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Health risk evaluation of nitrogen oxides. Exposure.

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2. Exposure

by Marika Berglund

Exposure assessment is an integral part of risk assessment. Accurate exposure data are crucial for the definition of dose-effect and dose-response relationships. Ideally, total exposure should be monitored when dose-effect and dose-response rates and the probability of risk for effects are evaluated.

The health risks posed by nitrogen oxides are determined by the personal exposure of individuals and not simply by indoor and outdoor concentrations. Long-term average concentration levels, diurnal variations, and short-term peak exposures, as well as the activity patterns and personal and home characteristics of individuals, are all important factors for exposure assessment.

Outdoor concentrations and human exposure

Data on ambient air levels of nitrogen dioxide (NO_2) from fixed stations in several urban areas have routinely been reported during the past decade, while levels of nitric oxide (NO) are seldom reported. Fixed stations are often located where maximum air pollutant concentrations are expected (and sometimes where background levels could be measured). Typically, the concentrations of NO_2 are 30-50% higher in the street than at the measuring point, which is generally situated several meters above street level (10-30 m).

The major source of human outdoor exposure to NO and NO_2 ($NO + NO_2 = NO_x$) in urban areas is traffic. There is a typical diurnal pattern of high concentrations during the morning and afternoon rush hours; hence substantial exposure can take place during commuting hours to and from work.

The concentration of NO usually follows the traffic intensity pattern closely, while the variations in the NO_2 concentration are more determined by meteorological factors. Typically, urban outdoor NO_2 concentrations are higher during the winter (heating season) and during periods of temperature inversion. During the summer season persistent anticyclone conditions (high pressure) can result in photochemical smog, which can lead to high concentrations of NO_2 in central city areas. (See chapter 1.)

Ambient data can be used to describe patterns and trends in NO_x levels over time, and they can adequately characterize the long-term average exposure of the general population to urban air pollution, but they may not be sufficient for the determination of dose-effect and dose-response relationships for NO_x, or for estimations of risks to various groups of the general population. Much effort has been put into the development of models for predicting personal exposure from ambient data.

Indoor concentrations and human exposure

Indoor air is not only contaminated by the infiltration of ambient air, but also by emissions from various indoor sources of NO_x (eg, gas stoves used for cooking, unvented gas and kerosene space heaters, unvented wood stoves, and tobacco smoking). The indoor NO_x concentrations are dependent on the infiltration rate of NO_x from outdoors, the type of ventilation (mechanical, forced, or natural), the air exchange rates, the presence of indoor sources and how they are used (eg, the use profile for cooking stoves is different from that of heaters), and removal processes (controlled, eg, by the type of furnishing and building materials and the relative humidity).

Indoor levels of NO_2 in homes without indoor sources are generally lower than outdoor levels, and they are higher in the summer than in the winter, partly due to more frequent ventilation. For the same reason, indoor levels in homes with indoor sources are generally higher than outdoor levels and lower in the summer than in the winter (1-3) (table 2.1). Indoor levels of NO are rarely reported, but are reflected by outdoor levels in homes without indoor sources. In Stockholm, indoor levels of about 25 $\mu g \cdot m^{-3}$ NO have been measured in homes close to a street with moderate traffic. During the night the NO levels can be higher indoors than outdoors due to the slow degradation and ventilation of NO (A Hadenius, Environmental and Health Administration, Stockholm, personal communication).

Microenvironmental monitoring

During the past decade, small passive monitors with high precision and accuracy have been developed for NO_2 (4-6). Passive samplers have been used to measure NO_2 concentrations in various microenvironments, as well as in personal exposure moni-

Table 2.1. Summary of indoor, outdoor, and personal nitrogen dioxide (NO_2) exposure measurements (NO_2 $\mu g \cdot m^{-3}$) in different microenvironments, and indoor:outdoor (I:O) ratios (I=home or bedroom if I:O not given by author).

