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File under
Anesthesiology

Anesthesia, Pregnancy, and Miscarriage:

A Study of Operating Room Nurses and Anesthetists

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Byron W. Brown, Jr., Ph.D.†

A survey was undertaken to evaluate the pos-
sible relationship between spontaneous miscar-
riage and exposure to the operating room. The
study was carried out by personal interview of 67
operating room and 92 general duty nurses. Re-
sults indicate that during the years 1966-1970,
2.7 per cent of pregnancies in operating room
nurses ended in spontaneous miscarriage, com-
pared 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, com-
pared 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 anesthet-
ics produce teratogenic responses in both
avian and mammalian species¹⁻³ has raised
concern as to their effects in an estimated
70,000 women in the United States who an-
nually undergo surgery and anesthesia during
gestation.^{4,10} 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 pre-
liminary reports suggest that such continued
low-grade exposure may be related to an in-

creased spontaneous miscarriage rate and to
an increase in the incidence of fetal anom-
alies.¹³⁻¹⁵ The present study was directed to-
wards this significant question.

Method

Two groups of women working in the op-
erating room were surveyed through a ques-
tionnaire designed to elicit information about
numbers of pregnancies, miscarriages,† contra-
ceptive techniques, birth defects, etc. The
first study was conducted by means of per-
sonal 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 in-
terviewed were selected at random, although
an effort was made to interview all duty per-
sonnel 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 spe-
cialty practice was limited to anesthesia. An-
other 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 so-
lited, but the participants were requested
not to alter their original responses.

All data were entered into an IBM 360-50

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

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where is the
fine line?

Information for 131
Other Physicians
ing 1965-1970*

Anesthetists	General Physicians
10	81
9.6	36.8
5.6	0
7	58
6 per cent	69 per cent
3	52
4	6
7.8 per cent	10.3 per cent

married and were between

Gynecologic Histories of
General Physicians

Anesthetists	General Physicians
82 per cent	91 per cent
18 per cent	14 per cent
12 per cent	15 per cent
54 per cent	54 per cent
4 per cent	5 per cent
7.5	9.5

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health, smoking, drinking, exercise habits, etc.
The most striking difference was the large in-
crease in the spontaneous miscarriage rate in
the operating room nurses. In this group,
29.7 per cent of pregnancies ended in miscar-
riage, compared with only 8.8 per cent in the
general duty nurses. This difference is sta-
tistically significant ($P = 0.045$) by Fisher's
exact test. Of interest, the operating room
nurses had more pregnancies (less contracep-
tion 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 operat-
ing room exposure upon subsequent preg-
nancies, 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 em-
ployment 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 respon-
sible 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 pos-
sible physical differences between the surviv-
ing 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), con-
genital defects (heart disease, surgery, etc.)
were detected among the groups. This find-
ing is not unexpected, since a much larger sur-
vey would be necessary to establish such dif-
ferences, if present.

Data derived from the two physician groups
surveyed by mail questionnaire (response rate
75 per cent after two mailings) are presented
in table 4. In these studies, the physician an-

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

esthetist group had a 37.8 per cent spontane-
ous 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).

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 differ-
ences between performances of the surviving
children produced by the two groups of phy-
sicians were found (table 6).

Discussion

There can be little doubt that the spontane-
ous miscarriage rate is significantly higher in
both operating room nurses and anesthetists
compared with their control groups. How-
ever, 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 differ-
ences 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 op-
erating 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 anesthesiologist 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.¹ Studies with rhesus monkeys or baboons exposed to chronic concentrations of the individual anesthetics, or anesthetics in combination, would help determine which anesthetic 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 anesthesiologists 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.*,¹⁹ 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 by approximately 10-15 per cent (or less) that previously present through the use of scavenging systems. Total elimination of 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.

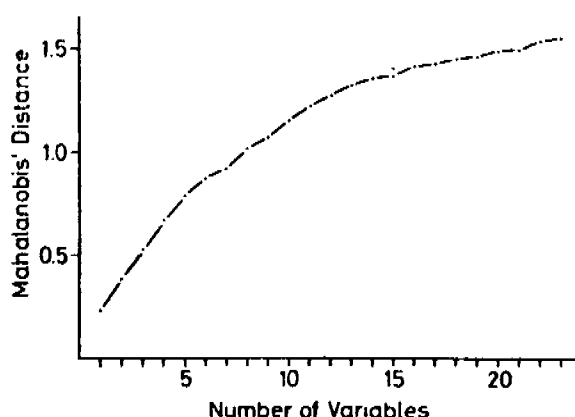
Addendum

Subsequent to the completion of this study, a report by Askrog and Harvald has indicated similar findings. (Teratogen effekt af inhalationsanesthetika, 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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the discrimination of vector of means can be tested for significance.

