Occupational Hazards for Operating Room-Based Physicians

Analysis of Data From the United States and the United Kingdom

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• Comparative analysis of data from three large retrospective surveys in the United States and the United Kingdom reaffirms an increased incidence of spontaneous abortion among female physicians working in the operating room. The live-born children of female physicians exposed in the operating room also had substantially more congenital abnormalities. Male anesthetists, compared with nonanesthetist physicians, had an increased incidence of hepatic disease; there was also an increased frequency of congenital abnormality in their children. The incidence of spontaneous abortion in wives of male anesthetists and in the rate of cancer among exposed male anesthetists was similar to control. Despite differences in survey methods and analysis, there was remarkable agreement in conclusions to be drawn from the independent studies.

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RECENT evidence suggests that personnel who work in the operating room are subject to serious occupational health hazards. Preliminary studies[1-5] have indicated an increase in rates of spontaneous abortion, congenital abnormalities in their children, and cancer among women working in the operating room. Subsequently, three large retrospective surveys examined the incidence of spontaneous abortion, congenital abnormalities in children, cancer, hepatic disease, and other illnesses in male and female operating room personnel in the United States and United Kingdom (UK).[6-8] Special note was made as to timing of the incident and the number of years that each respondent was exposed to the operating room.

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Particular interest focused on the relationship between operating room exposure and obstetric history. Although the original UK study of female anesthetists[6] used a slightly different format compared to later studies in both countries,[7,8] close similarity of the survey questionnaires permitted comparison of the data. The US survey included both physicians and nurses, while the two UK studies were restricted to physicians. Accordingly, comparison and analysis of the combined data have been limited to responses obtained from exposed physicians and physician control groups. Confidence in the conclusions to be derived from individual epidemiologic studies of this type is enhanced by the demonstration of comparable findings in similar populations. A preliminary comparison of data from the three studies suggested sufficient agreement to warrant further analysis. This report provides the results of such combined analysis.

METHODS

In each study, questionnaires were mailed to selected groups of physicians to provide a group of anesthetists and a control group not working in anesthesia. In the US study, the anesthetists were members of the American Society of Anesthesiologists, and the control group was comprised of members of the American Academy of Pediatrics. In the two UK studies, the anesthetist group was drawn from membership of various professional organizations, and from records of the Department of Health and Social Security and the Scottish Home and Health Department. The control groups were a random selection of physicians from the Medical Register. Study design, procedures em-

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ployed, techniques for data retrieval, and methods of statistical analysis are described in the individual publications.[6-8]

Female Surveys.—In the original US publication,[7] obstetric data for female anesthetists were included only if the respondent had worked in anesthesia for a period of not less than one year before onset of pregnancy. In our combined analysis, less stringent criteria have been applied. Since the UK data[6] relate to respondents working in an operating room at the beginning of pregnancy, irrespective of previous work history, similar criteria have been applied to the US data. The UK data have also been reanalyzed, defining spontaneous abortion as a gestation period of 20 weeks or fewer.

Male Surveys.—In the original UK survey of male physicians,[8] all respondents who worked in the operating room were regarded as a single "exposed" group. In our combined analysis, the UK test group includes only physicians who were working as anesthetists. Additional differences between the present summary of the UK male data and the previous analysis[8] are that obstetric data relate to events in the ten-year period from 1962 to 1972, and the definition of spontaneous abortion has been changed to a gestation period of 20 weeks or fewer, and the UK control group consists of several groups of physician specialists, while the US control group is taken from a single specialty. Each control group is comprised of physicians who have not worked in the operating room, and the criterion for entry as an exposed anesthetist is that the respondent was working in anesthesia at the beginning of his wife's pregnancy. The UK data have also been adjusted for age and smoking habit, by the direct method, following the procedures used in the US survey.

In providing comparisons of the results of the US and UK studies, rates have been presented in tabular form, side by side. Additionally, in certain cases the rates have been combined for the convenience of the reader, and statistical tests for the combined data have been carried out. Significance test P values have been provided. These are presented as one-tailed values so that each calculation indicates the sign of the difference as well as the actual strength of the statistical evidence.

