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Neuropsychological symptoms and occupational exposure to anaesthetics

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Abstract

***Objective*—To analyse the relation between symptoms regularly reported by hospital personnel and exposure to anaesthetics.**

***Setting*—Personnel of 18 hospitals in Paris from 1987 to 1989.**

***Design*—An exposed group that included all operating theatre members except for doctors, and which was divided into three subgroups depending on the degree of exposure—exposure was measured by the frequency of the use of the scavenging system—and a control group that included other hospital personnel matched by hospital, sex, occupation, age, and duration of service.**

***Subjects*—557 exposed workers and 566 unexposed workers.**

***Main outcome measures*—The groups were compared according to the crude rates of regular symptoms. Adjusted odds ratios were calculated to estimate the risks associated with exposure to anaesthetic gas. Liver transaminase activities (alanine aminotransferase, aspartate aminotransferase (s-ASAT, and γ-glutamyl transpepsidase) were measured and compared between groups of exposure.**

***Results*—After controlling for working conditions and matching factors, neuropsychological symptoms and tiredness were reported more by workers in less often scavenged theatres than by controls. No difference was found between workers of the well scavenged theatres and controls. Among the exposed workers, the members of paediatric surgical staffs reported a higher rate of neurological complaints (tingling, numbness, cramps) and tiredness than the members of the other surgical staffs. They had a high value of s-ASAT more frequently than the other exposed workers.**

***Conclusion*—These results strengthen the hypothesis of a causal relation between exposure to anaesthetics and neuropsychological symptoms, and show a dose-response effect. They suggest that the use of ventilating systems in operating rooms is an effective means of prevention.**

The effects of the exposure to anaesthetic gases on health has been investigated in various ways. Some authors have studied mortality.[1–5] High death rates from malignancies of the lymphoid and reticuloendothelial tissues and from suicides have been reported. Some chronic diseases such as neuropathies, liver diseases, and kidney diseases[6–9] have been examined but conclusions are inconsistent. The effects of anaesthetics on reproduction have been of particular concern.[10–19] An increased incidence of spontaneous abortions among female staff and among wives of exposed men has been found with a certain consistency,[8–13] despite the methodological difficulties associated with this type of study.[18] Also, some authors described a higher incidence of birth defects among children of workers exposed to anaesthetic gases.[19]

Few studies have analysed the symptoms of exposed workers.[20–22] Yet symptoms may be of interest either as indicators of the onset of an illness or as elements which disturb the wellbeing, the quality of life, and the competence of the workers. The purpose of this study was to analyse the relation between the symptoms reported by hospital personnel and exposure to anaesthetics under different conditions.

Patients and methods

SURVEY

The survey was carried out in 18 hospitals in Paris between June 1987 and June 1989. All operating theatre staff of these hospitals except doctors were interviewed. They filled out a questionnaire before their routine visit to the occupational practitioner; a yearly visit that is mandatory for all employees in

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France. If necessary, the occupational practitioner completed the questionnaire with the worker. An unexposed group included members of other departments, matched by hospital, sex, occupation, age, and duration of service. These controls were interviewed in the same way as the exposed workers; an essential criteria for inclusion was that they had never worked in an operating room other than perhaps for a short period during their studies.

QUESTIONNAIRE

Data that described the following working conditions were recorded: use of formol, solvents, ethylene oxide, or antineoplastic drugs; exposure to ionising radiations; standing position; carrying heavy loads; inconvenient lighting; irregular meals; stress. Technical data, especially the number of air changes an hour, were supplied by hospital engineers for each operating room. Workers were classified in the following manner: those who worked in an operating room with 20 or more air changes an hour, those who worked in an area with 11 to 19 air changes an hour, workers in recovery rooms, and those who were in an area with 10 or fewer air changes an hour. Other criteria pertaining to exposure, such as duration of daily exposure, number of patients anaesthetised, proximity of the worker to patients, and surgical specialty were also noted.

Health state was described by the prevalence of the following symptoms reported during or at the end of a working day at least once a week: nausea, headaches, dizziness, memory impairment, irritability, decrease in reaction time, tiredness, tingling, numbness, cramps in arms or legs. A syndrome of neuropsychological disorders was defined as the accumulation of at least two of the three following symptoms for the same worker: headaches, dizziness, decrease in reaction time. Peripheral neurological disorders were defined as the presence of at least one of the following symptoms: tingling, numbness, or cramps in arms or legs.

