D R A F T

CONSIDERATIONS RELATING TO ENVIRONMENTAL TOBACCO SMOKE AND THE NON-SMOKER

The Repace and Lowery article, Science 208:474 (1980), indicates that the concentration of tobacco smoke in public places that they sampled is in the range of 400 $\mu g/m^3$. They report some instances of higher and some of lower levels. A review of the literature indicates that a number of articles report the concentration of nicotine in public places with descriptions similar to those reported by Repace and Lowery. Most of these articles indicate the nicotine concentration to be in the range of 40 $\mu g/m^3$.

It may be estimated that the concentration of nicotine in sidestream smoke is about 10% and that a large portion of the smoke in the room environment is generated from the sidestream rather than by exhalation of mainstream smoke by the smoker. If we use this 10% estimate for the nicotine concentration, the total particulate may be calculated as 400 $\mu g/m^3$ or the same value as estimated by Repace and Lowery. However, nicotine does appear to have some limitations as a tracer for environmental tobacco smoke. Badre, et al., Annals Pharmaceutiques Francais 36: No. 9-10, 443 (1978), show that the disappearance of nicotine from the environment is exponential, whereas the particulate aerosol itself disappears at a more linear rate. We presume that the nicotine actually evaporates from the aerosol with time and undergoes a vapor state oxidation in the presence of ultraviolet radiation. This means that nicotine can be reliably used as a tracer on relatively fresh smoke but that as the smoke becomes older, progressively increasing underestimates of the aerosol concentration would be made on the basis of the nicotine concentration.

The amount of smoke received by the non-smoker when exposed to an environment containing 400 $\mu g/m^3$ can be estimated by comparison to the calculated amount of smoke obtained by the smoker. If we assume that man has a tidal volume of .5 liters for inspiration and respires at the rate of 12/minute, .36 m^3 of air will be inhaled per hour. If we further assume that all the inhaled material is retained, .14 mg of particulates will be inhaled and retained from an atmosphere containing 400 μg of particulates per m^3. If we further compare this to the average yield of American cigarettes of 15 mg and assume this to be the amount of smoke absorbed by the smoker, the non-smokers' value is about 1% of a cigarette per hour of exposure or about 10% of one cigarette for a 10-hour workday. This corresponds to about one puff. Confirmation that these estimates are of the correct order of magnitude can be obtained by reviewing the literature with respect to concentrations of nicotine and cotinine (the major metabolite of nicotine) found in serum and urine of smokers and non-smokers.

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Harke, Muensch. Med. Wochschr. 112:1 (1970), reported urinary cotinine and nicotine levels in non-smokers exposed to a smoke-filled room. They reported values for the non-smoker between 1.2% and 3.8% of the smoker. Horning, et al., Life Sciences 13:1331 (1973), report that non-smokers in the smoking environment had about 5% of the urinary nicotine level of the smoker. Russell and Feyerabend, The Lancet 1: 1979 (1975) report blood and urinary nicotine in non-smokers exposed for 78 minutes in a smoky room. The serum nicotine level of the non-smoker group was .9 ng per ml. which compares with an average smoker value of 24.5 ng per ml. or the non-smoker is about 3.7% of the smoker. However, the serum nicotine increase in the non-smoker exposed for 78 minutes was only .2 µg per ml. or less than 1% of the average smoker value. The urinary concentration of the non-smoker after exposure to the smoky room was about 6% of the value of the smoker.