RESULTS

Table 1 indicates the overall number of physicians surveyed and the percent of questionnaires returned for each of the respondent groups. The adjusted return rates (US response rates have been adjusted to correspond to definitions used in the UK analysis) vary from 45% for US male pediatricians to 82% for female anesthetists in the United States and United Kingdom.

The results of the independent surveys are described separately for female and male respondents.

Female Respondents

Table 2 shows that the mean age of female anesthetists in the United States (41.6 years) was greater than in the United Kingdom (39.3 years). Similar differences were present in the two control groups (47.2 and 41.8 years, respectively). All rates reported for the United States, but not the United Kingdom, were age-standardized to the same standard population.[7]

Of the 949 pregnant physicians examined in the US study, 596 were anesthetists and 355 were pediatricians. Of the 2,887 pregnant physicians examined in the UK study, 737 were anesthetists and 2,150 were nonanesthetist physicians.

Spontaneous Abortion.—In the original US study,[7] the rate for spontaneous abortion was reported as 17.1 per 100 pregnancies for exposed anesthetists compared with 8.9 for pediatricians ($P < .01$). In the UK study (spontaneous abortion of 20 weeks gestation or fewer), the rate for anesthetists was 17.5% compared with 14.0% for nonanesthetist physicians ($P < .05$).

Table 2 shows the rates for spontaneous abortion derived by pooling the adjusted data from the exposed anesthetists and control subjects in both countries. The combined rate for spontaneous abortion is 16.7% in anesthetists compared with 13.3% in control subjects ($P < .001$).

Congenital Abnormalities.—The earlier reported rate for congenital abnormalities (skin excluded) was 5.9% for female anesthetists in the United States, compared with 3.0% for female pediatricians ($P = .07$).[7] In the United Kingdom, the rate was 5.5% for female anesthetists and 4.2% in the control group of physicians ($P = .22$). If the adjusted US and UK data are combined (Table 2), the abnormality rate for exposed female anesthetists is 5.5%, and 4.0% for the control physicians ($P = .04$).

In the original studies, multifactorial congenital abnormalities (congenital hip, club foot, cleft palate or lip, spina bifida, hydrocephalus, atrial septal defect, patent ductus, pyloric stenosis, and anencephaly) were analyzed as a separate group. The incidence of these abnormalities in the United States was 1.2% for female anesthetists and 0.2% for female pediatricians ($P = .06$). In the United Kingdom, the respective values were 0.7% and 1.1% (not significant).

Male Respondents

Table 2 shows the mean age for male anesthetists studied to be less in the United Kingdom (39.8 years) than in the United States (45.2 years). The mean age of the control group of US pediatricians was 51.8 years, and 41.6 years for the nonanesthetist hospital physicians in the United Kingdom.

Excluding therapeutic abortions, there were 4,143 pregnancies in wives of the exposed male anesthetists in the United States, and 2,261 pregnancies in wives of pediatricians. In the UK study, there were 1,382 pregnancies in wives of male anesthetists, and 2,493 in wives of the nonanesthetist physicians, excluding therapeutic abortions.

Spontaneous Abortion.—The previously reported spontaneous abortion

Table 1.—Total Mailings and Response Rates by Various Medical Specialties and by Sex

	United Kingdom		United States	
	Total Mailings	Responses (%)	Total Mailings	Responses (%)
Males				
Anesthetists	1,901	1,407 (74.0)	9,793	6,558 (73.7)
Pediatricians	...	...	7,024	2,893 (45.0)
Nonanesthetist physicians	6,048	4,100 (67.8)	...	...
Females				
Anesthetists	1,034	849 (82.0)	1,399	1,059 (82.0)
Pediatricians	...	...	866	639 (79.4)
Nonanesthetist physicians	1,330	1,064 (80.0)	...	...

