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INDOOR AIR QUALITY IN RELATION TO SENSORY IRRITATION DUE TO VOLATILE ORGANIC COMPOUNDS

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ABSTRACT

The Sick Building Syndrome (SBS-syndrome) as defined by a WHO working group is discussed, and the existence of a sub syndrome is postulated, based on observations reported in the literature. This sub syndrome relates mucous membrane irritation - sensory irritation, dryness in nose and eye, which are very frequent symptoms within the Sick Building Syndrome - to the total concentration of volatile organic compounds (VOC) of the solvent type. This VOC syndrome may include other until now unidentified symptoms.

The postulated dose-response relation is supposed to be multifactorial and two thresholds are therefore of interest. Below a lower threshold, no irritation is expected due to VOC. Total concentrations above the higher limit are expected to cause irritation irrespective of any other exposure. Other exposures may, of cause, modify the intensity of the irritation. Concentrations in between the two limits may, depending on the effect of other exposures, promote irritation due to these other exposures.

A survey of the few observations reported in the literature indicates these two limits to be about 0.16 mg/m^3 and 2 mg/m^3 respectively. Most of the known total concentrations in the non industrial environment are above 0.16. Complaints were reported in all cases where concentrations were above 2 mg/m^3.

INTRODUCTION

Within the last decade an increasing number of indoor climatic complaints have been reported (1-4) from occupants in newly built or newly renovated buildings. A typical pattern of such complaints has been related to the nonindustrial indoor atmospheric environment, and these complaints are normally not found in similar older buildings. The increasing number of complaints coincide with changed building and housing practices, which include the use of new building materials and reduction in ventilation and tighter building envelopes. These all foster increased concentrations of indoor air pollutants.

The special pattern of complaints about indoor climate led the World Health Organization (WHO) to the definition of the Sick Building Syndrome (SBS) (5). This syndrome includes the symptoms shown on Table 1. The unspecific symptoms may all be caused by a combination of physical, chemical, biological, or psychological environmental factors. A number of such known or postulated causalities have been described in the literature (1-5). The known objective clinical signs are few and unspecific.

The diagnosis of SBS syndrome is therefore often established by comparison of known or supposed exposures with observed objective or subjective symptoms and by exclusion of other causes.

THE SICK BUILDING SYNDROME

The pattern of complaints called the Sick Building Syndrome (SBS) is similar to that observed in groups of persons exposed to irritating gases and vapors. Formaldehyde is such an example

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(6). The SBS syndrome, however, also occur in buildings with negligible formaldehyde concentrations in the air. Formaldehyde therefore cannot be the sole cause of the SBS syndrome.

Complaints of irritation of the mucous membranes in eye and nose, typically described as "dry mucous membranes", are often related to low air humidity by the occupants. Controlled exposure experiments with air humidity (7, 8) have, however, shown no effects of low air humidity by itself on the sensation of irritation. Moderately low humidity is therefore probably not the general cause of complaints about dry mucous membranes.

A number of other physical, chemical, and biological factors are known to cause complaints about the indoor atmospheric environment. They are summarized in references (9, 10). The total combined effect of simultaneously occurring exposures to several of these factors is unknown, but both additive and synergistic effects may occur.

The mechanism by which the many contributing atmospheric factors cause people to react is, in most cases, unknown. The Sick Building Syndrome may even have to be split into sub syndromes, each covering special reaction mechanisms. One such subdivision may include normal allergic reactions such as airway allergies (asthma, rhinitis, vasomotorica, and allergic alveolitis). These reactions have been found in several cases, but such allergic reactions must be excluded in many other cases, as the complaints are characterized by strong irritation and not by sneezing, tearing, and nose secretion, which are characteristic of airway allergies (11).

The irritation in eyes and airways may in some cases be explained by physical and chemical irritation of the common chemical sense (12, 13), which is known both in humans and in animals. This sense is composed of different types of nerve-endings in eyes, nose, throat, and lower airways. They may be activated by irritating gases and vapors. No qualitative separation is made between irritations caused by different chemical and physical exposures. Only the intensity of the burning and smarting sensations differs. In this paper this subdivision of the SBS in several subsyndromes will be illustrated in a discussion of the dose-response relation for irritation of the chemical sense in eye and nose caused by volatile organic compounds of the solvent type.