Source	Indoor			Outdoor	I:O ratios	Personal exposure	Reference
	Kitchen	Bedroom	Home				
Electric stove (no indoor source)	34	26		35	0.8		44[a]
	16	14		17	0.9	17	45[b]
			29	48	0.6	39	29[c]
		37	62	0.6	51		29[d]
	8	7		13	0.6		12[e]
	21	16	18	42	0.4	24	36[f]
	8	7	7	13	0.6		10[g]
					0.6		1[h]
					0.8		1[i]
	8	9		14	0.6		31[j]
	18	15		33	0.5		46[k]
	24	23		31	0.7		46[l]
	8	8	9	18	0.5	26	30[m]
Gas stove	211	57		35	1.6		44[a]
	59	37		17	2.8	41	45[b]
	66	37		16	2.2		12[e]
	45	28	34	15	2.3		10[g]
					3.2		1[h]
					2.4		1[i]
	80	46	61	42	1.4	48	36[n]
	70	41		23	1.8	86[o]	31[j]
	73	48		40	1.2		46[k]
	65	45		41	1.1		46[l]
Unvented space heater or geyser			80	51	1.6	67	29[c]
	39	32	37	13	2.8		10[g]
Gas stove + unvented gas appliances	139	60		46	2.1	88	35[p]
						75	35[q]
						70	35[r]
	74	68	67	14	4.8		10[g]

[a] Winter, about 500 households, Middlesborough, England.
[b] Summer, nine housewives, Topeka, Kansas, the United States.
[c] Winter and summer, 57 office workers, Tokyo, Japan.
[d] Winter and summer, 20 housewives, Tokyo, Japan.
[e] Integrated winter and summer data, 137 homes (25 electric and 112 gas), Portage, Wisconsin, the United States.
[f] Winter, about 30 homes, about 70 schoolchildren, Watertown, Massachusetts, the United States.
[g] Winter, about 300 homes (about 145 electric stove homes, 40 gas stove homes, 95 other indoor sources, 18 two indoor sources), New Haven, Connecticut, the United States.
[h] Winter, about 350 residents, about 85 homes (50 electric stove homes, 35 gas stove homes), rural area, Portage, Wisconsin, the United States.
[i] Summer, about 350 residents, about 85 homes (50 electric stove homes, 35 gas stove homes), rural area, Portage, Wisconsin, the United States.
[j] Winter, about 50 homes, 46 infants, Albuquerque, New Mexico, the United States.
[k] Winter and spring, about 300 gas stove homes, about 100 electric stove homes, Boston, Massachusetts, the United States.
[l] Summer, about 300 gas stove homes, about 100 electric stove homes, Boston, Massachusetts, the United States.
[m] Winter, 11 women, Stockholm, Sweden.
[n] Winter, about 100 homes, about 250 schoolchildren, Watertown, Massachusetts, the United States.
[o] 12-h waking day.
[p] Winter, 14 households, 13 housewives, Rotterdam, The Netherlands.
[q] Winter, 12 schoolchildren, Rotterdam, The Netherlands.
[r] Winter, nine preschoolchildren, Rotterdam, The Netherlands.

toring. A microenvironment has been defined as a particular location and time where a sufficiently homogeneous concentration of a pollutant exists and is significantly different from the concentrations at other locations (7). In general, sampling periods from 24 h to several weeks have been used, depending on the air concentration of NO_2 and the sensitivity of the sampler. If the passive sampler is sensitive enough, shorter periods, such as periods of peak exposures, can be measured (8).

Microenvironments with high levels of NO_2 have been identified, for example, homes and kitchens with gas stoves, homes with gas-fueled space heaters and water heaters, indoor ice-skating arenas, smoky environments, transportation environments, and close to a street with heavy traffic.

There is a great variation in the long-term average NO_2 levels among households with indoor sources (table 2.1). Households with gas-cooking stoves or space heaters have four to seven times higher 24-h average NO_2 levels than homes with electric stoves (9-11). Homes with both a space heater and a gas stove were shown to have two-week NO_2 levels averaging approximately double those of homes with one source only. Typically, the NO_2 concentration in the bedroom of a gas-cooking household is half that of the kitchen. Normal use of a gas stove has been reported to add 45 $\mu g \cdot m^{-3}$ to the background concentration in a home (12). Swedish data suggest that the use of gas for cooking adds about 10 $\mu g \cdot m^{-3}$ only to the weekly average NO_2 concentration in a home (13).

