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BLOOD AND URINARY NICOTINE IN NON-SMOKERS

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PURPOSE: THIS STUDY INVESTIGATES THE BLOOD AND URINE NICOTINE CONTENT IN NONSMOKERS.

METHODS: BLOOD AND/OR URINE NICOTINE CONTENT WAS MEASURED BY GAS CHROMATOGRAPHY IN 9 MALE AND 3 FEMALE NONSMOKERS BEFORE AND AFTER EXPOSURE TO THE SMOKE OF 80 CIGARETTES AND TWO CIGARS IN AN UNVENTILATED ROOM (38 P.P.M. CARBON MONOXIDE) AND, IN A SEPARATE EXPERIMENT, IN 12 MALE AND 15 FEMALE NONSMOKERS AND 9 MALE AND 9 FEMALE SMOKERS DURING THE AFTERNOON AFTER THEIR USUAL EXPOSURE TO TOBACCO SMOKE.

FINDINGS: OF 39 URBAN NONSMOKERS ABOUT HALF HAD MEASURABLE QUANTITIES OF NICOTINE IN THEIR PLASMA (RANGE 0 TO 5.5 NG. PER ML.) AND ALMOST ALL HAD NICOTINE IN THEIR URINE DURING THE EARLY AFTERNOON. THE AVERAGE CONCENTRATION OF URINARY NICOTINE IN NONSMOKERS UNDER NATURAL CONDITIONS WAS 10.7 NG. PER ML.

AFTER DELIBERATE EXPOSURE TO TOBACCO SMOKE IN AN UNVENTILATED ROOM, THE AVERAGE URINARY NICOTINE LEVEL (80 NG. PER ML.) AND PLASMA NICOTINE LEVEL (0.9 NG PER ML.) WERE SIGNIFICANTLY HIGHER THAN IN NONSMOKERS WHO HAD NOT BEEN DELIBERATELY EXPOSED TO SMOKE.

UNDER NATURAL CONDITIONS THERE WAS NO OVERLAP BETWEEN THE URINE LEVELS OF NONSMOKERS AND THE FAR HIGHER LEVELS OF 18 SMOKERS (MEAN 1236 NG. PER ML.).

DISCUSSION: "[T]HE TENDENCY FOR PLASMA-NICOTINE IN NON-SMOKERS TO INCREASE AFTER EXPOSURE IN THE SMOKE-FILLED ROOM WAS SMALL. URINARY

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NICOTINE, HOWEVER, WAS VERY MUCH HIGHER AFTER EXPOSURE...THE LESS IMPRESSIVE CHANGES IN PLASMA LEVELS SUGGEST THAT THE NICOTINE IS EXCRETED ALMOST AS FAST AS IT IS ABSORBED. THIS PROBABLY ACCOUNTS FOR THE ABSENCE OF ANY OBVIOUS PHYSIOLOGICAL EFFECTS IN NON-SMOKERS AFTER EXPOSURE IN A SMOKE-FILLED ROOM. HOWEVER, THIS RAPID EXCRETION WOULD BE SLOWED BY URINE ALKALINITY AND THIS MAY ACCOUNT FOR THE ISOLATED EXAMPLES OF NON-SMOKERS WITH AN ESPECIALLY HIGH PLASMA-NICOTINE. THE FACT THAT SOME NICOTINE IS PRESENT IN THE URINE OF ALMOST ALL NON-SMOKERS SUGGESTS THAT EPISODES OF PASSIVE SMOKING ARE COMMON IN URBAN LIFE.

"WE CONCLUDE THAT VIRTUALLY ALL URBAN NON-SMOKERS HAVE MEASURABLE AMOUNTS OF NICOTINE IN THEIR BODY FLUIDS THROUGHOUT MOST OF THEIR LIVES. IT IS DERIVED FROM THE INDOOR AIR THEY BREATHE AND IT REQUIRES NO MORE THAN ONE OR TWO SMOKERS TO CONTAMINATE A VEHICLE OR BUILDING."