A CLASSIFICATION OF FACTORS LEADING TO THE SICK BUILDING SYNDROME

In practice, the discussions in occupational hygiene normally focus on one health risk factor at a time and in such ranges of it, that this factor can be assumed by itself to cause complaints or illness. Such extreme values are typically not found in nonindustrial buildings. In consequence, the dose-response relationship may be multifactorial. A suggested classification of the many factors involved in such a multifactorial relationship is shown in Figure 1. From the physical, chemical, and biologically environment, a number of very different factors (temperature, concentration of pollutants, etc.) act upon the human organism. All these factors may interact (synergistically or antagonistically, etc.), thereby modifying their combined total effect. Each individual may react to this combined exposure with one or more symptoms. The intensity of each of these symptoms may be modified by additional factors such as age, smoking habits, sex, etc. The number of symptoms observed and their intensity may finally have a feedback effect on the individual's behavior, thereby causing them, for example, to change their environment or, in combination with an input from the social environment, to focus on certain symptoms and thus suppress others. It is characteristic of this model that each symptom may have several coinciding causes. The complaints therefore do not necessarily disappear if one cause is identified and removed from the environment. As another consequence, each subject may react differently to the mixed exposure and exhibit only a few of the symptoms from the spectrum of symptoms observed in the exposed population.

VOLATILE ORGANIC COMPOUNDS AND MUCOUS MEMBRANE IRRITATION

Mucous membrane irritation is one of the frequent symptoms in the Sick Building Syndrome (14). A number of physical, chemical, or psychological factors may individually or in combination lead to this symptom. The symptom is, however, similar to the irritation from the industrial environment where irritating volatile organic compounds are well known as irritants of mucous membranes in eyes and nose. In a toxicological evaluation of 62 chemicals found in indoor air and originating from building materials (15), 84% of the compounds were known or suspected irritants. Their irritating potency is known to vary much (16, 17), but for a wide variety of ordinary organic solvents, the potency is relatively similar when compared to more special compounds such as formaldehyde. It may therefore turn out that these ordinary organic compounds more conviently may be dealt with in combination and the special compounds treated as

separate problems.

The discomforting irritation related to the SBS may differ from that discussed in occupational hygiene. The occupational irritation refers to levels of reduced performance and to health risks. Even if the same sensoric mechanisms are involved for different compounds in the nonindustrial environments, these compounds may, as illustrated in Figure 2, show quite different slopes for the dose relations in the two ranges of concentrations characteristic of the industrial and nonindustrial environments. Very different potentials, as given for three different compounds in the occupational ranges, by their ED_{50}, may therefore not imply a similar difference for the same compounds at the low concentration found in the nonindustrial environment. This type of consideration leads to the hypothesis that the combined irritative effect of an atmosphere containing, e.g., 20 more compounds in concentrations well below the ED_{50} may be evaluated through the total concentration of these compounds.

Figure 3 shows Figure 2 modified for the relation between the total concentration of volatile organic compounds and the SBS syndrome. The pattern of symptoms to consider includes first of all irritation of mucous membranes but may include other symptoms unidentified until now. It follows from the figure that if the volatile organic solvents are related to a subsyndrome within the Sick Building Syndrome, the underlaying reaction mechanism should be multifactorial. In consequence, the dose-response relation will have to be divided in three ranges. A lower limit may exist below which no effects are observed from exposure to VOC. At concentrations higher that the upper limit, irritation will occur but the intensity may be modified by other exposures. In between the two limits, irritation may occur if other exposure factors are interacting. Each of these two thresholds in the dual threshold concept is, in principle, similar to the occupational TLV in the sense that they may be defined by, for example, the x-percentile reacting in the exposure group.

It cannot be ruled out that one or more compounds exist, until now undetected due to their low concentrations, which have a high enough irritating potency to produce irritation. Such strongly irritating compounds may exist (18), but if they were as widespread as the SBS has indicated, they should have been noticed in the industrial environment where much higher concentrations of these compounds may be expected. A reasonable hypothesis may therefore be that such undetected compounds are only involved in special SBS-cases, and they cannot be expected to be of general importance. Even if they do have a substantial effect on the indoor climate, the total concentration of volatile organic compounds may be a convenient tracer for their presence.