Table 2.—Adjusted Rates From Combined Surveys

	Age, yr	Pregnancies	Miscarriages/ Pregnancies, %	Live-Born Children	Congenital Abnormalities/ Live-Born Children, %
Exposed female anesthetists*					
United States	41.6	596	15.7±1.5	494	5.5±1.0
United Kingdom	39.3	737	17.5±1.4	599	5.5±0.9
Combined data	...	1,333	16.7±1.0	1,093	5.5±0.7
Control female physicians*					
United States	47.2	355	9.6±1.6‡	313	2.8±0.9
United Kingdom	41.8	2,150	14.0±0.8	1,817	4.2±0.4
Combined data	...	2,505	13.3±0.7	2,130	4.0±0.4
Significance for combined data§			P < .001		P = .04
Exposed male anesthetists†					
United States	45.2‖	4,143	12.1±0.5	3,597	5.3±0.4
United Kingdom¶	39.8‖	1,382	13.9±0.9	1,180	4.2±0.7
Combined data	...	5,525	12.6±0.5	4,777	5.0±0.3
Control male physicians†					
United States	51.8‖	2,261	12.0±0.7	1,970	0.9±0.4
United Kingdom¶	41.6‖	2,493	11.5±0.6	2,174	3.6±0.4
Combined data	...	4,754	11.7±0.5	4,144	3.7±0.3
Significance for combined data§			P = .10		P < .001

*Adjusted rates (±SE) from combined surveys of female physicians in the United States and United Kingdom. Rates are per 100; skin abnormalities are excluded.

†Adjusted rates (±SE) from combined surveys of male physicians' wives in the United States and United Kingdom. Rates are per 100; skin abnormalities are excluded.

‡Difference between US and UK control groups is significant (P=.01).

§Student t test for differences (D) in proportion where $t=D/SE\ (D)$, and SE/D is root sum of squared SEs. P values are one-tailed.

‖Fathers' ages.

¶Surgeons and radiologists excluded.

rate was 11.6 per 100 pregnancies among wives of male anesthetists in the United States, and 12.6% for wives of pediatricians (P=.84).[7] In the United Kingdom, the corresponding rate was 11.1% in the wives of exposed physicians (anesthetists and others), and 10.9% in wives of nonexposed physicians.[8]

When spontaneous abortion was redefined in the UK analysis as abortion within 20 weeks, as in the US survey, the difference in spontaneous abortion rates between wives of exposed male anesthetists and unexposed nonanesthetist controls was magnified. Before adjustment for age and smoking habit, the UK rates were 13.4%±0.9% exposed, and 11.5%±0.6% nonexposed. This difference was not statistically significant (P=.09). Adjustment for age and smoking habit was performed because of the lower incidence of smoking in the UK wives and because the group of pregnancies in women over 37 years of age was underrepresented in the UK anesthetist group. In this particular group of 96 UK pregnancies, the abortion rate was exceptionally high (26.0%). After adjustment, the UK rates became 13.9%±0.9% exposed, 11.5%±0.6% unexposed, and the difference was statistically significant (P=.02). The effect of male exposure, however, was not significant at the 5% level when US and UK data were combined (Table 2). The combined rate for spontaneous abortion was 12.6% for the wives of anesthetists, and 11.7% for wives of control subjects (P=.10).

Congenital Abnormalities.—The previously reported congenital abnormality rate (skin excluded) per 100 live births was 5.4% for wives of male anesthetists in the United States, and 4.2% for the wives of the pediatricians (P=.04).[7] In the UK survey,[8] the congenital abnormality rate, excluding skin abnormalities, was 3.9% in the wives of exposed male respondents, and 3.2% in the unexposed control group (P=.03) (Table 2). The difference in incidence of congenital abnormality in the two control groups was not significant.

When the age and smoking habit adjusted data for congenital abnormalities in the two countries were pooled, the combined rate for the wives of anesthetists was 5.0% and 3.7% for wives of control subjects. This difference is significant (P < .01).