"SOME CAUTION IS NECESSARY BEFORE ADVOCATING THE USE OF URINARY NICOTINE AS A MEANS OF TESTING OR CONFIRMING AN INDIVIDUAL'S SMOKING-STATUS. THIS WAS A SAMPLE OF FAIRLY HEAVY SMOKERS. ONLY 1 SMOKED LESS THAN TEN CIGARETTES A DAY. AMONG PEOPLE WHO SMOKE FEWER CIGARETTES THERE IS LIKELY TO BE SOME OVERLAP WITH NON-SMOKERS."

/AM/

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MAUDSL HOSP, LONDON, UK/
NEW CROSS HOSP, LONDON, UK

INHALATION STUDY, QUANTITATIVE STUDY, MALE FEMALE DATA, HUNDRED, BLOOD NICOTINE CONTENT, URINARY NICOTINE CONTENT, NONSMOKERS, PASSIVE SMOKING PHYSIOLOGICAL EFFECTS, NICOTINE ABSORPTION/ CIGARETTE SMOKING, CIGARETTE SMOKE EXPOSURE DURATION, CONFINED SPACE ATMOSPHERE, CIGAR SMOKE EXPOSURE, TOBACCO SMOKE EXPOSURE,

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AIR CARBON MONOXIDE CONTENT, TOBACCO SMOKE CARBON MONOXIDE, METHODOLOGY ANALYSIS, METHODOLOGY VALIDITY, NICOTINE ABSORPTION PASSIVE SMOKING ASSOC, NICOTINE EXCRETION, URINARY pH, URBAN FACTORS, AIR NICOTINE, SMOKING AMOUNT, SMOKING TEST, METHODOLOGY CONCESSION, NICOTINE EXPOSURE, PASSIVE SMOKING AMOUNT, INTERPRETATION VALIDITY CONCESSION/
BLOOD CARBON MONOXIDE, PASSIVE SMOKING HEALTH HAZARDS, PASSIVE SMOKING IRRITANT EFFECTS, GAS CHROMATOGRAPHY, EXSMOKERS/
ENGLISH LANGUAGE, LONDON RESIDENCE, UK RESIDENCE, GRANTOR UK MED RES COUNCIL, GRANTOR UK DEPT HEALTH SOCIAL SECURITY

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BLOOD AND URINARY NICOTINE IN NON-SMOKERS

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Summary Of 39 urban non-smokers about half had measurable quantities of nicotine in their plasma (range 0 to 5·5 ng. per ml.) and almost all had nicotine in their urine during the early afternoon. The average concentration of urinary nicotine in non-smokers under natural conditions was 10·7 ng. per ml., but after deliberate exposure to tobacco smoke (mean duration seventy-eight minutes) in an unventilated room (38 p.p.m. of carbon monoxide) the average urinary nicotine level (80 ng. per ml.) was significantly higher than in non-smokers who had not been deliberately exposed to smoke ($P<0.001$). Under natural conditions there was no overlap between the urine levels of non-smokers and the far higher levels of 18 smokers (mean 1236 ng. per ml.), suggesting that urinary nicotine may provide a more accurate assessment of an individual's smoking-status than blood-carboxyhæmoglobin. It is concluded that, as a result of passive smoking, most urban non-smokers have measurable amounts of nicotine in their body-fluids for most of their lives.

Introduction

PASSIVE smoking occurs mainly in poorly ventilated confined spaces in which people are or have been smoking. Compared with their usual intake it is of little consequence to the health of smokers. But non-smokers, besides experiencing annoyance and acute irritation to the eyes and respiratory passages, also absorb carbon monoxide [1-3] and nicotine.[3-5] Passive smoking may be harmful,[6,7] and infants are most at risk.[8]

Passive smoking has complicated the development of a reliable method for measuring nicotine in blood. This is because calibration curves were constructed by adding nicotine to plasma from non-smokers, despite the fact that gas chromatography showed peaks identical to nicotine in plasma from non-smokers. Earlier workers [9] did not believe that these peaks in non-smokers were in fact nicotine, and the plasma-nicotine levels obtained in smokers were, therefore, "corrected" by subtracting the plasma "blank" values derived from non-smokers. This would not have mattered so much had the levels in non-smokers been constant, but plasma-nicotine levels of non-smokers vary from 0 to 6·8 ng. per ml.[10] compared with a mean in smokers of 24·4 ng. per ml. just after smoking.[11] When these same non-smokers were instructed to avoid, for twenty-four hours, going near smokers or into places that had been frequented by smokers their plasma was free of nicotine. Our first experiment was designed to test whether non-smokers absorb measurable amounts of nicotine under conditions of extreme exposure in a smoke-filled room.

