Tobacco Smoking and the Pulmonary Surfactant System

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To explain enhanced retention of water insoluble gases and water insoluble particulate matter (tar) when smoke is inhaled we propose that these compounds interact physically with phospholipids forming the mono-molecular layer of surfactant lining the alveolar epithelium.

This would account for the alteration in surface tension lowering properties of surfactant when exposed to whole smoke but not gas phase. Also it explains the observed reversible reduction in 'free' surfactant as opposed to cellular contained surfactant in smokers.

Surfactant levels improve rapidly on abstinence from smoking and the time course of this improvement follows closely the reduction in alveolar epithelial permeability to a small hydrophillic molecule of diethylene triamine penta acetate (DTPA) and the improvement in homogeniety of ventilation as measured by the slope of alveolar washout (a measure of elusta properties of the peripheral airspaces of the lungs).

(Key Words: tobacco smoking, pulmonary surfactant system, water insoluble smoke constituents, lung function, slope of alveolar plateau, lung epithelial permeability)

Prompted by Niewoehners (8) observations interest has focused on the alterations in morphology of the terminal airspaces of the lungs of cigarette smokers. It was he, who demonstrated the prominence of inflammation of bronchioli and evidence of a macrophage alveolitis (8) in the lungs of young smokers. Associated 'early' disturbance in function of these terminal airspaces can be demonstrated in asymptomatic smokers, and reverses on abstinence from cigarettes (2).

I would like to present some observations which may explain the proclivity of tobacco smoke for the terminal airspaces and the rapid reversal of physiological disturbance when smokers abstain.

Tobacco smoke has both water soluble and insoluble compounds. Dalhamn (3) was able to show that water insoluble components, notably 'tar' (or particulate matter) was retained principally after inhalation whereas in contrast to water solubles little uptake occurred when smoke was held in the mouth. The importance of inhalation is not just the increased volume of disturbance, but the fact smoke comes into contact with the alveolar epithelium.

The unique feature to the alveolar epithelium as distinct from the airway epithelium is that in all probability it is covered with a mono-molecular layer of pulmonary surfactant made up of phospholipids with fatty acid chains facing the alveolar gas (1). this mono-molecular layer of phospholipids influences the elastic properties of the alveoli during breathing enabling a marked reduction in surface tension during exhalation perhaps preventing alveolar collapse. The release and manufacture of phospholipids to maintain the mono-molecular layer is achieved by the type II alveolar pneumocyte, one of the types of epithelial covering cells of the alveolus.

We have become interested as to how tobacco smoke interacts with a surfactant film. Using a Wilhemy balance (6) cycling from 100% to 50% of film surface area at 0.095 Hz we initially add whole tobacco smoke to saline. Eight
puffs of 35 mls from a single port smoking machine were added to the film. Surface tension fell, whole smoke acting like a surfactant producing a hysteresis loop. Addition of gas phase alone (smoke having passed firstly through a Cambridge filter) produced no effect (see Figure 1).

The study was then repeated using first bovine then rabbit surfactant. Whole smoke and surfactant whilst having reduced surface tension lowering properties also had no normal hysteresis loop (see Figure 2). Gas phase by contrast had only a minimal effect on the surfactant hysteresis loop. These observations are similar to those of Miller (6) but we interpret them as implying that the lipid soluble 'tar' physically interacts with the surfactant film.

When considering the chronic effects of tobacco smoke inhalation, cigarette smokers do not appear to have altered quality of surfactant (5) having similar percentages of dipalmityl phosphatidyl choline to non-smokers. However whilst total surfactant obtained at bronchoalveolar lavage is no different from non-smokers (4), smokers have reduced 'free' surfactant with a marked increased amount taken up into alveolar macrophages. Perhaps smoke altered surfactant is more readily phagocytosed. This may account for the increased numbers of alveolar macrophages seen in smokers (5).

There is evidence that on cessation of smoking, free surfactant levels rise within two weeks (4). We have therefore asked whether these changes in lung function observed to improve when smokers abstain, also follow a similar time course. We have been greatly aided by the measurement of clearance of an aerosol of technetium labelled diethylene trimine penta-acetate, a 495 dalton hydrophilic molecule, described by Jones and colleagues (7). The clearance of inhaled DTPA is greatly increased in cigarette smokers appearing to be related to tobacco smoke exposure.

As part of a longer study of abstinence 20 male smokers with normal lung function were selected (Table 1). Each was given nicotine containing chewing gum for 3 months. At the end of 6 months 10 had completely abstained whilst 10 continued to smoke. Each had epithelial permeability measured at onset, 1, 4, 12 and 24 weeks. To assess veracity of smoking history exhaled carbon monoxide was recorded at each visit. In addition measurements of airway function was recorded, specific airway conductance (Sgaw), forced expired volume in one scond (FEV1), maximal expiratory flow at 50% of vital capacity (Vmax 50) and closing volume (CV). In addition total lung capacity (TLC) and vital capacity (VC) were measured. A single breath nitrogen washout curve was used to assess closing volume together with homogeniety of ventilation recorded from the slope of phase III (Phase III N2 slope) which probably reflects the inhomogeniety of elastic properties of terminal airspaces.

Amongst abstainers exhaled CO level fell to zero after a week reflecting abstinence. This was not achieved by non-abstainers (see Figure 3). No significant changes occurred in lung function, as assessed by FEV1, Vmax 50, closing volume or Sgaw, or in TLC or VC (see Table 2).

However there was a significant increase observed in abstainers, of the half time clearance of DTPA indicating reduced permeability (see Figure 4). This was initially seen after a week, rising to a maximum at one month. A similar improvement of homogeneity of ventilation as seen by the N2 slope decreasing after a week of abstinence, no change was observed in abstainers (see Figure 5).

We suggest that tobacco smoke, principally 'tar', is associated with a reversible disturbance of permeability of the alveoli and elastic properties of the terminal airspaces. The time course of these changes are in line with the quantitative changes in pulmonary surfactant seen in smokers and may reflect the initial physical interaction between tar and surfactant.

REFERENCES

Table 1

**FOLUNTEES**

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<td>% Predicted FEV₁</td>
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Table 2

**LUNG FUNCTION**

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se ± .3 | se ± .3 | se ± .6 | se ± .57 | se ± .10 | se ± .09
**Fig. 1** The surface tension of saline film on a Wilhemy balance before and after addition of whole smoke. No change was observed when gas phase alone was added.

**Fig. 2** The surface tension of bovine surfactant before and after addition of whole smoke and gas phase.
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Fig. 3  The change in exhaled carbon monoxide in smokers and abstainers over a 6 month period. Mean values and standard errors are shown.

Fig. 4  The mean values of DTPA $T_1$ in abstainers and failed abstainers over 6 months together with 95% confidence intervals for comparing abstinence values with control values.
Fig. 5  The mean values of slope phase III in abstainers and non-abstainers together with 95% confidence intervals for comparing abstinence and control values.