

Occupational Exposure of Anesthetists to Halothane, Nitrous Oxide and Radiation

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To assess the exposure of operating room personnel to anesthetic vapors, measurements were made of the concentrations of nitrous oxide or halothane in the air of operating rooms while the anesthetics were being administered. Exposure of ten anesthetists to radiation in the operating room over a six-week period was also measured. The average concentration of halothane was 10, and that of nitrous oxide, 130, parts per million. Halothane was also found in the air expired by anesthetists, and fluorine-containing substances were found in their urine. The average radiation exposure was 13 milliroentgens per week.

OPERATING ROOM PERSONNEL, especially those who administer anesthetics, inhale anesthetic gases and vapors throughout their working lifetimes. They may also absorb ionizing radiation from x-rays or radioactive isotopes. Simultaneous exposure to these environmental factors is peculiar to operating room personnel. The hazards of ionizing radiation are well known, but toxicity from long-term inhalation of small amounts of anesthetic agents has not been defined. We believed it of interest to quantitate these exposures.

As early as 1893, Hewitt¹ noted that chloroform administered in the presence of open gas lights decomposed into hydrochloric acid and phosgene, leading to paroxysmal cough, throat irritation and headache. Recently, chronic toxicity from the inhalation of ether has been suggested. Wertham² observed symptoms in a surgeon, nurse and anesthetist

who had worked together for many years in operating rooms where ether was used. Symptoms experienced included depression, fatigue, headache, anorexia, nausea, loss of memory, and periodontal disease. The surgeon, with 15 years' exposure, had electrocardiographic changes and an increase in circulating lymphocytes. Symptoms disappeared after six weeks of vacation and did not recur after the installation of ventilating equipment in the operating rooms. Others have measured ambient ether vapor concentrations in poorly ventilated operating rooms during the administration of ether by the open-drop method and found concentrations between 20 and 500 parts per million (ppm).³ Vaisman, investigating the working conditions of 354 Russian anesthesiologists,⁴ found that most worked in poorly ventilated operating rooms administering ether by semiopen or semiclosed techniques, although halothane and nitrous oxide were used also. The majority complained of headache, fatigue, and respiratory-tract inflammation. Other complaints related to the central nervous, gastrointestinal and respiratory systems were registered. Among women in the group there were 31 pregnancies; 18 ended in spontaneous abortion, and only seven were uneventful. Vaisman attributed these problems to a combination of chronic inhalation of anesthetic vapors, emotional strain and excessive workload.

Workers exposed to ether vapor in the manufacture of smokeless gunpowder during World War I experienced gastrointestinal and central nervous system symptoms.⁵ Increased erythrocyte counts were common, although occasionally leukocytosis or anemia was present, and albuminuria often occurred. The concentrations of ether must have been high, since a suggestion of the excitement stage of anesthesia occasionally was seen.

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TABLE 1. Halothane in Ambient Air: 104 Samples Obtained in 21 Operating Rooms

Average Range	8.5 ppm 0-49 ppm
Halothane vaporized (ml vapor produced/min)*	
Average Range	50 10-330

* Calculated value: fractional concentration of halothane multiplied by total gas flow/min.

Materials and Methods

Environmental air was sampled by slow withdrawal into clean, well-fitting glass syringes, which were then capped. Expired air was obtained by aspirating air at the end of exhalation through a 16-gauge plastic catheter placed in the pharynx of the anesthetist. Room air was sampled in several patterns. In the first series (table 1), 10 ml of air were obtained near the anesthetist's nose in order to sample the air he breathed. These samples were analyzed for halothane. In the second series (tables 2 and 3) air was sampled above, below and at either side of the pop-off valve of the anesthesia machine, as shown in figure 1. Samples were taken from 21 operating rooms in two hospitals where air is changed approximately 12 times per hour. Samples were taken for nitrous oxide and for halothane on different days. No attempt was made to

alter the pattern of anesthetic practice during sampling. Nitrous oxide and halothane were administered to the patients as required. Since high flows were used in most cases, the pop-off valve was ordinarily open. Samples were taken at various times during the course of anesthesia.