As possible indicators of liver disease, the serum concentrations of alanine aminotransferase (s-ALAT), aspartate aminotransferase (s-ASAT), and γ-glutamyl transpeptidase (s-GGT) were estimated by the hospital laboratories for each subject. Workers who had values higher than the 90th percentile of the control distribution, stratified by sex, were distinguished from the workers who had lower values.

STUDY SAMPLE

One hospital in which the survey could not be conducted in a continuous way was excluded from the study. Among the remaining hospitals, 1429 persons were interviewed (765 exposed and 664 controls).

The information on the number of air changes an hour was missing for 67 persons, who were excluded. Among the exposed group, 141 workers were excluded because they reported being exposed for less than 30 minutes each day. All 65 workers in recovery rooms were kept in the exposed group even though they often answered that they had not been exposed or had been exposed for only a short period. Recovery rooms minister to several patients at the same time, and gases expelled by these patients are not collected, creating atmospheric pollution of an intermediate degree.

Among the control group, persons having worked in an operating theatre at any time, however short, during the last two years or during more than one year were excluded; 98 persons were in this category. The final sample included 557 exposed workers and 566 controls.

ANALYSIS AND STATISTICAL METHODS

The percentages of symptoms and excessive biological parameters have been compared among the four groups using the Mantel-Haenszel χ^2 test. The comparison of the four groups allowed a linear association to be tested. The differences in working conditions among the four groups were evaluated using Pearson's χ^2 test. Associations between symptoms and working conditions were tested with the Mantel-Haenszel χ^2 test adjusted for the group (exposed or control).

Factors that were significantly related both to the symptoms and to exposure were taken into account by logistic regression in order to analyse the relation between symptoms and exposure to anaesthetics. These models systematically included the following sampling factors: hospital, sex, age, duration of service, and occupation.

Among the exposed workers, the symptoms and the biological values were analysed in relation to the other exposure indicators described earlier.

The statistical analysis was carried out using SAS and BMDP software with the collaboration of the INSERM computer centre, SC5.

Results

Nausea, headaches, decrease in reaction time, neuropsychological syndrome, memory impairment, peripheral neurological disorders, and tiredness were reported more often by the workers of the less scavenged rooms than by all others (table 1). No significant relation was found between the serum values of s-ASAT, s-ALAT, and s-GGT and exposure to anaesthetic gas.

Table 2 describes the working conditions other than anaesthetic exposure for each exposure group. Some of these working conditions were related to the symptoms studied. The neuropsychological syndrome was reported more often by workers exposed to formol, by those using antineoplastic

Table 1 Symptoms and exposure to anaesthetics

Symptoms*	Controls (% with symptoms) (n = 566)	Exposed workers according to No of air changes an hour (% with symptoms) >20 (n = 142)	11–20 (n = 223)	≤10 (n = 192)	p Value
Headaches	17·3	26·0	33·2	37·7	p < 0·001
Dizziness	4·8	1·5	4·9	8·0	NS
Decrease in reaction time	13·3	12·5	13·5	24·9	p < 0·01
Neuropsychological syndrome†	6·6	4·0	10·5	22·0	p < 0·001
Irritability	23·4	19·3	23·8	21·4	NS
Memory impairment	10·3	13·3	12·4	16·7	p < 0·05
Peripheral neurological disorders‡	14·5	15·2	17·5	21·8	p < 0·05
Nausea	4·0	7·2	9·9	13·5	p < 0·001
Tiredness	31·1	37·6	36·6	49·7	p < 0·001

NS = Non-significant.
*These symptoms were perceived during or at the end of a working day at least once a week.
†Defined as the accumulation of at least two of the three following symptoms: headaches, dizziness, decrease in reaction time.
‡Tingling, numbness, or cramps of arms or legs.

Table 2 Working conditions and exposure to anaesthetics

Working conditions	Controls (%) (n = 566)	Exposed workers according to No of air changes an hour (%) >20 (n = 142)	11–20 (n = 223)	≤10 (n = 192)	p Value
Formol	12·6	41·3	53·9	62·4	p < 0·001
Solvents	16·3	29·4	33·5	42·3	p < 0·001
Ethylene oxide	24·0	76·8	79·4	79·8	p < 0·001
Antineoplastic drugs	23·9	2·9	1·9	2·8	p < 0·001
Ionising radiations	18·4	85·0	71·4	72·6	p < 0·001
Work standing up	75·0	73·8	78·6	74·6	NS
Carrying heavy loads	33·4	30·0	27·9	29·2	NS
Inconvenient lighting	27·4	33·3	33·5	36·5	NS
More than 8·5 h work a day	30·7	37·9	42·7	53·2	p < 0·001
Irregular meals	56·7	77·3	74·7	78·3	p < 0·001
Stress	8·3	15·1	11·8	17·9	p < 0·01