Peak levels of NO_2, measured 1 m from a gas stove were over 1100 $\mu g \cdot m^{-3}$ when the oven was on, and over 500 $\mu g \cdot m^{-3}$ when one single burner was on (9). Maximum 1-h averages ranged from 230 to 2055, and maximum 1-min averages ranged from 400 to 3808 $\mu g \cdot m^{-3}$ (14, 15).

Very high levels of NO_2 have been measured in indoor ice-skating arenas (16, 17). The weekly NO_2 concentrations that were reported ranged from about 200 to about 1500 $\mu g \cdot m^{-3}$, daily concentrations ranged from about 100 to about 5000 $\mu g \cdot m^{-3}$, and the maximum 1-h personal exposure concentration for a child playing ice-hockey was as high as 7500 $\mu g \cdot m^{-3}$. Probably, the very high levels of NO_2 result from the use of propane or gas-fueled machines used for resurfacing ice without adequate catalytic converters and adequate ventilation of the arena. Very high NO_2 levels have also been reported by Hedberg et al, about 7500 $\mu g \cdot m^{-3}$ (18), and by Dewailly et al, about 5600 $\mu g \cdot m^{-3}$ (19).

The levels of NO_x in smoky environments were reported to be 1-370 ppb NO (1-450 $\mu g \cdot m^{-3}$) and 0-50 ppb NO_2 (0-100 $\mu g \cdot m^{-3}$) higher than in similar control environments or outdoors (20). The extent of the increase varies with the number of smokers, the intensity of their smoking, and the ventilation rate of the indoor space. Leaderer et al (10) found a small but significant increase (1.1 $\mu g \cdot m^{-3}$) in the NO_2 concentration in the living room (not other rooms) of smokers (average 25 cigarettes per day), when they were compared with nonsmokers. No association was found between smoking at home and NO_2 levels, with the exception of smoking by the father and the child's exposure level (21). Cigarette smoke seems to be a significant but small source of NO_2 exposure among nonsmokers.

Commuting exposures to NO_2 seem to be similar to well-mixed ambient levels, probably due to the slow process of NO_2 formation from NO. Harlos et al (15) measured NO_2 continuously during commuting by car and bicycle. The average 1-h concentration was 75 $\mu g \cdot m^{-3}$ (maximum 100 $\mu g \cdot m^{-3}$), the 30-min average was 90 $\mu g \cdot m^{-3}$ (maximum 100 $\mu g \cdot m^{-3}$), and the 1-min average was 135 $\mu g \cdot m^{-3}$ (maximum 210 $\mu g \cdot m^{-3}$). Sega & Fugas (22) reported average transportation NO_2 concentrations of 100-150 $\mu g \cdot m^{-3}$ in the city and 50-80 $\mu g \cdot m^{-3}$ in the suburbs. The NO exposure levels were not reported, but they are probably reflected by the ambient levels.

Personal exposure assessment and activity patterns

Exposure is a function of concentration and time. People spend various periods in different types of microenvironments with various concentration levels (table 2.2). On the average, people spend about 90% of their time indoors (at home, work, school, etc), about 5% in transit (23, 24), and 7 (range 3-12) % near smokers (25). These values vary with the season, day of the week, age, occupation, and the like, but, definitely it is important to predict indoor pollutant levels when total exposure is being estimated.

Indirect and direct methods for personal exposure assessment are available. *Indirect* methods combine measures of concentrations at fixed sites in various types of microenvironments with information on where people have spent their time (time-activity patterns). Time-weighted average (TWA) exposure models have been developed to estimate total personal exposure (7, 26-28). The NO_2 exposure levels predicted from TWA exposure models have been shown to correlate closely with the exposure levels obtained by direct measurements of personal exposure (1, 22, 29). However, the large variation in NO_2 concentrations (distribution) within each type of microenvironment because of variability, in, for example, stove use, emission rates, ventilation frequencies, and the day-to-day and person-to-person variations in the use of time decreases the accuracy of the predicted exposure and increases the risk for misclassification of the exposure.

Table 2.2. Summary of the average amount (as percentage) of time (winter/summer) spent in various types of microenvironments for different sectors of the general population.

