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Birth Defects among Children of Nurse-anesthetists

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A survey of 621 female nurse-anesthetists in Michigan was performed to determine the incidence of birth defects among the offspring of this group. Two separate mailings and telephone interviews resulted in a response rate of 84.5 per cent. Of children whose mothers worked during pregnancy, 16.4 per cent had birth defects, while only 5.7 per cent of children whose mothers did not work during pregnancy had birth defects. This difference was significant ($P < 0.005$). Three neoplasms were reported in two children whose mothers worked during pregnancy. One neoplasm was reported among the offspring of mothers not working during pregnancy. (Key words: Toxicity: teratogenicity; Pregnancy: teratogenicity.)

LETHALITY and teratogenicity to the embryo of inhalation anesthetics administered in clinical concentrations has been demonstrated experimentally in several laboratory animals.[1,2] Nitrous oxide has even been shown to have lethal effects on embryos in rats when administered in concentrations far below those which are anesthetically effective, but which are nonetheless similar to concentrations found in the operating room environment.[3] Furthermore, transplacental carcinogenesis has recently been reported to occur in man.[4] Since several recent surveys have demonstrated high rates of spontaneous miscarriage of pregnancies among female operating room personnel,[5,6] we decided to study the incidence of birth defects, neoplasms, and other abnormalities in children of nurse-anesthetists. The incidence of birth defects was compared with the data of McIntosh *et al.*,[7] who studied the incidence of congenital malformations in 5,530 pregnancies in the general population. The incidence of neoplasms was compared with age-adjusted data from the Connecticut Tumor Registry.[8]

Methods

A survey of currently active female nurse-anesthetists in Michigan was made on the basis of a list of members provided by the American Association of Nurse Anesthetists. A questionnaire concerning pregnancy, birth defects, neoplasms, and other significant abnormalities among offspring in relation to operating room exposure was prepared. Information requested included the number of times the anesthetist had been pregnant, the date of birth and sex of the child, whether the anesthetist practiced anesthesia any time during the pregnancy, whether the pregnancy resulted in any congenital anomalies, birthmarks or other abnormalities of structure or function, whether the child is healthy at the present time, and whether the child had required surgery for any reason. These questions were interspersed with others, including age, training, and general health of the individual. Questionnaires were sent to 621 female nurse-anethetists. Those not responding within three weeks were sent a second questionnaire. Those not responding to either questionnaire were contacted by telephone when possible. The data obtained above permitted determination of the incidence of cancer among Michigan nurse-anesthetists.[9]

The analysis of birth defects consisted of comparisons between the frequencies of various types of congenital anomalies resulting from pregnancies during which mother-anesthetists practiced, the frequencies of congenital anomalies resulting from pregnancies during which the mother did not practice anesthesia, and the frequencies of congenital anomalies among non-anesthetists

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TABLE 1. Summary of the Michigan Nurse-anesthetist Survey

Total nurse-anesthetists surveyed	621
Respondents	525 (84.5 per cent)
Respondents who were mothers	268 (51 per cent)
Total births among respondents	695
Average births/mother	2.6
Total births—mother practiced during pregnancy	434 (62.4 per cent)
Total births—mother did not practice during pregnancy	261 (37.6 per cent)
Children with one or more birth defects	86 (12.4 per cent)
Total number birth defects reported	96
Children with birth defect—mother practiced	71/434 (16.4 per cent)
Children with birth defect—mother did not practice	15/261 (5.7 per cent)
Total mother anesthetists	268
Mothers with one or more children with birth defects	76 (28.4 per cent)
Mothers with only one child with birth defect (50 practice, 12 no practice)	62
Mothers with two children with birth defects	12 > 10 of these practiced during all pregnancies
Mothers with three children with birth defects	2
Children with neoplasms—mother practiced	2 (0.5 per cent)
Children with neoplasms—mother did not practice	1 (0.4 per cent)

as reported by McIntosh.[7] The statistical significance of differences was assessed using the chi-square test of independence, with continuity correction when the number of congenital anomalies exceeded 20. Otherwise, Fisher's exact test (two-sided) was used.