The existence of such a subsyndrome does not exclude the effect of strong irritating compounds. They may, like formaldehyde, contribute to or even dominate the cause for irritation. These cases may, however, more conveniently be considered as separate subsyndromes.

VOLATILE ORGANIC COMPOUNDS IN THE NONINDUSTRIAL ENVIRONMENT

Any human activity in the indoor environment is a potential source for air pollutants. Building and furniture materials are known to emit gases and vapors (19). Ventilation transports outdoor pollutants, such as sulphur dioxide and nitrogen oxides, to the indoor environment. Maintenance, cleaning, and cooking create their own sources. The human metabolism and human activities such as smoking are other sources for gases and vapors. To these sources may be added industrial sources such as copy machines, printing machines, glue, and spray cans, etc. (20). These sources may be important point sources and, for short-term intervals, create high concentrations. High concentrations, in a relatively short interval, however, do not necessarily indicate high dose, and mathematical models show that the emission from building materials account for the average concentrations of organic gases and vapors found in buildings (21).

The most characteristic feature of sources due to processes or human activity is their rapid variation with time and much higher maximum concentrations when compared to the more steady sources related to building materials and furniture. Such rapid, varying emission patterns would easily be correlated to any variations in the frequency of acute irritation. Such correlations are normally not observed in sick buildings. This type of source may, therefore, not play an important role in relation to the SBS when compared to the more steady sources.

A recent literature review performed by I.Johansson (22) contains 12 references to measurements of gases and vapors in the indoor environment. The most frequently seen group of organic compounds is the alifatic or alicyklic hydrocarbons with 6 to 17 carbon atoms. Toluene and three Xylenes are the most frequent compounds. Monoterpenes ($C_{10}H_{16}$) and halogenated alkanes are frequently seen too. The number of compounds identified may be as high as 250, but normally the

number is from 20 to 150. Generally 20 to 30 compounds are present in all samples and together account for between 50% and 75% of the total amount of these types of compounds in the air. All other compounds are only seen occasionally. Table 2 shows the total concentrations reported in these twelve (12) and a few other buildings (28, 29). The measurements have been divided into dwellings, offices, and schoolrooms. The concentration in older houses (range 0.02-1.7 mg/m^3) seems to be about 1/10 of that found in new houses, where the range of concentration is from 0.5 mg/m^3 to 19 mg/m^3. Corresponding occupational total concentrations will typically be in the range of 1/10 to one times their respective occupational threshold limit value (TLV), which is about 40 to 400 mg/m^3. The question therefore is whether the nonindustrial concentrations are so low that the VOC have no effect by themselves or do not even interact with other factors to result in noticeable effects.

HUMAN REACTIONS TO VOLATILE ORGANIC COMPOUNDS

The U.S.-recommended threshold for volatile organic compounds in the outdoor environment is 0.16 mg/m^3 (35). This recommendation is based on the importance of these compounds in photochemical smog pollution. No sufficient information is available about the presence of these processes in the indoor environment, although they have been postulated in relation to fluorescent lights in office buildings. This recommended outdoor concentration, therefore, can only indicate a lower limit below which VOC are without effect, alone or combined with other factors.

Occupational threshold limits are normally based on evidence from exposure experiments with concentrations much higher than those found in the indoor environment. Furthermore, such experiments often focus on health effects much more severe than the relatively harmless comfort-reducing mucous membrane irritation. Only a few experiments, therefore, can be used to extrapolate to the low concentration area. In an occupational, controlled exposure experiment with Toluene (36), which is the most frequent-found organic solvent both in the industrial and in the non-industrial indoor environment, subject were exposed to 0, 10, 40, and 100 ppm Toluene (TLV = 100 ppm = 350 mg/m^3). Both air quality and odor sensitivity were significantly impaired at 10 ppm Toluene (38 mg/m^3). All other factors in this experiment were within the comfort range. The effect of 10 ppm Toluene, therefore, is a direct consequence of the Toluene alone. Many other compounds found in the indoor environment are considered more mucous membrane irritative than Toluene (37). The effect of a mixed hydrocarbon exposure may, therefore, have a threshold concentration lower than 38 mg/m^3.

