IN CONFIDENCE

NITROGEN OXIDES

Paragraph 3(b) i mentions nitrogen oxides in relation to bronchitis and emphysema.

Smoke from a typical flue-cured cigarette contains about 100µg nitric oxide (NO) and 1µg nitrogen dioxide (NO_2). Levels in air-cured cigarette smoke tend to be much higher, though the ratio of NO to NO_2 is similar to that in flue-cured cigarette smoke (Sloan and Kiefer).

The effects of NO_2 on pulmonary tissue and respiratory function have been much studied. A Gallaher literature review, now two years old, is attached (Appendix A). Exposure of several species to NO_2 leads to changes resembling human emphysema. Table 1 compares this TLV value with concentrations known to cause emphysematous changes in animals and with possible concentrations in the lungs of a smoker (assuming either total or no oxidation of NO and NO_2).

Little information exists on the biological effects of NO, probably because of the difficulty of preparing a NO/air mixture not contaminated with NO_2. However, a recent paper by Hugod describes ultrastructural changes of unknown significance in rabbit lung caused by exposure to $6mg/m^3$ NO for 14 days. This is well below the likely concentration of NO in a smoker's lungs (Table 1); for this reason the experiment should be repeated and if the findings are confirmed, the significance of the ultrastructural changes should be established.

Equally important is the extent to which NO is oxidised to NO_2 in aged, diluted smoke (i.e. under conditions obtaining after inhalation). This oxidation is termolecular and therefore slow and highly dependent on the concentration of NO.

$$2NO \overset{+}{} O_2 \xrightarrow{\text{slow}} (NO_2) + O_2 \xrightarrow{\text{fast}} 2NO_2$$

If there is no absorption in the lungs and the concentration therein is $20mg/m^3$ (Table 1), after 1 min the kinetics of the reaction predict minimal oxidation to NO_2 (ITG Ltd., 1969). Moreover, during 1 min the smoker will take about 18 breaths which will reduce the concentration of NO to roughly 4% of that immediately after taking the puff.

However, if absorption of NO into lung tissue is rapid and is not accompanied by chemical reaction (for example with haemoglobin), then all the NO will eventually be oxidised to NO_2. Probably the true fate of NO in the lungs lies between these two extremes, but a situation in which the level of NO_2 exceeds the TLV (Table 1) is not impossible. Research is probably needed to clarify the situation.

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References

Hugod, C. (1979) Arch. Environ. Health 34 (i), 12.

Imperial Tobacco Group Ltd. (1969) TRC paper G731.

Sloan C.H. and Kiefer, J.E. (1969) Tobacco Science, 13, 180.

TABLE 1

NO_2 concentration (mg/m^3)		Reference
30	Concentration in lung of smoker if all NO oxidised to NO_2	*
9	T.L.V.	1
3.6	Lifetime exposure in rats caused emphysema - like changes	2
1.4	No effect in rats apart from tachypnoea	3
0.9	3 months exposure in mice causes emphysema - like changes	4
0.2	Likely concentration in lung of smoker assuming no oxidation of NO to NO_2	*
NO concentration (mg/m^3)		
20	Likely concentration in lung of smoker assuming no oxidation to NO_2	*
6	Concentration shown to produce minor changes in rabbit lung after 14 days exposure.	5

References

1. Documentation of Threshold Limit Values, American Conference of Governmental Industrial Hygienists.
2. Freeman et al (1968) Arch. Environ. Health 17, 181.
3. Freeman et al (1966) Arch. Environ. Health 13, 454.
4. Blair et al. (1969) Arch. Environ. Health 18.
5. Hugod (1979) Arch. Environ. Health 34, 12.

* Calculations assume 100µg/cig NO, 1µg/cig NO_2, puff number = 10, and smoker dilutes one puff to 500 ml with air before inhalation.