The incidences of neoplasms and other individual significant abnormalities reported in this survey were too low to calculate meaningful comparisons.

Results

Of the 621 questionnaires, 525 (84.5 per cent) were returned. Of the respondents, 268 (51 per cent) had delivered at least one viable child (table 1). There were 695 births among the respondents, an average birth rate of 2.6 children per mother. Of the 695 births, mothers practiced anesthesia at some time during pregnancy in 434 (62.4 per cent) of the pregnancies; mothers did not practice during 261 (37.6 per cent) of the pregnancies. One or more birth defects were present in 86 (12.4 per cent) of the children. Among the 434 children whose mothers practiced during pregnancy, 71 (16.4 per cent) had birth defects. Fifteen (5.7 per cent) of the 261 children whose mothers did not practice during the pregnancy had one or more birth defects. This difference was statistically significant, $p < 0.005$.

Of the 268 mother-anesthetists, 76 (28.4 per cent) had one or more children with birth defects. Of these, 62 mothers had one child with birth defects, 12 mothers had two children with birth defects, and two mothers had three children with birth defects.

Age was not a factor in the observed differences between exposed and non-exposed groups (table 2). In the McIntosh study, the average age of the mother during pregnancy was about three years less.

Table 3 compares the incidences of birth defects by organ system for the Michigan study (practice *vs.* no-practice groups) and the results of the study by McIntosh *et al.* Table 4 lists the incidences of birth defects by type in the Michigan study.

Of the 96 birth defects reported among 86 children in the Michigan study, 38 involved the skin. Among the exposed group, 33 (46.5 per cent) of the 71 birth defects were cutaneous anomalies, while five (33.3 per cent) of the 15 birth defects reported among the non-exposed were cutaneous. Excluding anomalies of the skin, the total number of birth defects in the exposed group was 38 (8.8 per cent), while the total among the non-exposed group was 10 (3.8 per cent). This difference was significant, $P < 0.025$. The differences between the incidences of defects in the exposed and non-exposed groups were significantly different in four groups: cavernous hemangiomas, total cutaneous anomalies, inguinal hernias, and musculoskeletal congenital anomalies. The differences between incidences of cardiovascular, gastrointestinal, and central nervous system congenital anomalies in the two groups were not statistically significant.

Comparison of the Michigan data with those of McIntosh reveals no significant difference between the incidences of the various anomalies when comparing the no-practice and McIntosh findings. However, there were significant differences in the incidences of cutaneous, musculoskeletal, and total anomalies when the practice and McIntosh groups were compared.

Three neoplasms occurred in two of the 434 children whose mothers practiced during the

pregnancy. One child had a neuroblastoma at birth and later developed a thyroid malignancy at puberty. Another offspring developed a parotid tumor at the age of 22 years. One neoplasm (acute leukemia, age 3 years) was reported to have occurred among the 261 children whose mothers did not practice during the pregnancy.

TABLE 2. Average Ages of Mothers at Birth, Tabulated by Practice Category during Pregnancy and Whether Congenital Anomaly Resulted

	All	Practice	No practice
All	30.60	30.90	30.09
Congenital anomaly	30.45	30.44	30.47
No congenital anomaly	30.62	20.96	30.06

TABLE 3. Incidences of Birth Defects by Organ System, Comparing the Michigan Practice and No-practice Groups and the McIntosh Group

