Anesthesiology
V 35, No 4, Oct 1971

Anesthesia, Pregnancy, and Miscarriage:

A Study of Operating Room Nurses and Anesthetists

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A survey was undertaken to evaluate the possible relationship between spontaneous miscarriage and exposure to the operating room. The study was carried out by personal interview of 67 operating room and 92 general duty nurses. Results indicate that during the years 1966–1970, 29.7 per cent of pregnancies in operating room nurses ended in spontaneous miscarriage, compared with only 8.8 per cent in the control group. A similar pattern was observed in a second study of 50 anesthetists and 81 physicians practicing in specialties other than anesthesia. During the six-year period 1965–1970, the anesthetists evidenced a 37.8 per cent spontaneous miscarriage rate, compared with 10.3 per cent in the control group. Miscarriages occurred earlier in both operating room nurses and anesthetists compared with their control groups (eighth versus tenth week). These results suggest a fetal lethality, possibly due to the anesthetic gases, although the studies do not incriminate any specific anesthetic agent, nor is a cause–effect relationship established. (Key words: Waste anesthetic gases; Spontaneous miscarriages; Fetal lethality.)

THE DEMONSTRATION that inhalation anesthetics produce teratogenic responses in both avian and mammalian species[1–8] has raised concern as to their effects in an estimated 50,000 women in the United States who annually undergo surgery and anesthesia during gestation.[9, 10] Recently it has been recognized that a second group of women is also exposed to the effects of inhalation anesthetics. These are the nurses and anesthetists who work daily in operating rooms contaminated with trace concentrations of anesthetics.[11, 12] Several preliminary reports suggest that such continued low-grade exposure may be related to an increased spontaneous miscarriage rate and to an increase in the incidence of fetal anomalies.[12–15] The present study was directed towards this significant question.

Method

Two groups of women working in the operating room were surveyed through a questionnaire designed to elicit information about numbers of pregnancies, miscarriages,‡ contraceptive techniques, birth defects, etc. The first study was conducted by means of personal interviews of 159 married operating room and general duty nurses between the ages of 25 and 50 years, employed in three large general hospitals in Northern California. The key questions were purposefully buried within a long detailed questionnaire, so that the nurses were unaware of the major purpose of the study. This precaution was necessary to try to avoid prejudice in response, as well as to avoid any undue personal concern on the part of those being interviewed. Nurses interviewed were selected at random, although an effort was made to interview all duty personnel working on a given nursing station or floor. Questions were carefully phrased and asked in a fixed format. All interviews were carried out by two observers, one a nurse, the other a psychologist.

The second group of 131 women included 50 physicians, aged 25–50 years, whose specialty practice was limited to anesthesia. Another group of 81 physicians in specialties other than anesthesia served as controls. After completion of a mail questionnaire by the participants, they were instructed to open a sealed envelope which explained the purpose of the study. Additional comments were solicited, but the participants were requested not to alter their original responses.

All data were entered into an IBM 360-50

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Received from the Departments of Anesthesia, Community and Preventive Medicine, Stanford University School of Medicine, Stanford, California 94305. Accepted for publication April 9, 1971. Supported by National Institutes of Health, Program Project No. GM-12527.

‡ Spontaneous loss of conceptus up to the twentieth week of pregnancy.

TABLE 1. Obstetrical Information for 159 Operating Room and General Duty Nurses during the Years 1966–1970*

	Operating Room Nurses	General Duty Nurses
Number in group	67	92
Mean age (years)	34.3	30.9
Years in the operating room (mean)	3.9	0
Number of pregnancies	36	34
Practicing contraception	45 per cent	55 per cent
Number of living children	26	31
Number of miscarriages	10	3
Miscarriages/pregnancies	29.7 per cent	8.6 per cent

* All nurses were married and were between the ages of 25 and 50 years.

TABLE 2. Medical and Gynecologic Histories of Operating Room and General Duty Nurses

	Operating Room Nurses	General Duty Nurses
Regular periods	78 per cent	87 per cent
Dysmenorrhea	34 per cent	29 per cent
Hypothyroidism	12 per cent	8 per cent
Nausea during pregnancy	37 per cent	26 per cent
Toxemia	6 per cent	2 per cent
Smoke	36 per cent	30 per cent
Drink	74 per cent	79 per cent
Regular exercise	55 per cent	69 per cent
Miscarriage by nurse's mother	64 per cent	59 per cent
Week of miscarriage	8.3	10.0

TABLE 3. Comparative Pediatric Histories of Children from Operating Room and General Duty Nursing Groups

	Children of Operating Room Nurses	Children of General Duty Nurses
Month sat	5.9	6.1
Month walked	11.3	11.5
Month talked	13.4	14.1
Heart disease	8 per cent	3 per cent
Operation	10 per cent	6 per cent

TABLE 4. Obstetrical Information for 131 Anesthetists and Other Physicians Practicing during 1965–1970*

	Anesthetists	General Physicians
Number in group	50	81
Mean age (years)	39.6	36.8
Years in the operating room (mean)	5.6	0
Number of pregnancies	37	58
Practicing contraception	66 per cent	69 per cent
Number of living children	23	52
Number of miscarriages	14	6
Miscarriages/pregnancies	37.8 per cent	10.3 per cent

* All physicians were married and were between the ages of 25 to 50 years.