Passive smoking also affects the results of the random measurement of urinary nicotine levels as a spot check on those claiming to be non-smokers after treatment at a smoking withdrawal clinic. Several genuine ex-smokers were falsely described as smokers after nicotine had been found in their urine. The second experiment we describe was undertaken to see whether there was overlap between the upper limits of urinary nicotine in non-smokers and the lower limits of smokers under natural conditions without control of urinary acidity.

Materials and Methods

First Experiment

12 non-smokers (group 1) spent an average of seventy-eight minutes seated among smokers in an unventilated smoke-filled room (volume approximately 43 cubic metres). The smoke was produced by burning or smoking eighty cigarettes and two cigars. The average ambient carbon monoxide was 38 p.p.m. Venous blood-samples were collected at an average of ten minutes before entry and twelve minutes after the volunteers left the room. The blood specimens were centrifuged within two hours and the plasma kept frozen until analysis for nicotine. The volunteers emptied their bladders just before entering the room. Urine specimens were collected on average about fifteen minutes after leaving the room and kept frozen until analysed for nicotine. This study has been described in detail in an earlier report of the changes in blood-carboxyhæmoglobin.[3] The experiment took place just after lunch. Urine pH was not controlled.

Second Experiment

Urinary nicotine levels were measured in three groups of volunteers over a one-hour period after lunch. This time of day was chosen to allow closer comparison with the first experiment. Again the urine pH was not controlled, but it was measured. In this instance special conditions were not imposed and the volunteers had undergone their usual exposure to tobacco smoke. 14 subjects (group 2) were non-smoking members of the Addiction

TABLE I—PLASMA AND URINE NICOTINE LEVELS OF NON-SMOKERS AFTER 75 MINUTES IN A SMOKY ROOM

No.	Sex	Plasma-nicotine (ng./ml.)		Urine nicotine (ng./ml.)
		Before	After	After
1	M	0·3	1·0	61
2	M	1·0	0·5	208
3	F	5·5*	1·2	98
4	M	0	0·8	93
5	M	0	0·5	33
6	M	0	1·0	35
7	M	†	1·0	45
8	F	0·5	0·7	13
9	M	0·7	0·7	157
10	M	0	0·9	†
11	F	0	1·4	92
12	M	0	1·2	45
Mean ± S.D. ..	..	0·73 ± 1·6	0·90 ± 0·29	80·0 ± 58·7

* This high level was found in the wife of M. A. H. R. who has never smoked. Three subsequent random levels at the same time of day were: 0, 1·5, and 2·5 ng. per ml.
† Specimens lost.

Research Unit staff. The other two groups (13 non-smokers [group 3] and 18 smokers) were from the staff of New Cross Hospital. In the case of the two New Cross groups, urine volumes were also measured so that the urinary nicotine excretion over the course of an hour could be calculated.

Blood and urinary nicotine were measured by gas chromatography. The method is accurate, reliable, and capable of measuring nicotine levels of 0·1 ng. per ml.[10]

Statistical correlations and significance levels were calculated by Wilcoxon, Mann-Whitney, and Spearman rank statistics.

Results

Plasma-nicotine

The average plasma-nicotine level was significantly higher after exposure to cigarette smoke (table I) ($P<0.01$). Furthermore, although plasma samples from 6 non-smokers contained no nicotine before exposure, no plasma samples were negative after exposure ($P<0.01$, Fisher's Exact test).

Urinary Nicotine

The average urinary nicotine of non-smokers after exposure in the smoke-filled room was 80 ng. per ml. (table I) compared with 12·4 and 8·9 ng. per ml. for the two groups of non-smokers who had not been deliberately exposed to cigarette smoke (table II). The difference between those non-smokers who had been heavily exposed to tobacco smoke and those who had not is highly significant statistically ($P<0.001$). The small difference between the two groups (2 and 3) who had not been exposed is not statistically significant (see accompanying figure).