To search for such a threshold, a controlled exposure experiment was established in the climate chamber at the Institute of Hygiene, Aarhus, Denmark (38, 39). In the experiment humans were exposed to a mixture of normal air pollutants in small concentrations. The aim was to investigate if mucous membrane irritation would occur. It follows from this experiment that air quality may be significantly reduced both at 25 mg/m^3 and 5 mg/m^3. The effect was acute and occurred within minutes after start of exposure and no adaptation was seen (40). The healthy subjects may have been more reactive than randomly selected subjects, and exposure factors other than concentration of VOC were slightly uncomfortable. Five mg/m^3 may therefore be in the lower end of the range for combined irritative effects.

In the exposure experiment, some indication of objective effects related to odor threshold, to chemical changes in eye and nose liquids, and to performance were seen as a result of the exposure (41, 42). Irritation of eye and nose is, therefore, not the only effect to consider as a result of exposure to volatile organic compounds, and a VOC subsyndrome may thus exist.

In eight of the twelve measurements reported by I.Johansson (22) human reactions was described. These eights measurements are shown at Table 3. The concentrations in houses with indoor climate problems are in the range from 0.09 to 13 mg/m^3 (average 1.3 mg/m^3), while the concentration in houses where no problems were reported is from 0.02 to 1.7 mg/m^3 (average 0.36 mg/m^3). The reported concentrations are improperly documented and may be biased in sampling. They do, however, indicate that the concentration of volatile organic compounds is generally higher in problem houses than in the houses without problems. The number of houses and the measurements are, however, insystematic and are insufficient for a final conclusion, but complaints seem to be present when the concentrations exceed 1.7 mg/m^3. Below 1.7 mg/m^3 complaints may occur with other types of simultaneous exposures. The conclusion of the available information is that no irritation should be expected due to exposure to volatile organic gases and vapors below 0.16 mg/m^3 . At concentrations higher than 1.7 mg/m^3 , complaints seem to occur in all reported cases, and at 5 mg/m^3 in a controlled exposure experiment, indication of objective effects was found besides the subjective irritation effect.

CONCLUSION

The observations found in the literature are scarce and in most cases improperly documented. They do, however, indicate that a subsyndrome may have to be separated from the Sick Building Syndrome. This subsyndrome is dominated by irritation symptoms in eye and nose but may include other effects related, for example, to performance. Such effects has not yet been identified. Volatile organic compounds are in this respect defined as organic compounds of the industrial type and with much less potential for mucous membrane irritation than formaldehyde. The proposed dose-response relation is multifactorial, which means that the effect of simultaneous exposure to other factors may be of importance for response.

The postulated relation is summarized in Table 4. At concentrations higher than 2 mg/m^3, irritation is expected in most cases, but the intensity and frequency in the exposed group may be modified by the effect of other exposures. In the range of 0.16 to 2 mg/m^3, VOC may cause irritation, but an added effect of other factors is needed for this to occur. Below 0.16 mg/m^3, no effects of VOC are expected.

To finally establish the proposed dose-response relation, future investigations should be done on total concentrations of VOC and irritation of eye and nose in buildings with and without complaints. The vast majority of investigations, however, has until now focused only on a limited number of tracer compounds, and no information is normally given about the sampling site selection and about complaints from the occupants. Future investigations should include both total concentration and number of compounds identified. Numbers of chemical groups represented and total concentration related to each group should be available, too. At the minimum, information on symptoms should include frequency of each of the symptoms included in the Sick Building Syndrome.