Sector of the population	Indoor			Outdoor	In transit	Reference
	Home	Work/school	Other			
Employed	50/50	33/32		8/7	9/11	29[a]
	66/59	19/16	6/7	3/12	6/6	1[b]
	57	23	10	4	6	30[c]
Unemployed/ housewives	82/88			18/12		29[a]
	81	1	10	7		35[d]
	83/75	3/0	8/7	2/13	4/4	1[b]
Schoolchildren/ students	77	9	8	6		35[d]
	65	23	5	6	1	36[e]
	66/68	20/4	7/9	4/15	3/3	1[b]
	68	14	10	8	2	16[f]
Preschool-children	83	4	8	4		35[d]
	88		8	<1	3	31[g]
Mixed population	67	14	7	12		47[h]
Total range	50-88	0-33	5-10	<1-18	1-11	

[a] Fifty-seven office workers, 20 housewives, Tokyo, Japan.
[b] About 130 workers, 30 nonworkers, 176 students (elementary, junior and high school), Portage, Wisconsin, the United States.
[c] Winter, 15 Swedish women, Stockholm, Sweden.
[d] Winter, 12 mothers, 11 schoolchildren (mean age 7.8 years), 10 preschoolchildren, Rotterdam, The Netherlands.
[e] Winter, about 370 schoolchildren, 12-14 years of age, Watertown, Massachusetts, the United States..
[f] Winter, 53 schoolchildren, Sundsvall, Sweden.
[g] Winter, 46 infants, Albuquerque, New Mexico, the United States.
[h] Integrated summer and winter data, about 500 households, N=1283 daily diaries, Los Angeles, California, the United States.

Direct measurements of the concentration in the breathing zone of a person using personal passive exposure monitors provides time-integrated measurements of exposure for a certain period across the various microenvironments where a person spends time. It is important to collect exposure data over time intervals consistent with the expected effects. Effects from long-term low-level exposure may be different from effects from short periods of high concentration (intermittent peak exposure). (See chapter 4.) Intermittent peak exposure, which occurs during cooking on a gas stove, may be significant to total exposure and adverse health effects. If effects from peak exposure are to be considered in the exposure assessment, the sampling time must be short enough to detect these peak exposures. Such a short sampling time is possible with the more sensitive passive samplers and with conventional air monitors, such as chemiluminescence NO_x monitors. However, direct methods of measuring personal exposure are relatively costly and time consuming. Within-person and between-person variability, both in personal exposure and personal use of time, can be large. Hence a sufficient number of personal exposure measurements must be collected for each person (repeated measurements), and a sufficient number of individuals must be sampled before the measurements can be considered to be representative. Personal daily exposures have been shown to vary between individuals on the same day by a factor of up to about 15 in the urban area of Stockholm and between days for the same individual by a factor of up to about 10 (13, 30).

Relationships between indoor, outdoor and personal measurements of nitrogen dioxide

The relationships between indoor, outdoor, and personal NO_2 exposure concentrations are shown in table 2.1 for several studies. The long-term indoor: outdoor ratio, when no indoor source is present, is on the order of 0.4 to 0.9, typically 0.5-0.6, and it is lower in winter than in summer. For homes with indoor sources, the indoor:outdoor ratios are larger than 1, typically 2-3, and they are larger in winter than in summer.

Indoor concentrations are strong predictors of personal exposure. Personal exposure has been shown to be closely related to the household indoor average concentrations, especially to bedroom concentrations, for homes with gas or electric stoves (1, 10, 31-33).

The average long-term increase in NO_2 exposure among children from the use of an unvented gas stove or a geyser ranges from about 10 $\mu g \cdot m^{-3}$ (Swedish data, 13) to about 30 $\mu g \cdot m^{-3}$ (meta-analysis of several studies) (34). The correlation between mothers' and children's exposure has been shown to be high (coefficient of determination 0.92), but the mothers' exposure was about 20% higher than the children's (35).

Outdoor concentrations, even if measured outside each residence, have been found to be relatively poor predictors of personal exposure (1, 10, 29, 32, 36). The association between personal exposure and outdoor levels of NO_2 is weakest during the winter for both gas and electric stove groups.