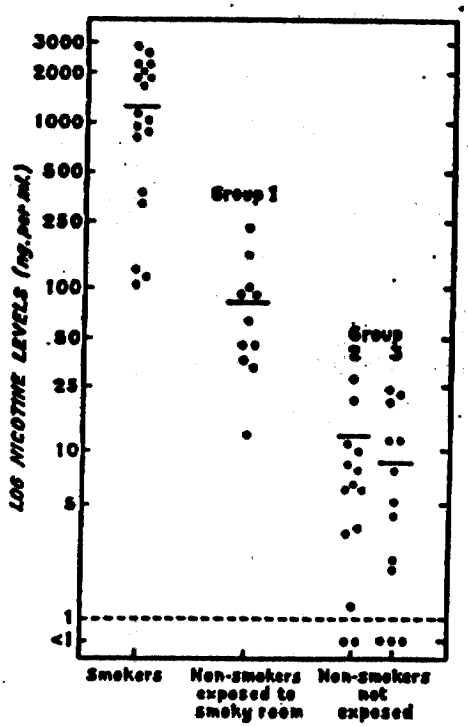
It was no surprise that the nicotine levels in smokers were considerably higher than in non-smokers. The overall average urinary nicotine concentration of the non-smokers was 10·7 ng. per ml., which is less than 1% of the average for the smokers (1236 ng. per ml.). The difference is even more pronounced when the nicotine excretions in ng. per hour are compared, the average of the non-smokers being less than 0·3% of the smokers' level (table II).

There was a slight negative correlation between urinary nicotine and the pH of the urine among the smokers, and this was also found for nicotine concentration in ng. per ml. ($r=-0.67$, $n=18$, $P<0.01$) and nicotine excretion in μg. per hour ($r=-0.56$, $n=17$, $P<0.05$). However, in the non-smokers these correlations were not significant ($r=-0.30$, $n=27$ and $r=+0.12$, $n=13$, respectively). The smokers' usual cigarette consumption correlated no better with urinary excretion in μg. per hour ($r=+0.70$, $n=16$, $P<0.01$) than with nicotine concentration in ng. per ml. ($r=+0.61$, $n=17$, $P<0.01$).

Discussion

After normal exposure to tobacco smoke, small amounts of nicotine were present in the plasma of about half of a small sample of non-smokers, but nicotine was almost invariably present in the urine. In only 1 out of 27 non-smokers was nicotine not found in the urine. The overall average urinary nicotine level of the 27 non-smokers under natural exposure conditions was 10·7 ng. per ml. (S.D. 13·6) and ranged from 0 to 64·3 ng. per ml. The lowest level among the 18 smokers was 104 ng. per ml. Under natural conditions, therefore, there was no overlap in urinary nicotine levels of smokers and non-smokers.

Some caution is necessary before advocating the use of urinary nicotine as a means of testing or confirming an individual's smoking-status. This was a sample of fairly heavy smokers. Only 1 smoked less than ten cigarettes a day. Among people who smoke fewer



Urinary nicotine levels of smokers and non-smokers with and without exposure to a smoke-filled room.

Group means are shown. Differences between the three groups are all highly significant ($P<0.001$), but the two samples of non-smokers who were not deliberately exposed do not differ significantly.