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TABLE 1

The Sick Building Syndrome as Defined by WHO (5)

- eye, nose, and throat irritation
- sensation of dry mucous membranes and skin
- Erytheme
- mental fatigue
- headaches, high frequency of airway infections and cough
- hoarseness, wheezing, itching, and unspecific hypersensitivity
- nausea, dizziness

TABLE 2

Total Concentrations in mg/m^3 of Volatile Organic Compounds Reported from Nonindustrial Atmospheric Environments

INHABITED	AGE	DWELLINGS ETC. mg/m^3	REF.	OFFICES ETC. mg/m^3	REF.	SCHOOLS ETC. mg/m^3	REF.
NO	NEW	0.48-18.7	23	-	-	-	-
	OLD	0.24-0.52	24	-	-	0.01 0.05	30a 31a,b
YES	NEW	12.9	25	-	-	0.86	32a,b
	OLD	0.02-1.7 0.25 1.05	26 27a,b 28	0.09-1.51 0.4-1.6	28 29c	0.13-0.18 0.14 0.29-0.50 0.22-0.31	30a 31a,b 33,34,a,b 32a,b

Notes:

a: Sum of selected compounds
b: See reference (22)
c: Estimated value
- No information

TABLE 3

Total Concentrations of Volatile Organic Compounds Measured in Occupied Nonindustrial Indoor Environments

COMPLAINTS	DWELLINGS mg/m^3	REF	OFFICES ETC. mg/m^3	REF	SCHOOLS ETC. mg/m^3	REF	WEIGHTED AVERAGE mg/m^3
NO COMPLAINTS OR NO INFORMATION	0.02-1.7	26	-		0.86 0.22-0.31 0.14 0.13-0.18	32a,b 32a,b 31a,b 30a	0.36 (N=47)
COMPLAINTS	1.05 0.25 12.9	28 27a,b 25	0.09-1.51 0.4-1.6	28 29c	0.29-0.50	33,34,a,b	1.31 (N=24)

Notes:
a: Sum of selected compounds
b: See reference (12)
c: Estimated value
- No information

TABLE 4

Concentration Thresholds for Irritation of Mucous Membranes Due to Volatile Organic Compounds of Solvent Type

TOTAL CONCENTRATION mg/m^3	IRRITATION	INTERACTIONS
< 0.16	NO EFFECT	
0.16-2	EFFECT POSSIBLE	PROVIDED OTHER EXPOSURES
> 2	EFFECT PROBABLE	MAY BE MODIFIED BY OTHER EXPOSURES

LEGENDS

Figure 1: Classification of factors relevant for investigation of the Sick Building Syndrome

Figure 2: Idealized dose-response relation for three different potential mucous membrane irritating compounds. Abscisses show logarithmic concentration and ordinate percent reacting persons in the exposed group. ED_{50} = Effective dose, 50% reacting.

Figure 3: Classification of factors relevant for investigations of irritation due to volatile organic compounds (VOC).

▬▬ : Direct action of VOC leading to irritation

—— : Reactions modifying the intensity of VOC-irritation

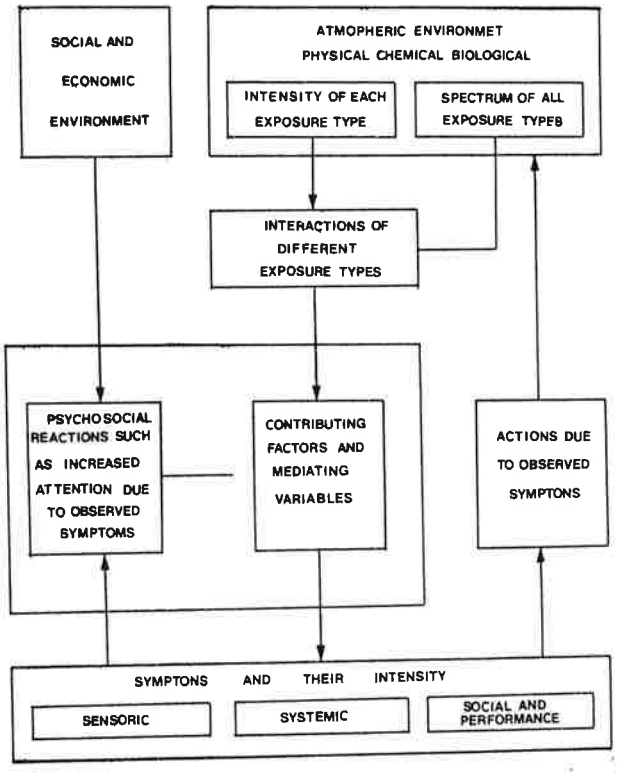

Figure 1. *Classification of factors relevant for investigation of the sick building syndrome*