TABLE 5. Medical and Gynecologic Histories of Anesthetists and General Physicians

	Anesthetists	General Physicians
Regular periods	82 per cent	91 per cent
Dysmenorrhea	18 per cent	14 per cent
Hypothyroidism	12 per cent	15 per cent
Nausea during pregnancy	54 per cent	54 per cent
Toxemia	4 per cent	5 per cent
Week of miscarriage	7.5	9.5

computer for storage, retrieval and statistical evaluation. For the purpose of analysis, assignment to the operating room group indicated any exposure to the operating rooms within the past five years in the case of the nurses, and within six years for the physicians. Only data relevant to these time periods were considered.

Findings and Comments

Selected information obtained from the operating room and general duty nurses relative to the immediate past five-year period, 1966–1970, is presented in table 1. The mean age of the operating room nurses was slightly higher (3.4 years), but otherwise the two groups were comparable in terms of general

health, smoking, drinking, exercise habits, etc. The most striking difference was the large increase in the spontaneous miscarriage rate in the operating room nurses. In this group, 29.7 per cent of pregnancies ended in miscarriage, compared with only 8.8 per cent in the general duty nurses. This difference is statistically significant ($P = 0.045$) by Fisher's exact test. Of interest, the operating room nurses had more pregnancies (less contraception practiced). Thus, despite their increased miscarriage rate, the same average numbers of living children per nurse were produced in the two groups during the five-year study period.

Since it proved impossible to determine with exactness the duration of effect of an operating room exposure upon subsequent pregnancies, any exposure to the operating rooms during the five-year study period arbitrarily assigned the nurse to the experimental group. During the five-year period, nurses in this group averaged 78 per cent time full-time employment in the operating rooms.

The medical and gynecologic backgrounds of the two groups of nurses were similar (table 2). Of interest, a high percentage of the operating room nurses experienced nausea with their pregnancies, suggesting adequate implantation. On the average, time of loss of the pregnancy occurred during the eighth week of gestation in the operating room group, compared with the tenth week in the control nurses. No obvious hereditary factors responsible for this difference were apparent, and similar miscarriage rates were obtained for mothers of the nurses in the two groups.

Some questions were designed to elicit possible physical differences between the surviving children of the two groups, but the data obtained did not establish any such differences (table 3). Thus, no differences in levels of physical performance (month sat up, or month walked), mental acuity (month talked), congenital defects (heart disease, surgery, etc.) were detected among the groups. This finding is not unexpected, since a much larger survey would be necessary to establish such differences, if present.

Data derived from the two physician groups surveyed by mail questionnaire (response rate 77 per cent after two mailings) are presented in table 4. In these studies, the physician anesthetist group had a 37.8 per cent spontaneous miscarriage rate, compared with 10.3 per cent for the control physicians ($P = 0.0035$ by Fisher's exact test) (table 4). Except for this finding and that of extensive exposure § to the operating room during the six-year period, the two groups appeared comparable (tables 5 and 6).

TABLE 6. Comparative Pediatric Histories of Children from Anesthetist and General Physician Groups

	Children of Anesthetists	Children of General Physicians
Month sat	5.3	5.6
Month walked	10.3	12.1
Month talked	15.2	16.8
Congenital anomalies	2.0 per cent	4.2 per cent

Of particular interest was the observation that loss of the fetus averaged almost two weeks earlier in the anesthetist group. The close similarity of these data to those obtained in the nurses is apparent. Again, no differences between performances of the surviving children produced by the two groups of physicians were found (table 6).

Discussion

There can be little doubt that the spontaneous miscarriage rate is significantly higher in both operating room nurses and anesthetists compared with their control groups. However, the precise etiologic factors involved are difficult to define. It is possible that the slightly greater ages in the experimental groups compared with their controls (34.3 *vs.* 30.9 years for the nurses, and 39.6 *vs.* 36.8 years for the physicians) might have influenced the rates of spontaneous miscarriage observed. On the other hand, an analysis of age incidence of abortion in 26,491 pregnancies indicates that only minor variations in miscarriage rates are usual at these age levels.[16] No other differences between the control and study groups were apparent except the extended periods of time spent by the latter in the operating rooms. The data suggest that there is a significant difference between the spontaneous miscarriage

§ During the period 1965–1970, the physicians in this group averaged 5.6 years' work in the operating room.