Analyses were performed with an F and M model 700 gas chromatograph, using a Beckman GC-2A gas-sampling valve with 1- or 5-ml sample loops. Halothane was separated in a six-foot-by- $\frac{1}{8}$ -inch column of 10 per cent diisodecyl phthalate on diatomaceous earth at 75 C. Nitrous oxide was separated on a two-meter-by-5-mm Poropak Q column at 50 C. The carrier gas in both instances was helium, at a flow rate of 20 ml per minute. The concentration of each sample was determined by comparing the chromatographic peak height with that of a standard. Halothane standards were prepared by dilution with air of a 0.12 per cent halothane-in-nitrogen mixture prepared by the Matheson Company. Nitrous oxide standards were prepared by serial dilution of the pure gas with air. The smallest detectable amount of nitrous oxide was 20 ppm; of halothane, 0.5 ppm. The flows and concentrations of anesthetics supplied to the breathing system and the patient were recorded.

Metabolic products of halothane in the urine were determined with a fluoride ion electrode

TABLE 2. Halothane Vapor in Air near Anesthesia Machine (Average Values in Parts per Million)

Halothane Vapor (ml/min)*	Number of Observations	Sampling Location†									
		a	b	c	d	e	f	g	h	i	j
10-15	3	1	1	1	1	2	1	2	2	0	1
16-20	8	2	4	2	2	2	3	4	2	2	3
21-25	1	11	8	9	8	8	9	8	11	7	7
26-30	3	2	6	9	3	3	3	3	7	2	3
31-35	2	0	0	0	0	1	1	3	3	4	5
36-40	5	5	3	2	2	2	3	3	3	3	3
41-45	1	—	14	1	3	5	2	0	3	0	2
46-50	2	2	7	2	0	2	2	3	3	1	1
51-55	4	4	5	3	4	3	5	3	3	2	3
56-60	2	5	17	6	5	5	6	4	11	5	4
120	1	12	25	7	7	10	26	14	8	8	—
220	1	22	8	4	6	—	4	27	3	5	4

* Calculated value: fractional concentration of halothane multiplied by total gas flow/min.

† See figure 1.

TABLE 3. Nitrous Oxide in Air Near Anesthesia Machine (Average Values in Parts per Million)

N ₂ O Flow (l/min)*	Number of Observations	Sampling Location†									
		a	b	c	d	e	f	g	h	i	j
0.5	1	27	11	14	0	11	11	11	16	14	0
1.5	1	—	105	42	21	21	21	42	252	84	—
2.0	5	78	118	35	32	73	119	59	55	52	47
2.5	2	51	136	166	69	66	73	49	177	119	73
3.0	4	225	84	54	48	39	45	54	75	51	42
4.0	1	—	—	—	—	42	53	78	89	105	78
5.0	2	354	428	60	59	148	59	163	74	74	45

* Undiluted nitrous oxide flow. Oxygen was added to the nitrous oxide as required.

† See figure 1.

(Orion). First, fluoride ion was measured directly in urine. The urine was then atomized into an oxygen-hydrogen flame where the organically-combined fluorine was converted to fluoride ion. The flame reaction products were trapped in aqueous sodium hydroxide. The total fluorine in urine, now in ionic form, was measured in this solution. Near the end of a working week (late Friday morning) urine specimens were obtained from four anesthetists who had given an average of 15 hours of halothane anesthesia during the week.

Exposure to radiation was measured by an electrostatically-charged chamber dosimeter (Victoreen) worn by each of the ten anesthetists while in the operating room. If the individual wore a lead apron during x-ray exposure, the dosimeter was worn outside the apron. Dosimeters were read at weekly intervals with an electrometer.

Correlation between anesthetic concentration in room air and the rate of delivery of these drugs was tested using Spearman's rank correlation coefficient and Student's *t* test.⁶

Results

In the first series, 104 air samples were obtained in 21 operating rooms in the two hospitals (table 1). In addition, 22 gas samples from the corridors outside were found to contain an average halothane concentration of 0.5 ppm, with a range of 0 to 4 ppm. The average concentrations of halothane at the ten sampling locations (fig. 1) in the 32 experiments of the second series are shown in table 2. Values are averaged for each group of

halothane vapor flow rates. Results of 16 tests for nitrous oxide are expressed similarly (table 3). The values obtained in the two hospitals did not differ enough to require separate presentation. The over-all average concentration of all of the measurements of nitrous oxide in all operating rooms was 130 ppm; that for both series of halothane measurements, 160 ppm.

