Mechanism by which Cigarette Smoke Attracts Polymorphonuclear Leukocytes to Lung*

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Cigarette smoking is a major risk factor in the development of pulmonary emphysema, a chronic disorder thought to be caused by excess protease activity in lung. Although inhalation of cigarette smoke is associated with accumulation of polymorphonuclear leukocytes (PMN; a major source of preformed proteases) in the lung, cigarette smoke, by itself, is not chemotactic for PMN. Since alveolar macrophages (AM) interact with cigarette smoke in vivo and are capable of releasing a chemotactic factor (CF) for PMN, the present study was undertaken to determine if cigarette smoke might stimulate AM to release a CF for PMN. To evaluate this concept, AM obtained by bronchoalveolar lavage (BAL) of five nonsmoking and six cigarette smoking individuals were evaluated for their ability to secrete a CF for PMN either spontaneously or following in vitro exposure to cigarette smoke for three hours. In smokers, AM from each patient spontaneously released CF for PMN (100±15 PMN/hpf) and, as an in vivo correlate, their BAL contained 6 ± 1 percent PMN. In nonsmoking controls, AM did not spontaneously release CF for PMN (5±1 percent PMN/hpf) and their BAL contained <1% PMN. In addition, normal AM could be stimulated to release CF for PMN by exposing them in vitro to cigarette smoke (85±10 PMN/hpf). AM supernatants containing the CF (but free of cigarette smoke) not only attracted PMN, but also activated PMN to release their performed proteases including elastase. These studies demonstrate: (1) inhalation of cigarette smoke is associated with PMN in the lung, (2) AM from smokers but not nonsmokers spontaneously release a CF for PMN, and (3) normal AM can be stimulated by cigarette smoke in vitro to release CF for PMN. Thus, the attraction of PMN to the lung in association with cigarette smoking may be mediated by the interaction of smoke with alveolar macrophages.

Q. (Kimbel): Do steroids inhibit release of chemotactic factor?

A. (Hunninghake): Yes, they may, but in the few patients we have studied we demonstrated no inhibitory effect.

Q. (Dreisin): Is it possible that the "neutrophil elastase" you measure is actually derived from an inactive proenzyme from the macrophage, the active form of which is released via proteolytic cleavage of the neutrophil?

A. (Hunninghake): I don't think so, because you can't account for all the activity you find in the neutrophil supernatants by that in the macrophage cultures. In addition, the release of elastase from neutrophils can be triggered with highly purified chemotactic factor which would exclude elastase derived from macrophages.

Q. (Mitchell): Why don't all smokers get emphysema?

A. (Hunninghake): I don't know. The protease-antiprotease balance in the lung is probably finely tuned. Cigarette smoking results in an added protease burden to the lung. In some individuals, it is likely that this added protease burden in the lung is adequately neutralized by increased antiprotease activity and these individuals have no lung damage. In other individuals this added protease burden may not be dealt with adequately by their antiprotease screen and these individuals get a destructive lung disease. Preliminary studies by Gadek have demonstrated that cigarette smoking may inhibit the antiproteases that are present in lavage fluid. In addition, recent studies by Strumpf have shown that the level of alpha,-antiproteinase in lavage fluid is increased in certain lung diseases. Observations such as these may add some insight into why certain individuals who smoke cigarettes get emphysema and others do not.

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