In the previous US study, the reported rate for congenital abnormalities of multifactorial origin was 1.6% for wives of anesthetists and 0.9% for wives of pediatricians (P=.03).[7] In the UK sample, the rate was 1.0% for wives of anesthetists, and 0.8% for the wives of control subjects (not significant). The pooled data indicate these rates to be 1.4% for the wives of the anesthetists and 0.9% for the wives of the control physicians (P=.01). The UK data were not adjusted for age and smoking habit.

Occupational Disease.—Comparative analysis of occupational disease rates is provided for male respondents only. Although the original US study indicated a significant increase in age-adjusted female cancer rates (3.0% in anesthetists vs 1.6% in pediatricians; P=.05), and in age-adjusted female hepatic disease rates (4.9% in anesthetists vs 2.9% in pediatricians; P=.04), equivalent data were not available from the UK study for comparison.[6]

Tabel 3 presents data, as noted by Cohen et al[7] and A. A. Spence (unpublished data), relating to other diseases reported by the male respondents. The incidence of cancer in the United States was 0.7 per 100 respondents in both male anesthetists and male pediatricians. The corresponding age-adjusted rates in the United Kingdom were 1.1% and 0.8% (P=.31). The rate for liver disease (serum hepatitis included) in the United States was 4.9% for anesthetists and 2.6% for pediatricians (P < .01). In the United

Table 3.—Disease Rates in the United Kingdom and the United States*				
	United Kingdom		United States	
	Anesthetists	Nonanesthetist Physicians†	Anesthetists	Pediatricians
Sample size	1,407	3,502	5,828‡	2,337‡
Cancer (excluding skin)	1.07	0.79	0.70	0.70
Gallbladder	1.34	0.48§	0.93	0.99
Liver disease	3.09	1.79‖	4.90	2.60§
Hepatitis	2.68	1.60‖	3.20	1.70§
Serum hepatitis	...	...	0.51	0.11§
Other liver disease	0.41	0.19	1.20	0.80
Myocardial infarction	1.72	1.78	1.75	1.61
Hypertension	1.80	0.80§	2.31	2.47
Arrhythmias	0.70	0.30§	0.75	0.70
Disk disease	1.44	0.53§	1.27	1.47
Peptic ulcer	2.30	1.20§	1.95	1.67
Ulcerative colitis	0.32	0.24	0.24	0.08‖
Migraine	0.15	0.00	0.23	0.06‖
Kidney disease (excluding pyelonephritis and infections)	1.70	2.10	4.20	4.60
Renal lithiasis	1.27	1.14	3.07	3.27

*Rates per 100 respondents for exposed male anesthetists and nonanesthetist physicians; UK data adjusted to US standard population.
†Excluding surgeons and radiologists. Seventy-four percent of the physicians were working outside the hospital.
‡Sample size varies slightly with type of disease.[7]
§Significant, $P < .01$.
‖Significant, $P < .05$.

Kingdom, the rates were 3.1% and 1.8% ($P < .05$). Kidney disease rate was 4.2% for anesthetists in the United States, and 4.6% for the control group ($P = .76$). In the United Kingdom, the rates were 1.7% and 2.1% ($P = .74$).

Incidence rates for peptic ulcer, gallbladder disease, arterial hypertension, cardiac arrhythmia, and lumbar disk disease among UK male anesthetists were significantly greater than in the UK male control group ($P < .01$). However, these differences were not noted in the US study. Rates for ulcerative colitis and migraine in US male anesthetists were higher than those in the pediatric control group and statistically significant ($P < .05$), but these differences, though confirmed in direction, were not statistically significant in the UK study.

COMMENT

Despite differences in methods of study and statistical evaluation, there is remarkable agreement in these three studies with respect to an apparent association between anesthetic practice and obstetric mishap. Both original surveys of female physicians point to a statistically significant increase in the risk of spontaneous abortion among women working in the operating room. There was also an increase in the overall risk of congenital abnormality of their live-born children.