Attempts were made to relate the delivery of anesthetic vapor from the anesthesia machine to the concentrations found in operating room air in the two series. In the first halothane series, no significant relationship could be found ($P > 0.05$). In the second halothane series, a significant ($P < 0.05$) correlation was found between vapor flow and concentration at points a, d, and j (fig. 1), but not at points g and b. Significant correlations were found for nitrous oxide at points a, d and g, but not at c, j and h. Data from other sam-

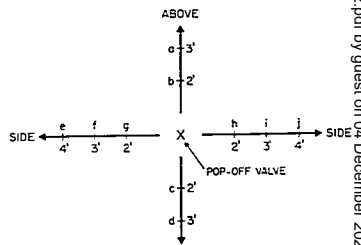


FIG. 1. Air sampling points. Distances are in feet from pop-off valve.

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TABLE 4. Halothane in Anesthetists' End-expired Air*

	Average	Minimum	Maximum
Halothane (ppm)	1.8	0.0	12.2
Exposure, hours	1.3	0.1	3.0
Time out of OR, hours	0.2	0.0	1.0

* 36 observations of 24 anesthetists.

pling points were not subjected to statistical evaluation.

End-expired air samples were obtained from 24 anesthetists while they were administering anesthesia or soon after they left the operating room (table 4). The time spent in a room with halothane in use and the length of time out of the room are also shown. For a few anesthetists, a comparison was made of halothane in end-expired air and in room air near the face (table 5).

Urine specimens from four anesthetists contained an average of 1.3 $\mu\text{g/ml}$ of fluoride ion and 8.1 $\mu\text{g/ml}$ of total fluorine (laboratory normal values, 1.0 and 5.0, respectively).

Amounts of exposure to radiation of ten anesthetists in six consecutive weeks are recorded in table 6.

Discussion

Anesthetists in the two hospitals studied inhaled modest amounts of halothane and nitrous oxide while working in operating rooms, and also were exposed to radiation. Halothane appeared in the end-expired air of anesthetists, and the amounts of fluorine in urine were increased. The anesthetic vapors appeared to be uniformly distributed in the room air near the anesthesia machine. The concentration of halothane in room air was about ten- to a hundredfold less than that of nitrous oxide, as expected from the differing rates of delivery of these two agents. No attempt was made to relate the anesthetist's exposure time and concentration of halothane in his end-expired air. To obtain meaningful data, it would have been necessary to know not only exposure time but concentrations to which he had been exposed. The end-expired concentrations were measured to confirm the fact that the anesthetist had been exposed and that halothane was present in his body. That room

air had less halothane than the end-expired air in some instances (table 5) indicated that the anesthetist had been exposed to higher concentrations in the recent past.

The flow of anesthetic agent delivered by the machine and the concentration of the agent in room air did not always correlate statistically, which probably was the result of nonuniform mixing of the gases with room air caused by air currents. Uptake or release of anesthetic by the patient also could have altered the amount of agent present in the room.

The concentrations of halothane and nitrous oxide observed in this study can be compared with those which would accumulate in a sealed, unventilated room with a volume of 100,000 liters (3,500 cubic feet). If 1 per cent halothane added to a 4 l/min flow of 50 per cent nitrous oxide in oxygen were delivered each minute, in ten minutes there would be 4 ppm of halothane and 200 ppm of nitrous oxide in the room; in one hour, 24 and 1,200 ppm; in two hours, 48 and 2,400 ppm.

We do not know if the observed concentrations of halothane and nitrous oxide present a hazard to individuals exposed over many years. It is interesting, however, to speculate on the relationship between anesthesia and certain toxic effects of volatile compounds. Benzene, which is anesthetic in concentrations of 1 to 2 per cent, affects bone marrow if chronically inhaled at lower concentrations (e.g., 100 ppm).^{7, 8, 9} Marrow biopsies of patients exposed for long periods to the vapor of benzene may show a spectrum of changes ranging from hypoplasia through leukemia.¹⁰ Nitrous oxide and halothane are known to produce bone marrow depression upon long expo-

TABLE 5. Halothane in Room and End-expired Air

Subject	Halothane in Air (ppm)		Exposure (hours)
	End-expired	Room	
JMK	9.6	3.8	2
HSB	12.2	12.9	2
AN	2.0	2.0	4
FR-1	0.5	6.0	0.5
MLB	1.0	3.1	2.3
PEH	0.8	0.6	3
JK	1.0	1.4	1
FR-2	2.7	12.4	1