Dose and biological markers

The only route of NO_2 exposure is inhalation. The dose is dependent on the inhalation volume and thus on, for example, physical activity and age. The lung absorption of NO_2 is about 80-90% during rest and over 90% during physical activity (37). (See chapter 3.)

Efforts have been made to find a sufficient biological marker for NO_2 exposure and dose. Increased urinary excretion of collagen and elastin (pulmonary connective tissue) breakdown products (including hydroxyproline, hydroxylysine, and desmosine) have been suggested as markers of diffuse pulmonary injury related to inhaled NO_2. A significant relationship between urinary hydroxyproline excretion and daily NO_2 exposure was found among housewives in Japan (38), but the hydroxyproline excretion fell within the normal distribution of healthy people. The majority of the housewives were exposed to active or passive cigarette smoke, and this exposure was independently related to the excretion of hydroxyproline. Other investigators have not been able to substantiate the relationship between urinary hydroxyproline excretion and NO_2 exposure (39, 40).

Measurements of the NO-heme protein complex in bronchoalveolar lavage (41) and 3-nitrotyrosine in urine (42) have been suggested as biological markers for NO_2 exposure. The work in progress to find a sufficient biological marker for NO_2 exposure at levels found in the general environment is promising; however, no metabolite has yet been proved to be sensitive or specific enough.

Estimates of nitrogen dioxide exposure among the general Swedish population

It has been estimated that about 3% of the Swedish population is exposed to NO_2 levels exceeding the 1-h national standard level of 110 $\mu g \cdot m^{-3}$ (98th percentile) (43). Most of the persons live on heavily trafficked streets in the main urban areas (26 and 13% of the residents of Göteborg and Stockholm, respectively). In smaller towns virtually no excessive exposure to ambient NO_2 has been noted. The estimations have been based on modeled results from emission inventories and on measurements of traffic emissions close to major roads. Possible exposure to NO_2 from the use of gas stoves has not been considered. The proportion of the population excessively exposed increases dramatically at an 1-h NO_2 standard level of 100 $\mu g \cdot m^{-3}$ (98th percentile), from about 300 thousand to about 1 million people. No estimation of NO exposure was made.

About 150 000 Swedish households, concentrated in the main cities of Sweden, use piped gas for cooking (Swedish Statistics 1992, personal communication).

Summary and concluding remarks

The major source of human outdoor NO_x exposure in urban areas is traffic. Outdoor concentrations are typically higher during morning and afternoon rush hours, the heating season, and periods of temperature inversion. During the warm season, persistent anticyclone conditions can lead to elevated levels of NO_2 in urban areas.

Indoor air concentrations reflect outdoor air concentrations when no indoor sources of NO_2 are present. The long-term average indoor:outdoor ratio is lower in winter than in summer when no indoor source is present, and is on the order of 0.4 to 0.9, typically 0.5 to 0.6,

Indoor levels in homes with indoor sources are typically higher than outdoor levels. Gas-fueled cooking stoves and water heaters with pilot lights are the major indoor sources of NO_2. There is a large variation in NO_2 levels within the gas-cooking home category, with some of them in the range of electric-cooking homes. Concentrations of NO_2 in the kitchens of households with gas stoves are often four to seven times greater than concentrations in kitchens of households with electric stoves. Kitchen concentrations are often higher than living room concentrations, which in turn are often higher than bedroom concentrations in homes with gas stoves. In homes with indoor sources, the indoor:outdoor ratios are greater than 1, typically 2-3, and greater in winter than in summer.

Exposure is a function of concentration and time.

On the average, people spend about 90% of their time indoors. In general, outdoor concentrations are relatively poor predictors of total personal exposure. Long-term personal exposure is closely correlated with home average concentrations and bedroom concentrations. Population distributions of activity patterns are similar across various studies, but there are large person-to-person and day-to-day variations in time use.

The work in progress to find a sufficient biological marker for NO_2 exposure at levels found in the general environment is promising; however, no metabolite has yet been proved sensitive or specific enough for this task. Currently, there is no useful biomarker for environmental NO_2 exposure.

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