TABLE II—URINARY NICOTINE EXCRETION OF SMOKERS AND NON-SMOKERS AFTER USUAL DAYTIME EXPOSURE TO TOBACCO SMOKE

Non-smokers (group 2)			Non-smokers (group 3)				Smokers				
Sex	pH of urine	Urinary nicotine (ng./ml.)	Sex	pH of urine	Urinary nicotine ng./ml.	Urinary nicotine µg./hr.	Sex	Cigarette consumption (no./day)	pH of urine	Urinary nicotine ng./ml.	Urinary nicotine µg./hr.
M	6·3	8·0	F	5·8	0	0	F	25	5·1	1967	102·3
M	6·4	0·8	F	5·7	4·2	0·18	F	18	5·5	802	..
F	5·7	21·0	F	6·6	9·0	0·49	F	20	6·8	128	28·2
F	7·3	10·3	F	5·9	12·0	0·33	F	15	6·0	104	11·4
F	6·6	3·3	F	5·9	2·0	0·22	F	30	5·0	2609	861·0
F	7·8	1·2	F	6·7	26·0	1·50	M	20	6·7	312	34·3
F	5·9	6·3	M	6·6	0·2	0·01	M	25	6·6	1990	167·2
M	6·2	8·6	M	5·9	12·0	1·50	M	30	5·5	1788	78·7
M	6·1	0·8	M	6·1	23·5	1·17	M	8	6·2	109	20·3
F	7·1	3·5	M	5·0	19·3	0·87	F	20	5·1	1620	130·3
M	6·7	6·2	M	5·5	2·2	0·32	F	15	5·7	833	114·9
F	5·1	28·6	M	5·0	5·2	0·33	M	40	5·1	2732	300·5
F	5·0	11·3	M	6·3	0·2	0·03	M	20	7·4	375	68·2
F	5·0	64·3	..	..	..	..	M	20	5·8	1049	106·9
..	..	..	..	..	..	..	F	70	5·6	937	380·4
..	..	..	..	..	..	..	M	Pipe smoker	5·7	2073	153·4
..	..	..	..	..	..	..	M	20	5·7	1006	110·6
..	..	..	..	..	..	..	F	10	5·4	1808	50·6
Mean ± S.D.	6·23 ± 0·85	12·4 ± 16·9		5·92 ± 0·55	8·9 ± 9·1	0·53 ± 0·54		23·9 ± 14·1	5·83 ± 0·67	1236 ± 861	160·0 ± 205·0

cigarettes there is likely to be some overlap with non-smokers. In addition, after exposure in a smoke-filled room, 2 out of 11 non-smokers had urinary nicotine levels over 150 ng. per ml., which is higher than the level of some smokers. However, the concentration of tobacco smoke in the experimental room was extreme and would not be tolerated by non-smokers, or indeed by smokers, under normal circumstances.

Urinary nicotine has certain advantages over blood-carboxyhæmoglobin as a spot test of smoking-status. It is not an endogenous product, it does not require skin puncture, and specimens can be kept frozen and tested in batches, whereas carboxyhæmoglobin must be measured within a few days. With more experience in light smokers and better use of the relation to pH, urinary nicotine may provide a more reliable spot check of tobacco use than blood-carboxyhæmoglobin since urinary nicotine values in smokers and non-smokers do not overlap to the same extent as carboxyhæmoglobin values.

How much of the nicotine in non-smokers is taken in with food, water, or inspired air is not known. One study found no nicotine in tap-water,[5] but it is well known to be present in air contaminated by tobacco smoke,[3-5] and smoky air is by far the most likely source. In our first experiment, the tendency for plasma-nicotine in non-smokers to increase after exposure in the smoke-filled room was small. Urinary nicotine, however, was very much higher after exposure, with a mean level of 80 ng. per ml. compared with 10·7 ng. per ml. for non-smokers under natural conditions ($P<0·001$). The less impressive changes in plasma levels suggest that the nicotine is excreted almost as fast as it is absorbed. This probably accounts for the absence of any obvious physiological effects in non-smokers after exposure in a smoke-filled room.[12] However, this rapid excretion would be slowed by urine alkalinity and this may account for the isolated examples of non-smokers with an especially high plasma-nicotine. The fact that some nicotine is present in the urine of almost all non-smokers suggests that episodes of passive smoking are common in urban life.

We conclude that virtually all urban non-smokers have measurable amounts of nicotine in their body fluids throughout most of their lives. It is derived from the indoor air they breathe and it requires no more than one or two smokers to contaminate a vehicle or building.

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"We trained hard, but it seemed that every time we were beginning to form up into teams, we would be reorganised. I was to learn later in life that we tend to meet any new situation by reorganisation, and a wonderful method it can be for creating the illusion of progress while producing confusion, inefficiency, and demoralisation."—CAIUS PETRONIUS, A.D. 66.