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TABLE 6. Exposure of Anesthetists to Radiation Over a Six-week Period (Milliroentgens per Week)

Subject	Week Ending						Average
	7/19	7/26	8/2	8/9	8/16	8/23	
29	10	5	*	10	3	2	6.0
30	95	25	5	15	10	15	27.5
31	*	5	10	5	3	5	5.6
32	10	2	*	5	3	5	5.0
33	42	35	12	30	15	22	26.0
34	12	10	5	5	2	5	6.5
35	12	5	*	8	8	5	7.6
36	8	5	20	25	5	12	12.5
37	10	5	*	6	2	5	5.6
38	70	5	18	8	3	5	18.2
Overall average							12.6

*No reading, dosimeter dropped.

sure.^{10, 11, 12} Whether these or other inhalation anesthetics will produce leukemia is unknown. Death rates from leukemia among anesthesiologists do not appear to be abnormal; however, the incidence of death from malignancies of the lymphoid and reticulo-endothelial systems appears to be appreciably higher in anesthesiologists than in the general population.¹³ A question that intrigues us is whether hazards exist in man when the period of exposure to traces of anesthetics occupies the majority of an adult life. We have undertaken studies^{13, 14} to answer this question.

Exposure to chemical vapors in industry is governed by threshold limit values (TLV's) set by the American Conference of Governmental Industrial Hygienists.¹⁵ These values are arrived at empirically on the basis of studies in animals and observations in man. The TLV represents a concentration at which observable toxic effects do not occur in long-term work exposure, based on a 40-hour work week. With the exception of diethyl ether and trichloroethylene, values have not been set for anesthetics. Those for trichloroethylene probably are not applicable to the anesthetic used clinically, since industrial trichloroethylene contains stabilizers which may be toxic. One "toxic" effect of diethyl ether which is taken into consideration in setting the TLV is that of narcosis, but this is not a toxic effect in the true sense. The TLV for ether is 400 ppm.¹⁵ It is not known if a

working-lifetime exposure to this concentration would produce toxic effects. Limits have not been set for industrial exposure to halothane or methoxyflurane. The manufacturers inform us that modern automated manufacturing techniques do not permit the escape of vapors into the working area.

Although the average exposure to radiation over the period of study was well below the currently acceptable limit of 100 milliroentgens per week (5 roentgens per year),¹⁶ two values in the first week approached this limit. After the first week, the individual and average values tended to decrease sharply and to level out. (This phenomenon is well known to health physicists; a dosimeter makes the wearer conscious of radiation and more cautious, thus his exposure soon drops). It does appear possible, however, that anesthetists could easily be exposed to excessive amounts of radiation, and the effects of radiation and anesthesia could be additive. The effects of long-term exposure to low doses of both radiation and anesthesia have not been reported. Such a study is in progress in our laboratory.

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Anesthesia

SPINAL ANESTHESIA IN PREGNANCY It has long been appreciated that the dose of drug required for spinal anesthesia is smaller in the pregnant than in the nonpregnant patient. This presumably is due to inferior vena caval compression, engorgement of the venous plexus surrounding the dural sac, and decreased volume of spinal fluid within the spinal canal. Three groups of patients received spinal anesthesia with 1 ml (4 mg) tetracaine. The first group consisted of 20 nonpregnant control patients of child-bearing age. Group 2 comprised 15 patients at term undergoing cesarean section. Group 3 consisted of 15 patients of child-bearing age who were given a spinal anesthetic after a tight abdominal binder had been applied. The usual dermatome level of group 1 was T11; of group 2, T8; of group 3, T7. Inferior vena caval pressure was elevated in group 3. Previous work had disclosed an elevated inferior vena caval pressure in pregnant patients in the supine position. Transient, though measureable, increases in spinal fluid pressure were noted in patients with vena caval compression. Added support is lent to the mechanical obstruction theory for explaining increased levels of spinal anesthesia in the pregnant patient. (Barclay, D. L., Renegar, O. J., and Nelson, E. W.: *The Influence of Inferior Vena Cava Compression on the Level of Spinal Anesthesia, Amer. J. Obstet. Gynec.* 101: 792 (July) 1968.)