Table 3 Symptoms and exposure to anaesthetics: adjusted OR by logistic regression. Comparisons with controls

	Exposure (No of air changes an hour) >20	11–20	≤10
Neuropsychological syndrome (n = 864):*			
OR (95% CI)	0·8 (0·3–2·4)	2·6 (1·2–6·1)	3·6 (1·6–7·8)
Significance	NS	p < 0·05	p < 0·01
Memory impairment (n = 993):†			
OR (95% CI)	1·5 (0·7–3·1)	1·4 (0·7–2·7)	1·4 (0·8–2·7)
Significance	NS	NS	NS
Peripheral neurological disorders (n = 896):‡			
OR (95% CI)	1·2 (0·6–2·4)	1·3 (0·7–2·3)	1·3 (0·7–2·3)
Significance	NS	NS	NS
Nausea (n = 945):§			
OR (95% CI)	1·0 (0·4–2·7)	2·1 (0·9–5·0)	1·4 (0·5–3·7)
Significance	NS	NS	NS
Tiredness (n = 896):|			
OR (95% CI)	1·2 (0·7–2·0)	1·1 (0·7–1·8)	1·8 (1·0–3·0)
Significance	NS	NS	p < 0·05

*Adjusted for exposure to formol, antineoplastic drugs, irregular meals, stress.
†Adjusted for antineoplastic drugs, irregular meals.
‡Adjusted for solvents, irregular meals, long working day.
§Adjusted for exposure to formol, ethylene oxide, irregular meals, stress, previous hepatitis.
|Adjusted for exposure to formol, solvents, irregular meals, stress, long working day.
The five models included sex, occupation, age, duration of service, and hospital.

drugs, and by those having irregular meals. Peripheral neurological disorders were reported more often by workers using solvents, those having long working days, and those having irregular meals. Memory impairment was more common among workers having irregular meals. Nausea was reported more often by workers reporting exposure to formol, those using ethylene oxide, and by those having irregular meals. Tiredness was more frequent among workers reporting exposure to formol, those exposed to solvents, those with long working days, and those with irregular meals.

Controlling for these working conditions and for sampling factors, the adjusted risks of the workers in operating rooms that were scavenged 10 times an hour or less were significantly higher than those of the control group (OR = 3·6, 95% CI 1·6–7·8 for the neuropsychological syndrome and OR = 1·8, 95% CI 1·0–3·0 for tiredness (table 3)). The risk of neuropsychological syndrome in operating rooms that were scavenged from 11 to 20 times an hour was roughly three times higher than that found in the control group. The risk of neuropsychological syndrome for workers in the operating rooms that were scavenged more than 20 times an hour was no higher than for the controls.

The workers of the less scavenged operating theatres were more often in paediatric surgery departments, exposed to a higher number of administrations of anaesthesia, and stood more frequently near the patient's head (table 4). Workers in paediatric surgery departments reported peripheral neurological disorders and tiredness twice as often as the other exposed workers (table 5). Their s-ASAT activities were more frequently higher. These associations were found even after controlling for the frequency of the use of the scavenging system. The same trend was seen for the neuropsychological syndrome and memory impairment. The other exposure indicators were not related to the symptoms nor to the biological values.

Discussion

This is a retrospective study in which some reporting bias cannot be ruled out. It is important, however, to make several points. Firstly, the purpose of the study was not specified in the questionnaire and the data were gathered on all occupational exposures in hospitals. Secondly, definition of the symptoms was restrictive and irregular or rare symptoms were not considered. To avoid placing too much emphasis on any one symptom, such as headaches, a neurological disorder syndrome category was created. This was accomplished by considering together several symptoms that were derived from answers given to questions concerning general symptomatology. Biological data were without systematic bias, even though their accuracy may be contested knowing that they came from several different hospitals. Thirdly, misclassification concerning exposures was avoided by obtaining data on exposure independently from the respondents.

