March 5, 1971

Sir Charles Ellis,
Westminster House,
7 Millbank,
London, S.W.1, England

Dear Sir Charles,

Thank you for your recent letter. Since I last wrote, the literature search on surfactant has been extended and summaries of some relevant papers are given below.

Miller, D. and Boncurant, S., AM. Rev. Resp. Dis., 1962, 85, 633.

In vivo and vitro studies on the effect of cigarette smoke on rat lung surfactant.

In vitro - smoke collected in a 100 ml syringe and poured on to surface.

In vivo - animals exposed to smoke for 8 half hour periods on 3 successive days.

Results. (values in dynes/cm.)

Saline	Saline & Smoke
71.0 ± 0.5	60.8 ± 0.5

Surface Tension of Rat Lung Extracts

	Before Smoke	After Smoke
At 100 cm^2	44.8 ± 10.6	30.6 ± 4.7
At 20 cm^2	17.0 ± 4.5	11.4 ± 5.1
Compressibility cm^2/dyne	4.1	5.7

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Surface Tension of Lung Extracts of Rats Exposed to Smoke

	Normal	Exposed
At 1 cm²	44.6 ± 12.1	33.8 ± 2.2
At 20 cm²	15.9 ± 3.7	14.5 ± 5.0
Compressibility	3.27	5.45

The author makes the general conclusion that smoke decreases the efficacy of surface forces in stabilising the alveoli.

Hall, P.W., Cook, W.A., Lanius, J.W. and Shaw, R.R., Am. Rev. Resp. Dis., 1967, 95, 244.

Effect of cigarette smoke and dust particles on dog lung surfactant obtained by bronchial washing.

	100% area	20% area
control	60.7 ± 0.4	7.1 ± 0.8
smoke	45.8 ± 0.7	19.7 ± 0.5
smoke passed through water	45.8 ± 1.1	22.0 ± 1.3
smoke dispersed as microbubbles through water	55.9 ± 2.0	8.0 ± 1.0
dust	62.0 ± 2.0	25.0 ± 2.0

Additional experiments - passing smoke through an acetate or charcoal filter does not remove smoke effect. Smoke passed through a Millipore filter does not affect surfactant.

Alteration of surface properties is attributed to physical effects of smoke particles.

Surface Tension of Lung Extracts of Rats Exposed to Smoke

	Normal	Exposed
At 100 cm^2	43.4 ± 12.1	33.8 ± 9.2
At 20 cm^2	15.1 ± 3.7	14.5 ± 5.0
Compressibility	1.27	5.45

The author makes the general conclusion that smoke decreases the efficacy of surface forces in stabilising the alveoli.

Webb, R.W., Cook, W.A., Lanius, J.W. and Shaw, R.R., Am. Rev. Resp. Dis., 1967, 95, 244.

Effect of cigarette smoke and dust particles on dog lung surfactant obtained by bronchial washing.

	100% area	20% area
control	60.7 ± 0.4	7.1 ± 0.8
smoke	45.8 ± 0.7	18.7 ± 0.5
smoke passed through water	45.8 ± 1.4	22.0 ± 1.3
smoke dispersed as microbubbles through water	55.9 ± 2.0	8.0 ± 1.0
dust	62.0 ± 2.0	25.0 ± 2.0

Additional experiments - passing smoke through an acetate or charcoal filter does not remove smoke effect. Smoke passed through a 1.μ filter does not affect surfactant.

Alteration of surface properties is attributed to physical effects of smoke particles.

Grammona S.T., Am. Rev. Resp. Dis., 1967, 96, 539

Experiments on dog, cat and guinea pig surfactant in vivo and vitro using tobacco, lettuce, avocado and pine leaves. Tobacco smoked in cigarette form; avocado and pine pyrolysed in flasks.

Results - tobacco smoke in vitro drop in surface tension at 100% area of 10-12 dynes/cm. No change at 2% area. No change at either area caused by vapour phase.

In vivo, whole smoke had no effect on dog or cat surfactant; guinea pigs showed decrease of 5 dynes/cm. at maximal area. Vapour phase had no effect on guinea pigs. The smokes from lettuce, avocado and pine leaves were tested in vitro on dog surfactant. All three left the maximal surface tension unchanged but caused an increase in minimal surface tension. Authors conclusion - tobacco smoke may cause emphysema while plant smoke would favor atelectasis.

Cook, C.A. and Webb, W.R., Am. Thorac. Surg. 1966, 2, 327.

Smoke vapour phase does not affect surfactant. Smoke particles and non-specific dust show similar effects.

Chronic smokers and patients with pulmonary disease have decreased surfactant activity.

Conclusions

The in vitro results observed in all the above papers suggest that tobacco smoke particles affect the maximal surface tension of surfactant and have little or no influence on the minimal surface tension. The fact that avocado, lettuce and pine smokes only affect the minimal surface tension seems difficult to explain but could probably be attributed to the mode of generation of the smoke.

The in vivo studies present a less cohesive picture. One group (Endurance) has reported lowering of maximal surface tension in rats exposed to smoke, while another (Grammona) reported no changes in cat and dog surfactant but observed a lowering in maximal surface tension in guinea pigs.

One surprising feature of in vivo and vitro tests is that vapour phase has no effect whatever and, if one makes the assumption that the majority of smoke particles are trapped before reaching the alveoli, it becomes difficult to rationalize the results observed with rats and guinea pigs. One might conclude that in small animals smoke particles can reach the extremities of the lung.

To clarify the situation, it would be necessary to observe the effect of whole smoke on a range of animals from rat to possibly lanish primates. The effect of vapour phase in vivo should be studied over prolonged periods of exposure and finally evidence of a chemical reaction between smoke of vapour phase and surfactant should be sought, since vapour is unlikely to cause any physical disruption in a surface and would probably exert more effect by chemical disruption of the surface active molecules.

If your analysis of the results quoted in these papers leads you to the same conclusions as mine, the final questions to be answered are whether we can expect important information from such experimentation and where could the work be undertaken. In Montreal we are not equipped to handle animals so you may wish to arrange to have the work done under a grant by some academic institution, or by contract in a research institute.

Yours sincerely,

M.A. Nisbet

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cc: Dr. S.J. Green
Mr. R.S. Wade

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