These differences in nicotine and cotinine levels between smokers and non-smokers can be taken at face value to indicate that the non-smoker absorbs qualitatively much less nicotine than the smoker. However, the quantitative assessment must consider the build-up and disappearance of nicotine from serum in the smoker and non-smoker. Similarly, rates of metabolism of nicotine to cotinine must also be considered when interpreting levels of exposure based on this metabolite. Figure 1 is derived from the literature data on the disappearance of nicotine from human serum, illustrating that the metabolic half-life of nicotine is about 40 minutes. The result of this fast clearance rate in the smoker is little build-up of serum nicotine levels with smoking at one hour intervals. If smoking is more rapid than this, some build-up does occur as shown by Russell and Feyerabend, Drug Metabolism Reviews 8:45 (1978), Figure 2. Thus, concentrations of serum nicotine do not afford a direct assessment of the total exposure, but more nearly reflect the amount of nicotine absorbed during the smoking of the last cigarette unless a high frequency of smoking occurs. In the case of the non-smoker, the exposure in a smoke-filled room would be continuous and the nicotine concentration in serum would rise to some equilibrium value where the input and disappearance per unit time were equal. Thus, it would appear to be impossible to relate serum nicotine levels in the population at large to daily amount of tobacco smoke absorbed. The amount of nicotine excreted in urine is small relative to the total intake and the amount found in urine is further compounded by pH of the urine, Feyerabend and Russell, Br. J. Clin. Pharma. 5:293 (1978). It, therefore, appears that nicotine excreted in the urine of the population at large would not be a useful measurement to describe daily amount absorbed.

Cotinine (the major metabolite of nicotine) has a much greater half-life in body fluids (30 hrs.) than nicotine

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(Zerdenberg, Jaffe, et al., Comprehensive Psychiatry 18(1), 93 (1977)) and therefore appears to have potential use as a measure of daily tobacco smoke absorption.

CONCLUSIONS

According to most articles in the literature, the nicotine concentration in environmental air of poorly ventilated rooms with smokers is in the order of 40 $\mu g/m^3$. Assuming sidestream smoke contains 10% nicotine, 400 $\mu g/m^3$ of particulates is estimated to occur in these poorly ventilated areas. This value is consistent with the Repace and Lowery article. It seems unlikely that measurements of nicotine or particulates in public places would yield data that would refute those reported by Repace and Lowery. However, simple calculations indicate that the amount received by the non-smoker in such an environment is very small even after a 10 hour period. Direct measurement of nicotine and cotinine in non-smokers' serum and urine indicates that detectable amounts are present. However, quantitative relationships between exposure and concentration in body fluids have not been established.

RESEARCH PROJECTS FOR CONSIDERATION

Measurements on the environmental air can only be used to make inferences as to the amount of tobacco smoke absorbed by the non-smoker. The anti-smoking groups will continually exaggerate these inferences as far as possible in support of their objectives. The only way to obtain a realistic measure of the amount is to measure a smoke-related component in the body fluids of the non-smoker. This component should be sufficiently long-lived in the body fluid so that its concentration reflects the amount absorbed on a daily basis by the non-smoker. The nicotine metabolite cotinine, with a 30 hour half-life and excreted in urine, has the potential of representing this measurement. Nicotine itself has too short a half-life for this purpose and no other component is present in sufficient quantities or is tobacco-specific. It is anticipated that a study involving smokers and non-smokers who frequent public places and who work under a variety of environmental conditions would show that the non-smoker absorbs less smoke than inferred by Repace and Lowery.

The following questions would need to be explored prior to a study within the general population.

1. The relationship between nicotine concentration and tobacco sidestream smoke particulates generated from an array of commercial brands should be determined. Although it is estimated that this number is about 10%, it would need to be determined and the range of error estimated when different brands are smoked.

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2. Elucidation of the relationship between the concentration of nicotine and the concentration of particulates in the room environment over time should be determined. Although it is felt that smoke in environmental air is relatively fresh and that nicotine would represent a satisfactory tracer, this needs to be quantitated.

3. It should be determined if any of the nicotine in environmental air is converted to cotinine. It is not anticipated that nicotine is converted to cotinine, but this must be evaluated as a possible source of error.

4. The relationship between nicotine in environmental air, duration of exposure, and urinary cotinine of the smoker and non-smoker must be established. It is anticipated that some variation in the metabolism of nicotine between individuals exists. Such metabolic differences as reflected in the concentration of urinary cotinine would represent part of the error of the method for determining exposure. This must be estimated by making measurements on a representative number of individuals exposed to environments of known concentrations. Hill and Marquardt, in press, have recently reported a relationship between serum cotinine and the amount excreted in the urine. We may, therefore, reasonably expect that a suitable relationship does exist between nicotine in environmental air and urinary cotinine.