These symptoms have been reported in previous studies. Vaisman *et al* [20] showed that anaesthetists frequently reported headaches, nausea, irritability, and tiredness, but this survey had no controls. More

Table 4 Characteristics of exposure to anaesthetics according to ventilation of operating theatres

	Exposed workers according to No of air changes an hour (%)			
	>20	*11–20*	*≤10*	*p Value*
Paediatric surgery department	9·9	17·6	60·9	p < 0·001
Worker positioned near the patient's head	21·2	35·5	39·9	p < 0·001
No of operations every two weeks:				
≥45	9·5	25·4	35·2	p < 0·001

Table 5 Odds ratio related to work in paediatric surgery department adjusted for No of air changes an hour among exposed workers

*Symptoms**	*OR*	*(95% CI)*	*p Value*
Neuropsychological syndrome†	1·8	0·9–3·5	NS
Memory impairment	1·6	0·9–3·0	NS
Peripheral neurological disorders‡	2·1	1·2–3·7	p < 0·01
Nausea	1·4	0·7–2·6	NS
Tiredness	1·7	1·1–2·6	p < 0·05
s-ASAT > 90th percentile	2·3	1·0–5·1	p < 0·05
s-ALAT > 90th percentile	1·3	0·7–2·6	NS
s-GGT > 90th percentile	0·6	0·3–1·4	NS

Paediatric surgery department compared with other surgery departments.
*These symptoms were perceived during or at the end of a working day at least once a week.
†Defined as the accumulation of at least two of the three following symptoms: headaches, dizziness, decrease in reaction time.
‡Tingling, numbness, or cramps of arms or legs.

recently, Cohen *et al*[21] described an excess of tingling, numbness, and muscle weakness in male dentists and in female dental assistants exposed to inhalation anaesthetics. These authors showed a dose-response effect when the degree of exposure was assessed by the number of hours the respondent was exposed. Lauwerys *et al*[22] described a higher prevalence of headaches among operating theatre personnel than among a control group.

Edling[28] has reviewed some studies of the effects of exposure to anaesthetics on the nervous system. In one of them, the results showed that the reaction time among the nurses working with anaesthetics was slower than among the reference group. In another, the results showed that exposed nurses reported experiencing prickling and numbness more often than the control group. Our results show an increase in the neuropsychological syndrome, which included dizziness, headaches, and decrease in reaction time, and increased tiredness. These symptoms seem to be the result of the first effects of the anaesthetics on hospital personnel. The long term effects and the development of these symptoms are unknown. Nevertheless, when the workers experience these symptoms frequently, morbidity becomes very real. Experiencing these symptoms may lead to a decrease in watchfulness that makes occupational tasks more constraining and that may impair the service given to patients.

These symptoms may be related to several other occupational characteristics that might be confounding factors. Working conditions differed between the exposed groups and the control group, showing that work done in operating theatres has its own special characteristics. Exposure to toxins other than anaesthetic gases, such as solvents used to clean medical instruments or ethylene oxide used as a sterilising agent, is frequent. The exposure to solvents was more frequent for workers in the less scavenged rooms. This can be explained by the surgical specialties of each theatre. For instance, in paediatric surgery, operations are usually shorter (amygdalectomy, adenoidectomy, appendectomy); therefore instruments are cleaned more often and hospital workers have more contact with the chemicals. The work organisation in a surgical ward, the coping with emergency situations, and the intervention on the human body accompanied by a feeling of great responsibility induce irregular work schedules and stress. These occupational characteristics were taken into account but they did not entirely explain the relation between exposure to anaesthetic gases and symptoms.

An important finding from this study is that the prevalence of the symptoms increases according to the degree of exposure, as measured by the use of the scavenging system. Firstly, this trend suggests a dose-response effect, which is an argument in favour of the hypothesis of causality.[30] Secondly, this result stresses the role of ventilation in the operating theatres as is discussed in several papers.[31 32] Various technical elements have an effect on the quality of the ventilation, especially the number, the position, and the kind of air vents in the system.[32 33] We did not have sufficiently detailed information to analyse these technical aspects and their relation with the reported symptoms.

The results also show effects specific to work in paediatric surgery units. They are concordant with the fact that operation rooms in paediatric surgery departments have a high concentration of airborne anaesthetics.[34] The effect of anaesthetic gases on hepatic function has been discussed[7 28] and a temporary increase in serum transaminase concentrations has been described.[28] We found no significant increase in transaminase concentrations in the exposed groups. A slight increase in s-ASAT concentration was found among the workers in paediatric surgery units, which strengthens the hypothesis of a specific exposure for these workers.

These adverse short term effects of anaesthetic gases show that the adverse effects do not concern all workers in operating theatres. Only those in the less scavenged operating rooms and those in paediatric surgery units are at risk. This finding allows us to recommend some preventive measures: operating theatres with old ventilation equipment should be modernised to guarantee an effective and comfortable ventilation of the ambient air. The situation in the paediatric surgery units should be studied further, especially from a technical standpoint and special scavenging equipment should be conceived for operating theatres for children. In the meantime however, the recommended norms[35 36] should be enforced, especially in paediatric surgery.

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