A high discrimination between the malformation group and its matched controls appeared within the first 10 of the 24 variables (see accompanying figure). Even with 8 variables a significant discrimination of both groups at 1% level was found. The discrimination of both groups was also possible without the two factors "abortions/stillbirths in mothers family" and "hours of daily work".

So, even in a sample with factors each not discriminating significantly between both groups, the linear discriminance analysis makes it possible to discriminate between the malformation group and the matched controls. This might mean that the malformations in our sample can be explained as caused by the combination of many minor factors (extrinsic and intrinsic).

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CONGENITAL MALFORMATIONS AND VINYL CHLORIDE

SIR,—In March, 1975, a significantly increased rate of central-nervous-system (C.N.S.) malformations was reported in 3 Ohio communities where polyvinyl chloride (P.V.C.) polymerisation plants are located;¹ the increase was not uniform and appeared more prominent in the Painesville area. There are two P.V.C. plants in Painesville, one of which began operation in 1949 and the other in 1967. The birth-defect rates were computed from birth-certificate data for 1970-73 and were compared with similar data for the entire State of Ohio. This study suggested a relationship between the higher rates of C.N.S. malformations and the increased risk of exposure to vinyl chloride in these communities.

By analysing data collected through the Center for Disease Control's hospital-based birth defects monitoring programme (B.D.M.P.),² we examined this relationship. Two hospitals participating in the B.D.M.P. are located in cities with polymerisation plants: one is in Pennsylvania, the other in Painesville, Ohio. C.N.S.-malformation rates for white infants born in these two hospitals in 1970-74 were compared with the rates for white infants in each State. No increase was seen in the Pennsylvania hospital, but an increase, primarily in anencephaly and spina bifida, was noted in the Painesville hospital for the total time 1970-74 (see table).

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ANENCEPHALUS AND SPINA BIFIDA IN OHIO STATE AND IN PAINESVILLE HOSPITAL, OHIO

Year	Anencephalus				Spina bifida			
	Painesville		State		Painesville		State	
	No. of cases	Rate*	No. of cases	Rate	No. of cases	Rate	No. of cases	Rate
1970	0	0.0	26	5.0	3	31.2	58	11.1
1971	1	10.3	38	7.3	3	30.9	44	8.5
1972	3	35.6	31	6.3	0	0.0	47	9.6
1973	2	24.9	27	5.4	2	24.9	46	9.2
1974	0	0.0	22	4.5	1	15.1	29	6.0
1970-1974	6	14.1	144	5.7	9	21.2	224	8.9

* Per 10 000 total white births.

The B.D.M.P. hospital data for Painesville were compared with birth-certificate data from the Ohio department of health, and 1 additional case not included in the B.D.M.P. report was added, bringing the total to 15. 30 controls, the first normal white infant born before and after each case, were selected from the hospital birth registry. Medical records for cases and controls were reviewed to confirm the diagnosis and to obtain, among other data, the parents' occupation and residence at the time of the infant's birth. In addition, parents of 14 of the affected children were interviewed about previous occupations and residences.

The study revealed that none of the interviewed parents of affected infants had ever worked at either of the two P.V.C.-polymerisation plants in Painesville (1 set of parents could not be located, but records show that they did not work at these plants at the time of their infant's birth); 2 of the fathers of controls had worked at one of the plants at the time of their infants' births. None of the parents in either group lived within 2 miles of the two plants. The chi-square test of significance was used in comparing the distances from residence and work-place of mothers and fathers to the P.V.C. plants for cases and controls. Comparisons were made at distances of 1 to 10 miles, in 1-mile increments. A significantly larger proportion of control mothers than case mothers worked (including housewives) within a 10-mile radius of the P.V.C. plant, at the 95% confidence level. This is probably a chance occurrence among multiple comparisons.

Vinyl chloride is a known carcinogen,³ and concern has arisen over its possible teratogenic effects. This concern stems from recent studies which have shown (a) an increase in mutagenicity in bacterial assay systems⁴ and (b) increased breakage in chromosomes of P.V.C.-polymerisation workers.⁵ The Ohio Department of Health study¹ is the only report that has suggested that vinyl chloride causes birth defects in man. Although the follow-up study reported here confirmed a moderate increase in C.N.S. malformations in Painesville, Ohio, no association was found with vinyl-chloride exposure.

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LATE COMPLICATIONS OF TUBAL LIGATION

SIR,—Unlike Mr Darwish and Dr Saafan (Nov. 15, p. 975), we are uncertain as to the aetiology of the late sequelae of female sterilisation, which they refer to as menstrual irregularity, but in our study it will be noted we looked specifically at menorrhagia and dysmenorrhoea. It seems unlikely that a psychosomatic cause could be present when two different tech-

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