When the preliminary work is completed and the relationships quantified, it is suggested that an experiment be considered involving a representative sample of the general population of smokers and non-smokers. Since it would be required to obtain urine samples over a number of hours, it will be necessary to arrange the study through a clinical or institutional environment. The number of individuals in the study would need to be determined after the preliminary work, but numbers in the order of 1,000 subjects in both the non-smoking and smoking groups would probably be necessary to insure groups that are representative of the general population.

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FIGURE 1

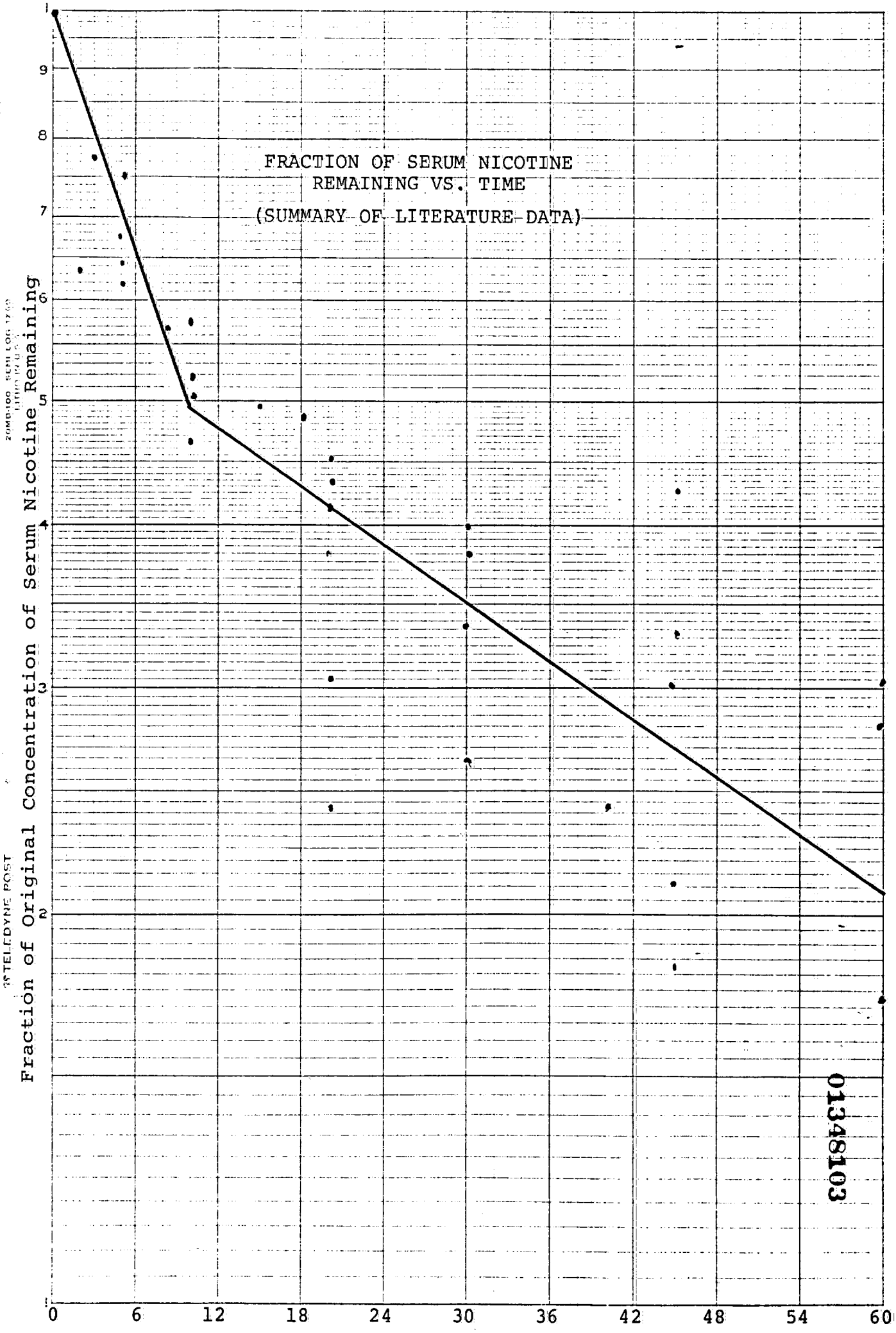

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FIGURE 2

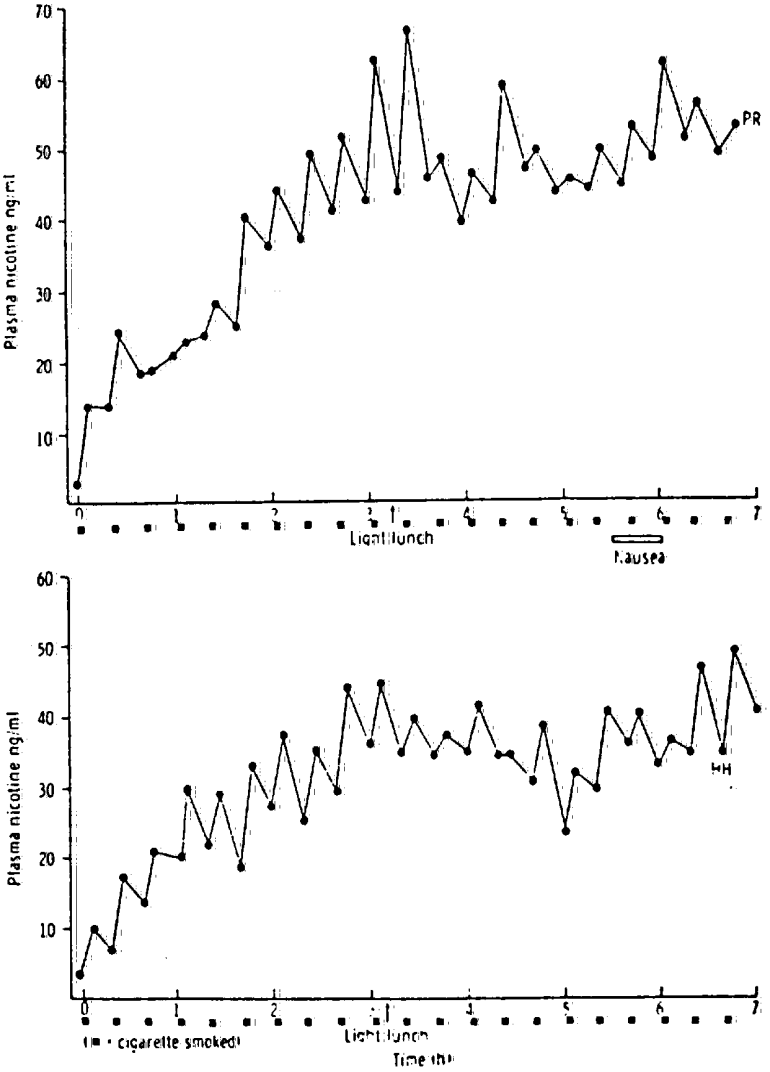

FIG. 7. Plasma nicotine levels during forced prolonged heavy smoking at a rate of three cigarettes per hour for 7 hr. Each cigarette was smoked over precisely 5 min, and blood samples were taken just before and 2 min after each cigarette. Both subjects were regular smokers whose usual smoking frequency was just over 20/day. Nicotine yields of the cigarettes were 1.3 for P.R. and 1.4 mg for H.H. Urinary pH was uncontrolled.

Source: Russell and Feyerabend, Drug Metabolism Reviews, 8, 45 (1978).

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