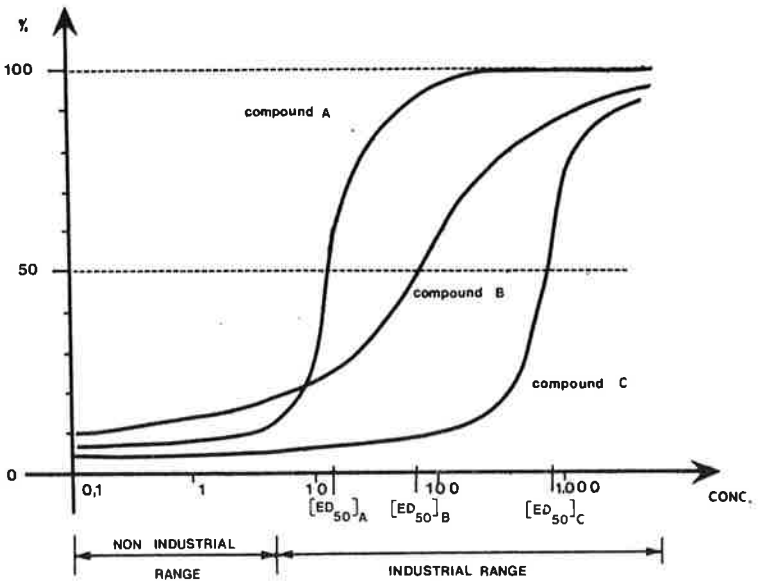

Figure 2. *Idealized dose-response relation for three different potential mucous membrane irritating compounds. Absises show logarithmic concentration and ordinate percent reacting persons in the exposed group*

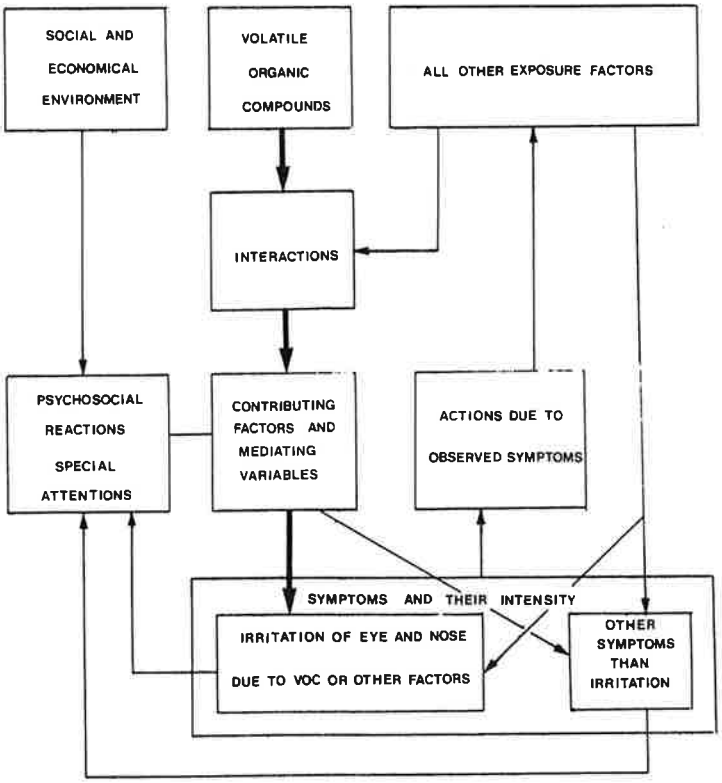

Figure 3. *Classification of factors relevant for investigations of irritation due to volatile organic compounds (VOC)*

———: *Direct action of VOC leading to irritation*

———: *Reactions modifying the intensity of VOC-irritation*

Discussion

W.S. CAIN, John B. Pierce Foundation, New Haven, CT: In the field measurements you reported, were measurements of humidity taken along with the measurements of concentration of volatile organic contaminants? If so, was there any attempt to correlate complaints with the combined effect of organic contaminants and humidity?

MOLHAVE: No systematic information on air humidity is available from the field measurements found in the literature, and consequently no analyses of correlation could be done.