	Corbett *et al.*				McIntosh *et al.* (n = 5,530)		Probability (*P*)		
	Practice Group (n = 434)		No Practice Group (n = 261)						
Type of Defect	Number	Per Cent	Number	Per Cent	Number	Per Cent	Practice vs. No-practice	Practice vs. McIntosh	No-practice vs. McIntosh
Skin	33	7.6	5	1.9	91	1.6	<0.005	<0.005	>0.10
Hemangiomas (cavernous)	12	2.8	1	0.4			<0.05		
Cardiovascular	7	1.6	3	1.2	42	0.8	>0.10	>0.10	>0.10
Urogenital	5	1.2	3	1.2	41	0.7	>0.10	>0.10	>0.10
Gastrointestinal	4	0.9	0	0.0	41	0.7	>0.10	>0.10	>0.10
Musculoskeletal	26	6.0	3	1.1	173	3.1	<0.005	<0.005	>0.05
Inguinal hernia	14	3.2	2	0.8			<0.05		
Central nervous system	3	0.7	1	0.4	65	1.2	>0.10	>0.10	>0.10
Miscellaneous	3	0.7	0	0.0	12	0.2	>0.10	>0.10	>0.10
Total	81	16.4	15	5.7	465	8.4	<0.005	<0.005	>0.10

TABLE 4. Incidence of Birth Defects by Type in the Michigan Practice and No-Practice Groups

	Practice Group (n = 434)		No-practice Group (n = 261)	
Type of Defect	Number	Per Cent	Number	Per Cent
Hemangioma (cavernous)	12	2.8	1	0.38
"Strawberry" birthmark	5	1.2	0	
Other skin anomalies (nevus, etc.)	16	3.7	4	1.5
Diagnosed heart defect	3	0.7	1	0.4
"Heart murmur" (no diagnosis)	4	0.9	2	0.8
Hypospadias	3	0.7	1	0.4
Undescended testicle	0		1	0.4
Other urogenital anomalies	2	0.5	1	0.4
Pyloric stenosis	3	0.7	0	
Malabsorption syndrome	1	0.2	0	
Inguinal hernia	14	3.2	2	0.8
Congenital dislocation of hip	3	0.7	1	0.4
Pectus excavatum	2	0.5	0	
Other musculoskeletal anomaly	7	1.6	0	
Microcephaly	2	0.5	0	
Hydrocephalus	0		1	0.4
Mental retardation	1	0.2	0	
Miscellaneous anomalies	3	0.7	0	

Discussion

Nitroso compounds and other carcinogens cause neoplasms in the central nervous system and other tumors in rats,[11] and certain compounds have been found to be embryotoxic in the first quarter of pregnancy, teratogenic in the second quarter, and carcinogenic in the latter half of pregnancy.[12] When carcinogenic, the effect may not be manifested until late in the offspring's life span.[11] The incidence of neoplasms in this survey is small, but the occurrence of several unusual tumors in this small population warrants further investigation into the possibility of transplacental carcinogenesis as an occupational disease among anesthesia personnel.

An estimated 7 per cent of children born in the United States have significant birth defects which are evident at birth or during infancy.[10] The present data suggest that offspring of practicing female anesthesia personnel are at increased risk in terms of congenital anomalies. This study is based on a relatively small population sample. However, the differences between the practice group (cutaneous anomalies, musculoskeletal anomalies, total anomalies) and both the no-practice group and the McIntosh data support the reliability of the conclusion that an increased risk of congenital anomalies exists in children born of female anesthetists.

Exposure to low concentrations of anesthetic gases, transmissible viruses, and radiation have been suggested as possible causes for the increased incidence of miscarriages reported among female operating room personnel. These factors can also be implicated as causes of birth defects. Acute high-dose exposure to inhalation anesthetics causes birth defects in laboratory animals. Certain viral diseases (*e.g.*, rubella) during pregnancy cause birth defects in man. Griem *et al.*[13] have reported a high incidence of hemangiomas (5.3 per cent) in children whose mothers were exposed to x-rays (x-ray pelvimetry) during pregnancy. The present survey was not designed to determine which of these factors explains the increased incidence of birth defects among female anesthetists. This and whether an increased incidence of neoplasms or other abnormalities exists among offspring of anesthetists can be determined only by a larger study, including additional data not only from female anesthetists, but also from non-operating-room personnel in hospitals.

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