The US abortion and congenital abnormality rates have been corrected for both age and smoking habit, and relate to female anesthetists who were not only working during the first trimester of pregnancy, but who also had been employed in anesthesia in the year preceding pregnancy. In the UK survey,[6] no information was available as to smoking habit or age of the respondent at the time of the pregnancy. Moreover, the criterion for regarding the respondent as an anesthetist was simply that she was working in an operating room during the first trimester of pregnancy. Adjustment of the UK data by excluding cutaneous congenital abnormalities, using the US definition of spontaneous abortion, and recalculation of the female anesthetist data from the US survey to coincide with the less stringent criteria of the UK study, slightly reduces the estimate of relative increase in the risk of spontaneous abortion (United States, +64%; United Kingdom, +25%) and congenital abnormality (United States, +96%; United Kingdom, +31%). The number of respondents in the US control group is small and represents pediatricians only, which may account for the apparent difference between the US and UK control groups (Table 2). The combined estimate of an increased risk of spontaneous abortion is +26%, and for congenital abnormality, +38%.

The combined data suggest a slightly higher rate of abortion for the wives of male anesthetists, but the difference is not statistically significant ($P = .10$). The sample of UK pregnancies alone, however, shows a 21% increase in risk, which is significant after adjustment ($P = .02$). This may be a chance finding due to a low number of pregnancies in the older age group. It is unlikely to represent a risk since careful retrospective matching of the UK data[8] shows no effect of anesthetic exposure in male anesthetists. Thus, the combined data do not establish an increased incidence of spontaneous abortion in wives of male anesthetists, but do indicate an increase in the reported rate of congenital abnormality in live-born children of practicing male anesthetists. Analysis by type does not demonstrate an increase in any particular category of abnormality.

We believe that comparison of these three studies strongly suggests that the practice of anesthesia, specifically among those working in the operating room, is associated with an increased risk of congenital abnormality for the live-born children of both exposed men and women. Previous publications[6-8] discussed possible etiologic considerations, and pollution of the operating room air with anesthetic gases and vapors is high on the list of possible causal factors.

Analysis of the data on other health conditions suggests that in both countries, male anesthetists are not at higher risk with respect to cancer, leukemia, or myocardial infarction. Significant increases ($P < .01$) in the reporting of peptic ulcer, gallbladder disease, arterial hypertension, and lumbar disk problems by UK anesthetists (A. A. Spence, unpublished data) are not reflected in the replies from the US anesthetists.[7] Similarly, the increased frequencies of ulcerative colitis and migraine among US anesthetists were not observed in the UK data. Both of the UK studies and the US study show that male and female anesthetists have increased rates of hepatitis. A recent study in the United Kingdom, however, shows no evidence of an increase in chronic liver disease in anesthetists.[9]

Dentists who use inhalation anesthetics in their practice also have a large and statistically significant increase in the incidence of hepatic disease when compared with a control group of dentists not using general anesthesia. The incidence of hepatic disease (serum hepatitis excluded) per 100 respondents in the exposed group was 5.9% compared with 2.3% in unexposed dentists and oral surgeons ($P < .01$).[10] Although there is no difference between anesthetists and other physicians with respect to the incidence of renal disease, there was an approximate three-fold increase in the overall reporting of renal disease by US physicians in both study and control groups compared with the physician groups in the United Kingdom. This difference is due almost entirely to an increased incidence of renal lithiasis in US physicians. The explanation for the above differences remains presently undefined, although both genetic and environmental factors may be operant. The latter would include preferences in dietary intake, alcohol consumption, and chemical pollution. Such discussion is beyond the scope of this analysis.

In view of the strong corroborating evidence of increased obstetric health hazards for anesthetists shown in the present comparison of US and UK data, there would seem to be justification for taking all reasonable steps to monitor and minimize this risk. Although it should be stressed that a cause-effect relationship has not been proved, the possibility that these findings may be a consequence of operating room pollution by anesthetic gases would seem to warrant active steps to reduce the level of pollution in all operating rooms. At the same time, one must also be cautious in assuming that by reducing operating room pollution, the problem has necessarily been solved. The continued monitoring of health problems of the operating room workers is an important requirement.

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