rates in the two groups, and that this may be related to something in the operating room environment, possibly the trace concentrations of anesthetic gases present. A somewhat higher miscarriage rate in the physician anesthetist group *vs.* the operating room nurse group may reflect the former's exposure to the higher gas concentrations adjacent to the anesthesia machine.[17]

Teratogenicity of the volatile anesthetics in the experimental animal has been well established, although in most studies the anesthetic agents were provided in high concentrations and during short periods of exposure.[1-8] The suggestion that results of the present study reflect a fetal lethality of the anesthetics is supported by an earlier mean time of miscarriage in both operating room groups (two weeks earlier than controls). This is a common effect of teratogenic drugs. The similarity of the spontaneous miscarriage rates in the mothers of the operating room nurses and the general duty nurses helps to rule out the likelihood of a hereditary tendency toward more spontaneous miscarriages in this experimental group. Since a number of measurable physiologic effects, *e.g.*, headache, nausea, enzyme induction, have been shown to result from prolonged exposure to trace concentrations of certain anesthetics,[17] it seems reasonable to consider a possible relationship between the increase in spontaneous miscarriage rate and other physiologically influencing (toxicologic) factors. One must remember, however, that factors unmeasured by the present study may also have contributed to the results observed. It is possible, for example, that periods of unusual high stress in the operating room, special sprays and solvents used in the operating room (antiseptic solutions, propellants, adhesive solutions, etc.), as well as other unknown factors may be incriminated. It is even possible that biases in selection of study subjects or in study methods could have caused the differences reported, though great efforts were made to minimize bias. The similarity of the results of the two separate studies is reassuring.

To confirm whether the trend revealed by these surveys is real, a number of additional studies are indicated. Cytogenetic examination of the abortuses of operating room personnel would help define genetic damage and contribute to our understanding of fetal lethality.[18] Second, expansion of the present study to include an annual survey would permit us to evaluate the effects of adequate scavenging precautions upon the rates of spontaneous miscarriage. If, over a period of years, following the institution of clean air in the operating room, the miscarriage rate were reduced to that of the control group, we would be more confident of a relationship to the trace anesthetic concentrations formerly present in the operating room. Third, we believe that a large-scale survey may be indicated. This would look at the question of whether there is an alteration in the male–female infant ratio among wives of anesthesiologists, as well as among women working in the operating room. Furthermore, a large survey could provide valuable information about the incidence of congenital deformities among offspring of operating room personnel. Finally, it has been shown that certain primates are satisfactory models for studying the teratogenicity and fetal lethality effects of drugs.[19] Studies with rhesus monkeys or baboons exposed to chronic concentrations of the individual anesthetics, or anesthetics in combination, would help determine which anesthetics may be implicated in this syndrome.

Our earlier study of pollution of the operating room by anesthetic gases indicated that trace concentrations of halothane were present in the operating room atmosphere and were measurable in the exhaled air of both anesthetists and nurses.[17] Since concentrations of nitrous oxide, ether, and presumably other anesthetic agents, are also present in the operating room atmosphere, one cannot associate the observed increase in spontaneous miscarriage rate with any particular anesthetic agent. In the preliminary report by Vaisman *et al.*,[13] the only anesthetics used were nitrous oxide and diethyl ether. Thus, until proven or disproven, all volatile agents present in the operating room must remain suspect!

Of practical importance is the recent demonstration that contamination of the operating room by anesthetic gases could be reduced to approximately 10–15 per cent (or less) of that previously present through the use of scavenging systems. Total elimination of all waste gases is, of course, the goal, and should

be attainable. In the meantime, we recommend that all possible corrective measures be initiated as rapidly as possible. In addition to installing adequate scavenging devices, it would seem prudent to restrict the assignment of nurses or doctors planning pregnancy to those operating rooms where volatile anesthetics either are not being used or have been removed.

Although absolute indications for such precautions are not available at the present time, they are reasonable measures and readily undertaken. On the other side, there remains the likelihood that trace anesthetic concentrations do produce fetal lethality in chronically exposed female personnel. Under such circumstances, we choose not to be complacent, and our institution is proceeding towards rapid elimination of this potential hazard.

Addendum

Subsequent to the completion of this study, a report by Askrog and Harvald has indicated similar findings. (Teratogen effekt af inhalationsanaestetika, Nordisk Medicin 16:498–500, 1970.) This survey included 754 persons in 80 anesthesia services in Denmark, and indicated that spontaneous abortion and perinatal death occurred in approximately 10 per cent of pregnancies prior to employment. Following employment in the anesthesia service, this percentage rose to 21 per cent. Additionally, more female infants were born to personnel working in the operating room, and especially to the wives of male anesthetists. This would suggest that chronic exposure to anesthetics induces male lethality. We did not observe this in our study, although male lethality with drugs that are embryotoxic has been reported.

The authors gratefully acknowledge the help of Mrs. Lynne Bellville and Mrs. Sylvia Cohen in conducting personal interviews with the nursing staff. Mrs. Marie Hu was responsible for computer programming.

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