yet it is equally difficult to envisage several smoke constituents each causing similar increases in the numbers of quite distinct types of leucocyte. If nicotine is the cause, it might raise the white cell count directly or indirectly. Evidence for indirect action is the fact that the count takes more than six weeks to fall to non-smoking levels after someone has stopped smoking.⁸

whereas the plasma half life of nicotine is only a few hours.⁵ Although nicotine promotes the release of adrenal steroids and catecholamines,⁹ which can cause leucocytosis, this action cannot explain the raised white cell count in smokers because these hormones cause neutrophilia. Nicotine has no known direct action to increase the white cell count, and it may not be possible to examine its role by administering nicotine chewing gum because this does not reproduce exactly the plasma nicotine pattern caused by smoking.⁵

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